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Risk reduction through family therapy (RRFT): Protocol of a randomized controlled efficacy trial of an integrative treatment for co-occurring substance use problems and posttraumatic stress disorder symptoms in adolescents who have experienced interpersonal violence and other traumatic events

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ABSTRACT

Decades of research demonstrate that childhood exposure to traumatic events, particularly interpersonal violence experiences (IPV; sexual abuse, physical abuse, witnessing violence), increases risk for negative behavioral and emotional outcomes, including substance use problems (SUP) and posttraumatic stress disorder (PTSD). Despite this well-established link—including empirical support for shared etiological and functional connections between SUP and PTSD –the field has been void of a gold standard treatment for adolescent populations. To address this gap, our team recently completed a large randomized controlled trial to evaluate the efficacy of Risk Reduction through Family Therapy (RRFT), an integrative and exposure-based risk-reduction and treatment approach for adolescents who have experienced IPV and other traumatic events. The purpose of this paper is to provide a detailed description of the design and methods of this RCT designed to reduce SUP, PTSD symptoms, and related risk behaviors, with outcomes measured from pre-treatment through 18 months post-entry. Specifically, the recruitment and sampling procedures, assessment measures and methods, description of the intervention, and planned statistical approaches to evaluating the full range of outcomes are detailed. Clinical and research implications of this work are also discussed.

1. Introduction

Interpersonal violence experiences (IPV; sexual abuse, physical abuse, witnessing violence) and other forms of traumatic events (e.g., traumatic grief, disasters, accidents involving injury) during childhood serve as strong and consistent predictors of substance use problems (SUP) [1–5], posttraumatic stress disorder (PTSD) [6], depression [7], and risky sexual behaviors [8,9] during adolescence and adulthood [10,11]. Evidence-based treatments have been developed and evaluated for treating pediatric PTSD and depression among adolescents who have experienced IPV and other traumatic events through individual, office-based approaches [12]. Trauma Focused-Cognitive Behavioral Therapy (TF-CBT) [13], an exposure-based treatment that teaches youth and caregivers skills for managing trauma-related behavioral and emotional problems, is the most widely-disseminated pediatric trauma-focused, evidence-based treatment, with an abundance of RCTs to support its safety, efficacy, and effectiveness with trauma-related mental health concerns [12,14]. Existing treatments for adolescent SUP emphasize teaching youth new cognitive and behavioral skills for responding to internal and external substance use cues and often involve the caregiver in establishing contingencies for achieving and maintaining substance use reductions (e.g., CBT, Motivational Enhancement Therapy with CBT, Multisystemic Therapy [MST], Contingency Management, etc.) [15]. Among youth who have experienced IPV and other traumatic events, substance use may result from feelings of distress in relation to trauma cues and expectancies that using substances will help the young person cope with such distress. Long-standing, siloed approached to treatments for SUP versus

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mental health problems has resulted in a fragmented set of treatment offerings wherein interventions for substance using populations rarely address common co-occurring mental health disorders, such as PTSD, despite the fact that they may be functionally related [16,17].

Prior to the current trial, only two small pilot RCTs (*N*'s < 34) had been published to evaluate integrated approaches to treatment of co-occurring SUP and PTSD among adolescents [18,19]. Although both pilot studies supported the feasibility of integrated approaches, only one found significant main effects for both SUP and PTSD [18]. Neither study was adequately powered to establish efficacy, leaving the field without a gold standard treatment for this vulnerable population.

Risk Reduction through Family Therapy (RRFT) [18,20] is an integrative, exposure-based treatment approach for adolescents who have experienced IPV and other traumatic events. To address the need for an empirically-supported psychosocial therapy for adolescents with co-occurring SUP and PTSD, our team recently completed the first large, sufficiently powered randomized controlled efficacy trial of RRFT, focusing on the SUP and PTSD outcomes [73]. While a concise overview of the Methods specific to those outcomes are included in the published paper, it does not provide a full description of the recruitment and sampling procedures, assessment measures and methods, description of the intervention, and planned statistical approaches to evaluating the full range of outcomes. Thus, the current paper describes the full protocol of this NIH-funded Stage II RCT designed to evaluate the efficacy of RRFT in comparison to treatment as usual in reducing SUP, PTSD, HIV sexual risk behavior, and putative risk mechanisms (e.g., emotion regulation, parenting) among a sample of adolescents who had experienced IPV and other traumatic events who were treated in a "real world" setting.

2. Method

2.1. Study overview

A Stage II RCT was conducted to examine the efficacy of RRFT in comparison to treatment as usual in reducing SUP, PTSD, and related problems (e.g., HIV sexual risk behaviors) when delivered in a community-based mental health treatment setting under the supervision of the treatment developer. Beyond serving as the first large RCT to date to address the long-standing question of efficacy of an integrative treatment targeting co-occurring SUP and PTSD for adolescents, the study aimed to 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) [21]; 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 may or may not meet diagnostic thresholds.

A sample of 140 adolescents with current SUP and PTSD symptoms was recruited between December 2012–January 2017. Each participant and a designated caregiver completed a structured clinical interview and standardized questionnaires at five timepoints: pre-treatment (baseline), three months post-baseline, six months post-baseline, 12 months post-baseline, and 18 months post-baseline. The first five cases enrolled into the study were assigned to the RRFT clinicians as pilot cases to practice implementation of the treatment and were not entered into the RCT. Families entering the study after the pilot cases ($n = 135$) were assigned to either an experimental condition or a control condition. One hundred twenty-four cases were urn randomized to condition (described below in detail) and 11 of these cases were not randomized bur rather assigned to a specific condition either because they had a sibling already enrolled in the study (and a family could not receive both treatments due to contamination factors) ($n = 2$) or because of case load issues (e.g., if therapists in the control condition were on a wait list and the RRFT clinician had several open slots, it was preferable not to have the participant wait to receive treatment and thus were assigned to RRFT or vice versa) ($n = 9$). See CONSORT diagram (Insert Figure here). Participants randomized to the experimental condition were assigned to a therapist who was trained and supervised in RRFT. Participants randomized to the control condition received Treatment as Usual (TAU). These treatment conditions are described in greater detail below (see Interventions).

2.2. Participants

The final sample in the RCT consisted of 124 adolescents who met the following inclusion criteria: 1) Aged 13 to 18 years; 2) Reported at least one memorable experience of IPV (other traumatic events were permitted and included—but IPV was required); 3) Reported current non-tobacco substance use as defined by at least one substance using day in the past 90 days; and 4) Reported five or more PTSD symptoms. Youth were excluded from the current study if they: 1) Were previously identified as having a Pervasive Developmental Disability or Moderate to Severe Mental Retardation; 2) Were actively suicidal or homicidal; or 3) Reported active psychotic disorder. Statistical power was estimated for the difference between RRFT and TAU in change from baseline to each follow-up assessment. Using G*Power [37], the design effect formula was used to calculate the effective number of independent observations provided by each pair of measurements [36]. Results showed that at an alpha of 0.05 and with 165 independent observations from 124 participants, the study was adequately powered (i.e., power = 0.80) to detect a small-to-medium effect of $f = 0.13$ for the between-group differences in change.

2.3. Recruitment

Youth were primarily recruited through two local child advocacy centers (CACs). CACs provide victims of child maltreatment with a variety of services, including forensic interviewing, medical examination, advocacy, and outpatient mental health treatment. CACs are among the most common entry points to community services for abused children, and IPV 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. While use of community-based therapists required the investigative team to create more extensive training and supervision protocols than a trial conducted at the academic medical center, it provided a realistic evaluation and promoted future transportability and dissemination [22].

2.3.1. Screening and enrollment

As part of routine care, all adolescents who presented to the CACs for evaluation and/or treatment underwent a semi-structured intake assessment to determine traumatic event history, trauma-related symptoms, and appropriateness for outpatient care. Findings were then used to determine study eligibility. Eligible youths and their families were informed about the study and referred to research study staff for further screening and potential enrollment. Research staff confirmed youth used non-tobacco substances (alcohol and/or drugs) at least once in the past 90 days using the Timeline Followback (TLFB) [23] and the presence of five or more PTSD symptoms using the Global Appraisal of Individual Needs (GAIN) [24]. Adolescents who met these criteria and their caregivers were then asked to provide written consent/assent for recruitment into the study, sign a release of information (allowing for chart reviews), and schedule the pre-treatment assessment. All consent procedures were approved by the Medical University of South Carolina institutional review board (IRB).

2.3.2. Urn randomization

An adaptive randomization procedure, known as urn randomization, was used to balance potentially confounding variables among the participants randomized to each condition [25]. This approach to

randomization reduces pre-treatment variability between groups on these factors. The urn randomization procedure was implemented using an adaptation of the Microsoft Access application gRand [26] and was set up by the study statistician (JC). To keep assessors blind to condition, participants were urn randomized to the RRFT or TAU conditions by a trained CAC staff member (not a study clinician) using this program immediately following completion the baseline assessment. Specifically, once the Research Assistant screened and consented a new participant entering the study, she or he provided the necessary information to the CAC staff member to enter into the urn to produce the condition assignment. Specifically, condition assignment was balanced based on pre-treatment PTSDs severity (score on UCLA-PTSD-RI [24–26] ≥ 38), frequency of pretreatment substance use (≥4 substance using days over past 30 days); and the gender of the adolescent. Once the condition was identified, the CAC staff member informed the PI and the TAU supervisor of the condition assignment. The PI (for RRFT assignment) or the TAU supervisor (for TAU assignment) would then determine therapist assignment (based on case load and participant schedule match) and then inform the clinician about the new client.

2.4. Clinicians

Treatment for participants in both the RRFT and TAU conditions was provided by 14 master's level clinicians (7 clinicians in the RRFT condition and 7 clinicians in the TAU condition) housed at the two CAC settings. All of the clinicians were female and white. Clinician effort dedicated to treating study participants across both conditions were covered by the grant. All CAC clinicians had previous training in trauma-focused treatments, but no prior training in substance use treatment. RRFT clinicians completed intensive formal training in RRFT and received weekly supervision from the developer of RRFT, while TAU clinicians completed gold-standard training in TF-CBT and received weekly supervision from an experienced clinician with expertise in TF-CBT. Each clinician was assigned to one treatment condition exclusively. For all cases in this study, effort for clinicians in both conditions was covered by the grant funding which supported the study, and treatment was provided at no cost participants and their families.

2.5. Intervention

2.5.1. Risk reduction through family therapy (RRFT)

RRFT is an adaptation and integration of preexisting empirically-supported, cognitive-behavioral interventions and principles designed to address the adolescent behavioral health problems targeted here including: TF-CBT [27], Multisystemic Therapy [10] [28], and empirically-supported psychoeducation strategies for prevention of high-risk sexual behaviors [29] and sexual revictimization [30]. Based on the integration of these models, the RRFT manual outlines seven treatment components: (1) psychoeducation and engagement, (2) family communication, (3) substance abuse, (4) coping, (5) PTSD, (6) healthy dating and sexual decision making, and (7) revictimization and risk reduction.

Several theoretical models underpin RRFT intervention strategies. First, the RRFT treatment model draws upon ecological theory [31] by assessing and targeting the web of social influences (e.g., family, peer, community) that promote risk (e.g., substance using peers) [32] and resiliency (e.g., family activities) [33] for substance use and related risk behaviors at each level of an adolescent's ecology. For example, the youth and caregivers work with the therapist to determine what maintaining factors (“drivers”) contribute to a given risk behavior at each level of their ecology (e.g., substance use as a coping strategy; low parental monitoring; substance-using peers) and how those drivers can be modified to reduce substance use and promote emotional resilience (e.g., teach positive coping skills, involve other family members or neighbors for monitoring, connect the youth with structured activities that provide a forum for meeting non-using peers).

Second, Mowrer's Two-Factor Theory [34] is applied in RRFT, as therapists aim to extinguish distress and fear that an adolescent who has experienced IPV and other traumatic events has paired with memories and cues of the trauma. According to this theory, fear is acquired through a classical conditioning process by which the individual pairs a neutral stimulus (e.g., the dark; a certain word/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, as individuals can reduce a fear response during exposure to the feared stimuli without the feared aversive consequences. Based on its adaptation from TF-CBT, RRFT includes *gradual exposure* therapy to address PTSD symptoms via the development of a detailed written or verbal account of the IPV experiences and other 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 that they have developed in relation to the traumatic events (e.g., “I am damaged goods”; “The abuse was my fault”; “I am unlovable”; “Being high is the only way to deal with what happened.”) 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 and relaxation skills.

Third, the connection between substance use and trauma-related symptoms can be conceptualized in the context of negative reinforcement theory [35], which posits that escape and avoidance of negative affect (in this case, trauma-related distress) is an important motive for substance use. Sometimes referred to as the “self-medicating hypothesis,” a decrease in trauma-related substance use is thought to occur with improvement of self-regulation deficits [36], such as emotional reactivity. The Coping and PTSD components of RRFT focus on improving such skills—with a particular focus on reducing emotional suppression and empowering the youth with safe, healthy, prosocial skills to withstand distress and negative affect.

RRFT is individualized in that the different needs, strengths, preferences, and developmental factors of each adolescent and family are incorporated into case conceptualization and tailored treatment planning. The RRFT manual provides suggested language in introducing and teaching specific skills, session activities, and therapy homework ideas. The order in which the components (Table 1) are administered is determined by needs of the youth/family and is based on severity of the problems. The RRFT protocol is typically administered through weekly, 60–90 min individual sessions. When feasible and applicable, brief joint family sessions are also conducted. Therapists are encouraged to engage in brief phone or SMS/text check-ins with families between sessions to promote treatment engagement, particularly when new skills have been taught or during times of family crisis. Duration of treatment is not fixed in RRFT; rather, treatment is ended when the youth and family's goals have been met. Treatment progress is tracked systematically with standardized tools (questionnaires, urine drug screens) as well as ongoing updates to the functional assessment of risk and protective factors. Although pharmacological interventions were not implemented as part of this trial, participants were not prohibited or discouraged from pursuing medication from outside providers.

2.5.2. Control condition: treatment as usual (TAU)

Adolescents assigned to the TAU condition received the standard treatment that a IPV victim would typically receive at the CAC where the trial took place. At the study site, TAU clinicians had completed gold-standard training in TF-CBT (i.e., 2-day in person clinical training workshop, approximately 6 months of follow-up consultation calls delivered by experienced national TF-CBT trainers) and received on-going weekly supervision in TF-CBT. In addition to treatment that is typically offered at the CACs, TAU included capacity to refer to other agencies in the community (e.g., group therapy for substance use problems), which was documented in their charts. TAU has been utilized as a comparison

Table 1
Overview of RRFT components.

Component	Key concepts and objectives
Psychoeducation and Engagement	• Review privacy and confidentiality • Review RRFT intake assessment feedback • Personalized goal-setting • Identify treatment motivators for youth and caregiver ("finding the carrot") • Identify and address anticipated barriers to session attendance and engagement • Safety planning as needed, including run-away risk assessment and protection plan • Education about (a) trauma and traumatic stress, (b) mental health impacts of trauma, (c) substance abuse and connection with trauma, (d) risky sexual behavior and connection to trauma; e) resiliency • Provide overview of RRFT treatment components and expectations • Prioritize intervention components per family needs
Family Communication	• Review and establish family rules, as well as contingencies tied to following or breaking these rules • Assess family's communication norms • Teach effective communication skills (e.g., active listening) • Implement strategies for increasing family cohesion • Role-play solutions for common conflicts
Coping	• Define coping and differentiate between healthy and unhealthy coping (e.g., substance abuse, self-harm) • Emotion identification, labeling • Emotion acceptance (less suppression and reactivity, emphasis on building distress tolerance) • Anxiety reduction, relaxation via a range of strategies (crisis survival kit) • Change thoughts via cognitive processing • Problem-solving
Substance Abuse	• Goal setting around substance use and enhancement of motivation to cut back on substance use as needed • Identify factors ("drivers") contributing to substance use (i.e., fit circles) and develop and implement interventions based on those drivers • Contingency management to reduce substance use • Increase caregiver and school monitoring • Increase prosocial activities (monitored, with non-using peers, etc.) • Teach realistic refusal skills • Urge surfing • Review links between trauma and substance use and how of completion of the PTSD component will address trauma-related drivers (e.g., substance use as a way of coping with intrusive memories and/or inaccurate or unhelpful trauma-related beliefs • Prevention (i.e., of future use, relapse, etc.)
Posttraumatic Stress Disorder	• Review PTSD symptoms and connection with substance use • Exposure to trauma-related memories and cues/triggers through trauma narrative or similar strategies • Address inaccurate and unhelpful beliefs that developed from the trauma • Share trauma narrative or 'story' with appropriate caretaker • Skill building to reduce risk of future PTSD and/or trauma exposure

condition for several behavioral treatment evaluations involving adolescent substance abuse [28] or trauma [37].

The primary reason TAU was selected for the control condition was that no "standard of care" exists for co-occurring substance use problems and PTSD among adolescents. Alternative comparison conditions were considered, including evidence-based substance use treatment only, evidence-based PTSD treatment only, and waitlist control. These approaches were deemed insufficient because they would effectively result in withholding treatment for known problems in participants. A pre-defined course of parallel or sequential treatments for each presenting problem (i.e., delivered as separate treatments, likely by separate providers and possibly in separate clinics) was also considered but deemed unnecessarily burdensome for participants. Thus, given the ethical need to provide treatment to the control group (adolescents with current substance use and clinically significant PTSD symptoms) and a deficiency 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.

2.6. Design & data collection procedures

2.6.1. Treatment characterization

The frequency and nature of services provided was closely monitored and recorded using several strategies. First, a comprehensive chart review was conducted of the therapy session notes across both conditions, where study staff recorded information regarding characteristics of each session (e.g., duration of session, who participated in the therapy session, focus of session, and contact in between sessions), as well as whether outside for referrals were made (for the TAU condition). Second, all therapy sessions across both conditions were audiotaped to measure therapist adherence to RRFT and to characterize TAU. The audio recordings of 20% of sessions across both conditions (560 sessions total) were coded by 3 raters trained to > 80% inter-rater reliability. Tapes were coded using the Family Therapy Scale from the Therapy Procedures Checklist [38], which is an assessment of techniques used in session (e.g., improving family communication patterns), and an RRFT Therapist Adherence Measure (RRFT-TAM) [39]. The RRFT-TAM was developed using guidelines from the Standards for Educational and Psychological Testing [40] and accompanying Rasch methods [41]. Because RRFT represents an integration of TF-CBT for PTSD and MST for SUP, the RRFT-TAM was designed to capture key features of those models. Finally, caregivers also completed the Services Assessment for Child and Adolescent [42] at the final assessment point to report on a wide range of services that had been accessed over the course of participation in the study.

2.6.2. Outcome monitoring

Both the control and experimental groups were assessed at five timepoints: pre-treatment (T1), 3 months post-baseline (T2); 6 months post-baseline (T3); 12 months post-baseline (T4); and 18 months post-baseline (T5) by a highly trained research assistant who was blind to condition. Assessment time points were anchored to study entry/baseline assessment rather than treatment completion due to variable duration of treatment. The full assessment battery lasted approximately 2 h (see Table 2 for research instruments).

2.6.3. Retention

Several strategies were employed to maximize retention. First, to establish a long-term collaborative relationship with families, assessments were scheduled at the family's convenience, contacts were as

Table 2
Research instruments.

Assessment	Data	A/C
Demographics and ipv history		
Demographics Questionnaire	Information such as age, sex, ethnicity, Hollingshead [43] socioeconomic data, and family composition	AC
Chart Review of information from Intake Interview	Semi-structured interview to assess lifetime history of IPV and IPV incident characteristics [44]	AC
Substance use and abuse		
Timeline Followback (TLFB) [23]	Type, quantity, and frequency of non-tobacco substance use over past 90 days	A
Urine Drug Screens [45]	The urine toxicology screen to validate TLFB self-report	A
Diagnostic Interview Schedule for Children (C-DISC) [46]	Diagnosis of Axis I disorders	AC
Substance use risk and protective factors		
Family Environment Scale (FES) [47]	Cohesion and conflict subscales; social and environmental characteristics of families	AC
Bad Friends subscale [48]	Youth's peer relations	AC
Alabama Parenting Questionnaire (APQ) [49]	Parenting practices across the following domains: Corporal Punishment, Inconsistent Discipline, Poor Monitoring and Involvement, Positive Parenting, Rules and Expectations	AC
Direct Supervision subscale of the OSLC Monitoring Scale [50]	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)	AC
Parent Happiness With Youth Scale [51]/ Youth Happiness With Parent Scale [52]	Degree of satisfaction with the parent-child relationship across multiple domains	AC
Drinking Motives Questionnaire [53]	Motives or reasons for substance use (Coping, Enhancement, Social Facilitation)	A
Trauma-related psychopathology and risky sexual behaviors		
UCLA PTSD Index for DSM-IV [54]	Trauma history, Severity of PTSD symptoms	AC
Child Depression Inventory (CDI) [55]	Severity of depressive symptoms	A
Sexual Risk Behavior Scale [56]	Severity of risky sexual behaviors (e.g., condom use)	A
Other trauma-related treatment targets and mechanisms		
Emotion Regulation Questionnaire (ERQ) [57]	Tendency to regulate emotions in two ways: (1) Cognitive Reappraisal and (2) Expressive Suppression	A
UPPS-R-C Child Version [58]	Impulsivity traits	A
Hopelessness Scale for Children (HSC) [59]	Current level of hopelessness	A
Child Attributional Style Questionnaire – Revised (CASQ) [60]	Causal explanations for positive and negative events.	A
Treatment assessment		
RRFT Therapist Adherence Measure (RRFT-TAM) [39]	Content & skills that were addressed (and not addressed) at each session	N/A[a]
Therapy Procedures Checklist [38]	Techniques used in each session based on those from the most commonly used youth interventions (e.g., CBT)	N/A[a]
Services Assessment for Child and Adolescent (SACA) [42]	Interview to assess any additional services (e.g., church counseling, inpatient hospitalizations) that had been accessed over the course of participation in the study	C
Client Satisfaction Questionnaire-8 [42]	Consumer satisfaction with treatment	AC
Chart Reviews	See description above in Control Condition: Treatment As Usual.	N/A

Note. A/C denotes person completing the assessment A = Adolescent, C = Caregiver.
[a] N/A indicates measure was used for coding of therapy session tapes across both conditions, as described below.

friendly and personalized as possible, and families were reimbursed for their participation in each assessment session. Second, at consent, we requested up to eight phone numbers of the caregivers' and adolescents' best friends, closest relatives, and places of employment to facilitate contact each time the family is assessed; we also asked if participants had plans to change their place of residence. Third, we received consent to reach the adolescents (and caregivers as applicable) through text messaging and social media in addition to phone and mail. Fourth, direct contact with the families helped to maintain the cohort, as all families were tracked monthly for therapist adherence and school placement reports. When possible, participants were followed by the research assistant responsible for the initial research interview, which promoted rapport and a sense of involvement.

The research assistant administered the assessment battery in each family's home or at the CAC, based on the participant's preference and availability. To compensate for their time, families were paid $70 for completing the intake interview and $50 for each subsequent assessment. Data from all timepoints were collected on all families who were randomized into the study, even if they dropped out of treatment.

2.7. Planned data analysis strategy

The statistical analyses will follow intention-to-treat methods, with youth and caregivers included in the randomly assigned condition independently of their participation in the clinical intervention. The data are structured with five repeated measurements (level-1) nested within participants (level-2). To address this, the primary statistical models will be implemented as mixed-effects regression models [61], with continuous outcomes analyzed according to a normal sampling distribution and discrete outcomes analyzed using Bernoulli (dichotomous), negative binomial (count), or ordinal (ordered categories) sampling distributions. Primary outcomes focus on substance using days and PTSD symptom severity, with secondary outcomes targeting marijuana use and marijuana using days, alcohol use and alcohol using days, and polysubstance use (i.e., the use of at least two different substances). Sexual risk behaviors, as measured by the Sexual Risk Behavior Scale [56], are secondary outcomes that will be evaluated as well. To model change over time, polynomials and/or time-related indicators will be entered at the level of repeated measurements. For instance, by including linear and quadratic polynomials, the model would estimate an instantaneous rate of change that, over time, can slow down or speed up. Alternatively, more basic formulations, such as the use of dummy-coded indicators for the post-baseline assessments, could test for change between baseline and each subsequent assessment occasion. The effect of RRFT will be tested using a dummy-coded indicator for intervention condition (0 = TAU, 1 = RRFT), which will be entered at participant-level along with cross-level interactions between condition and the level-1 time term(s). Significance testing will be based on the Wald test (i.e., β/SE), and tests that are not directly provided by this formulation (e.g., the significance of within-group change for RRFT) will be obtained using planned contrasts. A number of potential control variables will be considered. For instance, at level-1, an indicator may be included for treatment status at each measurement occasion. This would test for an overall shift in the level of the outcome

trajectory following the end of treatment. Likewise, at level-2, variables may be included to control for participant demographic variables (e.g., age, sex, race) and/or indicators of treatment intensity (e.g., duration, frequency). The models will be implemented using SuperMix [61] or similar software for mixed-effects regression models.

3. Discussion

The objective of this paper was to describe the rationale and methods for a recently completed NIDA-funded Stage II RCT to rigorously evaluate the efficacy of RRFT, an integrative and exposure-based treatment approach for adolescents who had experienced IPV and other traumatic events, in comparison to treatment as usual. This study was conducted to address a significant gap in the field with regard to integrative treatment for co-occurring SUP, PTSD, and related problems (e.g., HIV sexual risk behavior) among adolescents. That is, although significant progress has been made in treating trauma-related psychopathology among adolescents and in treating SUP among adolescents independently, significantly less is known about treatment of SUP and PTSD in an integrative fashion among adolescents who have experienced IPV and other traumatic events.

Research with trauma-exposed adults suggests that integrated approaches to the treatment of comorbid PTSD and SUP are safe and efficacious [21,62,63]. However, a review noted that few studies examining integrated approaches to SUP and PTSD have included sufficient follow-up assessments [63]. Given that post-treatment substance use relapse rates are high, including among youth [63–70], assessments that extend to the year following treatment are critical in determining whether gains are indeed maintained after treatment. A substantial strength of the Stage II trial was that it included 12- and 18-month post baseline assessments to determine if indeed RRFT was successful in targeting long-term improvements in SUP and PTSD symptoms, as well as sexual risk behaviors.

Another strength of the Stage II trial is that it evaluated the safety and efficacy of an *exposure-based*, integrative approach to treatment of these co-occurring problems. Exposure-based approaches (i.e., intentionally approaching and recalling specific thoughts, feelings, memories, and cues of traumatic event experiences) have strong empirical support for the treatment of PTSD among adults [71] and youth [13,14]. Integrated intervention approaches for PTSD and SUP that do not incorporate exposure have had less robust findings [19,36].

The Stage II builds upon the prior research completed with RRFT. Prior to the Stage II study, a Stage Ia feasibility trial [20] and a Stage Ib pilot RCT [18] evaluating RRFT have been completed. The Stage I work resulted in a treatment manual, a clinician training protocol, and a quality assurance system. The results from these prior studies were promising, indicating that RRFT can be readily learned and implemented with fidelity, and that it can lead to improvements in drug use, drug use-related risk and protective factors, PTSD symptoms, and HIV sexual risk behaviors. The first outcome paper for the current trial indicates that the results hold true for SUP and PTSD symptoms.

Numerous other strengths of the Stage II RCT design are noteworthy. First, this study focuses on a 'real world' population of adolescents—where the focus was on heterogeneous symptoms (e.g., current substance use, PTSD symptoms), rather than requiring meeting full diagnostic criteria (e.g., severe substance use disorder + PTSD diagnosis). This ensures the study results will generalize to a broader population of youth who are highly vulnerable for the wide range of negative sequelae that can follow IPV and other traumatic event experiences. The multi-faceted clinical needs of this population call for an innovative solution to bridge the gap between early intervention and treatment, resulting in an inclusive risk-reduction approach with the potential for a wider-spread impact. Second, establishing an integrative treatment option for this population directly addresses issues related to client burden (having to navigate separate, parallel or sequential treatments for SUP and PTSD delivered by different therapists in different settings) and clinician preferences [72] to have tools to address the multi-faceted problems most representative of their clients. Third, the Stage II trial affords a unique opportunity to pursue mechanisms of action research, which can direct improvements to treatment models and inform important next steps in this line of research. As noted in the Methods, we assessed several empirically-informed skills specifically targeted in RRFT (e.g., emotional regulation; parenting) that may lead to improvements in SUP and PTSD.

Next steps with the study will involve evaluation of the sexual risk behavior outcomes and the putative targets of treatment as mechanisms of action. The details provided in this protocol paper allow for a complete picture of the study design, as well as promote opportunities for reproducibility in future clinical trials that may be designed to evaluate other treatment options for adolescents who have experienced trauma and engage in high risk behavior. This may be particularly timely (at the time of the manuscript writing) given the world-wide COVID-19 pandemic that may further increase the need for both research and clinical services targeting traumatic stress and substance use behavior [74] among adolescents.

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