Study Protocol (without Appendices)

1) Protocol Title

Treatment of Suicidal and Self-Injurious Adolescents with Emotional Dysregulation.

2) Background

Suicide is the third leading cause of death among adolescents in the US and yet there is a paucity of research on effective treatments for this population. The primary aim of the research described in this application is to evaluate the efficacy of dialectical behavior therapy (DBT) for suicidal adolescents. DBT has an empirical track record with suicidal adults of reducing the incidence, frequency and medical risk of suicide attempts and non-suicidal self-injuries among individuals meeting criteria for borderline personality disorder (BPD). While DBT is widely used in the community with suicidal adolescents, particularly those with difficulties characteristic of BPD such as poor emotion regulation and impulse control, no randomized trial of DBT with suicidal adolescents has ever been conducted. And, while non-randomized trials indicate that the intervention is both safe and effective, without a randomized trial we simply do not know whether DBT for suicidal adolescents is efficacious or not. Given the severity of the problem and the lack of alternative treatments for high-risk adolescents, addressing this question is of great importance.

This project is a collaborative, two site study using identical procedures and protocols at each site. Two sites, Seattle and Los Angeles, are necessary in order to recruit the 170 intent-to-treat adolescent participants needed for sufficient power to provide clinically and scientifically meaningful findings in a timely fashion. The Seattle site is composed of two research groups: University of Washington-Behavioral Research and Therapy Clinics (UW-BRTC) (PI, Marsha Linehan) and UW Child Psychiatry/Seattle Children's Hospital (SCH) Behavioral Health (PI, Elizabeth McCauley). The UW-BRTC houses the original DBT program, has been the site for numerous clinical trials, is currently expanding to provide care to adolescents as well as adults, and boasts a team that is expert in suicide behaviors treatment research. The UW-BRTC site is the principle site and will take leadership in training and oversight of the DBT component of the study as well as in the management of all data using a UW web based application. The UW will also be the principle corresponding site with National Institute of Mental Health, the project funder. The SCH clinic has been the site for a number of clinical research trials with adolescents who have mood disorders and has an ongoing program for suicidal adolescents, which can be readily extended to accommodate the needs of this clinical trial. The SCH site is a subcontract awardee of the principle grant. The University of California, Los Angeles (UCLA) site is also composed of two sub research groups: the UCLA School of Medicine and Neuropsychiatric Hospital and Clinics (PI, Joan Asarnow) and Harbor-UCLA Medical Center (PI, Michele Berk). Both sites have experience conducting high quality clinical trials with depressed youth and collaborating in multisite research studies. For the Los Angeles team, the Harbor-UCLA site is the principle grant recipient with UCLA as the subcontract awardee.

SPECIFIC AIMS: The overall study was designed to address multiple aims/hypothesis and exploratory research questions related to both specific suicide and self-harm behaviors as well as broader functional outcomes.

The Aims addressed in this paper are as follows:

AIM 1 is to evaluate the efficacy of individual and group DBT for adolescents by comparing it to a combined individual and group supportive therapy control condition (IGST) chosen specifically to maximize internal validity by controlling for 1) hours of one-on-one contact offered; 2) hours of group contact offered; 3) availability of between-session telephone calls, 4) availability of clinical team support for therapists; and 5) availability of clinical supervision.

Hypo 1: Suicide events (suicide, suicide attempt) will be less likely in DBT vs. IGST during the treatment and follow-up period.

Hypo 2: Non-suicidal self-injuries (NSSI) will be less likely in DBT vs. IGST during the treatment and follow-up period.

Hypo3: Days in treatment will be higher and treatment dropout will be lower in DBT vs. IGST.

Overall Study Aims:

AIM 1 is to evaluate the efficacy of individual and group DBT for adolescents by comparing it to a combined individual and group supportive therapy control condition (IGST) chosen specifically to maximize internal validity by controlling for 1) hours of one-on-one contact offered; 2) hours of group contact offered; 3) availability of between-session telephone calls, 4) availability of clinical team support for therapists; 5) availability of clinical supervision and 6) psychotropic medication management.

Hypo 1: Suicide events (suicide, suicide attempt, ER or hospitalization for suicidality) will be less likely in DBT vs. IGST during the treatment and follow-up period.

Hypo 2: NSSI will be less likely in DBT vs. IGST during the treatment and follow-up period.

Hypo 3: Days in treatment will be higher and treatment dropout will be lower in DBT vs. IGST.

Hypo 4: Time to both suicide events and to NSSI will be longer in DBT vs. IGST.

Hypo 5: Functional outcomes, as reflected in improved family relationships, will be greater in DBT vs. IGST.

Exploratory Research Question 1*: In comparison with IGST, does DBT differentially impact functional* outcomes such *as school attendance and peer relationships?*

Exploratory Research Question 2*: Is DBT a cost effective treatment for suicidal behaviors and NSSI? We will collect data to generate cost estimates for each of the interventions, including costs such as ER visits, and conduct exploratory analyses of incremental cost-outcome ratios comparing the two approaches.*

The first aim of this research is not to demonstrate that DBT works better than usual treatment or other manualized psychosocial treatments but rather to test whether DBT is itself efficacious at producing change. That is, we want to interpret significant effects supporting our hypotheses as evidence that gains in the target areas of the treatment are in fact due to DBT and not to non-specific factors associated with any treatment.

AIM 2 is to analyze mediators of reduced suicide events and NSSI in adolescents.

DBT is based on a theoretical model that suicidal behavior is a combined outcome of both stressful life events and emotion dysregulation together with inadequate skills for solving such events or regulating negative emotions. Our meditational hypotheses are based on the underlying theoretical foundation of DBT.

Hypo 6: Decreases in family conflict will mediate reductions in both suicide events and NSSI.

Hypo 7: Increases in parent DBT behavioral skills will mediate reductions in family conflict.

Hypo 8: Reductions in emotion dysregulation will mediate reductions in both suicide events and NSSI.

Hypo 9: Increases in DBT behavioral skills will mediate reductions in emotion dysregulation.

3) Study Design

This study is a randomized controlled trial of DBT compared to an active control condition (individual and group supportive therapy; IGST). The study consists of an assessment component (screening/intake plus outcome assessments occurring at 3 month intervals) and a treatment component (6 months).

Subjects will be adolescent patients and at least one of their parents/legal guardians or other responsible adult authorized to participate by the parent/legal guardian. Data will be obtained by telephone and in-person, using interview, questionnaire, and self-monitoring methods. Potential patient subjects and the corresponding parent/other adult subject will be asked to authorize the research team (via separate written consent forms) to obtain treatment records and school records which may be used to abstract data relevant to diagnosis and treatment experiences, and treatment effects on school performance. All assessment and treatment sessions will be video or digitally recorded for research purposes. Study therapists will also be enrolled as subjects and asked for self-report data pertaining to domains such as burn-out, therapeutic alliance and treatment expectancies.

Screening and Enrollment

Screening has two phases, telephone screening and in-person evaluation. (Each is described below.) To minimize subject burden, individuals progress to the next screening phase only upon meeting eligibility requirements.

Telephone Screening. Individuals are either self-referred or referred to one of the four participating clinical sites by the mental health treatment community. Interested individuals contact us or, at their request, arrange for us to contact them and are screened on the telephone by our Participant Coordinator (PC). The phone screen serves as a preliminary screening tool in determining subject eligibility. Pre-screening information will be gathered by phone from the parent/guardian. Target areas include: intentional self-injurious behavior, suicide attempts and related behaviors (e.g., suicidal thinking, plans) and emotional difficulties associated with suicidal and self-injurious behaviors. Individuals are provided with a general overview of the screening process including the type of questions that will be asked and are told that they are free to skip questions or end their participation at any time.

The average amount of time required to complete the telephone screening is approximately 30 minutes. Individuals are also told that at the conclusion of the interview they may be asked to come for an in-person assessment prior to determining if they are an appropriate fit for the study. Any caller not eligible for continued screening (either due to failed inclusion criteria or self-discontinuation from screening) will be offered a treatment referral list. (See Appendix II for the phone screen and intake protocols, Appendix III for the phone screen measure and Appendix IV for the treatment referral list.) Adolescents who call expressing interest in the study will be told to that their parent/legal guardian must initiate the call.

In-Person Screening Interview. The screening interview is the principle method for determining participant eligibility. Screening starts with a description of the study purpose and procedures. Prior to beginning the interview questions are answered and individuals are asked to sign an audio/video/digital recording consent form as well as the study consent form. (See Appendix I for consent forms.) If an individual chooses not to participate or sign forms, the screening interview is ended and a treatment referral list is offered. The screening assessment includes several measures and sub-scales of measures used to determine the individual's match to the inclusion/exclusion criteria (see sections D3 and D4 of this application). Some measures are assessor-administered interviews, others are self-report assessments. Assessments may be conducted using paper and pencil as well as direct computer entry methods. The time required to complete the intake screening battery is 2-4 hrs. (2 hrs. for parents). Parents and adolescents will be assessed separately. Assessments may be divided into smaller sessions on the basis of subject preference and scheduling availability. (See Appendix II for assessment protocols and Appendix III for assessment instruments used as part of the in-person screening.)

Randomization

A computerized adaptive randomization procedure will be used to match patient subjects to treatment conditions (DBT, IGST) within sites on five variables : 1) number of non-suicidal self-inflicted injuries in the last year(low=$\leq$6, high = >6); 2) number of lifetime suicide attempts (none, $\geq$1) 3) gender; 4) age (young= <16; older = >16); and 5) currently taking psychotropic medications (no, yes (including ADD/ADHD medications). Assessment personnel will be kept blind to condition assignment throughout the study. Adolescent patient subjects and their parents will be kept blind to treatment condition until the first treatment session.

Subjects

A total of 170 subjects will be enrolled in the study across sites. This is a multi-site study. The four study sites are: 1) The University of Washington Department of Psychology, 2) Seattle Children's Hospital, 3) Harbor-UCLA/LA Biomed, and 4) the Semel Institute at UCLA Medical Center.

Inclusion and Exclusion Criteria

Inclusion Criteria:

1. Elevated suicide ideation operationalized as ≥ 23 on the SIQ-Jr (initially SIQ-Jr cutoff was $\geq$ 31 modified to 23 to facilitate recruitment.

2. Recurrent intentional self-injury operationalized as at least 3 intentional lifetime self-injuries including at least one in the 12 weeks before the telephone screening.

3. At least one lifetime suicide attempt.

4. Meets at least 2 BPD criteria besides the recurrent intentional self-injury criterion.

5. 12-18 years old

6. At least one family member or responsible adult agrees to participate in assessments and in the multi-family group therapy if required by condition assignment.

7. Lives within commuting distance.

8. Youth must speak English and parent must speak either English or Spanish.

Exclusion Criteria:

1. IQ less than 70
2. Court ordered to treatment.
3. Psychiatric or medical symptoms (such as psychosis, mania, neurological impairment, substance dependence or abuse, severe eating disorders) that would interfere with the ability of the youth to participate in the assessments and treatment.

Both self-report measures and structured interviews will be used to screen for eligibility during the baseline assessment (See Question #9a for a detailed explanation of screening for eligibility and the baseline assessment). The Suicide Ideation Questionnaire-Junior (SIQ Jr.) will be used to measure suicide ideation. Although designed for younger adolescents, the SIQ-Jr. has been widely used with both younger and older adolescents to evaluate suicidal ideation. Use of the SIQ-Jr. for all participants allows us to keep measurement constant and minimize both participant burden (15 items) and reading comprehension problems. A raw score of 23 or above has been empirically established as the clinical cutoff indicating potentially significant suicide risk. The Structured Clinical Interview for DSM-IV, Axis II (SCID-II) Borderline Scale and the Borderline Personality Features Scale for Children (BPFS-C) will be used to assess Borderline Personality Disorder features. The Kauffman Brief Intelligence Test (KBIT-2) verbal scales will be used to rule out mental retardation. The Suicide Attempt Self-Injury Interview (SASII) is a structured interview that tabulates the client's prior self-injuries and suicide attempts. This measure has been used successfully with adolescents and their parents in previous studies conducted at the University of Washington and in previous treatment-outcome research with self-injuring adolescents.

Subject Payments

Subject payments are an important incentive and compensation for participation in our research. All subjects in the study will be paid for each completed assessment. The amounts listed below are total amounts, to be divided between the youth and parent. Payment will be given to the parent, who will have the responsibility of giving money to their child as they feel is appropriate. We will suggest that parents and teens split the money equally, however, we will leave it up to the parent's judgment how the money is handled. A larger sum of money is offered for lengthier assessments and those occurring after the study treatment ends.

Assessment	**Payment**
Telephone Screening	$0
Baseline Assessment	$50
3-month Assessment	$25
6-month Assessment	$25
9-month Assessment	$25
12-month Assessment	$50

If the youth and parent do not complete an assessment, they will be offered a partial payment of $10 and provided the remainder of the payment once the full assessment is finished. If an assessment is missed and cannot be rescheduled before the next assessment is due, the assessor will gather information about both time periods and offer a partial payment of $10 for the missed assessment as well as full payment for the current assessment. If the adolescent has been repeatedly difficult to contact, the assessor will administer a Brief Phone Interview with the adolescent and parent, consisting of 6 questions representative of the major study outcome domains. Participants will not be paid for the brief phone interview.

Study Timelines

Subjects enrolled in the study will participate in 6 months of psychotherapy and a total of 5 assessments (baseline, 3 months, 6 months, 9 months, and 12 months). Enrollment of subjects is estimated to begin in December, 2011 (began 1/2012) and all subjects are estimated to have been enrolled by the end of 2013 (last subject enrolled 8/2014). The estimated date of study completion is April, 2015 (Follow-ups continued through 2015).

Study Endpoints

The primary objective of the study is to determine if DBT is effective in reducing suicide attempts and self-harm behaviors in adolescents who have previously engaged in these behaviors, as compared to IGST. Because of the nature of the study population, these behaviors are likely to occur during participation in the study. Hence, these events would not necessarily lead to removal from the study treatment/study. Participants will be considered to have completed the study treatment after receiving 6 months of treatment.

Any adolescent who misses four consecutively scheduled weeks of either individual therapy or group therapy/skills training is considered a dropout from treatment. This rule was instituted because it can be very difficult to know exactly when an emotionally dysregulated patient has actually dropped out of therapy. Patients often say they have dropped when in fact they don‘t mean it and even when they do mean it, they often change their minds within a short period of time. This dropout rule is explained to patients and family members during the first session of individual and/or group therapy and has been a standard part of DBT since its inception (Linehan, 1993).

During the course of treatment, the adolescent/family, the therapist or the study PIs may question the appropriateness of a particular patient continuing in the study or whether the treatment should be modified. The DSMB will be kept apprised of adverse and notable events on an ongoing basis and serve as the final arbiter of whether individual patients should be removed from the protocol. With some adolescents, it may become clinically necessary to arrange for ancillary services such as a case manager or brief inpatient admission. If the youth is determined to be a possible danger to self or others, he/she will be referred for emergency evaluation and possible hospitalization. In such cases an outside clinical expert consultant to be designated at each site may be called in to evaluate the adolescent for purposes of determining whether the treatment being provided is related to the deterioration in the adolescent‘s psychiatric status and whether the adolescent‘s treatment should be changed in any way.

Study Treatments

Individual and Group Dialectical Behavior Therapy (DBT) for Adolescents

Model Underpinning DBT. DBT is based on a combined capability deficit and motivational model that states that 1) adolescents with suicidal behaviors and borderline features lack important interpersonal, self-regulation (including emotional regulation) and distress tolerance skills, and 2) personal and environmental factors often both block and/or inhibit use of behavioral skills that adolescents do have, and at times reinforce dysfunctional behaviors. The term dialectical conveys both the multiple tensions that co-occur in therapy with teens and their parents well as the DBT emphasis on providing and teaching a synthesis of acceptance and change. DBT for adolescents is an adaptation of standard DBT described by Miller, Rathus and Linehan (2007). The primary adaptation is the inclusion of family in the DBT skills training portion of therapy as well as a much greater inclusion of parents in the management of high suicide risk.

DBT Strategies are divided into eight sets: 1) dialectical strategies, 2) core strategies (validation and problem-solving), 3) communication strategies (irreverent and reciprocal communication), 4) case management strategies (consultant-to-the-patient/family; environmental intervention), 5) structural strategies (e.g., targeting within sessions), 6) attachment-to-the-patient strategies, 7) multi-family skills training, and 8) specific protocols covering suicide crisis intervention, therapy-interfering behavior and compliance issues and relationship problem-solving.

DBT for Adolescents Components consist of the following: **1 hr/wk individual sessions**, **2 hr/wk multi-family skills training,** as needed **telephone consultation** (which may also include email and text messages) and a **1 hr/wk team consultation**. Individual session agendas are determined by hierarchically ordered treatment targets as follows: 1) reduce imminent life-threatening behaviors), 2) reduce behaviors interfering with treatment, 3) reduce quality-of-life interfering behaviors (e.g., Axis I disorders, family, school problems), 4) increase behavioral skills and 5) adolescent goals. Family therapy and collateral sessions will also be scheduled as needed. Skills training is highly structured and didactically focused with a heavy emphasis on modeling, instructions, behavioral rehearsal, feedback and coaching, and homework assignments. Skills training includes the four standard DBT skill modules 1) mindfulness skills, 2) interpersonal effectiveness, 3) emotional regulation, and 4) distress tolerance plus 5) walking the middle path, a skills module designed specifically for adolescents and their families which includes training in dialectical skills, behavioral principles

and validation. (See Miller et al. 2007 for a description). Phone consultations focus on crisis intervention and skills coaching; individual therapists coach the adolescents and family members. Consultation team meetings of therapists are aimed at maintaining treatment fidelity. This meeting is conducted by the therapists following guidelines in the treatment manual.

Individual and Group Supportive Therapy (IGST) for Adolescents

Model Underpinning IGST. The treatment is an adaptation of the supportive therapy treatment manual developed by Dr. David Brent and his colleagues in a CBT vs. supportive therapy RCT for depressed adolescents and Dr. Judith Cohen in Trauma-focused CBT v. supportive therapy RCTs for traumatized children. We have modified the treatment by adding a group component to it match the provision of group therapy in DBT. Supportive therapy is an active therapeutic approach that can be applied from a variety of theoretical approaches and, as such, is essentially atheoretical in itself. The aim of IGST is relief or reduction of symptoms, the promotion of personal growth including enhancement of patients' strengths/coping skills and capacity to use environmental supports, and to help suicidal adolescents increase their sense of self-esteem. The treatment will be effective in reducing suicidal behavior and emotion dysregulation by helping the adolescent patients learn to trust and validate themselves. The overarching assumption in IGST is that adolescents become suicidal for a variety of reasons, but they often report feeling isolated, misunderstood, unloved and unwanted. The opportunity to share their innermost concerns and feelings with an interested, empathic adult may be a very beneficial experience. This model of suicidal behavior is compatible with Joiner's theory that an absence of a sense of belongingness is a major risk factor for suicidal behavior.

IGST Interventions. There appears to be reasonable agreement in the field about the interventions in supportive treatments. These interventions include providing a strong therapeutic alliance where the therapist provides an environment that is completely trusting and validating. We selected IGST because it represents a commonly used therapeutic approach that also includes the components included in most currently used approaches to reduction of suicidal and self-injurious behaviors. It can also be readily adapted to match DBT in terms of hours of treatment provided, inclusion of group and family work, and supervision structure. IGST techniques include 1) attending skills conveying actively being with the patient, 2) listening skills conveying a sense of unconditional positive regard by observing and reading the patient's non-verbal behavior, listening to and understanding the patient's verbal messages, listening to the whole person and tough-minded listening that aims at hearing any distorted perceptions the patient may have, 3) empathy by communicating understanding, 4) probing and questioning to help patients talk about themselves and define their problems concretely, 5) eliciting adolescent interests, 6) clarification by summarizing, paraphrasing, and organizing of thoughts, emotions, and 7) identifying feelings and attending to affect. There are as well, a number of specific behavioral treatment protocols covering suicide crisis intervention and therapists will follow the standard of care in the field for management of suicidality, as described in the Practice Parameter for the Assessment and Treatment of Children and Adolescents with Suicidal Behavior, published by the American Academy of Child and Adolescent Psychiatry (AACAP, 2000).

IGST Components consist of the following: 1 **hr/wk individual sessions**, **2 hr/wk supportive group therapy**, as needed **telephone consultation** and a **1 hr/wk therapist supervision** meeting. Individual sessions start with a basic orientation to supportive therapy with both the adolescent and his/her family member(s). The first session also includes a discussion of the factors that contributed to the adolescent's suicidal behavior, analyses of risk factors and a discussion of lethal means. All patients are asked to make a no-suicide contract and procedures for risk management are discussed with both the adolescent and family. Thereafter, each session starts with a mood and suicidality check and, if the patient wishes to record experiences in a diary, the diary is reviewed. The session agenda is set by the patient each week. As noted above, the primary target of sessions is the relief or reduction of symptoms and the promotion of personal growth. As needed family and collateral therapy sessions are also scheduled as needed for psychoeducation of family members, providing feedback to parents and giving time for parents to ask questions about the patient's progress. The aim is to assure greater alignment of parents and teens goals for therapy. In weekly supportive group therapy, group members, in consultation with the therapist, set the agenda each week. The only stipulation is that each member is given some time to address his or her personal concerns. The therapist both models and instructs participants in supportive interaction styles. The group focuses on the overarching assumption in IGST that adolescents become suicidal for a variety of reasons, but they often report feeling isolated, misunderstood, unloved and unwanted. The goal of the group, which will focus on the completion of group activities (such as arts and crafts projects and reading and discussing books and movies), is to provide a

community where each adolescent can feel at home and included as an insider instead of an outsider. Phone calls with the therapist are used for brief crisis intervention during office hours. Families will be directed to local emergency rooms, 911, psychiatric emergency response teams (e.g., the DMH Access line/PMRT) and local and national suicide hotlines (e.g., 1-800-273-TALK) outside of business hours. IGST therapists and a supportive therapy supervisor will meet weekly to address supervision issues relevant to provision of IGST.

Standard Treatment Protocols Common to DBT and IGST

Intensity of Treatment. Both conditions include 1 hr weekly individual sessions including as needed family and collateral sessions, 2 hr group therapy, phone consultation with both adolescents and parents, and a 1 hr weekly therapist consultation team meeting to enhance therapist fidelity to treatment model. In both treatment conditions, the first therapy session will include a meeting with the parent(s). Thereafter, parent/collateral meetings will be held on an as needed basis, with a limit of no more than 7 total sessions during the 6-month treatment period (including the first session). Phone contact with parents will be unlimited and the therapist may go over the 7 sessions if an emergency session with parents is needed. In DBT, the therapist may choose to meet either with the parent alone or with the parent and teen together. In the IGST condition, the therapist will only conduct joint meetings with parent and child to conduct crisis management (e.g., suicidality, potential child abuse reporting). Given that the primary focus of IGST is the therapist/teen relationship, family sessions are not typically a focus of treatment in this model (although the therapist will meet with the parent individually, as described above). One difference between conditions is that parents attend group skills training in DBT but do not attend the supportive group therapy in IGST. Because topics in supportive group therapy often are about family problems or topics adolescents do not feel comfortable discussing with their parents, the focus of the group on support can be lost when parents are present. In both conditions, undergraduate or bachelor's level research assistants will assist group leaders with setting up the room, providing refreshments and group materials, monitoring videotaping equipment, accompanying youth to the restrooms, and recording basic information about each group meeting, such as which members were present and what topics were covered.

Crisis Management: Both interventions will develop safety plans at treatment start and will employ active crisis intervention in accordance with current standards of care (AACAP, 2000) when needed. Parents will be asked to provide contact information for additional responsible adults to be contacted in the event the therapist is unable to reach the parent in an emergency (Emergency/Alternative Contact Form). As dictated by the standard of care (AACAP, 2000), therapists in both interventions will schedule additional sessions for crisis intervention when needed and will provide after-hours crisis intervention either directly or by use of local crisis/emergency services, as described above. Adolescent inpatient services and EDs are readily available across conditions and across sites. In both conditions, adolescents will be instructed to not discuss suicidal thoughts or behaviors with each other in order to prevent contagion effects common among teens.

Assignment to Therapist. Newly admitted patients will be discussed in the weekly DBT and IGST therapist meetings and assigned to therapists on a space available basis. Patient requests for a change in therapist are reviewed by the team and granted on the basis of clinical judgment and caseload space.

Drop Out Policy. Any adolescent who misses four consecutively scheduled weeks of either individual therapy or group therapy/skills training is considered a dropout from treatment. This rule was instituted because it can be very difficult to know exactly when an emotionally dysregulated patient has actually dropped out of therapy. Patients often say they have dropped when in fact they don't mean it and even when they do mean it, they often change their minds within a short period of time. This dropout rule is explained to patients and family members during the first session of individual and/or group therapy and has been a standard part of DBT since its inception (Linehan, 1993).

Use of Psychotropic Medications During the Study. Medications/medication management will <u>not</u> be offered as part of this study. Adolescents who enter the study on psychiatric medications can continue these medications under the care of their prescribing provider. If at any time during the study the adolescent, parent or therapist would like the youth to be evaluated for medication, then he/she will be referred to a community-based provider. This may include a provider within the study therapist's institution but medication treatment will not be provided through the study. In accordance with the DBT philosophy of "consultation to the patient," in the DBT condition, when possible, adolescents/parents will be coached by the therapist on how to consult with the medication provider themselves regarding questions/concerns about their medication treatment. In the IGST condition, the therapist and/or the adolescent/parent may consult with the medication provider as needed. In both study conditions, therapists may consult directly with medication providers regarding any issues directly affecting safety. A psychiatrist will be designated at each study site who will be available to

consult with therapists in both conditions to answer questions about medications so they can make appropriate recommendations to the adolescent/parent regarding safety concerns (e.g., lethality of various medications, to assess if medication type and dosage is adequate for managing acute exacerbation of symptoms). Medication use (type, dosage, adherence) will be documented by independent evaluators during study assessments.

Hospitalization Policy. Because of the nature of the population, patients may be hospitalized at their own or their parent's request, or due to the concerns of their care providers (usually due to high suicide risk). No DBT or IGST therapist will serve in a responsible position (e.g., attending) for any patient during inpatient treatment. Study treatment is not terminated due to hospitalization.

Treatment Fidelity Ratings. In order to insure that therapists in both conditions are practicing fidelity to each treatment model, a subset of video recordings of both individual and group therapy sessions will be coded for adherence by expert DBT and IGST therapists. Both DBT and IGST have existing measures of fidelity that have been created by the treatment developers that will be used in this study (both are attached to this submission).

Adherence coding for IGST will be conducted locally and by Dr. Judith Cohen at Allegheny Singer Research Institute in Pittsburgh.

ASSESSMENT

Schedule of Assessments: Assessments will be conducted at intake, month 3, month 6 (treatment end), month 9 and month 12 (six month post-treatment). In addition to these longer assessments, weekly measurement will be completed in the form of the daily diary card, adolescent rating of suicidal ideation and planning (SBQ, see below), therapist note, and pre- and post-individual session ratings. We estimate that the full assessment battery (which will be completed at intake) will take approximately 3 to 4 hours (2 hrs. for parent). The extended assessment (which will be completed at months 6 and 12) will take approximately 2 hours (1 hr for parent). Finally, the abbreviated assessment battery (to be completed at 3, and 9 months) will take approximately 1.5 hours to complete (45 min. for parent). All measures will be computerized (see Section I on Data Management for more details). A table listing all assessment measures to be used in the study and a brief description of each measure are provided below.

Following each assessment, the interviewer will complete the **University of Washington Risk Assessment Protocol** (UWRAP) which includes (1) assessment of suicide and self-injury risk pre- and post-assessment, (2) strategies to decrease distress and related suicidal and self-injurious urges, (3) strategies to improve mood (4) procedures for when to increase level of response (e.g., escorting the subject to the hospital). Of note, there is no evidence that assessment of suicidal behavior (whether for treatment or research purposes) may "prime" vulnerable individuals and lead to increased suicide risk or risk of non-suicidal self-injury. Research investigating the potential of iatrogenic effects of youth suicide screening among high-risk and general student body groups (Gould et al., 2005) found that high-risk students in their sample who were asked about suicide were no more likely to report suicidal ideation after the survey than unexposed students (4.7% and 3.9%, respectively; P = .49) and high-risk students (defined as those with depression symptoms, substance use problems, or any previous suicide attempt) who were asked about suicide were neither more suicidal nor distressed than high-risk who were not asked about suicide; on the contrary, depressed students and previous suicide attempters in the assessment group appeared less distressed (P = .01) and suicidal (P = .02), than high-risk students not asked about suicide. However, given that self-harm and suicidal behaviors are inherent risks in a study that recruits expressly for highly suicidal persons, the UWRAP will be administered as a standard part of each assessment battery. If an adolescent is determined to be at risk of self-harm, it will be handled by the Principal Investigator or a licensed clinical psychologist/social worker who is part of the study team. A licensed clinician will be available at all times. If needed, the assessor might facilitate the subject contacting his/her treatment provider or parent/other adult or, if necessary, arrange hospitalization. For cases in which a telephone assessment is conducted and issues of self-harm risk arise, the participating parent/caregiver and any alternatively identified adult present in the physical vicinity of the teen subject will be immediately notified and guided through appropriate interventions. The UWRAP includes a very specific protocol for calling in a supervisor to speak with the subject before s/he is allowed to go home should the other elements of the protocol not sufficiently reduce distress. To date, the supervisor has been called in to an assessment to debrief a severely distressed or suicidal client less than 5% of the time. Additionally, all assessment team members have access to master's level or doctoral level consultants/supervisors 24-

hrs/7days a week should additional consultation/intervention be necessary. A modified version of the UWRAP (not including assessment of suicidality) will be used with parents/guardians who participate in assessments, in order to measure any distress they may have experienced as a result of the assessment process. The majority of this assessment requires that the assessor provide information about details regarding the assessment such as the timing (e.g., within the window), the type of modality (e.g., face to face vs. over the telephone), the informant participating in the assessment. Two items ask that the parent/guardian rate the level of stress that they are experiencing.

At the conclusion of the assessments, assessors will read a script ("End Script") to parents/guardians and youth. The script reminds parents/guardians that although specific information from the evaluation will not be provided, they should seek emergency services if they are concerned about the safety of the youth. Spanish speaking parents/guardians will receive the script in Spanish. Additionally, youth are reminded that they should inform their parent/guardian or call emergency services if they are at risk of harming themselves or are feeling suicidal.

Measures Included in this Study:

Screening Tools: (Not reported here but used in screening for study participation):

Self-Injury Screening Tool. The Self-Injury Screening Tool is a brief 6-item interview that measures history of self-harm and suicidal behaviors in order to determine if the adolescent meets study inclusion criteria. It will be administered to both adolescents and parents.

Kauffman Brief Intelligence Test (KBIT-2) are verbal scales that will be used to rule out mental retardation.

Study Inclusion and Major Outcome Measures;
The Suicide Attempt Self-Injury Count (SASI-C) was developed as a very brief survey of past intentional self-injuries and categorizes them into suicide attempts and non-suicidal self-injuries. This measure has been used successfully with adolescents and their parents in previous studies conducted at the UW and in previous treatment-outcome research with self-injuring adolescents.
The Suicide Attempt Self-Injury Interview (SASII measures the topography, intent, medical severity, social context, and outcomes of self-injurious behavior (including suicide attempts). Psychometric properties are good.
The Suicide Ideation Questionnaire-Junior (SIQ Jr.) will be used to measure suicide ideation. Although designed for younger adolescents, the SIQ-Jr has been widely used with both younger and older adolescents to evaluation suicide ideation. Use of the SIQ-Jr. for all participants allows us to keep measurement constant and minimize both participant burden (15 items) and reading comprehension problems. A raw score of 23 or above has been empirically established as the clinical cutoff indicating potentially significant suicide risk.
Structured Clinical Interview for DSM-IV, Axis II (SCID-II) Borderline Scale will be used to assess borderline personality disorder features, which will be measured continuously rather than applying diagnostic cut-offs that may not be relevant for adolescents.

Sample Descriptive Measures:
Adolescent Demographic Data Scale (ADDS): The ADDS is a brief interview conducted with the parent information is gathered about a wide range of demographic data such as date of birth, racial background, religious background, school performance, and developmental disorders.
Adolescent Family of Origin (AFOI): This AFOI is a brief interview conducted with the parent and/or teen, as part of the ADDS, that asks information about the family composition and individuals that the adolescent has lived with in the past and present (e.g., duration, relationship of individual to adolescent, marital status, occupation, etc.)
Measures of Adolescent's Behavioral Health Status:
The Child Behavior Checklist (CBCL) and Youth Self-Report (YSR): are widely used self-report measures of child and adolescent psychopathology. Parents complete the CBCL (Achenbach & Edelbrock, 1981), a dimensional measure assessing a broad range of behavioral and emotional symptoms with well documented

reliability and validity. This instrument provides a relatively quick assessment of youth symptoms and social functioning standardized to national norms.Youth complete the YSR (Achenbach, 1991), which parallels the parent completed CBCL. Extensive data support the psychometric adequacy of the YSR (Achenbach et al., 1995). The YSR and CBCL provide scores for total behavior problems, externalizing symptoms, internalizing symptoms, as well as narrow band symptom scales assessing depression/anxiety, attention problems, delinquent behavior, aggressive behavior, somatic complaints, social problems, conduct problems, and ADHD symptoms. These dimensional measures have well established procedures for determining the clinical significance of symptom scores.

Kiddie-Schedule for Affective Disorders and Schizophrenia—Present and Lifetime Version (K-SADS-PL) including the introductory interview and the depression, mania, GAD, PTSD, Panic Disorder diagnostic modules will be administered with both the parent and the teen.

Safety Procedures

Although the population studied is a high-risk population, study procedures are judged to present minimal risk. It is possible that participants will not like some of the assessment questions and some questions may focus on feelings or experiences that may be uncomfortable for participants. However, the questions are similar to what would typically be asked in a medical setting and do not involve any specific risk or discomfort beyond those of a standard clinical evaluation. Participants will be informed that they are free not to answer questions and to terminate participation in the project at any time. All study staff conducting assessments will be trained in emergency procedures and will have access 24-hour to the PIs and senior study clinicians for emergency consultation and crisis management.

The treatments to be studied pose no greater risk than standard psychotherapy interventions. During the treatment, feelings and topics that are upsetting to participants may arise and temporarily lead to negative emotions. Study clinicians will be available to help participants manage any negative reactions that may occur and the study treatments are designed to enhance youth's abilities to manage these reactions more adaptively without resorting to suicidal behavior. Suicidality will be routinely monitored and study clinicians will be trained in emergency procedures to follow if youth report active suicidality. Participants will be informed that they may decline participation in therapeutic procedures and that they may terminate participation in the treatment at any time. There are some risks associated with any treatment, as well as no treatment, and not all youth respond to treatment. This is a high risk population and participants are at risk for suicide attempts, suicide, and other adverse outcomes. While there is no discernible adverse reaction to the psychosocial treatments offered in this study (DBT and IGST), psychotherapy and the process of changing one‘s life is often experienced as very painful and it is not inconceivable that an adolescent might attempt or complete suicide in reaction to a difficult interaction with his or her therapist. We do not know whether the risk of suicide will be substantially lower in DBT or IGST but our prior research and clinical work with youth who engage in suicidal and self-inflicted injurious behavior suggests that this work can be done safely with the use of well-trained personnel and appropriate crisis management protocols. Study investigators have a great deal of experience working with these high risk samples of adolescents and implementing crisis management as needed. Participants will be receiving treatment as part of a research study conducted by nationally recognized suicide experts. As part of the study, they will be carefully monitored by highly trained personnel and receive state-of-the-art psychotherapy approaches. Hence, participation in the study is likely to lower risk as compared to treatment as usual in the community. Termination of therapy may also be a cause of distress. As the six-month treatment draws to an end, progress of each patient will be reviewed by their individual therapist with the patient, their parent(s) and the treatment team. If additional treatment is thought necessary or requested, a referral to non-study treatment in the community will be made. Subjects will be informed that there is a minimal risk of loss of confidentiality. All study personnel will be trained in the research ethics and protocols for maximizing integrity and confidentiality of clinical information and research data. Further, we have obtained a NIH Certificate of Confidentiality to help protect against outside attempts to gain access to research data.

A Data Safety Monitoring Board (DSMB) will be created to monitor the safety of participants throughout the trial. The DSMB will monitor the execution of the research protocol and study procedures and will ensure that reporting of adverse events follows the requirements of the respective institutions and NIH. The DSMB will meet to review the protocol and procedures at study start, including review of how adverse events will be defined in the course of the trial and the reporting procedures. The DSMB will conduct regular reviews thereafter to determine whether patient safety is being adequately safeguarded and study goals are being met. At each review, the DSMB will examine whether the emerging pattern of findings alters the risk-benefit ratio to the point that the study needs to be discontinued. The DSMB will be kept apprised of adverse and notable events on an ongoing basis and serve as the final arbiter of whether individual patients should be removed from the protocol. During the course of treatment, the adolescent/family, the therapist or the study PIs may question the appropriateness of a particular patient continuing in the study or whether the treatment should be modified. With some adolescents, it may become clinically necessary to arrange for ancillary services such as a case manager or brief inpatient admission. If the youth is determined to be a possible danger to self or others, he/she will be referred for emergency evaluation and possible hospitalization. In such cases an outside clinical expert consultant to be designated at each site may be called in to evaluate the adolescent for purposes of determining whether the treatment being provided is related to the deterioration in the adolescent‘s psychiatric status and whether the adolescent‘s treatment should be changed in any way. Should the consultant believe that the patient is being harmed by the treatment or research protocol, the consultant will discuss possible termination from the study. All subjects who wish to receive additional treatment at the conclusion of their participation (regardless of whether they dropped from treatment, completed treatment, or were terminated at consultant recommendation) will receive appropriate referrals. It is possible that youths will be enrolled in the study but that information obtained after enrollment will raise questions regarding inclusion/exclusion criteria (e.g. evidence of psychotic symptoms might emerge). In these instances, we will assist in linking the youth to appropriate treatment and withdraw them from the study.

The DSMB will be chaired by Dr. Donald Guthrie. Dr. Guthrie has previously consultant to the investigators at the UW site and has served as DSMB chair for several studies with the UCLA investigators. The remainder of the board will (minimally) consist of one psychiatrist with expertise in treating highly suicidal and depressed adolescents, one mental health specialist (MSW, PhD, PsyD or MD) in the area of suicidal and life-threatening behaviors, one mental health specialist (MSW, PhD, PsyD or MD) in the area of child/adolescent mental health, and one biostatistician. The primary role of the Data Safety Monitoring Board (DSMB) is to monitor the safety of participants throughout the trial at the respective sites. The DSMB will monitor the execution of the research protocol and study procedures and will ensure that reporting of adverse events follows the requirements of the respective institutions and NIH.
Any patient who commits suicide during the course of the study will be reported immediately (i.e., within 24 hours of discovery of the event by research personnel) to the IRBs at each site and to the Chair of the DSMB. Drs. Linehan and McCauley (Seattle sites) and Drs. Berk and Asarnow (Los Angeles sites) will be responsible for understanding and adhering to the most recent IRB policies and will also be responsible for the accurate documentation, investigation, and follow up of all study-related adverse and notable events.

4) Data and Specimen Banking

At the end of the study, an anonymized and de-identified database will be created and retained for future analyses in a data repository. This is required of all NIMH-funded studies, receiving funding levels over $500,000. Other researchers may be permitted access to the data repository in order to maximize the usefulness of the data for improving mental health and health outcomes. The repository will not include video or audio recordings.

Repository data are saved on server computers located in a locked, nonpublic, dedicated server room in the Behavioral Research and Therapy Clinic’s (BRTC) research offices on the University of Washington (UW)

campus. These systems have enabled firewalls, antivirus, regular patching and updates, and authenticated access. Environmental control is provided via temperature monitoring and air conditioning. An uninterruptable power supply unit provides battery backup power in case of power failure. Data are protected via daily backup. Repository data are stored indefinitely.

Data are stored in access-controlled SQL databases. Access to the databases is limited, and all repository data are strictly confidential. Database access is restricted to essential staff and their designees and to only the context relevant to their roles on the project. Access is limited to those who have completed HIPAA and Human Subjects Research training and who have applied to their immediate supervisor and been approved by the BRTC Director (or her designee) for access. Users access the databases via individual user accounts with individual passwords. Approved individuals are required to sign a confidentiality form stating they will not take data out of the databases or the locked and secure research clinic premises.

Repository data (including data from the CARES study) are covered by an active federal Certificate of Confidentiality that protects the investigators from being forced to release any research data in which subjects have been identified. The certificate's purpose, limitations, and specific areas of reporting are noted for the participants in the consent form.

Repository data are taken from questionnaires, interviews, computerized behavioral tests, and ambulatory physiological monitoring and consist of (a) descriptive data about participant characteristics, (b) outcome data on participants, (c) process data about participants and therapists, and (d) behavioral performance. The data may include information about participants' behavioral and emotional problems, psychiatric history, traumatic events, drug and alcohol use, suicidal behavior, interpersonal relationships, HIV risk behaviors, task persistence, implicit self-associations, sleep and activity patterns, sleep quality, gender and sexual orientation, service use, and feelings about treatment the participants received.

Requests to access repository data require an application that is reviewed by the principal investigator (PI) for the repository database. External investigators submit their curricula vitae and documentation of ethics and HIPAA training. The PI determines whether the purpose of the request is research-related and whether the requester has the appropriate credentials. If the PI deems the purpose and credentials to be appropriate, then approval from the UW IRB for use of repository data is sought. Access to data is provided only if the IRB grants approval.

Vetted users interact with data via a remote access portal. Access to the BRTC portal requires that external investigators sign the BRTC Confidentiality Agreement and, if not affiliated with UW Medicine, complete a UW Medical Center Temporary Workforce HIPAA Self-Study form. Data required for project analysis (as described in the project description) are pulled from the SQL databases by the BRTC Data Manager and placed in de-identified SPSS files.

5) Data Management

Primary Outcomes for this paper:

There are three primary outcome domains: suicidal attempts, non-suicidal self-injury and suicidal ideation. Treatment maintenance and functional improvement is also assessed. Suicidal events will be defined as either a suicide, suicide attempt (defined as self-injurious behavior with some non-zero intent to die as a result of this behavior) and suicidal ideation. We will also examine the number of non-suicidal self-injury behaviors. The primary measure of treatment maintenance will be days in treatment.

Statistical Analyses

As stated above, our hypotheses are as follows:

Hypo 1: Suicide events (suicide, suicide attempt, suicidal ideation) will be less likely in DBT vs. IGST during the treatment and follow-up period.

Hypo 2: NSSI will be less likely in DBT vs. IGST during the treatment and follow-up period.

Hypo 3: Days in treatment will be higher and treatment dropout will be lower in DBT vs. IGST.

In the presence of a large proportion of data stacked at one response such as zero, which may occur, no transformation can successfully spread out this stack of common responses. If this occurs we will consider implementing zero-inflated Poisson (ZIP), zero-inflated Negative Binomial (ZINB) regressions which model the zeroes in the structural portion of the model, and/or Ordinal models as was implemented in Linehan et al. (2006) for similar measures. ZIP and ZINB models are mixture models in which the complete distribution of the outcome is approximated by mixing two component distributions.

The most common approach is to assume a logistic regression model for the "zero, not zero" aspect of the outcome and either a Poisson or Negative Binomial distribution for the count portions of the model. ZIP and ZINB models with random effects, will accommodate the clustering present in the repeated assessments. Ordinal mixed effects model (see Hedeker et al., 2000) will address the clustering of the repeated measures within subject as well as providing the mechanism to contrast between groups. For Hypothesis 1 and Hypothesis 2, we will examine the data separately through the Treatment year and the Follow-up year with linear contrasts between treatment groups performed at the end of the treatment year and the end of the follow-up year.

With repeated assessments, missing data is inevitable, but the key thing is that the specified contrasts are not effected due to the presence/absence of data. This ZINB models, mixed effects, and ordinal mixed effects framework are robust with respect to dropout and missing data, unless the dropout mechanism or cause of missing is informative. We will use pattern-mixture models to assess if there is bias due to drop out or missing data. As described by Hedeker and Gibbons (1997), these mixed models allow us to assess whether important estimates (e.g., average suicide attempts for Groups) are dependent on missing data patterns, and provide overall estimates of effects by averaging over the various missing-data patterns. In addition, we will consider the extension of the Pattern-Mixture models as described by Guo, Ratcliffe, and Ten Have (2004) which includes the incorporation of random effects in the Pattern mixture model, which allow subject-to-subject heterogeneity. To examine if medication effects potentially bias our inferences, we will parallel the pattern mixture approach above to see if the medication dosage affects the inference. All proposed frameworks allow for the inclusion of covariates. With the multi-site design, we will control for site in all analyses.

Power Analysis

We plan on enrolling 170 subjects, 85 per treatment group.

Based on the specific aims, one simplistic assessment of treatment efficacy is based on the occurrence of events (suicide events, attrition from therapy). Therefore, to determine sufficient sample size, we base the derivation on the sample size needed to detect a significant effect, illustrating a contrast between groups, with 80% power. Analytical methods such as survival models or repeated measures models will have more power than the simplistic chi-square contrast between groups.

We calculated a power curve based on a 30% difference between groups. The 30% difference is based on the comparable difference Diamond et al. (2010) saw in their treatment of Attachment-Based Family Therapy compared to a treatment as usual control. To protect against inflated type I errors, we adjust the alpha-level of the test by a factor of 5, corresponding to the five key outcomes/analyses of interest: reduction in suicide attempts and in ideation, days in treatment, functional improvement, and assessment of mediation. Based on the figure, we found that 65 subjects per group is sufficient to yield at least 80% power to detect a 30% different between groups. This 65 per group implies we would need 72.2% retention, which is in line with the 72.4% retention rate reported by Stanley et al. in her investigation of CBT in this population.

We also calculated a power curve based on a 25% difference between groups. For a 25% difference between groups, with 85 subjects per group, the analysis will have power in excess of 80% to yield a statistically significant result at the alpha=0.05. Adjusting the alpha-level to 0.01, the study would need retention rates in the line of 88% to guarantee sufficient size per group (75 per group).

For mediation, Fritz and MacKinnon (2007) documented sample size requirements to guarantee 80% power under the sequential regression framework (i.e., Baron and Kenny, 1986). Under the assumption of a medium effect for intervention with the mediator and a medium effect for intervention on outcome covarying the mediator, the sample size required for partial mediation is 118. Therefore, our sample size of 170 even with an anticipated attrition rate of 25% is sufficient for detecting our mediation hypothesis. (Not part of current paper).

Data Management

Data will be managed by the University of Washington site. The Behavioral Research and Therapy Clinics (BRTC) at the UW site maintains an independent server network that supports computer workstations for all research projects at the BRTC. Additionally, they have developed a user- and

researcher-friendly computerized data entry and management system that can be accessed on-line from both the UW and from other sites with internet access. The system is a three-tier web-based application hosted on one of the BRTC servers. Interface screens are presented as web pages with some integrated display logic on the patient side, the application tier includes more formal data logic and cleaning, and the database layer stores the data in an organized manner consistent with previously collected research data. The application tier and data tier are implemented on a two-node failover cluster providing redundancy and security of research and clinical data.

There are currently 128 instruments available for use, including multi-path interview assessments with skip logic and instant reporting. Instrument preparation included creating a variable naming and coding structure consistent with previously collected data as well as clearly defining logical constraints for both data integrity and display purposes. Before study start, the instruments for the current study will be entered into the database and thoroughly tested before going on-line. Concurrent with instrument development, a clinical management system was designed and implemented to track subjects, which has now been expanded to manage five research studies. Subject progress from initial contact through study drop or completion is also largely automated, integrated with the assignment and tracking of completed outcome measures, weekly treatment assessments, and other pertinent data.

During instrument creation, a substantial amount of metadata was entered for each instrument (and will be entered for new instruments), resulting in the creation of a comprehensive data dictionary indexing over 8,500 variables with explanations of value coding, variable labels, and usage information indicating quality of current records and historical usage within other studies. This dictionary is used to programmatically generate SPSS syntax files for ease in analysis. Initial deployment of the system in single-site and multi-site research has been extremely successful.

Data will be entered at each site by the on-site clinical research assessors for interview data, by participants for questionnaire data, and by therapists for therapist notes and data collected during treatment sessions. Data is segregated in the UW system by site and each site has complete access to data they have entered. The UW will provide a help-desk and a data manager to be sure that data entry goes smoothly at each site. The UCLA site will also have a data manager to oversee data entry at the UCLA site and to work collaboratively with the UW data manager. Each site will be responsible for cleaning the data that they enter and for verifying that the data entered by their site is ready for aggregation into data files combining data from the two sites. Both sites will have equal access to the aggregated data files that can be downloaded to onsite computers for analysis.

Data will be stored in locked files. Names will be kept separately from data, which will contain only an identifying number. With the exception to confidentiality noted above, only study personnel will have access to the data and be involved in coding data and protecting identifying information. All study staff will be trained in confidentiality procedures and sign a confidentiality agreement prior to gaining access to the data. When the research is completed, raw data will be destroyed. Electronic files without identifiers will be maintained until all papers are completed. Names, contact information of participants, and informed consent forms will be destroyed when the research is completed.

6) Confidentiality

Confidentiality will be maintained by coding all data with identification numbers, not names. Research data will not be released to any outside person or agency. We have obtained a NIH Certificate of Confidentiality that will be upheld by the respective institutions at each site. Clinical information will only be released to designated individuals or agencies with explicit written request by the patient. Electronic information is similarly separated into clinical/identifying information and de-identified research information and stored in computer files that will be protected by passwords. Video recordings of sessions will be made in an effort to assess treatment adherence and assessment reliability. While participants may be identifiable in these videos, the recordings will only be labeled with participant number. Video recordings will be kept for 15 years after the ICF and PHI forms have been signed. At the end of this time period, the recordings will be destroyed. Recordings will be kept in a locked safe, which is housed inside of a locked research office. As an additional precaution, recordings are encrypted (e.g., made unreadable) prior to being stored and require a password or “key” to remove the encryption and view the files. Only approved research staff will have access to the password, which will be stored separately from the recordings. Subjects will be informed that they have the right to review their

recordings at any time and request that recordings be edited or erased, in part or in whole. Clients will not be given copies of their recorded sessions. They may, however, request to view their recordings in our offices. Because these recordings may contain sensitive and emotionally charged information, we feel it is best for clients to view these tapes with their study therapist or another study staff member present.

All video recordings that are shared with other study sites (i.e., University of Washington, UCLA, Allegheny Singer Research Institute) will be shared via the University of Washington server. The procedures for transmitting these videos securely is as follows:

The video file will be put into an encrypted volume via TrueCrypt software, which uses government-standard Advanced Encryption Standard (AES) to secure files. (AES is a Federal Information Processing Standards (FIPS; http://itl.nist.gov/fipspubs/) approved cryptographic algorithm used to protect electronic data. AES is widely used across the healthcare industry to secure data-at-rest, data-in-motion and data-in-transit.) The encrypted volume can only be opened with the correct password. The encrypted volume is uploaded to the UW BRTC server via a web-based portal. The portal can only be accessed with a unique user ID. Once uploaded, the encrypted volume will be kept on the secure server until the video-coding task is complete. The UW BRTC server has Windows Server 2008 R2 running on it and has an enabled firewall, antivirus, regular patching and updates, and authenticated access to both the databases and the data capture application. It is physically controlled in a locked room in a non-public building on the UW campus. External access to the server is encrypted in transmission using SSL encryption. The environmental control is provided through temperature monitoring and air conditioning. An uninterruptible power supply unit provides battery backup power in case of power failure. Furthermore, the data on our servers is protected through a daily back-up solution. In order to view videos, the viewer has to log into the UW BRTC web-based portal to download the encrypted volume to her desktop. He/she opens the volume using the correct password and views the video inside the encrypted volume. The encrypted volume appears to the user as a new disk on the computer, but remains encrypted on the computer hard disk at all times, even as the viewer watches the video. Once done viewing, the viewer "dismounts" or exits the volume. After the encrypted volume is dismounted, the video cannot be viewed again without supplying the correct password through TrueCrypt. Lastly, the viewer permanently deletes the volume so that no trace of the volume remains on his/her desktop.

All materials are kept in locked facilities and only essential study personnel will have access to recordings. All research data will be reported as group aggregates that cannot be associated with any given individual. Finally, all staff will be required to sign a confidentiality agreement to complete Human Subjects and HIPAA training certifications.

In accordance with state law, if we obtain information about suspected child abuse or elder abuse during the course of the research study, we are mandated to report this information to relevant authorities. In addition, if we determine that a study patient is a danger to self or others, the law allows us to share this information with individuals/entities needed to maintain safety. These exceptions to confidentiality will be clearly stated in the informed consent/assent documents and will be carefully reviewed with youth and parents/guardians. Because the study population is suicidal and self-injurious adolescents, it is likely that these situations will occur. All study staff will be trained in procedures for reporting child and elder abuse and in safety procedures for psychiatric emergencies. The PI at each site will oversee all instances in which confidentiality must be breeched.

7) Withdrawal of Subjects

During the course of treatment, the adolescent/family, the therapist or the study PIs may question the appropriateness of a particular patient continuing in the study or whether the treatment should be modified. With some adolescents, it may become clinically necessary to arrange for ancillary services such as a case manager or brief inpatient admission. If the youth is determined to be a possible danger to self or others, he/she will be referred for emergency evaluation and possible hospitalization. In such cases an outside clinical expert consultant to be designated at each site may be called in to evaluate the adolescent for purposes of determining whether the treatment being provided is related to the deterioration in the adolescent's psychiatric

status and whether the adolescent's treatment should be changed in any way. Should the consultant believe that the patient is being harmed by the treatment or research protocol, the consultant will discuss possible termination from the study. All subjects who wish to receive additional treatment at the conclusion of their participation (regardless of whether they dropped from treatment, completed treatment, or were terminated at consultant recommendation) will receive appropriate referrals. It is possible that youths will be enrolled in the study but that information obtained after enrollment will raise questions regarding inclusion/exclusion criteria (e.g. evidence of psychotic symptoms might emerge). In these instances, we will assist in linking the youth to appropriate treatment and withdraw them from the study.

8) Risks to Subjects

Although the population studied is a high-risk population, study procedures are judged to present minimal risk. It is possible that participants will not like some of the questions and some questions focus on feelings or experiences that may be uncomfortable for participants. However, the questions are similar to what would typically be asked in a medical setting and do not involve any specific risk or discomfort beyond those of a standard clinical evaluation. Participants will be informed that they are free not to answer questions and to terminate participation in the project at any time. All study staff conducting assessments will be trained in emergency procedures and will have access 24-hour to the PIs and senior study clinicians for emergency consultation and crisis management.

The treatments to be studied pose no greater risk than standard psychotherapy interventions. During the treatment, feelings and topics that are upsetting to participants may arise and temporarily lead to negative emotions. Study clinicians will be available to help participants manage any negative reactions that may occur and the study treatments are designed to enhance youth's abilities to manage these reactions more adaptively without resorting to suicidal behavior. Suicidality will be routinely monitored and study clinicians will be trained in emergency procedures to follow if youth report active suicidality. Participants will be informed that they may decline participation in therapeutic procedures and that they may terminate participation in the treatment at any time. There are some risks associated with any treatment, as well as no treatment, and not all youth respond to treatment. This is a high-risk population and participants are at risk for suicide attempts, suicide, and other adverse outcomes. While there is no discernible adverse reaction to the psychosocial treatments offered in this study (DBT and IGST), psychotherapy and the process of changing one's life is often experienced as very painful and it is not inconceivable that an adolescent might attempt or complete suicide in reaction to a difficult interaction with his or her therapist. We do not know whether the risk of suicide will be substantially lower in DBT or IGST but our prior research and clinical work with youth who engage in suicidal and self-inflicted injurious behavior suggests that this work can be done safely with the use of well-trained personnel and appropriate crisis management protocols. Each of the PIs have experience working with these high risk samples of adolescents and implementing crisis management as needed. Participants will be receiving treatment as part of a research study conducted by nationally-recognized suicide experts. As part of the study, they will be carefully monitored by highly trained personnel and receive state-of-the-art psychotherapy approaches. Hence, participation in the study is likely to lower risk as compared to treatment as usual in the community. Termination of therapy may also be a cause of distress. As the six month treatment draws to an end, progress of each patient will be reviewed by their individual therapist with the patient, their parent(s) and the treatment team. If additional treatment is thought necessary or requested, a referral to non-study treatment in the community will be made. Subjects will be informed that there is a minimal risk of loss of confidentiality. All study personnel will be trained in the research ethics and protocols for maximizing integrity and confidentiality of clinical information and research data. Further, we will obtain a NIH Certificate of Confidentiality to help protect against outside attempts to gain access to research data.

9) Potential Benefits to Subjects

Youth and families participating in the research study will receive potentially effective treatments by skilled therapists that may result in reductions in suicidal behavior and psychopathology in the youth and improved family functioning. The benefits also include modest payments for completing assessments. The benefits of this study to society are likely to be large. Potential benefits of this study include the development of an effective treatment approach for suicidal youth. Information from this study should advance knowledge

regarding the problem as well as care for future patients. Youth suicide and suicide attempts are major public health problems, leading to a number of national initiatives to address this critical problem. As explained above, the risks of study participation are minimal. Therefore, we believe that the potential benefits of this research far outweigh the risks.

10) Compensation for Research-Related Injury

Since this study involves teenagers with a history of suicide attempts and deliberate self-harm, these youths are at risk for suicide attempts and self-injury regardless of whether they choose to participate or not participate in the study. Psychiatric emergencies and injuries will be addressed by referring subjects to the appropriate level of medical care. Subject's insurers and/or their families will be responsible for covering any costs related to treatment for injuries.

11) Economic Burden to Subjects

Subjects will not be responsible for any costs due to their participation in the research.

12) Consent Process

The location of the informed consent process will depend on the referral source and timing of contact and will either be in the ED/hospital, at an outpatient clinic, at the participant's home, or another agreed upon location (e.g., research offices). For parents/youth who give their permission to hear more about the study, the process of participation will be explained using the informed consent/assent forms by study staff trained in informed consent and assent procedures. It will be explained that participation is voluntary, will not affect the relationship between the patient and the ED/hospital/clinic providers or other mental health providers, and that the participant is free to withdraw consent at any time. Subjects in the hospital setting will be approached only after (a) ED/hospital staff have determined that it is an appropriate time to present the study to the parents and youth, and b) ED/hospital staff have briefly described the study (using the script) and parents have expressed an interested in learning more about the study. Subject referred by staff at the Child & Adolescent Psychiatry Clinic or other outpatient clinics (e.g. pediatrics) will only be contacted directly only after they have given permission for providers to give their contact information to study staff or have contacted study staff on their own in response to referrals or advertisements. Following explanation of study procedures using the informed consent/assent forms, potential participants will be asked whether they are interested in participating. Participants who sign the appropriate forms will be enrolled in the study. Parents will be required to provide consent for their teens and themselves to take part in the research. Youth will be required to provide assent using the same consent form as their parents. Every effort will be made to perform informed consent in a quiet, private location. Potential participants will be given time to determine whether they wish to participate and/or to perform informed consent in a different location/at a different time. Participants will be told that they are free to change their minds and decline to participate after signing the informed consent form. Informed consent will be conducted with Spanish-speaking parents. This includes parents who are monolingual Spanish speakers as well as those who speak some English, but prefer to conduct the informed consent process in Spanish. Youth must speak English fluently to be included in the study. With Spanish-speaking parents, informed consent will be conducted by study staff who are fluent in Spanish, using a Spanish-language consent form**.**

13) Vulnerable Populations

As documented above, youth ages 12-18 will be included in the research. The research does not involve greater than minimal risk. Safety procedures are documented above.

14) Multi-Site Human Research*

This project is a Collaborative R01 grant from the NIMH. This a multi-site study consisting of two primary sites - LA Biomed/Harbor-UCLA and the University of Washington, Department of Psychology. Each primary site has a sub-site (subcontract) where subjects will also participate in the study, the UCLA School of Medicine/Neuropsychiatric Institute and UW/Seattle Children's Hospital. The University of Washington is the lead site and Dr. Marsha Linehan, the creator of DBT, is the Principal Investigator of the overall project and of the Seattle sites. Dr. Michele Berk is the Principal Investigator of the Los Angeles sites. Dr. Joan Asarnow is

the Principal Investigator of the UCLA site and Dr. Elizabeth McCauley is the PI of the UW/Seattle Children's Hospital site. Each PI will be responsible for the project operations at their respective site. In Seattle, Dr. Linehan will oversee the University of Washington Behavioral Research and Therapy Clinics (UWBRTC) site and Dr. McCauley will oversee the UW/Seattle Children's Hospital (SCH) site. In Los Angeles, Dr. Berk will oversee the Harbor-UCLA Medical Center site (Harbor-UCLA) and Dr. Asarnow will oversee the UCLA School of Medicine and Neuropsychiatric Hospital and Clinics (UCLA) site. The University of Washington will serve as the coordinating site with Dr. Linehan as the corresponding PI.

There is also a subcontract from LA Biomed/Harbor-UCLA to Dr. Judith Cohen at Allegheny General Hospital/Research Institute. Dr. Cohen's role will be to train study therapists in the IGST treatment and to monitor treatment fidelity in this study condition via phone calls to local IGST supervisors and therapist, and by watching videotapes of IGST sessions. Power analyses indicate that in order to detect differences between the Dialectical Behavior Therapy (DBT) and Individual and Group Supportive Therapy (IGST) treatment conditions (given the significant though low base rate of the outcomes), a sample size larger than could be recruited at any single site is required for the proposed study. Further, conducting the study in partnership at two culturally and geographically different sites such as Seattle and Los Angeles improves the diversity of the sample, thus aiding in study generalizability.

Expertise of Sites: Our respective sites bring together a team of investigators with unique as well as overlapping areas of expertise. Dr. Linehan is the treatment developer of DBT and co-author of the book on DBT for suicidal adolescents. She has been the principal investigator on six different NIH-funded treatment development/evaluation clinical trials, three of which have focused specifically on highly suicidal individuals with borderline personality disorder (BPD). Much of Dr. Linehan's research has focused on treatment of exceptionally difficult and highly suicidal individuals. She has extensive experience in training and supervising therapists treating suicidality and has developed a large array of suicide management and monitoring protocols for both assessors and therapists. She was very active in the writing of the DBT treatment manual for adolescents with special emphasis on management of suicidality and of keeping the manual within the DBT algorithm. Dr. McCauley has been (or is currently) the principal investigator on two RCTs funded by the NIMH, a recently completed (497 participants) trial of a school based preventive intervention for adolescents at risk for depression and an ongoing study of the efficacy of a Behavioral Activation treatment for clinically depressed adolescents. She is currently a co-investigator on two additional RCTs, studying the management of depression in community settings (primary care and schools) and has been (or is currently) the PI on three longitudinal studies documenting the developmental course of depression in youth. Dr. Berk was previously a member of the Beck (Beck, Brown et al., 2005) research team that demonstrated the effectiveness of cognitive therapy with suicidal adults, and has translated that experience into applications for adolescents at Harbor-UCLA where she is the founder and director of the adolescent DBT program at Harbor-UCLA and has been the co-PI of a trial evaluating cognitive-behavioral approaches for youths presenting with suicide. Dr. Asarnow has extensive experience with multi-site trials evaluating the efficacy and effectiveness of interventions for depression and suicidality in adolescents. She has been PI of 7 different RCTs, including three current NIMH-funded RCTs focusing on youth depression and/or suicidality. She was the PI of the Youth Partners in Care project which demonstrated the effectiveness of a quality improvement intervention that improved access to evidence-based cognitive-behavior therapy and pharmacotherapy for adolescent depression across 6 sites within 5 major health care organizations. She is also the PI of two trials evaluating cognitive-behavioral approaches for youths presenting with suicide attempts and was PI at the UCLA site for the multi-site Treatment of Resistant Depression in Adolescents (TORDIA) study. Thus, both sites are centers of excellence in the conduct of clinical trials and are well equipped to conduct all aspects of the proposed research. While this will be the inaugural collaboration for the four sites, all four investigators have experience working on multi-site studies. Drs. McCauley and Linehan have worked collegially for the past several years. Dr. McCauley is a consultant for the DBT Adolescent Clinic underway at the Behavioral Research and Therapy Clinics at UW under Dr. Linehan's supervision. Dr. Linehan is a consultant to Dr. McCauley's post-doctoral fellow. Given their shared focus on adolescent depression, Dr. McCauley and Dr. Asarnow have been close academic colleagues for the last twenty years. They have worked together on a number of meeting symposia and panel presentations and Dr. McCauley has consulted with Dr. Asarnow in relation to the development and implementation of her work involving treatment of depression in primary care. Dr. Berk and Dr. Asarnow have

collaborated for the past 7 years, and during that time have conducted two treatment trials with suicidal adolescents and published multiple articles together. Additionally, Dr. Berk is a regular attendee at the University of Washington hosted DBT Strategic Planning Meeting, a workgroup of active DBT researchers who come together annually to discuss the latest advances in DBT research and to work collaboratively to solve shared research problems and promote scientific advancement of treatments for BPD, other difficult to treat populations and treatment-resistant disorders. Finally, this past spring Dr. Linehan traveled to Los Angeles where she met with both Drs. Berk and Asarnow for the purpose of collaborating on this grant submission as well as to consult on on-going adolescent cases in Dr. Berk's DBT clinic.

Administrative Structure and Operations: The UW site will serves as the coordinating center, the organizing and administrative unit for the research. Dr. Korslund at UW will provide overall operations coordination between the sites, the DSMB and NIH. To capitalize on the strengths of the each site and reduce duplication of resources and costs, key functions (as outlined below) will be consolidated by site. At the start of the project, the UW will hold an extensive meeting with all key personnel. This meeting will serve to structure the administrative infrastructure and quality control procedures. To ensure on-going close collaboration, the site PIs will have (bi-weekly or more frequent if needed) telephone conferences to discuss operations, client enrollment, issues with inclusion/exclusion criteria, client withdrawal, transfer of data files, protocol modifications and any problems as they arise. In addition, annual investigator meetings of all key personnel will take place, alternating between the two sites, and will include ongoing maintenance of high inter-rater reliability of ratings and review of implementation of study procedures and protocols. Each site's PI will monitor recruitment/enrollment, general implementation of study procedures at their respective sites and maintenance of the treatment blind. Dr. Linehan and Dr. Anthony Dubose, an expert adolescent DBT trainer in Seattle, will provide the DBT intervention training and will provide as needed supervision at both sites for therapists who fall out of DBT adherence during the study. Drs. McCauley and Linehan will provide clinical oversight of DBT teams at UW and Dr. Berk will provide clinical oversight of DBT teams at UCLA, supported by Dr. Asarnow and the UW team. The UW will conduct adherence coding for all sites for DBT. Dr. Judith Cohen, a consultant who has expertise in supportive therapy, will provide the IGST training as well as supervision at both sites for therapists who fall out of IGST adherence during the study. She has an ongoing collaboration with Dr. Asarnow at UCLA where Dr. Cohen has led the training in supportive therapy for an RCT with depressed children and collaborated with the study team on training, implementation, adherence ratings, and quality assurance monitoring for the supportive therapy condition. Similarly, Dr. Cohen will provide the training of IGST at both sites and will provide clinical consultation, assistance and supervision when needed for IGST therapists. Each site will also have site-specific IGST supervisors. The Los Angeles sites will conduct the adherence coding for IGST, with Dr. Cohen co-rating tapes for adherence and reliability checks.

Dr. McCauley will provide oversight for the assessment functions of the study and together with her counterpart at the UCLA site, Dr. Asarnow, will provide training and quality assurance monitoring for the assessment procedures, ensure that recruitment efforts are aggressive and that assessment procedures and policies are followed.

The UW will hold primary responsibility for data management and for coordinating statistical analysis. The computerized database will be housed and managed at the UW site and this site will coordinate data entry and data scoring of treatment and outcome assessments for both sites.

Data collection will be monitored through a data tracking system from the beginning of a given assessment through delivery to the data analyst. Data from assessment interviews, assessors, subject and therapist self-report measures, adherence coding, and therapist notes and reports are entered directly into the computerized database, which eliminates the necessity of double-entry and minimizes substantial entry error. The UW will manage a help-desk that provides timely assistance to assessors, clinicians, and staff at both sites. This computerized database adheres to the data management and sharing system mandated by NIH.

Dr. Robert Gallop will conduct data analysis. Dr. Gallop has extensive experience and expertise in the development and coordination of data analytic plans for large clinical trials with data demands similar to the proposed trial and has worked collaboratively in this manner with Drs. Linehan, McCauley and Harned across

several on-going and completed RCTs. With this population of interest, Dr. Gallop has served as the statistician for the recently published studies dealing with suicidality in adolescents as well as depression in adolescents. Therefore, Dr. Gallop is very familiar with the measures to be used in this study. With respect to multi-site studies, Dr. Gallop has served as the Director of Data Management and Statistics for the NIDA funded Multisite Cocaine Collaborative Treatment Study as well as the Director of Data Management and Statistics for the two-site Penn-Vanderbilt Treatment of Depression Study. In addition to Dr. Gallop's recent collaborations with our group,

A Study Executive Committee (SEC), comprised of key personnel from both sites, will be the vehicle for ensuring study cohesion across the lifecycle of the project. Dr. Linehan will chair the SEC and with Drs. McCauley, Berk, Asarnow, and Gallop form the functional governing body. The SEC will be responsible for final approval of the study protocol and thereafter for any changes in the protocol, all of which will be documented in writing as part of the SEC minutes. The committee will monitor recruitment rates, quality of assessments and treatment, and data collection and management. If difficulties arise, the committee will work to resolve the problems. The SEC will also function as the Publications Committee and be responsible for making decisions about authorship of publications and sharing and use of data. The SEC/publications committee will review all proposed data analytic procedures, proposed publications, and make authorship decisions. Modeled after procedures used in other multi-site projects, the site PIs and co-investigators will be on all primary papers. Other individuals may propose secondary papers. The SEC will review and make final decisions on these proposals. These procedures aim to ensure fairness, maintain quality control, facilitate opportunities to address secondary questions, and allow junior collaborators to develop and lead publications on secondary questions.

Dr. Linehan, as Chair, will be responsible for monitoring overall project progress, recruitment milestones, and quality assurance across teams, and be the primary link to the Data Safety and Monitoring Board. The UW will host annual in person meetings of the SEC in years 1 and 3. UCLA will host the SEC meeting in years 2 and 4. As stated previously, SEC conference calls will be held bi-weekly (or more frequently if needed) to discuss on-going operations and any problems**.**