Integrative Risk Reduction and Treatment for Teen Substance Use Problems and PTSD

An estimated 1,800,000 adolescents are victims of child sexual abuse (CSA) in the United States alone. When other forms of interpersonal violence (IPV) are considered, such as child physical abuse and assault (CPA), these figures rise dramatically: nearly 70% of youth aged 13-18 report lifetime exposure to physical assault, and 40% of youth in this age range report a lifetime history of maltreatment by a caregiver. **CSA is one of the strongest and most consistent predictors of adolescent problems.** In particular, youth who have experienced CSA are at **significant risk for substance use problems, including early initiation, use, and abuse**. For example, adolescent CSA victims are over 3.5 times more likely to report marijuana abuse/dependence and are over 8.5 times more likely to report hard drug abuse/dependence compared to non-CSA victims (Kilpatrick et al., 2000). Other alarming sequelae, such as posttraumatic stress disorder (PTSD) and risky sexual behaviors, also have been clearly linked with CSA. Gender differences have been observed in rates of exposure to CSA, CPA, and other potentially traumatic events. Whereas boys and men are more likely to experience CPA and potentially traumatic events overall, girls and women are more likely to experience CSA. In general, childhood exposure to violence is a strong, reliable predictor for a host of negative outcomes. Youth with histories of CSA and/or CPA often experience earlier substance use initiation and elevated risk for substance use disorders (SUD) later in life, as well as mental health problems like PTSD, depression, and risky sexual behaviors. These problems frequently co-occur, which complicates recovery for both SUD and mental health problems. Remarkably, no behavioral interventions have been developed and rigorously evaluated for this population that accomplish the following: a) take an **integrated approach** to targeting such sequelae through use of existing empirically supported interventions (e.g., exposure therapy for trauma symptoms, contingency management strategies for substance use problems); and b) incorporate **risk reduction for less symptomatic youth** (e.g., adolescent IPV victims with subsyndromal PTSD who have different degrees of substance use problems – abusing, using, at high risk for initiating). Risk Reduction through Family Therapy (RRFT) was developed and currently is being evaluated by the principal investigator, **an early stage and new investigator**, through a NIDA-funded K23 award (K23DA018686) to address this gap in the field. RRFT is an integrative, ecologically-based approach to **risk reduction and treatment.** A Stage 1a feasibility trial and a Stage 1b pilot randomized controlled trial (RCT) evaluating RRFT have been completed. This Stage 1 work has resulted in a treatment manual, a clinician training protocol, and a quality assurance system. Preliminary findings from these studies are promising, indicating that RRFT can be readily learned and implemented with fidelity, and that it can lead to improvements in drug use and drug use-related risk and protective factors, PTSD symptoms, and risky sexual behaviors. Preliminary findings from the pilot RCT also support the feasibility of conducting a larger RRFT efficacy trial and have established the existing research team as prepared to conduct a Stage II RCT. Thus, the overall goal of this application is **to conduct a Stage II RCT to more rigorously evaluate the efficacy of this promising, integrative risk-reduction and treatment approach for adolescent CSA victims to reduce substance use problems, PTSD, and related outcomes (risky sexual behavior) from pre-treatment through 18 months post-entry**.

**Specific Aim 1:** To evaluate the efficacy of RRFT in reducing substance use problems and prognostic factors among adolescents experiencing PTSD symptoms. **Specific hypotheses for this aim are:**

**A)** Adolescents receiving RRFT and their caregivers will report significantly less substance use during treatment and follow-up than control adolescents who receive Treatment as Usual (TAU).

**B)** Adolescents receiving RRFT and their caregivers will report improvement in empirically-demonstrated risk and protective factors for initiation and continuation of substance use at the individual level (e.g., coping) and at each level of an adolescent's ecology (e.g., increased number of positive family activities, reduced family conflict, reduced number of peers who use drugs, improved school attendance, increased involvement in pro-social community activities) during treatment and follow-up than control adolescents who receive TAU.

**Specific Aim 2:** To evaluate the efficacy of RRFT in reducing PTSD and risky sexual behavior among adolescents: **Specific hypothesis for this aim is:**

**A)** Adolescents receiving RRFT will experience less PTSD overall symptoms and PTSD criterion symptoms (per youth and caregiver reports), and less risky sexual behavior, during treatment and follow-up than control adolescents who receive TAU.

In order to maximize the data obtained from this proposed efficacy trial and to inform potential next steps in this line of treatment research, preliminary investigation on mechanisms of action in RRFT will be pursued as an exploratory aim.

**Exploratory Aim:** To investigate intermediate targets (e.g., skills) of RRFT as putative mechanisms of action for improvements in substance use and PTSD. **Specific hypotheses for this aim are:**

**A)** Changes during treatment in family relations (familial cohesiveness and conflict, satisfaction with caregiver-youth relationship) and parenting practices (monitoring) will mediate changes in substance use.

**B)** Changes during treatment in emotional reactivity will mediate changes in PTSD symptoms.

The results of the proposed study will have a **significant impact on public health** by informing treatment for adolescent victims. **This population is at high risk for drug use and other problems in adolescence and adulthood.** Demonstrating the efficacy of this promising risk reduction and treatment approach, as well as closer examination of the mediating factors that may lead to clinically meaningful outcomes, could provide a valuable clinical tool for community-based therapists to employ with this high-risk population.

**(A) Significance:** An estimated 1.8M adolescents are victims of child sexual abuse (CSA) in the United States. Further, nearly 70% of youth aged 13-18 report lifetime exposure to physical assault, and 40% of youth in this age range report a lifetime history of maltreatment by a caregiver. Data from large community and clinical samples indicate that IPV exposure significantly increases risk for a range of negative outcomes. With regard to substance use problems, IPV has been associated with early substance use initiation (e.g., Rothman et al., 2008)--which in turn is strongly linked with substance abuse and dependence in adulthood (e.g., Anthony & Petronis, 1995; Grant & Dawson, 1997)--as well as the development of alcohol and drug abuse disorders in adolescence (e.g., Clark & Bukstein, 1998; Kilpatrick et al., 2000). Other sequelae in adolescence empirically related to CSA include Posttraumatic Stress Disorder (PTSD) (Finklehor et al., 2005), depression (Danielson et al., 2005), and risky sexual behaviors (e.g., Parillo et al., 2001; Rotheram-Borus et al., 1996). For example, epidemiological studies demonstrate that youth 12-17 who have experienced IPV are **over six times more likely to report comorbid PTSD and substance use disorders** than those who do not report CSA (Kilpatrick et al., 2003). The risk for IPV-related negative sequelae continues into one's adult years (e.g., Danielson et al., 2009; McLean & Gallop, 2003), highlighting the **public health impact of CSA.**

**Specific risk and resiliency factors for substance use problems (including initiation, use, and abuse) among adolescents** have been consistent with Ecological Systems Theory (Bronfenbrenner, 1979), which proposes that the individual, family, peer, school, and community environments (i.e., each level of a youth's ecology) play a role in psychological development. This results in a heterogeneous array of possible risk reduction and treatment targets, such as individual maladaptive coping strategies (Carrigan et al., 2008), family conflict (Johnson & Pandina, 1991) participation in family activities (Lewis & Petry, 2005), association with substance using peers (Guo et al., 2002), poor school attendance (Hallfors et al., 2002), and limited participation in positive, structured community activities (Mahoney & Stattin, 2000). Utilizing this ecological framework, interventions can be used to alter or reduce these risk factors—as well as bolster resiliency factors.

**While progress has been made in the treatment of IPV-related PTSD and depression, significantly less is known about risk reduction and treatment of substance use problems among IPV victims—and about how to target or reduce risk for these heterogeneous outcomes using a comprehensive approach.** Research with trauma-exposed adults suggests that integrated approaches to the treatment of comorbid PTSD and substance use problems can be efficacious (Brady et al., 2001) when exposure therapy (involving direct confrontation of feared memories, thoughts, feelings, situations) is included, as exposure has the most empirical evidence for the efficacious treatment of PTSD (e.g., Foa et al., 1999). Integrated intervention approaches for PTSD and substance use disorders that do not include exposure (Seeking Safety) have had less robust findings (Hien et al., 2009). No studies have been published on the efficacy of integrated approaches to risk reduction and treatment of substance use problems and PTSD (that include exposure) among adolescents. Thus, a clear gap remains in the clinical literature regarding this public health need.

Risk reduction and treatment tailored to adolescent IPV victims, which address the individual, family, and community risk and resiliency factors for adolescent substance use problems (initiation, use, and abuse) and incorporate exposure-based interventions for PTSD symptoms, are warranted. **Risk Reduction through**

**Family Therapy (RRFT; Danielson et al., in press) has been developed by the PI for this purpose**. RRFT is a risk reduction and treatment approach for adolescents with ann IPV history that integrates principles and interventions from existing empirically supported treatments (including exposure therapy) for adolescent substance use problems, PTSD, and other negative sequelae. Preliminary data suggest that RRFT is feasibly delivered and potentially efficacious (see Preliminary Studies). The proposed study is the next step in this important line of research—to evaluate the efficacy of RRFT in a larger scale RCT. If found to be efficacious, RRFT will improve clinical practice by offering: 1) a more efficient alternative to the current compartmentalized approach to treatment of this population (which often involves referrals to multiple agencies; e.g., Cocozza et al., 2005); and 2) a risk reduction option for youth at elevated risk for developing substance abuse and related mental health problems in the future, but who are not currently meeting diagnostic threshold. President Obama's recent national proclamation (April, 2010) to recognize and help "heal lives" of victims **further highlights the significance of this proposed Stage II clinical trial.**

**(B) Innovation:** The innovativeness of the proposed approach to this Stage II efficacy trial is three-fold. First, this study **focuses on a 'real world' population** of adolescents with IPV histories who are at high risk for substance abuse in their lifetime but may present with heterogeneous symptoms. Rather than focusing on a diagnosis (e.g., drug dependence), RRFT targets a broader population of youth who are highly vulnerable for substance use problems, as well as other negative outcomes. The multi-faceted clinical needs of this population call for an **innovative bridging of the gap between early intervention and treatment,** resulting in an inclusive risk-reduction approach with the potential for a wider-spread impact. Second, the proposed comprehensive approach to risk-reduction treatment is **novel for adolescents**. Standard of care for risk reduction and treatment of substance use problems and for treatment of trauma-related psychopathology for youth populations are usually offered in isolation of one another, but there has been a recent call for "integrative, concurrent treatments" for a trauma-exposed adolescent population (Blumenthal et al., 2008; pg. 250). The very limited research in this area has not included exposure-based treatment for PTSD symptoms; the proposed treatment addresses this gap. Third, the proposed clinical trial **affords a unique opportunity to pursue preliminary mechanisms of action (MOA) research**, which can direct improvements to treatment models and inform important next steps in this line of research. We will identify specific skills and processes targeted in RRFT (e.g., emotional reactivity) that lead to improvements in substance use problems and PTSD. This is consistent with NOT-DA-019, which notes MOA research as a major programmatic priority of NIDA, to ultimately inform the development of more powerful behavioral interventions. Finally, this proposal includes **several novel applications of advanced quantitative methods** (see Data Analytic Plan). For example, use of phase-specific, or discontinuous, change models in the context of an RCT has been encouraged in the recent literature (Hayes et al., 2007) and will yield highly tailored tests of the proposed hypotheses.

**(C) Approach**

**C1. Preliminary Studies: RRFT Pilot Work.** A NARSAD Young Investigator Award and a K Award (K23DA018686) funded the PI to develop the RRFT Treatment model, manual, and quality assurance protocol, as well as conduct an open pilot feasibility trial, followed by a pilot randomized controlled trial (RCT). Below, the RRFT development phase is briefly summarized, followed by results of the two trials. The RRFT manual and quality assurance protocol, and a paper (Danielson et al., in press) describing the results of the open pilot trial in greater detail, are in the Appendix.

**Overview of RRFT Treatment Model and Manual Development.** RRFT is an adaptation and integration of already-existing empirically supported interventions with similar theoretical rationales targeting similar populations, including: 1) Multisystemic Therapy (MST; Henggeler et al., 2002), 2) Trauma Focused-Cognitive Behavioral Therapy (TF-CBT; Cohen et al., 2006), and 3) empirically supported psychoeducation strategies for prevention of high risk sexual behaviors (e.g., Diclemente et al., 2004) and sexual revictimization (Marx et al., 2001). The PI consulted with the developers of these interventions to adapt the principles and procedures from these treatments to be more applicable to the multiple needs of this population and more user friendly for treatment providers. Based on the integration of these models, the RRFT manual is devised into 7 treatment components shown in Table 1 below.

Multiple theories are incorporated in RRFT via multiple intervention strategies. First, the RRFT treatment model involves **ecological theory** (Bronfenbrenner, 1979) by assessing and targeting the web of social influences (e.g., family, peer, community) that form the context of human risk (e.g., substance using peers; Guo et al., 2002) and resiliency (e.g., family activities; Lewis & Petry, 2005) factors related to substance use as well as risky sexual practices, at each level of an adolescent's ecology. RRFT, like other ecological models of substance abuse treatment (e.g., MST), adopts a family-based approach to intervention and encourages therapists to intervene in multiple social systems. Second, **Mowrer's Two-Factor Theory** (1960) is applied in RRFT, as therapists aim to extinguish distress and fear that an adolescent victim has paired with memories and cues of the IPV experience. Per this theory, fear is thought to be acquired through a classical conditioning process by which the individual pairs a neutral stimulus (e.g., the dark or a certain word or smell) with a stimulus that invokes a fear response (e.g., sexual assault) --such that the neutral stimulus elicits the fear/distress response in the absence of the feared stimulus. Change occurs through **exposure therapy** where individuals are able to diminish a fear response when they are exposed to the feared stimuli without the feared aversive consequences. Based on its adaptation from TF-CBT, RRFT includes gradual exposure therapy with adolescent victims with PTSD symptoms via the development of a detailed written or verbal account of the IPV experiences and other potentially traumatic events. As part of this exposure-based trauma narrative work, **cognitive-behavioral therapy** also is involved where the therapist helps adolescents identify and replace inaccurate and/or unhelpful beliefs they have developed/attributed to the event(s) (e.g., I am damaged goods;). Skill building in the area of coping (e.g., emotional reactivity) is an important preamble to the exposure work and is accomplished by teaching distress tolerance skills, relaxation, etc. Third, the connection between substance use and trauma-related symptoms can be conceptualized in the context of **negative reinforcement theory** (Baker et al., 2004), which posits that escape and avoidance of negative affect (in this case, trauma-related distress) is the primary motive for addictive drug use. Similarly referred to as the 'self-medicating hypothesis,' a decrease in trauma-related substance use is thought to occur with improvement of self-regulation deficits (e.g., Hien et al., 2005), such as emotional reactivity and tolerance. RRFT focuses on improving such skills through the Coping and PTSD components of the model. Finally, **psychoeducation and skills building approaches** are incorporated to address risky sexual behaviors and revictimization risk in the Healthy Dating and Sexual Decision Making and Revictimization Risk Reduction sections respectively. Guidelines are provided to guide clinical decision making in determining whether a participant will receive the **prevention versus the treatment content of the Substance Abuse component**. Substance Abuse Prevention focuses on reducing risk factors (e.g., time spent with substance using peers; addressing substance abuse in family members) and bolstering protective factors (improving family communication) for substance use at each level of a youth's ecology, including the individual level (e.g., improving adaptive coping skills). RRFT is individualized in that the different needs, strengths, and developmental factors of each adolescent and family are incorporated into treatment. The manual provides suggested language in introducing and teaching a skill, session activities, and therapy homework ideas.

Table 1. Overview of RRFT Components

| Component | Content |
|---|---|
| Psycho-education | • Provide information to youth and caregiver about: a) prevalence of CSA and other forms of traumatic events; b) reactions to such traumatic events; c) the relation between substance use and other risky behaviors and PTSD/depression.<br>• Discuss family focus of treatment and begin to set family rules. Set treatment goals.<br>• Introduce RRFT treatment model and components.<br>• Emphasize importance of consistent attendance/participation, even when symptoms begin to improve. |
| Coping | • Provide an overview of helpful vs. unhelpful coping<br>• Skill building (with you and caregiver) in: a) feelings identification /expression; b) relaxation techniques; c) distress tolerance skills; d) understanding connection between thoughts, feelings, and behaviors; e) thought changing; f) problem solving |
| Family Communication | • Review/establish family rules (e.g., curfews, substance use), including privileges earned for following rules and consequences for not adhering to rules. Adolescent and siblings are actively engaged in this process.<br>• Skill building in: a) active listening; b) effective speaking (e.g., use of I statements, use of non-blaming language, reduction of caregiver 'over explaining'/lecturing vs. interaction/discussion<br>• Role-play of "hot-spots": re-occurring arguments in the family ('do-overs' with new skills taught) |
| Substance Abuse | • Treatment: Determination of specific risk factors (based on youth and caregiver input) that appear to be driving the substance use in the youth and selection of interventions based on these factors, such as:<br>• Contingency management (caregiver use of rewards and consequences as tied to random drug tests & breathalyzers)<br>• Increase caregiver and school monitoring (e.g., helping parent modify work schedule)<br>• Increase in participation in positive, monitored community-based activities (e.g., YMCA, jobs) so as to increase opportunities for |

| | |
|---|---|
| | meeting non-using peers and to find activities to replace drug-related activities<br>• Realistic refusal skills<br>• Psychoeducation regarding relation between substance use and PTSD symptoms<br>• Motivational interviewing and starting with smaller, achievable goals as movement towards change<br>• Prevention: Reduction of present risk factors (e.g., reduce time with using peers) and increase in resiliency factors (increase positive family activities). |
| PTSD | • Exposure to trauma-related memories and cues and addressing inaccurate and unhelpful beliefs regarding trauma through creation of trauma narrative; making meaning of the CSA experience;<br>• Sharing trauma narrative with family members as appropriate. |
| Healthy Dating and Sexual Decision Making | • Interactive discussion and skill building in: a) healthy vs. unhealthy relationships; b) factors considered when engaging in sexual activity (e.g. how does this fit with adolescent's 5-year plan); c) psychoeducation on sexually transmitted diseases, particularly HIV, and consistent condom use; d) role-playing of assertiveness in romantic relationships (e.g., condom insistence); e) importance and role-playing of on-going communication between adolescent and caregiver on these topics. |
| Revictimization Risk Reduction | • Psychoeducation regarding risk for revictimization<br>• Identification of risky situations, people, and places and role-playing of how to recognize and respond to these situations |

**RRFT Open Pilot Feasibility Trial** (Danielson et al., in press; Appendix). We evaluated the feasibility of implementation and initial efficacy of RRFT through an open pilot trial (N=10) of female adolescents recruited through an urban university-based clinic specializing trauma treatment. Participants (13-17 years old; *M*=15.0, *SD*=1.7) a) had experienced at least one memorable sexual assault (defined as unwanted/forced vaginal or anal penetration by an object, finger, or penis; oral sex; or touching of one's genitalia) in their lifetime; and b) were able to understand and engage in treatment. Three adolescents reported single incident events and seven reported a series of sexual assaults by the same perpetrator. In addition, four of the adolescents had experienced multiple sexual assaults (i.e., sexual assaults that occurred at different points in time by different perpetrators). Time since most recent sexual assault ranged from 3 weeks to 9 years (*M*=2.8, *SD*=3.1). Caregivers participating in treatment included the biological parent(s) in 6 cases, an extended family member as legal guardian in 3 cases, and a step-parent in 1 case. A research assistant administered a 90 day TLFB, urine drug screen, and a range of self- and caregiver-report measures on substance use risk and protective factors, PTSD, and depression at pre- and post-treatment, as well as 3 and 6 months post-treatment. Two participants received RRFT from the PI and the remaining received RRFT from master's level clinicians rigorously trained and supervised in the model by the PI. Average length of treatment was 24 sessions (*SD*=8).

Substance Use. Reductions were reported in substance use (among the 4 substance using adolescents in the sample; Table 2) and substance use-related risk factors (among all adolescents in the sample). Frequency of substance use at each time point is reported in Table 1 for the 4 youth who reported using substances prior to treatment. As can be seen, there were reductions in use among these participants through 6-month follow-up. Urine drug screen results were consistent. Of the 6 participants not using substances prior to treatment, none initiated use, according to self-report and urine analysis.

Table 2. Substance Use at Pre- and Post-treatment Among Participants Reporting Use (N=4)

| | | Substance | TLFB -% days[1] | TLFB -uses/day[2] |
|---|---|---|---|---|
| Participant | | | | |
| 1 | Pretreatment | Cocaine, Alcohol | 40 | 3 |
| | Posttreatment | None | 0 | 0 |
| | 3-month | None | 0 | 0 |
| | 6-month | None | 0 | 0 |
| 2 | Pretreatment | Marijuana | 27 | 1 |
| | Posttreatment | None | 0 | 0 |
| | 3-month | None | 0 | 0 |
| | 6-month | None | 0 | 0 |
| 3 | Pretreatment | Marijuana | 1 | 1 |
| | Posttreatment | Marijuana | 1 | 1 |
| | 3-month | None | 0 | 0 |
| | 6-month | None | 0 | 0 |
| 4 | Pretreatment | Alcohol (hard liquor) | 27 | 4 |
| | Posttreatment | None | 0 | 0 |
| | 3-month | Alcohol (Beer) | 4 | 1.5 |
| | 6-month | Alcohol (Beer) | 7 | 1 |

[1]% of days with substance use over the past 90 days as reported on the Time Line Follow Back (TLFB); [2]=Average number of drinks/drugs per using day as reported on the TLFB.

Modest improvements were observed in risk factors for substance use, including family cohesion and conflict levels (Table 3). Improvement in other areas of ecological functioning also was observed. A brief, semi-structured interview developed for this study assessed substance abuse risk and resiliency factors at each level of a youth's ecology. Clinician ratings on this measure at pre-treatment were based primarily on youth and caregiver reports; however, post-treatment ratings included clinician's knowledge or observation of these behaviors. Sixty percent of youth reported consistently attending school or GED classes and/or working at pre-treatment vs. 90% at post-treatment and 6-month follow-up; 10% reported consistently engaging in at least one positive family activity per week at pre-treatment vs. 100% at post-treatment and 6-month follow-up; 10% reported consistently engaging in at least one structured social activity per week at pre-treatment vs. 90% at post-treatment and 70% at 6-

month follow-up; 10% reported spending time with at least one friend that does not use alcohol or drugs at pre-treatment vs. 100% at post-treatment and 6-month follow-up.

Mental Health Symptoms. Large effects (corrected for small sample bias using the formula specified by Hedges and Olkin [1985]) were found with regard to improvements in PTSD and depression symptoms (see Table 3). Multilevel Longitudinal Models (MLMs) were used to estimate the direction and rate of change (i.e., linear slope) for each outcome variable over time. The MLMs revealed negative linear slopes on the youth-report (β = -1.66) and caregiver-report (β = -0.76) versions of the UCLA PTSD Index and on the CDI (β = -1.23), indicating that the mean scores on these scales decreased from pre-treatment to 6-month follow-up.

Table 3. Effect Sizes for PTSD, Depression, and Family Functioning Scores

| | Pre-Treatment vs. Post-Treatment | | Pre-Treatment vs. 3-Month Follow-Up | | Pre-Treatment vs. 6-Month Follow-up | |
|---|---|---|---|---|---|---|
| Outcome | *ES* | CI (95%) | *ES* | CI (95%) | ES | CI (95%) |
| UCLA-A | -1.81 | -2.85 to -0.77 | -2.07 | -3.15 to -0.98 | -2.45 | -3.61 to -1.29 |
| UCLA-C | -1.18 | -2.13 to -0.23 | -1.23 | -2.18 to -0.27 | -1.02 | -1.95 to -0.09 |
| CDI | -1.51 | -2.50 to -0.51 | -1.64 | -2.66 to -0.63 | -2.17 | -3.27 to -1.06 |
| FES-Coh-A | 0.60 | -0.29 to 1.50 | 0.99 | 0.06 to 1.92 | 0.75 | -0.16 to 1.65 |
| FES-Coh-C | 0.70 | -0.20 to 1.60 | 0.84 | -0.08 to 1.75 | 0.49 | -0.40 to 1.38 |
| FES-Con-A | -0.67 | -1.57 to 0.23 | -0.80 | -1.71 to 0.11 | -0.77 | -1.68 to 0.14 |
| FES-Con-C | -0.38 | -1.27 to 0.50 | -0.13 | -1.00 to 0.75 | -0.51 | -1.40 to 0.38 |

UCLA-A=UCLA PTSD Index-Adolescent Report; UCLA-C= UCLA PTSD Index-Caregiver Report; CDI=Children's Depression Inventory; FES-Coh-A=Family Environment Scale-Cohesion-Adolescent Report; FES-Coh-C= Family Environment Scale-Cohesion-Caregiver Report; FES-Con-A= Family Environment Scale-Conflict Scale-Adolescent Report; FES-Con-C= Family Environment Scale-Cohesion-Caregiver Report.

Implementation. Successful recruitment and retention of participants for RRFT is feasible (100% of adolescents approached consented to participate; 100% treatment completion). Successful administration of RRFT is feasible (treatment adherence, as monitored by audiotaped sessions, weekly individual supervision with PI, and completion of RRFT adherence checklist by participants=95%).

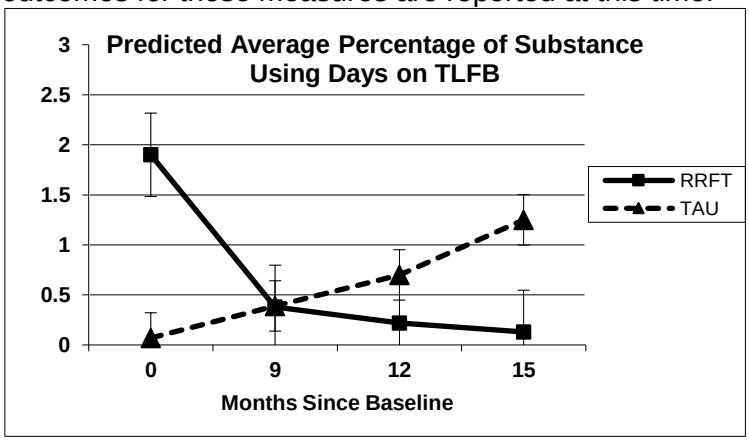
Following the treatment phase of the open pilot trial, focus groups were conducted with RRFT therapists and leadership in the clinic to collect qualitative feedback regarding the perceived utility of the RRFT model and manual and the feasibility of its implementation. Results of the focus groups resulted in unanimous positive feedback, with therapists noting the following strengths of the model: 1) preference for the component versus a session-driven model (e.g., treatment focusing on completion of the 7 RRFT components rather than the completion of a certain number of sessions); 2) flexibility in terms of component order, allowing them to focus on most relevant/high risk concerns first; 3) user-friendly manual. Suggestions for improvement to the manual included: 1) providing to caregivers anticipatory guidance for expected/developmentally appropriate behavior changes among adolescents at various ages near end of treatment; 2) increasing the frequency of joint youth-caregiver sessions (following individual sessions) to provide additional opportunities to practice family-level problem-solving throughout treatment; 3) Adding skill "check-outs" to confirm completion of each RRFT treatment component (to help therapist determine when a skill has been mastered). These revisions were incorporated into the manual and training prior to beginning the Stage 1 pilot RCT study.

**RRFT Pilot RCT.** A pilot trial (N=30) comparing RRFT to Treatment As Usual (TAU) has been completed. The aim of this pilot trial was to establish the feasibility of research methods, as well as to determine if RRFT had promise to be an efficacious treatment. Participants were recruited through an urban university-based clinic specializing in trauma treatment (NCVC) and a local Child Advocacy Center. Participants ranged in age from 12-17 years (*M*=14.80, *SD*=1.51), with 27 girls and 3 boys. Fifteen were African-American, 10 were Caucasian, 2 were bi-racial, 2 were Hispanic, and 1 was Native American. CSA incident characteristics and other traumatic event history were as follows: a) 19 of the 30 (63.3%) reported that the first CSA was a series of abuse experience versus a single event; b) 9 (30%) reported 2nd, 3rd (n=5), and 4th (n=1) CSA revictimzation experiences; c) age of first or only CSA experience ranged from 4-15 years; d) 23 (67.7%) reported having experienced other traumatic events as well. Fifteen were randomly assigned (via blocked randomization methods) to receive RRFT, with the remaining 15 assigned to receive Treatment As Usual (TAU). TAU was defined as standard care that a CSA victim and family would typically receive in the local community following presentation at the NCVC. Fourteen of the 30 youth were also receiving

psychopharmacological intervention at the time of the pre-treatment assessment. Significant pre-treatment differences (*p*>.05) between groups were observed on the following measures: substance use per the TLFB (RRFT>TAU), UCLA-PTSD Parent-reported scores (RRFT>TAU), and family cohesion (adolescent and parent report) (RRFT>TAU); no other differences in demographics, CSA characteristics, or pre-treatment status were found. Data analytic procedures were used to account for these differences. All participants but two (93.3%) were retained through post-treatment assessments. Inclusion criteria and assessment methods are identical to those described for the open trial, plus the addition of the Youth Risk Behavior Survey (YRBS; CDC, 2005) and the Behavior Assessment System for Children (BASC; Reynolds & Kamphaus, 1992).

**Treatment Descriptive Results**. Mean treatment length for the RRFT condition was 23 sessions (*SD*=13 sessions). Treatment completers were defined as having completed 5 of 7 RRFT treatment components. All but three RRFT participants completed all 7 components; one participant completed 5 components (Psychoeducation, Coping, Family Communication, Substance Use, Healthy Dating and Sexual Decision Making); and two participants in the RRFT condition dropped out (one due to moving out of state and the other was due to caregiver stating she was no longer interested in services). Based on review of audiotapes, supervision, and treatment fidelity checklists, therapists adhered to the RRFT model 94% of the time. Approximately 60% of the participants in the TAU condition received TF-CBT (as measured by a treatment fidelity measure (see Appendix), the Services Assessment for Children and Adolescents, and chart review) and the remaining 40% received a shortened version of trauma-focused treatment (primarily consisting of psychoeducation); *M* number of sessions=13, *SD*=6).

**Treatment Outcome Results**. Data Analysis*:* Data were 4 repeated measurements (pre-treatment, post-treatment, 3-month follow-up, 6-month follow-up; level-1) nested within 30 youth/caregivers (level-2), yielding a two-level Mixed-Effects Regression Model (MRM). Data from the TLFB was used to compute a count variable representing the number of instances of self-reported substance use over the previous 90 days and a count variable representing the number of days during which substance use occurred over the past 90 days. The remaining outcomes were modeled as continuous variables. To account for variability in the length of time between measurement occasions, all outcomes were modeled according to a linear time term computed as the number of months elapsed between baseline and subsequent assessments (Singer & Willett, 2003). Treatment condition was coded such that RRFT = 0 and TAU = 1. MRMs were performed using HLM software (v. 6.08; Raudenbush et al., 2004), with restricted maximum likelihood estimation for continuous outcomes and a Bernoulli model with a logit link function and Laplace approximation of maximum likelihood for dichotomous (Bernoulli model) and count (Poisson model) outcomes. Specification of random effects was based on the likelihood ratio test when possible and otherwise was based on the Wald test for variance components (Singer & Willett, 2003). Unit-specific results were interpreted for all outcomes (Raundenbush & Bryk, 2002). The MRMs account for differences between groups in pre-treatment symptom levels and include all participants in the analysis, thus, the results are a conservative estimate of efficacy. Given limited variance in the Ecological Functioning measure and the YRBS, only descriptive outcomes for these measures are reported at this time.




Outcome variables and results: Significant linear effects in the expected directions were yielded by the MRMs demonstrating **improvements in symptoms from baseline to six months post-treatment for RRFT participants on all outcomes,** except BASC-Adaptability Scale (p>.05). Thus, substance use (percent of days of non-tobacco drug use)(p<.001), as well as ratings on measures of PTSD (both adolescent and parent report)(p's<.001), depression (p<.001), family cohesion and conflict (p's<.05-.001), and Internalizing, Externalizing, and Behavioral Scales on the BASC (p's<.05-.001) improved over time for RRFT participants. **In comparing RRFT to TAU, the following condition X linear effects were significant in the expected direction, meaning RRFT participants yielded greater reductions over time when compared to participants receiving TAU: Percent of days of non-tobacco**

**substance use** ($\beta_{11}$ = .37, *SE* = .03, *T* (88) = 11.25, *p* < .001)(see Figure).; **PTSD** (parent report) ($\beta_{11}$ = 1.07, *SE* = .42, *T* (28) = 2.54, *p* < .05), and **family cohesion (parent report)** ($\beta_{11}$ = -.75, *SE* = .32, *T* (88) = -2.32, *p* < .05); a trend also was found for adolescent report of family cohesion: ($\beta_{11}$ = -.80, *SE* = .44, *T* (28) = -1.84, *p* = .07). On the remaining outcomes, the RRFT and TAU groups evidenced similar reductions in symptoms over time. **There were no outcomes on which TAU outperformed RRFT**.

**With regard to other selected risk and protective behaviors**, 17 youth reported having previously engaged in consensual sexual intercourse at the pre-treatment assessment (per the YRBS). Given the small sample sizes at each time point, responses were aggregated to reflect whether a participant endorsed each behavior at any given post-treatment or follow-up assessment. Results (based on the YRBS and Ecological Functioning Measure) were as follows: used alcohol or drugs before last sexual experience: RRFT = 0% vs. TAU =6.3%; used a condom during last sexual experience: RRFT = 93.3% vs. TAU =73.3%; were pregnant: RRFT = 6.3% vs. TAU =13.7%; had an STD: RRFT = 0% vs. TAU =13.7%; engaged in weekly positive family activities: RRFT = 86.7% vs. TAU =73.3%; attended school or work consistently: RRFT=73.3% vs. TAU =53.3%; spent time with non-substance using peers: RRFT = 86.7% vs. TAU =80%.

Relevance to current study: These Stage 1 pilot studies support the feasibility and utility of the RRFT manual and quality assurance system, while also providing initial support for efficacy with regard to substance use behaviors, substance use risk, and PTSD. The studies also illustrate the highly vulnerable nature of this population (30% of these youth had already been sexually revictimized at the time of pre-treatment), and thus the need for the proposed intervention. In addition, the studies demonstrate the PI's capacity to successfully recruit this high risk population for treatment research and retain them through 6-month post-treatment and to direct all other aspects of an RCT, such as training therapists and overseeing RRFT implementation with fidelity. This experience has guided and informed the proposed trial described in detail below. The knowledge gained from successful completion of the research has the capacity not only to reduce substance abuse and enhance mental health among young victims of interpersonal violence but also to bring a critical, gender-based perspective to this research area and inform personalized intervention that can extend to other areas of substance abuse treatment.

**C2. Overview of Methods:** The proposed RCT follows a 2 (treatment type) × 5 (timepoints) factorial design. We will recruit 140 local Child Advocacy Center clients who are 13-18, have a memorable CSA history, and report PTSD symptoms. Participants randomized to the experimental condition will be assigned to a therapist trained and supervised in RRFT. Participants randomized to the control condition will receive Treatment As Usual (see below). Research assessments with youth and caregivers will be conducted at pre-treatment and at months 3, 6, 12, and 18 post study entry (i.e., participants will be followed 18 months after initiating treatment).

**C3. Recruitment:** C3a. Recruitment source: Lowcountry Child Advocacy Centers (CACs): CACs provide victims of child maltreatment with a variety of services, including forensic interviewing, medical examination, advocacy, and outpatient counseling. Two local CACs (Lowcountry Children's Center/LCC and Hope Haven/HH) serve the Lowcountry of South Carolina (SC), which includes a population across 8 counties that exceed 750,000. The National Crime Victims Center (NCVC; clinic where PI and Co-Is Saunders and de Arellano are housed) has worked closely with these CACs for over 15 years. The research team has a strong track record of having successfully recruited research participants from LCC/HH (See Letters of Support). Referral Data: In closely tracking referred youth over the past 12 months, approximately 573 youth 12-17 years were referred to LCC/HH following an allegation of child maltreatment, with 344 (60%) of these referrals based on allegations of CSA (ethnic/racial breakdown of these are youth are as follows: 32% Non-Hispanic White, 54% African-American, 4% bi-racial, and 9% Hispanic). Approximately 85% (292) of these cases resulted in disclosed and/or substantiated CSA. Tracking data suggests that at least 60% (175) of these youth present with significant PTSD symptoms. Thus, approximately 14 youth a month will be eligible for recruitment into the proposed study.

Rationale for CACs as targeted recruitment sites: Multiple service systems often are involved in child abuse cases; often with poor coordination (Glisson & Hemmelgarn, 1998). CACs were developed to reduce the system intervention burden to abused children, to better coordinate investigations and services, and to provide

direct services. There are now over 600 CACs nationwide, with 18 in SC alone. CACs are among the most common entry points to community services for abused children, and CSA victims make up ~73% of the cases seen at CACs nationally (www.cac-sc.org). CACs are mandated by their accreditation standards to provide mental health treatment for abused children or have strong referral relationships with professionals and organizations that do. This mandate, in conjunction with the referral rates reported above and the research team's long and successful history of conducting clinical research and projects with LCC/HH, indicates that this is the ideal setting to recruit adolescent CSA victims for the proposed Stage II efficacy trial.

C3b. Screening: LCC/HH have existing outpatient clinics with strong collaborative working relationships with community referral sources. LCC/HH host monthly task force meetings where representatives from all community referral sources are typically present. Drs. Danielson and Saunders, in conjunction with LCC/HH Directors Ralston and Capps and clinic staff, will meet with referral sources before and during the study to ensure strong community buy-in. The project coordinator will attend monthly meetings to address any questions that may arise. All cases presenting to the CACs for evaluation and/or treatment undergo a semi-structured intake assessment to determine traumatic event history, trauma-related symptoms, and appropriateness for outpatient care. This assessment will be used to determine entry because: a) it is more comprehensive than using only a diagnostic instrument; b) youth are more likely to disclose CSA and other forms of trauma when asked in a behaviorally specific way (Resnick et al., 1993); c) it more closely mirrors how adolescents with trauma history present to clinics under "real world" conditions; and d) these assessments are routine and the cost will not be borne by the research study. Based on this assessment, youths and their families will be referred to research study staff for recruitment into the study. Specifically, if inclusion criteria are met (see below), the therapist who conducted the initial assessment will inform the family about the study and ask for consent to share contact information with research study staff. If consent is given, the referred youth and family will be contacted by research staff to describe the research project and confirm the presence of five or more PTSD symptoms using the UCLA PTSD Index (see Assessment Table). Adolescents confirmed to meet these criteria and their caregivers will be asked to provide written consent/assent and sign a release of information (to allow for chart reviews) and they will be scheduled for the pre-treatment assessment. All forms and consent procedures will be approved by the Institutional Review Board at MUSC.

C3c. Research Recruitment and Retention Strategies: The current research team has been very successful at recruiting research participants from challenging clinical populations. For example, in a clinical trial examining MST as an alternative to the hospitalization of youth presenting with psychiatric emergencies (Henggeler et al., 1999), 156 of 175 eligible families (88%) were successfully recruited; and 98% of the participating families were retained in the study 2 years post referral. Moreover, of the 77 families randomized to the MST condition, 95% completed a full course of MST. Similarly, in a trial with youth with comorbid substance use and internalizing problems and their families (Sheidow, 2008), 41 of 43 (95%) of eligible families were recruited; 92% of families completed all assessments through the 6-month follow-up; and 98% of families referred to the experimental condition completed a full course of treatment. The pilot work with RRFT has been no exception to our ability to recruit challenging adolescents and their families, with 100% recruitment and retention rate with the open pilot trial through 6 month follow-up (N=10) and a 89% recruitment rate and 93% retention rate in the RCT. Several strategies account for the excellent research retention rates. First, to establish a long-term collaborative relationship with families, assessments are scheduled at the family's convenience, contacts are as friendly and personalized as possible, and families are reimbursed for their participation in assessments. Second, at consent, we ask for up to eight phone numbers of the caregivers' and adolescents' best friends, closest relatives, and places of employment to facilitate tracking of each time the family is assessed; we also ask if they are planning to move. Third, we also receive consent to reach the adolescents (and caregivers as applicable) through modern technology strategies, such as text messaging and Facebook pages. Fourth, direct contact with the families helps to maintain the cohort, as all families are tracked monthly for therapist adherence and school placement reports. When possible, participants are followed by the research assistant responsible for the initial research interview to encourage rapport and a sense of involvement.

**C4. Participants:** C4a. Inclusion criteria: Participants will be: **1)** 13-18 years old; **2)** Present to LCC/HH for evaluation or treatment; **3)** Report having experienced IPV in their lifetime, including: **CSA**, defined as forced or unwanted: (a) vaginal or anal penetration by an object, finger, or penis; (b) oral sex; (c) touching of the respondent's breasts or genitalia; or (d) respondents' touching of another person's genitalia; ***CPA****, defined as having been (a) attacked or threatened with a gun, knife, or some other weapon; (b) attacked by another person with perceived intent to kill or seriously injure; (c) beaten and injured (i.e., "hurt pretty badly") by another person; (d) spanked so forcefully that it resulted in sustained welts or bruises or required medical care; or (e) cut, burned, or tied up by a caregiver as a punitive consequence;* ***Exposure to Domestic Violence****; and being victim of or bearing witness to* ***Community Violence***[***]. **4)** Have a memory of the incident(s); **5)** Self-report five or more DSM-IV PTSD symptoms. Rationale: Minimum PTSD criteria for inclusion in previous treatment outcome research with CSA populations has ranged from 3 (Deblinger et al., 1996) to 5 symptoms (Cohen et al., 2004). **6)** Self-report one or more substance-using day(s) in the previous 90 days.

C4b. Exclusion criteria: Potential participants will be excluded from the study if the adolescent meets any of the following criteria: **1)** Has previously been identified as having a Pervasive Developmental Disability or Moderate to Severe Mental Retardation; **2)** Is actively suicidal or homicidal; **3)** Reports active psychotic disorder. Rationale: The proposed intervention would likely not be sufficient for these adolescents, who may either have a diminished capacity to benefit from CBT and/or who would require more intensive treatment.

C4c. Urn randomization. An adaptive randomization procedure, known as urn randomization, will be used to balance potentially confounding variables among the participants randomized to each condition (Hedden et al., 2006). Urn randomization was used in Project MATCH (Stout et al., 1994) and adopted in Co-I Sheidow's current treatment outcome study. The factors on which the adaptive randomization procedure will operate are pre-treatment substance use frequency, PTSD symptom severity, and gender. This will decrease pre-treatment variability between groups on these factors, and the literature indicates that these variables are related to substance use outcomes (Kilpatrick et al., 2003). The urn randomization procedure will be implemented using an adaptation of the Microsoft Access application gRand.

**C5. Interventions:** C5a. Experimental Condition: Risk Reduction through Family Therapy (RRFT): RRFT (Danielson, 2007) is described in the Preliminary Studies section (Manual in Appendix). The order in which the components (Table 1) are administered is determined by needs of the youth/family and based on severity of problems. On average, the RRFT protocol is administered through weekly, 60-90 minute sessions. However, therapists are encouraged to do phone check-in's with families between sessions, particularly when new skills have been taught, when contingency management and/or caregiver monitoring plans are first implemented for substance use or other risky behaviors, when the family is experiencing a crisis, and when exposure therapy has begun. The duration of treatment is dependent on the symptom level of the youth. When feasible and applicable, individual sessions and briefer, joint family sessions are conducted each week. However, if family members are not available for in person sessions, phone-based check-ins are implemented (e.g., to ensure caregiver is modeling adaptive coping at home, to discuss monitoring, to assess application of positive family communication and problem-solving skills learned in treatment, to ensure adolescent is engaging in positive activities in the community). Nonetheless, individual sessions still address the family system and other layers of the ecology (e.g., role-playing communication). As with the pilot studies, participants receiving psychopharmacological interventions at pre-treatment will maintain their medication regimens; however, no participants will receive any other simultaneous psychosocial intervention in addition to RRFT.

C5b. The Control Condition: Treatment As Usual (TAU): Adolescents assigned to the TAU condition will receive the standard treatment that an IPV victim would typically receive at LCC/HH. In addition to treatment that is typically offered at the CACs, this will include a referral for substance abuse evaluation and may include referrals to other agencies in the community. TAU has been utilized as a comparison condition for several behavioral treatment evaluations involving adolescent substance abuse (Henggeler et al., 2002) or trauma (Zatzick et al., 2004).

[***] Italicized inclusion criteria denotes changes approved by the DSMB, IRB, and study sponsor.

Rationale for TAU: No "standard of care" exists for the heterogenous risk reduction and treatment needs of this population. Although TAU may not seem optimal for an efficacy trial, the decision to rely upon TAU was based on a number of factors. First, an evidence-based substance abuse intervention was considered (e.g., contingency management), but given that youth will have moderate to severe PTSD symptoms and some members of the population are not using substances at the time of pre-treatment assessment, this would not be sufficient (i.e., it would be unethical to not offer youth with PTSD some form of trauma treatment). Similarly, an evidence-based treatment for PTSD (e.g., TF-CBT) was considered; however, such interventions do not address substance use (i.e., this would not be sufficient for substance using adolescents). Third, provision of parallel or sequential treatments for each presenting problem was considered. Depending on the pre-treatment symptom presentation of the youth, this would potentially require that control participants and their families attend numerous treatment programs (e.g., a research-based outpatient treatment for substance use and a research-based treatment for PTSD and depression, as well as psychoeducation for healthy dating and sexual decision making); placing significant burden on these families. Finally, a waitlist control was considered, but it was determined that the needs of this population for immediate treatment ethically outweighed the value of a waitlist comparison condition. Thus, given the ethical need to provide treatment to the control group, but a dearth of information regarding how to address the heterogeneous clinical needs of this population, TAU was selected as the most appropriate comparison condition for this study. Close monitoring of the treatment provided has been incorporated into the study design and the services and techniques administered to each youth and family in each condition will be closely measured to ensure appropriate evaluation comparisons, including: a) therapists and supervisors across both conditions will complete the Therapy Procedures Checklist (Weersing et al., 2002), which is an assessment of techniques used in session (e.g., cognitive-behavioral) following each session; b) Chart review across both conditions (see below and Appendix); c) audio-taping and random selection of one tape per family a month for audit (to compare with therapist responses on the Therapy Procedures Checklist).

**C6. Assessments:** C6a. Design & Data Collection Procedures: Both the control and experimental group will be assessed at five timepoints. A pre-treatment (T1) assessment will be scheduled to occur at the time of consent to participate. Follow-up assessments will be obtained at 3-months post entry (T2), 6-months post entry (T3), 12-months post entry (T4) and 18-months post entry (T5). The full assessment battery, which is very similar to the protocol used in the pilot studies where no problems with participant completion have occurred, will take approximately 1.5-2 hours to complete. The research assistant will administer the assessment battery in the family's home or at LCC/HH based on the participant's preference. To compensate for their time, families will be paid $70 for completing the intake, $50 for completing the 3-months and 6-months post-entry assessments, and $100 for completing the 12 months post entry assessment. In addition, families will be paid $150 for completing the 18-month post-entry assessment and compensate for time spent responding on 12 monthly reports of school placement and therapist adherence. Data from all timepoints will be collected on all families who are randomized into the study even if they drop out of treatment. For families with barriers to attending assessments, a de-identified RedCap survey of all time point measures can be sent through the participant's private email address which they will have provided at the pre-treatment assessment. Ms. White, who served as the project coordinator for the pilot RCT study, and Dr. Danielson have carefully planned for adequate staff training and coverage for the proposed study based on their experience in the pilot work (see Appendix). Ms. White will assist in training the research staff on specific assessment measures and protocol, and will conduct weekly meetings, quarterly reviews, and booster trainings with research assistants.

C6.b. Research Instruments (a more detailed description of these measures are in the Appendix)

| ASSESSMENT | DATA | A/C* | REFERENCE |
|---|---|---|---|
| **DEMOGRAGHICS AND CSA HISTORY** | | | |
| Demographics Questionnaire | Information such as age, sex, ethnicity, Hollingshead (1975) socioeconomic data, and family composition | A, C | N/A |
| Chart Review of information from Intake Interview for Trauma | Semi-structured interview to assess lifetime history of CSA and other forma of maltreatment and CSA incident characteristics | A, C | e.g. Resnick et al., 1993 |
| **SUBSTANCE USE AND ABUSE** | | | |

| | | | |
|---|---|---|---|
| Timeline Followback (TLFB) | Quantity + frequency data over past 90 days | A | Sobell & Sobell, 1992 |
| Urine Drug Screens | The urine toxicology screen will tap marijuana, cocaine, benzodiazepine, and opiate use. | A | AACC, 1988 |
| **SUBSTANCE USE RISK AND RESILIENCY FACTORS** | | | |
| Family Environment Scale (FES) | Cohesion and conflict subscales; Social and environmental characteristics of families | A, C | Moos & Moos, et al., 1986 |
| Bad Friends subscale | Youth's peer relations | A, C | Loeber et al., 1998 |
| Alabama Parenting Questionnaire (APQ) | Parenting practices across the following domains: Corporal Punishment, Inconsistent Discipline, Poor Monitoring and Involvement, and Positive Parenting, Rules and Expectations | A, C | Shelton, Frick, & Wootton, 1996 |
| Direct Supervision subscale of the OSLC Monitoring Scale | Level of parental monitoring (the amount of adult supervision at parties and friends' houses, and the caregiver's knowledge and accuracy of youth's location and whereabouts | A, C | Brown, Dishion, & Kavanagh, 1991 |
| Children's Attributional Style Questionnaire (CASQ) | Assesses how children explain positive and negative events through 3 dimensions of causality; internal-external, stable-unstable, and global-specific | C | Seligman et al, 1984 |
| K-UPPS Impulsive Behavior Scale | Facets of impulsive behavior: negative urgency, lack of premeditation, lack of perseverance, and sensation-seeking | A | Whiteside & Lynam, 2001 |
| Parent Happiness With Youth Scale/ Youth Happiness With Parent Scale | Degree of satisfaction with the parent-child relationship across multiple domains | A, C | Donohue et al., 2001; Decato et al., 2001 |
| Hopelessness Scale | Degree of hopelessness; positive/negative expectations for future | A | Kazdin et al, 1986 |
| Emotion Regulation Questionnaire (ERQ) | Assesses the habitual use of emotion regulation strategies: cognitive reappraisal and expression suppression | A | Gross & John, 1998 |
| Drinking Motives Questionnaire | Frequency of use for 3 motives (Coping, Enhancement, Social Facilitation) | A | Cooper et al., 1992 |
| **TRAUMA-RELATED PSYCHOPATHOLOGY AND RISKY SEXUAL BEHAVIORS** | | | |
| UCLA PTSD Index for DSM-IV | Trauma history, Severity of PTSD symptoms | A, C | Pynoos et al., 1998 |
| Child Depression Inventory (CDI) | Severity of depressive symptoms | A | Kovacs, 1992 |
| Sexual Risk Behavior Scale | Severity of risky sexual behaviors (e.g., condom use) | A | Jemmott et al., 1999 |
| **TREATMENT ASSESSMENT** | | | |
| RRFT Fidelity Checklist | Content & skills were addressed and not addressed each session | IR | Danielson, 2007 |
| Therapy Procedures Checklist | Techniques used in each session based on techniques from the most commonly used youth interventions (e.g., CBT) | IR | Weersing et al., 2002 |
| Youth Service Utilization Form | Assesses utilization of mental health placements, inpatient/ outpatient treatment, school attendance and medication management | A,C | N/A |
| Client Satisfaction Questionnaire-8 | Consumer satisfaction with treatment | C | Attkisson & Greenfield, 1994 |
| Chart Reviews (completion by RAs | Close monitoring of each treatment protocol (for both conditions) and includes frequency and type of therapist contact and specific efforts made by therapist to maintain engagement | N/A | N/A |

- *Denotes Adolescent Report (A) and/or Caregiver (C) Report; IR denotes independent raters

C7. Data Analysis Strategy. **Data structure**. The research design is characterized by *t* repeated measurements per participant *i* ($n_{ti}$ = 5); therefore, the hypotheses will be evaluated using a series of two-level Mixed-Effects Regression Models (MRMs; e.g., Raudenbush & Bryk, 2002). Longitudinal MRMs account for dependency in outcome variation attributable to nesting of repeated measurements (level-1) within participants (level-2). The standard MRM for continuous outcomes (Goldstein, 2003) is readily extended to dichotomous (i.e., Bernoulli; Gibbons & Bock, 1987) and count distributed outcomes (Poisson; Hedeker & Gibbons, 2006).

**Model building & estimation**. Prior to analysis, to check the effectiveness of the urn randomization procedure, the proportion of participants randomized to each condition who are substance using, male, with significant PTSD symptoms will be compared. "Spaghetti plots" will be used to illustrate the level of and variability in the outcomes as well as the patterns and amount of change over time (Hedeker & Gibbons, 2006). This information, and consideration of the phase-specific change models presented by Singer & Willett (2003), will inform the methods used for modeling change. Preliminary models also will test for differences by site referral source, and differences will be controlled in subsequent models. The model building approach detailed by Singer & Willett (2003) will be employed for the specification of fixed and random effects. Linear and non-linear change patterns will be modeled at level-1, intervention phase will be modeled at level-1 (i.e., differentiating measurements occurring during treatment from those following treatment), intervention condition will be modeled at level-2, and cross-level interaction terms will be entered for level-1 and level-2 terms. A linear change term will be computed and modeled based on each participant's actual assessment dates (e.g., number of months from start of treatment). Orthogonal polynomials will be used to model non-linear trajectories (Biesanz et al., 2004). An Intention-to-treat (ITT) analytic strategy will be used, with each research participant retained in the intended intervention group. MRMs will be performed using HLM software (v6.08; 2004). Prior to analysis, each outcome will be inspected to determine the most appropriate outcome distribution.

**Evaluation of specific aims**. Following inspection of spaghetti plots, evaluation of outcome distributions, and completion of model building, the hypotheses for each specific aim will be evaluated as detailed below.

**Specific Aim 1:** To evaluate the efficacy of RRFT in reducing substance use problems and prognostic factors among adolescents experiencing trauma-related symptoms. **Specific hypotheses for this aim are:**
**A)** Adolescents receiving RRFT and their caregivers will report significantly less substance use during treatment and follow-up than control adolescents who receive Treatment as Usual (TAU).
**B)** Adolescents receiving RRFT and their caregivers will report improvement in empirically-demonstrated risk and protective factors for initiation and continuation of substance use at the individual level (e.g., coping) and at each level of an adolescent's ecology (e.g., increased number of positive family activities, reduced family conflict, reduced number of peers who use drugs, improved school attendance, increased involvement in pro-social community activities) during treatment and follow-up than control adolescents who receive TAU.

Hypotheses A and B for Specific Aim 1 will be evaluated according to two-level MRMs with a maximum of 5 repeated measurements (level-1) nested within participants (level-2). The final model specification will depend on inspection of the spaghetti plots and preliminary model building results. The level-1 model will include the linear polynomial term (e.g., 0, 3, 6, 12, 18, corresponding to the timing of the measurements relative to the start of treatment) and a dummy-coded variable indicating whether the measurement occurred during treatment or post-treatment completion (0 = during, 1 = following). The level-2 model will include the dummy-coded intervention condition variable (0 = TAU, 1 = RRFT). In addition, cross-level interactions will be specified for condition × linear and condition × post-treatment. According to this specification, the model will test for: TAU v. RRFT differences at baseline, TAU v. RRFT differences in the rate of change over time, and TAU v. RRFT differences in the "shift" in the level of the outcome associated with treatment completion. This model is readily extended to accommodate non-linear (e.g., quadratic) change and/or slopes specific to each phase. To gauge the magnitude and clinical significance of the effects, 95% *CI*s will be computed for each coefficient.

**Specific Aim 2:** To evaluate the efficacy of RRFT in reducing PTSD and risky sexual behavior among adolescents. **Specific hypothesis for this aim is:**
**A)** Adolescents receiving RRFT will experience less PTSD overall symptoms and PTSD criterion symptoms (per youth and caregiver reports), and less risky sexual behavior, during treatment and follow-up than control adolescents who receive TAU.

The Hypothesis for Specific Aim 2 will be evaluated according to a series of two-level MRMs as detailed for specific Aim 1.

**Exploratory Aim:** To investigate intermediate targets (e.g., skills) of RRFT as putative mechanisms of action for improvements in substance use and PTSD. **Specific hypotheses for this aim are:**
**A)** Changes during treatment in family relations (familial cohesiveness and conflict, satisfaction with caregiver-youth relationship) and parenting practices (monitoring) will mediate changes in substance use.
**B)** Changes during treatment in emotional reactivity will mediate changes in PTSD symptoms.

The product of coefficients test for mediation effects, reviewed by MacKinnon et al. (2002) and extended to multilevel applications by Krull & MacKinnon (2001), will be used to evaluate Hypotheses A and B. The test requires specification of an initial variable (treatment condition), putative mediator (family relations indicators &

emotional reactivity), and outcome variable (substance use & PTSD symptoms). A key feature of the mediation hypotheses is that one change process is hypothesized to mediate another change process. The statistical test for mediation requires estimation of two coefficients and their *SE*s. The first coefficient, the "a-path," represents the association between condition and the putative mediator process. The second coefficient, the "b-path," represents the association between the putative mediator process and the outcome process, holding constant the effect of condition. Thus, the standard representation of multilevel mediation models described by Krull & MacKinnon is complicated by the longitudinal nature of the outcomes and the mediators. To accommodate this, parallel process latent growth curve models will be used to evaluate two change processes and the extent to which change in one process influences change in the other process. The proposed methods are detailed by Cheong et al. (2003) and will be implemented in Mplus (v. 6.00; Muthén & Muthén, 2005).

The "a-path" coefficient and *SE* will be obtained from the model specifications for Specific Aims 1 and 2 as implemented in Mplus. The "b-path" coefficient and *SE* will be obtained from a separate model where the outcome slope is regressed on the mediator slope in a parallel process latent growth curve model. The significance of the mediated effect will be tested using asymmetric confidence limits and critical values for the product of coefficients as implemented in PRODCLIN (MacKinnon, Fritz, Williams, & Lockwood, 2007; MacKinnon, Lockwood, & Williams, 2004). Importantly, this method offers greater statistical power relative to the traditional "causal steps" approach to testing mediation (MacKinnon et al., 2002).

**Missing data**. Participants dropping out of the clinical intervention will be retained in the research portion of the study according to ITT principles (e.g., Nich & Carroll, 2002). In the event of missing data, the methods recommended by Schafer and Graham (2002) will be used to evaluate missing data assumptions and guide the analytic strategy. For a small proportion of missing data and evidence supporting a Missing at Random mechanism, the MRM-based procedures detailed above will be applied to available data. For a non-trivial amount of missing data and evidence supporting a MAR mechanism, multiple imputation for repeated measurements (Goldstein et al., 2008) will be used to generate complete data. For a non-random missing data mechanism (i.e., MNAR), pattern mixture models will be used to evaluate and control the effect of the missing data patterns (Hedeker & Gibbons, 1997; Verbeke & Molenberghs, 2000).

**Statistical power**. Estimating statistical power for MRMs is complex because the methods must account for the number of participants, the number of measurements, the proportion of variance at level-2, and the level of measurement of the covariates (Snijders & Bosker, 1999). This is further complicated when the effect of interest is a condition × time interaction effect. The targeted sample size of $N = 140$ is sufficient to detect a small-to-medium effect of RRFT on substance use and PTSD symptom outcomes (assuming .80 power, 5% significance, 10% attrition, and 1:1 allocation).

**C8. Impact and Future Directions:** Given the **established feasibility** of the proposed approach (supported by the preliminary investigations of RRFT and extensive **experience of the research team** in conducting RCTs with other high-risk adolescent populations), in conjunction with **an innovative, integrative approach** that targets a population at high risk for substance use problems and bridges the gap between early intervention and treatment, **the results yielded from accomplishing the aims of the proposed project will have a significant impact on adolescent public health.** With up to 45% of trauma-exposed youth meeting criteria for an substance use disorder and up to 75% of youth with a substance use disorder reporting having experienced a traumatic event (Blumenthal et al;., 2008), the impact of moving science forward in evaluating an integrative risk-reduction approach to treatment for this population will be far-reaching. In addition, data yielded from this study (irrespective of treatment group comparisons) will address an empirical question often raised in the trauma field regarding the potential utility of exposure therapy among adolescents with substance use problems (e.g., Cohen et al., 2003; Nace, 1988). Provided positive results for RRFT, the current study opens the doors for the next steps in this important line of research, including Stage 3 research (i.e., larger scale, multi-site RCT), a closer examination of MOA in RRFT, and investigations into the effectiveness, dissemination, and adaptation of RRFT (e.g., for web-based delivery)--ultimately yielding a valuable clinical tool for community-based therapists to employ with this high-risk population.