

Official Title: Text-Message-Based Depression Prevention for High-Risk Youth in the ED (iDOVE)

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RESEARCH PLAN

SPECIFIC AIMS:

A history of violence strongly correlates with adolescent depression.[1-5] Approximately 50% of teens with a history of physical peer (non-partner) violence, as compared to 5-10% of teens in the community, report depressive symptoms;[3, 6-9] and teens with a history of peer violence are at increased risk of subsequent major depression.[10-12] Conversely, adolescents with depressive symptoms have higher rates of future peer victimization and aggression than non-depressed peers.[13-17] Peer violence and depression have mutual, reinforcing negative impacts on emotional and behavioral regulation strategies.[13, 18-20] Teens with a history of peer victimization or aggression are also at higher risk for other negative consequences, including anxiety, post-traumatic stress disorder (PTSD), risky sexual behaviors, and substance/alcohol abuse.[3, 4, 9, 21-24]

The emergency department (ED) is an ideal location to initiate interventions for high-risk adolescents.[25-27] Multi-session cognitive behavioral therapy (CBT) for teens' co-occurring depression and violence may effectively reduce depressive symptoms.[28, 29] However, many teens lack access to these services.[30] The ED is the primary source of care for most high-risk teens.[31, 32] An ED visit therefore provides an important opportunity to initiate preventive interventions, to complement existing mental health treatment or to stand alone for those who never seek formal care.[33-36] Innovative techniques are needed to engage ED patients. Most teens use text-messaging.[37] Personalized text-message interventions for adolescents, including for depression prevention, are accessible, feasible, and may be effective.[38-41]

In this K23 research plan, we will create an indicated depression prevention intervention for teens seen in the ED with depressive symptoms and a history of peer violence. Drawing on effective CBT and motivational interviewing (MI) depression and violence prevention interventions,[42-45] a brief in-person session ("ED") will introduce basic cognitive and behavioral strategies. Following ED discharge, eight weeks of tailored CBT-informed daily text messages ("text") will be sent, to enhance skills and remind participants of self-determined goals. The "ED+text" intervention may be more accessible and disseminable for this high-risk population.[46]

My long-term goal is to become an expert in easily-disseminated, technology-assisted mental health interventions for high-risk ED patients. Although such interventions may have a modest effect, I am purposely designing them to have a broad reach for the large group of ED patients who do not access any mental health care. My short-term goals, for this K23 award, are to gain training in development and analysis of technology-assisted ED depression prevention interventions, and to test the hypothesis that an "ED+text" indicated depression prevention intervention is acceptable and feasible. This study will lead to an R01 application to conduct formal efficacy testing.

We are currently completing our recruitment for, and analysis of, Aim1 (qualitative interviews to develop the intervention). THIS APPLICATION IS FOR APPROVAL OF AIMS 2 and 3.

Aim 2: Refine intervention content. Eligible participants will be iteratively enrolled, 4 at a time, in the "ED+text" intervention (n=16-20). Through semi-structured interviews and measures of protocol adherence, we will refine content and improve feasibility, acceptability, usability, and clarity of the intervention components.

Aim 3: Conduct a randomized pilot trial (n=120) of the "ED+text" preventive intervention vs. enhanced usual care (attention-matched nutritional text messages).

3a: Primary outcomes will be intervention acceptability (defined as 65% enrollment rates and 80% agree/strongly agree ratings[42, 47] on the Client Satisfaction Questionnaire-8[48] and exit interviews), feasibility (defined as 80% completion of in-person and text-message sessions[42, 47]) and fidelity of in-person sessions (defined as 80% adherence to session manual[49-51]).

3b: Preliminary hypothesis testing: Although not powered to detect efficacy, we will look for a trend toward a primary outcome (a decrease in depressive symptoms at 8 and 16 weeks), and an exploratory secondary outcome (decreased number of peer fights) relative to enhanced usual care.

This proposal is innovative: it will develop a feasible, acceptable depression prevention intervention for a high-risk population of adolescent ED patients with a history of peer violence. It also has high significance and impact: utilizing the ED location, it addresses a current lack of easily-accessible preventive services and reflects NIMH Strategic Objectives 3 and 4. It will potentially lead to an efficient means to reduce depressed mood in high-risk teens with little access to traditional mental health care. If effective, this intervention will be

translated to other at-risk patients seen in the ED. Finally, it is essential for my career development as an ED-based mental health intervention researcher.

RESEARCH STRATEGY

(a) SIGNIFICANCE: Prevention of adolescent mental health disorders and peer violence are critical research goals according to Healthy People 2020, NIMH, and the Institute of Medicine.[52-55] Mood disorders are epidemic among teens,[6-8, 56] and strongly correlate with a history of physical peer violence (assault or victimization).[5, 14, 15, 57-59] Rates of youth violence are also high,[60, 61] many causing severe injury: over 650,000 youth presented to the ED for violent injuries in 2008 alone.[62] In a national study of 4023 adolescents, 39% of teens with a history of assault (vs. 5% of teens with no trauma history) met criteria for major depressive disorder (MDD).[3] My pilot work shows that 40-60% of adolescents with a history of physical peer violence report past-month depressive symptoms, as compared to 17-20% of all teens seen in the ED.[9, 63-65] These rates are substantially higher than the 5-10% average 30-day prevalence of depressive symptoms in community samples of teens.[7, 66] Just as EDs screen for high-risk alcohol use or partner violence, a positive screen for past-year peer violence is a marker of being high risk for both MDD and future violent injury.[25, 67-72]

A strong theoretical basis exists to explain the bidirectional relationship between depression and violence. Many risk factors for depression—such as poor problem-solving skills, misreading of social cues, and inability to regulate one’s emotional responses—also predict involvement in peer violence.[2, 13, 73] Depressive symptoms may therefore increase their risk of peer violence.[4, 5, 57, 74, 75] Conversely, peer violence may increase stress reactivity and reinforce maladaptive coping skills and negative world-views, thereby worsening depressive symptoms and potentially leading to MDD.[4, 10, 59, 69, 76-78] Targeted enhancement of cognitive and behavioral skills, to reduce both depressive symptoms *and* future peer violence, may be more effective for these high-risk adolescents.[28, 59, 79]

In sum, there is a strong bidirectional relationship between peer violence and depression in adolescents, due to common cognitive and behavioral errors. [1-4, 9] **This preventive intervention for adolescent ED patients, uniquely tailored to reduce depressive symptoms in the context of peer violence, therefore has the potential to decrease depressed mood in the short-term within an extremely high-risk group.**[34, 52, 80] If this research is successful, it could have a significant impact on the health of adolescents with minimal access to mental health services, high risk of developing more severe depressive disorders, and high rates of co-morbidities.

This K23 research plan therefore aligns with NIMH’s Strategic Objective 3, to develop “new and better interventions for mental disorders that incorporate the diverse needs and circumstances of people with mental illness,” and Objective 4, to “strengthen the public health impact of NIMH-supported research.”

(b) INNOVATION:

1: Development of an ED-initiated indicated depression prevention intervention for high-risk adolescents

Primary-care and school-based targeted CBT preventive interventions, some of which include elements of motivational interviewing (MI) to increase participant engagement, are effective at reducing depressive symptoms, mental health sequelae of violence (including PTSD), and psychosocial dysfunction.[28, 43, 81-85] A single ED-based study using MI has been conducted (by Co-Mentor Cunningham), showing decreased aggression among adolescents with both alcohol use and a history of peer violence.[42, 44, 86] Despite the strong relationship between violence and depression, and the shared cognitive and behavioral deficits of these disorders, no indicated depression prevention interventions exist for youth with a history of peer violence.

Adolescents with depressive symptoms and a history of peer violence often use the ED as their primary source of care.[31, 32, 87] They are unlikely to receive referrals to existing mental health services from the ED, unless they are seeking care specifically for psychiatric-related complaints.[8, 36, 63] Even when they do receive a referral, adolescents lack accessible mental health services.[30, 36, 88] Moreover, depression and violence are associated with low adherence to treatment.[89, 90] Therefore, while longer interventions may be more effective,[84, 91] *multi-session in-person interventions are unlikely to be successful with our population.*[89]

Brief ED-based interventions are effective at reducing recurrent suicidality and violence.[42, 44, 92-94] A brief, theory-based, ED-initiated depression preventive intervention for adolescents with a history of peer violence is therefore both indicated and innovative. **The proposed intervention aims to decrease depressive symptomatology, and possibly prevent future violence-related episodes, in high-risk adolescents.**

2: Use of state-of-the-art technology to improve reach, engagement, and outcome of this novel intervention

Text messaging provides an ideal delivery mechanism to longitudinally engage and deliver content to these high-risk adolescents. Between 87% and 91% of teens, including those seen in the proposed study site ED,

own cellphones,[37, 64, 95] and adolescents average more than 50 text messages per day.[37] Theoretical benefits of a text-message-based longitudinal intervention protocol include continued engagement, real-life practice (e.g. daily text-message-based mood monitoring, goal-setting), increased dosage of therapeutic content, and the ability to tailor messages to participants' current emotional state.[41, 96-100]

Text-message-based interventions have been shown to be *acceptable, feasible, and in some cases effective at delivering interventions addressing a variety of psychosocial issues*, ranging from smoking to bipolar disorder.[38, 96, 101-103] A recent study in New Zealand showed acceptability, feasibility, and self-reported improvements in mood among adolescent participants in a school-based cell phone adaptation of a universal CBT depression prevention intervention.[39] Recent studies in American EDs showed that text-message-based alcohol[104] and diabetes[105] interventions are acceptable and feasible with young adult ED patients. **No ED-based in-person or text-message interventions exist for reducing depressive symptoms.**

Dr. Ranney (PI) has conducted surveys of the target population, showing their preferences for technology-based intervention formats,[64, 95] and is currently using text-messaging to assess adolescent girls' daily mood. Drs. Cunningham & Boyer have extensive experience developing technology-augmented interventions,[44, 106-110] although not for depression prevention. In this research project, Dr. Ranney will learn from her mentors' and advisors' previous research experience to develop an acceptable, single-session "ED" + longitudinal "text" depression prevention program for youth with a history of violence.

(c)APPROACH:

OVERVIEW OF PROJECT: This project will develop, refine, and pilot a novel, single-session in-person + daily text-message ("ED+text") depression prevention intervention to reduce depressive symptoms among adolescents with a history of violence presenting to the ED for any reason. The intervention will target cognitive, affective, and behavioral strategies through a single, brief in-person introductory session ("ED") followed by 8 weeks of theoretically-informed text messages ("text") (Table 11.2). It is based on existing depression and violence prevention interventions as well as text-message preventive interventions developed for other populations.[38, 39, 104, 111]

The intervention has been designed, and will be tested, via an iterative process. In Aim 1 (ongoing, near completion) semi-structured interviews and expert consultation informed preliminary intervention content and format. In **Aim 2**, a series of small open trials and further qualitative analysis will refine it. In **Aim 3**, we will then conduct a randomized, controlled pilot trial of the novel intervention among adolescents with depressive symptoms and a history of peer violence. We will use the same setting and participant screening/enrollment procedures throughout the study.

Inclusion	Exclusion
<ul style="list-style-type: none"> • Age 13-17 • English-speaking • Parent present and able to consent • Medically/physically able to assent 	<ul style="list-style-type: none"> • Acute suicidality/psychosis • Sexual assault chief complaint • Child abuse chief complaint • In police custody

Study Setting and Patient Population: This study will be conducted in the pediatric ED of Rhode Island Hospital, which serves over 50,000 pediatric patients per year. The patient population is diverse, with 40% publicly insured, 40% Hispanic, and 25% African-American. Dr. Spirito has successfully conducted numerous studies of high-risk adolescents at this site.[47, 89, 112]

Patient Screening: The Research Assistant (RA) will be present on a random selection of shifts covering all days of the week, weighted by patient volume. Every patient meeting screening inclusion/exclusion criteria (see Table 11.1) who presents during an RA shift will be approached, in accordance with Dr. Cunningham's protocols. Only English-speakers (~95% of ED population) will be recruited for this development grant. *Should* Potentially eligible participants will be identified by RAs from the electronic ED tracking log. After obtaining parental consent/ adolescent assent, RAs will administer a computerized screen for depressive symptoms and past-year peer violence. The screen will also include basic demographic questions from the National Longitudinal Study of Adolescent Health (Add Health).[113] Additionally, to reflect my experience with 2 different screening processes during my pilot grant, we will administer some additional questions drawn from Add Health, YRBS, and other pertinent relevant measures of other behaviors (which I and my mentors have found increases participant honesty on all questions; in studies where we only administer the screening questions of interest, rates of self-report have decreased significantly). See **Appendix 1** ("CODEBOOK") for questions.

Mentors Spirito and Cunningham have used similar screening protocols to recruit participant samples similar to the general ED population. All screened patients will be able to choose a small gift (\$1-\$2 in value) as compensation for their time.[86, 114]

Eligibility and Enrollment: Participants are eligible for enrollment if they screen positive for self-report of: (a) **depressive symptoms**, defined as a Patient Health Questionnaire-9 (PHQ-9)[115] score of ≥ 5 , and b) **past-year peer (non-partner) violence** (victimization or perpetration), using a modified version of the Revised Conflict Tactics Scale 2

[CTS2].[116] If meeting eligibility criteria, a second consent/assent and a detailed contact information form will be completed. If PHQ-9 score is ≥ 20 or a positive answer to the suicidal ideation question, the attending emergency physician will be notified. Participants with severe depressive symptoms (PHQ-9 ≥ 20) will be INELIGIBLE for participation in Aims 2 or 3. See [Human Subjects](#) for details.

Refusal to permit audio-taping of ED sessions will be an additional exclusion criteria.

- **Justification of eligibility criteria:** (1) Use of PHQ-9: As per other depression prevention interventions, PHQ-9 is a standard screening tool to determine eligibility for targeted and indicated depression prevention studies.[43, 82, 83, 85, 117, 118] A cutoff of 5 accords with that used by other intervention studies.[119-121] (2) Adolescents reporting any past-year peer physical violence. “Peer” violence is non-partner, non-family-perpetrated physical violence.

Adolescent peer victimization and perpetration strongly overlap, and teens with any past-year fights (not just those with acute injury) are high risk for future injury and depressive symptoms.[3, 122] Co-Mentor Cunningham has used the modified version of CTS2 for multiple ED-based studies addressing peer violence.[44, 86, 113, 116, 117]

- **Justification of enrollment feasibility:** Each month ~1200 patients age 13-17 present to the RIH ED. Based on AIM 1 results, approximately 20% of teens will screen positive for both current depressive symptoms and past-year peer violence; in Aim 1, 70% of eligible teens consented for interviews. At a very conservative 50% consent rate, at least one participant would consent per eight hour recruiting shift (~20 pts/month). High retention rates (~80%) are reported by her mentors and others in similar longitudinal intervention studies.[39, 42, 47, 96, 104] See [Figure 11.1](#) (under **Aim 3**) for flow chart.

AIM 2: Refine intervention content:

In this Aim, the newly developed depression prevention intervention will be iteratively refined, recruiting four adolescents per round (two of each gender) for at least four rounds of open pilot testing (a total of at least 16 adolescents). Under the guidance of her entire mentorship team, Dr. Ranney will use semi-structured interviews and measures of protocol adherence to evaluate and then improve the intervention’s appropriateness and comprehensibility for the target population. The open trials will also provide an opportunity to assess the feasibility of inclusion and exclusion criteria, and recruitment and assessment procedures.

- Study setting, eligibility, and enrollment are as above. Additionally, participants will need to own or have access to a cellphone that can receive text messages. A subset of the participants in Aim 1 (who have previously consented to be contacted) will be contacted via mail and cellphone to see if they want to participate in Aim 2. We will limit cross-enrollment to a maximum of 1/3 of our sample.

Open trials will last for the full anticipated intervention duration of 8 weeks.

Theory/Model	Technique/strategy	Intervention Component	Delivery Method
CBT, MI	Elicit recognition of problem(s)	-Feedback on depressive symptoms and peer violence - Identify “thought-feeling-action” triangle for negative thoughts & violence	In-ED + Text
CBT, MI	Goal-setting	-Offer range of personal change goals for depression & violence, including option to create own goals - Separate personal goals from peer standards, particularly for violence -Convey respect & empathy for goals - Define “rewards” for meeting goals	In- ED + Text
CBT	Cognitive restructuring: - Challenge negative thoughts - Problem-solving	- Identify negative thoughts, their triggers, and their results (emphasizing violence’s role as trigger/outcome) - Identify alternatives to negative thoughts and violence - Encourage non-violent assertiveness - Put negative events in perspective	Text
CBT	Affect regulation: - Emotional regulation - Distress tolerance	- Identify alternative ways of dealing with common stressors and potential fights (“coping plans”) - Provide strategies to calm down and deal with stress and threats	Text
CBT	Behavioral activation:	- Develop a list of fun, non-violent activities (social, physical, and indulgent) - Elicit pro-social behavioral skills - Reminders of community mental health/violence-prevention resources	Text

- **Incentives:** \$25 for completing the baseline assessment and in-ED intervention, \$10/month for text-messaging plans, \$5 for completing follow-up survey prior to the follow-up interview and \$50 at follow-up interview.

- **“ED” session (~20-30 minutes):** This session will take place during waiting periods in the ED stay; average ED visits are 3-5 hours. The session is a manualized adaptation of the first session of an effective CBT-based depression prevention program (provided to the PI by Dr. Paul Rohde, who is available to advise on an as-needed basis)[43, 82] and of Cunningham’s MI-based violence interventions.[44] Using Spirito’s and Cunningham’s brief ED interventions as a model, the trained interventionist will provide participants with immediate feedback, using computerized baseline assessment scores (a very brief version of the planned baseline assessment, to help us refine the intervention). The interventionist will then give a brief overview of Beck’s Cognitive Triad (the interplay between thoughts-emotions-behavior); and will conduct personalized goal-setting using MI techniques (**Appendix 2**, “ED SESSION”). Participants will also be oriented to the text-message system, including potential human subjects concerns (see **Human Subjects**).

During the session, the parents will be asked to step out of the room. They will be given publicly-available content regarding adolescent depression prevention to review, both to enhance their buy-in to the project and to occupy them during the intervention.

All sessions will be audio taped. Following each session, the interventionist will complete an adherence rating form to indicate how well the protocol was followed. Adherence manuals will be developed by Dr. Ranney and Spirito based on session content, the Cognitive Therapy Rating Scale (CTRS),[49] and the Motivational Interviewing Treatment Integrity Code (MITI),[50] well-validated methods of assessing competence and adherence. **Mentor Spirito will listen to all sessions with Dr. Ranney as a training activity**, and as part of the treatment development process. After each round of open pilot testing (4 participants each), the “ED” protocol will be modified according to participant and interventionist feedback.

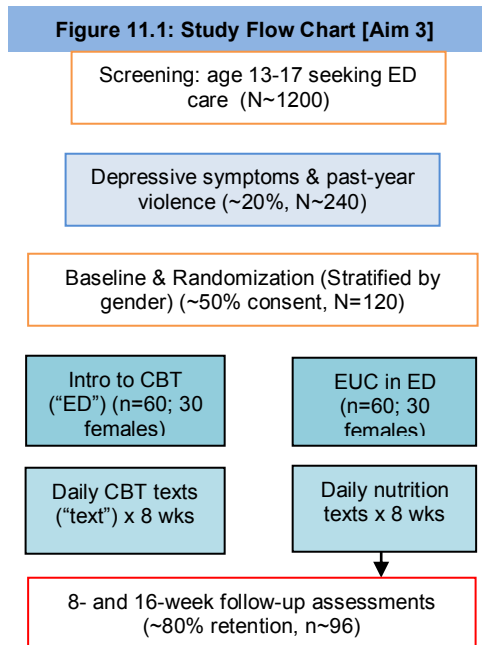
- **“Text” component (daily for 8 weeks):** Based on results from Aim 1, we will sending *one automated assessment followed by one tailored CBT-informed text message each day*, at a time of the participant’s choice. Each week, a variety of messages will be delivered to create both (a) a natural progression in skill-building; (b) continued motivation for participation; and (c) responsiveness to participants’ needs, through tailoring. This daily text-message system will maximize active engagement and increase participants’ practice of key CBT-based concepts, which has been shown to correlate with change in depressive symptoms.[84] We will also provide *participant-driven text-messages*: e.g., if the participant texts “FIGHT” or “MOOD” to the automated program, indicating need for additional support on that topic, s/he would receive an appropriate skill-based message.

After each round of open testing, message prompts, content, and frequency will be **iteratively refined based on qualitative and quantitative assessments**. Final content will be submitted to the IRB prior to the start of Aim 3 (at which point the intervention will not be further revised). The current conception of the messages and the delivery algorithm are attached as **Appendix 3** (“TEXT MESSAGES”).

Messages will be delivered to participants’ own cell phones using an automated computerized system developed by an outside company, Reify Health, based on pre-specified delivery algorithms. Any responses that deviate from expected requests will receive an automated “crisis message.” Data from the responses will be reviewed weekly, and will be visible ONLY to members of the research team (see **Human Subjects**). (see **Appendix 3** and **Human Subjects** below).

PI Ranney used this system to conduct daily mood assessments of high-risk adolescent girls in a pilot grant funded by a private foundation with over 80% response rates to 9 daily messages and overwhelmingly positive feedback during a post-assessment interview. Mentor Spirito is currently using Reify Health to deliver text-messages for an NIMH-funded R34 for adolescent suicide prevention. Advisor Boyer has successfully delivered interventions to participants using a similar system.

- **Assessments:** In addition to the assessments in the screening protocol, we will administer assessments at the close of the open intervention to guide refinement of the “ED+text” intervention. Specifically, we will



collect data on feasibility: study recruitment and refusal rates, program completion, follow-up rates, reliability and range of responses to baseline and follow-up questionnaires, and rates of study attrition (see **CODEBOOK AIM 2**). Participants will also complete detailed qualitative debriefing after the in-person and text-messaging components of the intervention (see **QUALITATIVE ASSESSMENT**). This evaluation necessarily occurs on a clinical, non-statistical level. Participant acceptance of the text-messaging will also be assessed by: (1) The *System Usability Scale*, a participant-completed, reliable and valid metric for measuring usability and acceptability of technologies.[123, 124] Higher scores equate to higher usability.[125, 126] (2) *Relative Subjective Count (RSC)*, the quotient of the participant’s estimate of the number of times the system delivers a text, divided by the actual number of texts delivered.[127, 128] As text-message systems are unable to track actual number of texts opened, this measure is a reliable surrogate measure of acceptability.[127, 128] Low RSC (e.g., <1.0) correlates with increased participant satisfaction, while elevated RSC (>1.0) reflects poor acceptability of a technology (e.g. that the messages were intrusive).[127, 128] Lastly, in recognition of the NIH’s move toward “learning healthcare system” outcomes, we will include a review of Lifespan electronic medical records (EMR) to determine participants’ ED visits and admissions over the 8 weeks of the study period, to show the feasibility of tracking this data. We will extract only the number, category, and disposition of the visits (specifically, whether the visit was related to injury, psychiatric complaints, or medical complaints, and whether the patient was discharged, transferred [as well as transfer location], or admitted to Hasbro) from the Lifespan EMR.

Aim 3: Conduct a pilot randomized trial of the novel “ED+text” intervention versus enhanced usual care (EUC).

This Aim corresponds to **Stage 1b of intervention development (pilot testing and refining the intervention)**. [129] In Years 3-5, a two-group randomized design will be used to measure intervention feasibility (numbers of patients recruited, retained, randomized, and completing all follow-ups) and acceptability (satisfaction questionnaires and exit interviews), as well as exploratory hypothesis testing. In Year 5, analysis and grant authorship will occur. The entire mentorship team will guide Dr. Ranney in this Aim.

- Intervention Recruitment: Participant screening and enrollment processes will remain the same. Study setting, eligibility, and enrollment are as per above, with the additional requirement (as per Aim 2) that participants own or have access to a cellphone that can receive text messages.

- Content: Per above.

- Study Randomization and Intervention Conditions: Eligible participants will be randomized to *experimental* (ED+text, n=50) or *enhanced usual care* (EUC, n=50) care. As gender is a known moderator of depressive symptoms and violence,[12, 58, 73, 136] randomization will be stratified by gender and baseline depressive symptoms, using block randomization. See **Figure 11.1** for flowchart. All participants will complete a baseline assessment in the ED. If randomized to ED+text, they will complete the introductory session during waiting periods in their ED visit (as per Drs. Spirito’s & Cunningham’s ED-based interventions), then will receive daily tailored CBT-based text-messages for 8 weeks. EUC will consist of a brief introduction to home safety and nutrition, as well as an introduction to the text-message service in the ED, followed by eight weeks of regular text messages on safety, diet and nutrition. *The current standard of care for these patients is, in essence, no care*: no depression or violence screening assessment protocols are currently used in our ED. Both “ED+text” and EUC conditions therefore exceed current levels of care.

- Assessments: At screening participants will be asked additional questions from the Child & Adolescent Services Assessment, the Short

Table 11.3: Schedule of Participant Assessments

Construct	Measures	Baseline	8-week	16-week
Depressive symptoms	BDI-II[130, 131]	X	X	X
Peer violence	CTS-2 (physical subset)[116]		X	X
	YRBS Physical Fight	X	X	X
	CADRI (physical subset)[132]		X	X
Cognitive/behavioral skills	IPAS	X	X	X
	Positive Affect	X	X	X
	Violence Self Efficacy	X	X	X
	Short Hopelessness Scale		X	X
	Emotional Regulation	X	X	X
	Rumination	X	X	X
Associated co-morbidities	Substance Use		X	X
	Child PTSD Symptom Scale[134]	X		X
Resource utilization	Child & Adolescent Services Assessment[135]			X
Process measures	Client Satisfaction Questionnaire-8[48]		X	
	Relative Subjective Count		X	
	Qualitative assessment		X	

Hopelessness Scale. Other question types include: medication use, delinquency, drug use and binge drinking, community violence, intimate partner violence (CADRI physical subset), symptoms of Post-Traumatic Stress Disorder (PTSD), safety and nutrition factors, cell phone use, cyberbullying, access to medical services, and demographics. These will be in addition to screening eligibility questions (CTS-II and PHQ-9).

We will assess depressive symptoms, violence, cognitive/behavioral skill-sets, and resource utilization at baseline; 8 weeks (at the close of the text-messaging portion of the study); and 16 weeks. Although a longer follow-up period would be preferred, these follow-ups were chosen based on budgetary and time constraints of this training grant. In accord with mentors' ED studies,[42, 47] assessments are expected to take ~30 minutes to complete. They have been modified based on Aim 2 data. Although limited in the baseline assessment due to in-ED time constraints, we recognize that a number of important co-morbidities, such as substance use and PTSD, may relate to our intervention's effectiveness. We will measure these at screening, baseline and follow-up. At the 8-week follow-up, standardized quantitative process measures will be administered to assess acceptability, usability, and feasibility; qualitative interviews will be administered to a purposefully sampled subset of a maximum of half of both the intervention and control groups.[124, 137] (See [Table 11.3](#) and [Appendix F](#) for details on assessment schedule and psychometric properties). Lastly, in recognition of the NIH's move toward "learning healthcare system" outcomes, we will include a record of maximum heart rate during the ED visit, and review of the EMR for ED visits and admissions over the 6 months following enrollment in the study, as described in the Aim 2 protocol above.

- **Fidelity Protocol:** The fidelity of the text-message component is assured, as all text-messages will be automated. To assess fidelity of in-person ED sessions, all will be audio-taped. The interventionist's first 10 tapes will be rated by Drs. Spirito and Ranney, *according to guidelines to be developed in Aim 2*, to objectively evaluate if there is protocol drift. If tapes meet the 80% criterion, 20% of recordings thereafter will be coded. Criteria for adherence to the ED session will be defined in terms of specific content areas, as well as adherence to basic CBT and MI principles.[49-51] **This will serve as a training activity.**

- **Incentives:** Maximum compensation for completion of the entire trial will be \$150 (\$25 for baseline, \$40 for 8-week follow-up, \$50 for 16-week follow-up, \$20 for unlimited text-messaging plan for 8 weeks, \$5 for alerting us to a change in phone number, \$5 each for finishing the 8 & 16 week follow-ups online). Spirito and Cunningham have successfully recruited and retained 80-90% of participants for 12-month follow up across multiple trials with high-risk adolescent ED patients, using similar protocols and compensation.[42, 47, 89]

Mental Health Safeguards and Data Management: The research assistants will be extensively trained by the PI and Mentor Spirito to recognize and manage participant distress. In case of severe depressive symptoms, suicidality, or other crises during in-ED screening, the interventionist will immediately notify the PI and the attending emergency physician. If mental health crises are identified during interviews outside the ED, the research team will contact the PI at time of identification and refer appropriately, according to the drafted crisis plan. Mentor Spirito, a licensed clinical psychologist, will be available by phone for clinical decision-making. Please see **Human Subjects** for further details.

STATISTICAL ANALYSIS

PHASE ONE, Aim 2: Using data collected during the open trials, we will perform a preliminary process analysis, examining study recruitment and refusal rates, study completion rates, use of text messages, follow-up rates, reliability and range of responses to assessments, and overall study attrition. We will study exit interview transcripts for acceptability, treatment satisfaction, and comprehensibility. Exit interviews will also undergo thematic analysis, similar in methodology to Aim 1. Because the interview topics are restricted to review of the revised materials and feedback on planned intervention components, it is likely that most codes will be deductive. Analysis will also focus on key domains that are also covered by the quantitative evaluation instruments so that the qualitative data can provide additional context for that quantitative data.

In addition, as described in Aim 2: Assessments, above, we will assess the text-messages' usability and acceptability by calculating the mean score for the System Usability Scale (SUS)[124, 125] and the Relative Subjective Count (RSC). [127, 128] The SUS will be administered at the close of the 8-week intervention; a higher score correlates with higher usability. The RSC will be calculated based on information obtained in the exit interviews, as successfully used by Dr. Boyer; lower scores correspond to higher acceptability.[127, 128] We will also review the number and type of ED visits and hospital admissions for the duration of the study to examine trends in hospital admission as an effect of study participation.

Based on these formative data, we will further refine our intervention and study protocol.

PHASE TWO, Aim 3:

- Sample size: For this intervention pilot study, we chose to recruit 120 subjects in the RCT. Conservatively estimating that 20% may be lost to follow-up, 96 subjects will complete the 16-week assessment. This number will be sufficient to allow us to make judgments regarding feasibility and acceptability. Despite problems in the stability of effect size calculations with small samples, if a small effect size is detected between groups, and the intervention is shown to be feasible and acceptable, then further testing in a larger trial may be indicated given the innovative nature of the intervention and its potential disseminability.[138, 139] Based on our Aim 1 results, we anticipate that the mean PHQ-9 score of our participants will be 10.0, with a standard deviation of 4.5. If we wish to show a delta-PHQ9 of 2 (with alpha 0.05 and beta 0.8), we would need to successfully follow up 63 participants.

- Data management: Data from text messaging, including time of delivery and any participant responses, will be stored in a de-identified database on a HIPAA-compliant server. This de-identified data will be imported into Stata 12 (Stata Corp, College Park, TX), with which I and my mentors are skilled. Stata 12 is suitable for the multi-level modeling necessary for a fully-powered longitudinal study.

- Acceptability and feasibility (Aim 3a): *Acceptability* will be measured using descriptive analysis of enrollment rates, participants' ratings of the clarity and structure of the in-person and text-message sessions, Client Satisfaction Questionnaire-8,[48] *Feasibility* will be measured using percent of in-person sessions completed, the RSC (as described in Aim 2).[127, 128] and therapist adherence ratings.

- Exploratory hypothesis testing: We will calculate total scores for depressive symptoms (PHQ-9, BDI-II) and violence exposures (CTS-2, CADRI) at baseline and follow-up. We will calculate descriptive statistics for study sample demographics, baseline mediators/moderators (e.g. IPAS, hopelessness), co-morbidities (CPSS) and service utilization (CASA). T-test and chi-square comparisons will be used to detect baseline between-group differences.

The *primary exploratory outcome* of interest is depressive symptoms (measured by BDI-II); the *secondary outcome* is peer violence (CTS-2). Under Dr. Papandonatos' guidance, we will first calculate preliminary estimates of the between-groups differences in depressive symptoms (continuous) and peer violence (counts), with 95% confidence intervals, at 8- and 16-week follow-up assessments, adjusted for baseline values. An intent-to-treat approach (all patients randomized to intervention will be retained in analysis) will be used to address potential problems inherent in following only treatment completers and the potential for differential attrition across conditions.[140, 141] In cases of loss-to-follow-up, baseline observations will be carried forward.

Generalized linear mixed models (GLMM)[142, 143] that employ likelihood-based estimation approaches will then be used to evaluate changes in depressive symptoms and number of fight episodes at the 8-week and 16-week follow-ups. Intervention condition will be considered the primary predictor variable. Race and gender will be included as secondary predictors. We will control for baseline levels of the outcome variable (e.g. severity of baseline depressive symptoms and peer violence) as well as the linear and quadratic effects of time. We will also examine potential moderators of the intervention effect, including gender, race, and baseline coping skills. In GLMM, no missing data imputation will be employed, as the models produce consistent estimates in the presence of data missing-at-random.[144, 145] **Analyses will serve as a training activity.**

Potential Problems & Alternative Strategies: Parental involvement: According to pilot data, 99% of eligible adolescents seen in our ED are accompanied by a parent. We recognize the importance of parents in teens' mental health, but we have chosen not to include parents any further than the consent process, in order to focus on acceptability for adolescents,[146] and to increase feasibility and eventual disseminability. Difficulty completing in-person session during time in ED: My mentorship team has successfully completed multiple studies with 45-60 minute CBT- and MI-based interventions for teens in the ED. Enrollment biases: Patients who are more symptomatic or more comfortable with technology may be more likely to enroll. In our planned R01 we will correct for these characteristics by stratifying by baseline symptom severity, and by including technology use as a covariate; we will also adapt the intervention for Spanish speakers. Attrition of participants: Our study recruitment location has a strong track record in retaining our target population in long-term studies. I will conduct weekly meetings with staff to identify potential threats to participant retention. The native attraction of text-messaging to adolescents should help prevent fatigue from intervention use.[39, 147, 148] Although we anticipate 15-20% attrition based on past work, we believe that we can respond rapidly and effectively to any potential difficulties. Technology difficulties: Through the PI's foundation grant and Dr. Spirito's NIMH-funded R34, we have successfully piloted the text-message technology that we propose to use in this project. Cell phone concerns: Participants will be compensated for their monthly text-messaging plans. See **Human Subjects** for details on protection of confidential information, and for mechanism to regain contact in case of changed phone numbers.

14. PROTECTION OF HUMAN SUBJECTS

Summary: For this clinical study, all data collection sheets and computerized databases will use a unique numeric code to identify specific subjects. The code sheet will be kept in a locked file cabinet in Dr. Ranney's locked office, and on password protected files on secure hard drives owned by Dr. Ranney's institution. We intend to seek approval for this study from the human protection committees at Rhode Island Hospital; no study activities will be initiated without full institutional review board approval. All members of the research team have already completed training and received certification in Human Subjects Research Protection (CITI Program) and HIPAA regulations. They will continue to renew this training in compliance with Rhode Island Hospital and Brown University policies. Additionally, **a Certificate of Confidentiality will be obtained** for this study from NIH once IRB approval has been granted.

14a. Risks to the Subjects

14a.1. *Human Subjects Involvement and Characteristics:*

In Specific Aim 2, approximately 16 adolescents will participate in a series of open trials of the ED-based preventive intervention. In Specific Aim 3, the novel "ED+text" intervention will be studied in a randomized controlled pilot trial, with 50 participants in the "ED+text" arm and 50 participants in the enhanced usual care (EUC) arm. The ethnic and racial composition of the study group will be expected to represent that of the pediatric population seen in the Rhode Island Hospital ED, identified to be approximately 40% Hispanic and 25% black or African American by my own pilot study (data analysis in progress). Children aged 13 to 17 will be included in the study.

Inclusion Criteria. To recap what was described in Section 11c above: *Inclusion criteria for screening include:* being medically stable; mentally and physically able to assent; English-speaking; and having a parent present to consent. *Exclusion criteria for screening include* a chief complaint of sexual assault or child abuse; a chief complaint of acute suicidality or psychosis; or being in police custody. *Additional inclusion criteria for enrollment (in Aim 2 or Aim 3) include* a PHQ-9 score ≥ 5 and past-year peer violence (according to CTS2).

Potentially eligible participants will be **excluded** from enrollment if they or their parents do not consent to audio-taping of the in-ED session or if they meet criteria for severe depression (PHQ-9 > 20). Additionally, patients who are deemed (based on in-ED assessment by a clinician, after notification about a positive screen for suicidality) to need a psychiatric hospitalization will be ineligible.

Participants in Aim 1 may be eligible for Aim 2, but will be restricted to less than 1/3 of the Aim 2 sample. Participants will be ineligible for Aim 3 if they have participated in Aims 1 or 2.

Rationale for including special classes of subjects. This research will involve children between the ages of 13 and 17 inclusive. The age range is dictated by the prior research showing elevated risk for depression and peer violence among teens in this age range. It is of utmost importance to study this "vulnerable population" because they are an understudied population; a population at high risk of negative outcomes; a population with limited access to and use of traditional mental health services; and a population with high possible benefits if effective, accessible preventive services can be developed.

All ethnicities and races will be equitably included. Only English-speaking patients will be eligible for two reasons. First, our previous and ongoing studies show that the vast majority of Hispanic adolescents speak fluent English.[9, 149, 150] Second, due to budgetary constraints inherent in this training grant, it would be difficult to fund a bilingual interventionist and translation of all materials into Spanish.

14a.2. *Sources of Materials:*

Materials will be collected from adolescent participants in the study. Data will be collected from participants primarily using a tablet laptop computer and audio-taped interviews; some de-identified data may be collected through secure text messaging services in Aims 2 and 3. Minimal data will be collected from Medhost and Lifelinks regarding participants' ED utilization and hospital admissions after initiation of the study. Data that are obtained specifically for research purposes will be collected only with written assent from youth and written consent from a parent or guardian. Minimal clinical data will be collected on patients that refuse to participate in the study, on patients that the research assistants fail to approach about the study, and on patients that are excluded from the study. This data will be obtained from de-identified emergency department medical records, to assess characteristics of patients not approached or who refuse participation.

Linkages to subjects and access to subject identities. For each stage of the research, participant names and contact information will be maintained in a secure, password-protected recruitment/enrollment database. Once individuals enroll in the study, names will be linked to participant ID number *only* in this database, which will be kept in a restricted access folder on a secure server. This file will be assigned a code name unrelated

to the name of the study. Baseline, follow-up, and focus group data will be coded according to participant ID number, and will contain no protected health information.

To facilitate scheduling the 8 week follow-up interview during Aim 2 only, participants *may* choose to participate in the YouCanBookMe Limited scheduling service. This is a voluntary third party, encrypted service that schedules appointments using the participant's email address, first initial, and last initial. The data will only be scanned by the system for the purposes of scheduling and rescheduling the participant's follow-up interview. Once the scheduled interview is complete, members of the research team will erase the participant's email from the YouCanBookMe encrypted server. While this information will be kept in confidence by the research team, and while YouCanBookMe assures that it will not access the information for any promotional purpose, we cannot prevent outside forced entrance into the YouCanBookMe server.

Signed consent and assent forms will be kept in a double-locked file cabinet in the PI's locked office, separate from any other project data. Once data collection for each stage of the study is completed, the corresponding recruitment/enrollment database will be deleted as it is unnecessary to maintain the link between participant identity and study data. All information collected as part of this study will be accessible only to research staff that has completed mandatory training in the protection of human subjects.

Data collection. Data will be collected solely for the purposes of this research project. All information collected as part of this study will be obtained only by research staff employed by the project. Data sources include: 1) participants' responses to baseline and follow-up questionnaires, 2) confidential audio-taped semi-structured interviews, and 3) participants' responses to text-messages. In Aim 2, data will be collected at screening, baseline and after the intervention. In Aim 3, data will be collected at screening, baseline, 8 weeks post-enrollment, and 16 weeks post-enrollment.

14a.3. *Potential Risks:*

Every effort will be made to ensure that study participants are protected from risks. The risks are as follows: 1) potential coercion, 2) loss of confidentiality, 3) emotional discomfort during the assessment and/or program sessions, and 4) further violence if an assailant is made aware of program involvement. The protection against each risk is described in detail in **Section 14b.2, below**.

14b. Adequacy of Protection Against Risks

14b.1. *Recruitment and Informed Consent:*

Screening and Consent. A research assistant (RA) will be present in Hasbro Children's ED on randomly selected shifts (selection weighted according to patient volume). All patients between ages 13 and 17 will be pre-screened by the RA. If the patient is triaged as stable, and is not presenting for with a chief complaint of suicidality, psychosis, sexual assault, or child abuse, the RA will approach the patient and his/her family once the patient is put in a private treatment room. After reading a script to the parent and child, verbal consent/assent will be obtained from the parent/legal guardian and the child. Then, youth will complete a computerized screening survey. The adolescent and his/her parent will be informed that the adolescent's answers to study questions may be used to determine their eligibility for a research program. After completion of assent/consent, the teen will then be administered the screening questionnaire, including PHQ-9, and CTS-2. Additionally, to reflect my experience with 2 different screening processes during my pilot grant, we will administer additional questions drawn from Add Health, YRBS, and other relevant materials about other behaviors (which I and my mentors have found increases participant honesty on all questions; in studies where we only administer the screening questions of interest, rates of self-report have decreased significantly). All participants will be able to choose a small gift (worth \$1-2) as compensation for their time.

If an adolescent screens positive for mild-to-moderate depressive symptoms (PHQ-9 between 5 and 20) and past-year peer violence, s/he will be informed that they are eligible for the research program. Adolescents and their parents will be informed that their responses to screening questionnaire indicate that they are eligible for a program to help build mental health and prevent fights. Screened participants who agree to be part of the study will complete an additional *written* assent/consent form for Aims 2 and 3.

All individuals who agree to participate in the screening will be given referral information for a variety of community resources including community mental health services and violence prevention organizations.

During recruitment, research staff will inform the subject of the general nature of the study, their privacy rights, expectations for their participation, the voluntary nature of their participation, and that their participation can be withdrawn at any time. Participants will be assured that refusal to participate will not affect their care in any way. At all times, research staff will make explicit the voluntary nature of the subjects' participation as well as potential situations for breaking confidentiality. Recruitment procedures will be HIPAA compliant and have been IRB approved in past studies.

Referrals. All participants in the screening will receive a handout of mental health and violence prevention resources. If an adolescent screens positive for severe depressive symptoms at any time during the study, regardless of eligibility for the study, the RA will discuss the score with the family, notify the attending pediatric emergency physician, and offer to contact the adolescent's pediatrician.

If an adolescent discloses suicidality or if the patient's family so desires, the RA will alert the patient's clinician (if appropriate) who will immediately initiate a psychiatric evaluation in the ED, or will contact the patient and his/her parent if disclosure occurs outside of the ED. (See "Mandatory Reporting & Crisis Management," below). If a patient is deemed to need psychiatric hospitalization based on the screening, they will be withdrawn from the study.

Assessments and Remuneration. In **Aim 2**, participants will complete a baseline assessment, an 8-week follow-up assessment and interview; in **Aim 3**, participants will complete a baseline assessment, an 8-week interview and an 8-week and 16-week computerized follow-up assessment. Follow-up assessments will take place online, on the telephone, or in private rooms at the PI's departmental office (separate from the ED) where privacy and confidentiality can be maintained (i.e., making sure no one can overhear the conversation).

Participants will be remunerated with a gift worth ~\$1-2 for the screening survey. In **Aim 2**, participants will be compensated \$25 after completing the baseline assessment and in-ED intervention, \$10/month for text-messaging plans, an additional \$5 incentive if they complete the 8-week follow-up survey *prior* to the 8-week follow-up interview, and \$50 for completing the 8-week follow-up. In **Aim 3**, participants will be remunerated \$25 after completing the baseline assessment and in-ED intervention, \$40 for completing the 8-week follow-up, \$50 for 16-week follow-up, and \$10/month for text-messaging plans. Participants will also receive \$5.00 for notifying us of any address/telephone changes, and an additional \$5 for completing the 8-week and 16-week surveys *prior* to their due date.

14b.2. *Protection Against Risk*

Risk 1): Potential Coercion.

The risk of potential coercion will be minimized by following standard procedures for obtaining the informed consent from parents and assent from teens. Study personnel will fully explain the study procedures, risks, benefits, and alternatives to teens and their parents. Participants and their parents will also be reminded that study participation is voluntary and that refusing to participate or withdrawing from the study at any time will not result in any negative consequences on their care.

Risk 2): Confidentiality

Potential risk will be minimized by strictly adhering to the guidelines for research outlined by the Lifespan IRB, Rhode Island state law, the Federal Health Insurance Portability and Accountability Act of 1996 and its regulations ("HIPAA"), and the DHHS Federal Policy for the Protection of Human Subjects (45 CFR Part 46 Subpart D). In particular, the risk of loss of confidentiality will be minimized by the following specific procedures:

UNIVERSAL:

- (a) All research staff will sign a pledge of confidentiality and will understand that violation of confidentiality is reason for dismissal. Training of staff includes information about the importance of confidentiality and techniques to maintain confidentiality of all information reported by research participants.
- (b) Any collected information will be referenced only by participant ID #.
- (c) The only list connecting the participant ID # to the participants' names will be kept in a password-protected folder on the PI's password-protected computer (which is owned by the hospital, and which is on the hospital's HIPAA-secured research server). This list will be deleted as soon as each phase of the study is completed.
- (d) The consent forms and research materials will be kept in separate double-locked cabinets in the PI's locked office.
- (e) All computerized information will be maintained on password protected, HIPAA-compliant computers owned by the PI's hospital which use only HIPAA-compliant research server.
- (f) All computerized surveys will be completed using REDCAP.
- (g) No names, only identification codes, will be used in presenting data in lectures, seminars, and papers.

SEMI-STRUCTURED INTERVIEWS:

- (a) Semi-structured interviews will take place in a private room at the site of the participant's choosing (e.g. ED, PI's departmental office, library, telephone) where confidentiality can be assured

- (b) Ground rules will be set at the beginning of the interviews, instructing participants to not identify themselves or others by name, and emphasizing the confidentiality of everything discussed [with the exception of suicidality/homicidality/child abuse].
- (c) Participants will be not be referred to by name on the audiotapes.
- (d) Prior to transcription, the digital tapes will be kept in a password protected format on a password-protected Lifespan hard-drive accessible only to the PI and the RA. The recordings will be maintained for 5 years in compliance with human subjects policies.
- (f) Transcripts will be reviewed only by the PI and her research team.

TEXT-MESSAGING:

- (a) All text-messages will be sent using a secure text messaging system (hosted by Reify Health, a company that we have worked with in the past for similar projects) that will not store data remotely; the text-message server is located behind a research-compliant firewall.
- (b) Text-message data will be maintained in a password-protected, restricted-access hard drive in the Department of Emergency Medicine.
- (c) Text-message data will be monitored exclusively by the PI and her research team.

Participant confidentiality will be breached only to protect the safety and welfare of research participants and only in accordance with state and federal law. The exceptions to confidentiality include if the adolescent reports suicidality, homicidal thoughts, or that he/she is the victim of child abuse or neglect. If the adolescent reports suicidality or homicidality, parents will be notified, and an emergency psychiatric evaluation for inpatient hospitalization will be facilitated with the Pediatric Emergency Psychiatric Service at Rhode Island Hospital. If necessary, authorities will be notified. If child abuse or neglect is reported, a report will immediately be filed with the Department of Children, Youth and Families. This exception to breaking confidentiality – the case where a participant reveals child abuse, suicidality, or homicidality – will be explained in detail to both participants and parents prior to completing the assent/consent.

Finally, information collected in this research study will not be available to clinicians, parents, or to other researchers. All data will be collected specifically for use on this project.

Risk 3) Emotional Discomfort

Of note, members of the proposed mentorship team have substantial prior clinical and research experience with high-risk populations as evidenced through their biographical sketches. Dr. Spirito has extensive clinical and research experience developing interventions for depressed, suicidal, and alcohol-abusing adolescents. Dr. Cunningham has extensive clinical and research experience with adolescent violence and substance abuse prevention.

Parental distress: If parents report feelings of distress as a result of being notified that their child is eligible for this research project, clinical resources will be offered. These include referrals for mental health counseling and information about violence hotlines and local community organizations.

Assessments: The assessment instruments are commonly used in research and clinical practice. We will minimize distress by presenting questions/program techniques in a supportive manner, assuring participants that they may refuse to answer questions that make them uncomfortable, and reminding them that they may terminate the assessment and/or intervention at any time.

Although there is extremely low risk of an adverse reaction to the screening survey or qualitative interviews (and, in fact, benefits to participation in similar research have been demonstrated),[151] all potential participants will be provided with a list of community resources at the same time that they are approached by the RA about participation in the study. To minimize negative consequences from the screening survey or semi-structured interviews, the RA will be trained to immediately terminate the assessment and alert the PI and the patient's clinician in the case that the subject demonstrates physical or psychological instability.

Additionally, on completion of baseline and follow-up assessments, the RA will be alerted by the computer if a participant has reported suicidality or severe depressive symptoms. The RA will contact Dr. Ranney or Dr. Spirito at that time, and the teen will be further evaluated for risk of harm to self or others. To the extent that the adolescent is determined to be a risk to himself/herself or others, the parent will be notified and a referral to an emergency evaluation with the Pediatric Emergency Psychiatric Service at Rhode Island Hospital will be made.

Regarding the text-messaging component of the study, text message assessments do NOT induce depression despite repeated assessments of negative mood.[152] Momentary assessments have also been shown to be acceptable, feasible, and appropriate when used to ask sensitive assessments (e.g., suicidality,

mood, alcohol and substance use, eating disorders, and violence) among a variety of populations, including school-age adolescents, schizophrenics, the homeless, drug addicts, recently hospitalized suicidal patients, and college students.[153-163]

Text-message Data: Participants and parents will be explicitly instructed during the consent process that no one will be monitoring text-message data in real time. In the case of a crisis situation, the adolescent should call the provided crisis hotline number or the PI's phone number rather than text the program. Nonetheless, some participants may misinterpret these guidelines. Hence, text-message data will be reviewed regularly by the PI and her mentorship team. The software will also be designed to send participants a message that directs them to a crisis phone number, if data that is not expected by the text-message algorithm is received.

OF NOTE: This protocol mirrors that used by other text-message-based interventions for mental health and other potentially sensitive behaviors/disorders (e.g. [39, 104, 164-168]), including one that is currently ongoing with Dr. Spirito and Dr. Ranney at Brown University (for suicidal adolescents). Moreover, as the text messages include *no* PHI and *no* sensitive information regarding diagnoses, they easily meet or exceed HIPAA regulatory standards [169].

Ongoing Safeguards: Due to the association between violence and mental health sequelae, it is possible that some participants will experience psychiatric symptoms during the course of the program that may warrant mental health care. In order to minimize the risk of mental health deterioration, all subjects may receive mental health treatment at any time during the study. Clinical need will determine whether it is appropriate for the participant to continue in the study.

The PI's email and phone number, and a crisis hotline number, will be provided to every participant. The participant will be instructed to call the PI in case of any problems with the study, or if s/he has an immediate mental health crisis. S/he will be encouraged to call the crisis number, or 911, as well, if in need of immediate mental health services. The participant will also be provided with a wallet card explaining why she is responding to text messages, in case s/he is asked by a teacher or employer.

If a participant is identified as needing mental health treatment, the PI or her mentors will contact the participant individually for further assessment, and will notify the participants' parents of any clinical needs. Evaluation by the Pediatric Emergency Psychiatric Service at Rhode Island Hospital will be initiated on the PI's discretion at any sign of suicidality, homicidality, or child abuse. Suicidal or homicidal attempts or completions, and hospitalizations, will be monitored as serious adverse events, and will be reported our hospital's IRB according to our Data Safety & Monitoring Plan. If a patient is deemed to need psychiatric hospitalization based on the screening, they will be withdrawn from the study.

That said, we will be clear during the assent/consent process with the parents and child that we will not be conducting ongoing, real-time monitoring of the text messaging. We will emphasize that if a child needs immediate assistance, s/he or his/her parents should call 911, the child's doctor, or call one of the crisis numbers provided.

By notifying parents/guardians of the teen's risk, providing parents with the information they need to monitor their child's risk, and by conducting ongoing monitoring of the safety of the teens, **we are maintaining the highest ethical standard for our participants.**

Risk 4) Violence

The emergence of increased aggression is important and needs to be monitored. If a subject discloses increasing frequency of involvement in violence, severe physical injury, homicidality, or high risk of retaliatory violence she will be contacted by the PI for further evaluation. Although no questions will be specifically asked about child abuse or sexual assault during the study, the staff will be trained to assess and respond to participants for whom these issues arise.

Risk 5) Mandatory Reporting and Crisis Management:

As described above and in the Data Safety & Monitoring Plan, below, all instances of potential mental health or violence risks, staff will follow a written protocol regarding reporting these incidents to Dr. Ranney or Spirito based on call schedule, and will take appropriate referral or legal action as indicated. In addition, the IRB board at Rhode Island Hospital will be informed of any incidents. Drs. Ranney and Spirito will be responsible for providing training to all research staff who are conducting assessments with participants regarding procedures for identifying, managing, and responding appropriately to acute warning signs of distress that could occur as a result of the survey. Such strategies include maintaining an empathic response, acknowledging the distress through reflection, and eliciting or encouraging use of relaxation and cognitive

calming strategies. Staff will receive training in crisis assessment and management procedures in the event that participants reveal suicidal and/or homicidal ideation, child physical/sexual abuse, or concerns about safety. Drs. Ranney (M.D., Emergency Medicine) and Spirito (Ph.D., Clinical Psychology) will be responsible for providing regular supervision to research staff who have direct contact with patients including crisis procedures for suicide and homicide risk and clinical assessment and referral procedures for participants who are a danger to themselves or others. Supervision will focus on procedures for managing issues that could arise given the patient population, including potential crisis situations and/or adverse events.

Our crisis management procedures mirror those used by the Rhode Island Hospital Department of Psychiatry and Emergency Medicine clinical services. Dr. Ranney has successfully used these safety protocols in studies at the proposed study site.

It is possible that situations will arise in which researchers are provided with information by children or families which they are legally and ethically obligated to disclose (e.g., suicidal or homicidal intent, harsh disciplinary practices, sexual abuse). All participants are informed in advance through the process of informed consent of the legal and ethical obligations of study staff should these issues arise. The consent and assent forms will clearly describe times when confidentiality must be broken, i.e., suicidality, homicidal thoughts, and a report of child physical or sexual abuse. Participant confidentiality will be breached only to protect the safety and welfare of research participants and only in accordance with state and federal law.

As additional safeguards, **if a child reveals substantial mental health problems, such as suicidal ideation/attempts, homicidal ideation, or clinical deterioration, or if such problems are identified during the course of the study**, the child will be evaluated as soon as possible, by the PI, the primary mentor, and (if indicated) the on-call RIH psychiatric crisis team, to make a clinical determination about whether the child requires hospitalization or other clinical services. The primary mentor is a licensed child clinical psychologist and has training and experience in intervening in similar crisis situations. Project staff will carry cell phones with them during all participant contact and will be instructed to contact the PI (who is on call and always carries a phone) immediately to inform her of any clinical emergency. Additionally, Dr. Spirito and Dr. Ranney will carefully monitor the symptom progression of all participants. **If a patient is deemed to need psychiatric hospitalization based on the screening, they will be withdrawn from the study.**

If any mental health problems are reported or identified at the time of the follow-up and the family is not in treatment, appropriate referral for psychological intervention will be arranged.

Whenever possible, study staff will handle these situations therapeutically. For example, if time limits and safety concerns allow, parents will be informed in advance and provided the opportunity to participate in the mandated report process. Research staff will contact the PI who will be responsible for any on-site clinical decision-making.

Over the past 10 years, in several ED studies conducted by myself and my mentors, staff have encountered only 2 cases of harm to others that involved crisis management procedures leading to breaching confidentiality and involving authorities, less than 10 cases of child abuse requiring mandatory reporting to the police, and regular suicide risk assessments (~10 participants per study, per month).

14c. Potential benefits of the proposed research to the subjects and others:

Participation in this project could potentially benefit participants in a few important ways. The instruments used to obtain information in this study are commonly used in clinical and research practice but may invoke some emotional discomfort. Efforts will be made to minimize this discomfort by presenting questions in a supportive manner, assuring participants that they may refuse to answer questions that make them uncomfortable, and may terminate participation in the study at any time. It is also possible that the questions or assessments themselves may be beneficial to all participants by asking them to review their affect and peer violence. The screening and baseline assessments may therefore act as a very minimal intervention (as could any study with interviews regarding risky behaviors). Indeed, study participants in Dr. Spirito's and Dr. Cunningham's previous, similar studies have commented that they have found the questions to be helpful.

Additionally, we hope that our intervention will be successful in preventing/reducing depressive symptoms, and possibly peer violence, in our subject population. The intervention offers the possibility of a relatively low-resource, highly-disseminable preventive intervention for a needy population. We therefore think that the clear examination of these questions outweighs the previously mentioned risks.

Because all youth participating in the study self-report depressive symptoms and peer violence, we felt it was necessary to enhance usual care (typically no violence-prevention or mental health information is routinely provided during the ED visit) for all youth. Thus, all youth participating in screening will review a health information brochure, with referral information for mental health problems including suicide hotlines, substance

use, and violence prevention and treatment services, anger management, etc. This pamphlet will be similar in style and content to that used in my mentors' prior work. In addition, as described above, participants that meet criteria for severe depressive symptoms or suicidality on the screening survey will be offered a clinical assessment and individualized referral in the ED, which exceeds the current standard of care.

In sum, potential benefits for the research far outweigh the risks for the participants. The proposed research also has significant benefits for society in general, as described in **Importance of the Knowledge to be Gained** (14d, below).

14d. Importance of the Knowledge to be Gained

Given the high rates of both depression and peer violence among youth; the interdependence of these problems; the individual and societal cost of violence and its mental health consequences; the fact that most of these teens use the ED as their primary source of care; and these teens' lack of access to traditional mental health services; the development of effective targeted interventions are clearly needed. Given the paucity of accessible existing interventions, the knowledge to be gained from this research is significant. The risks to participants are reasonable in relation to the importance of this knowledge to be gained.

14e. Vertebrate animals:

n/a

14f. Data and Safety Monitoring Plan

To address the NIH policy for Data and Safety Monitoring, the PI (Dr. Ranney) and her mentorship team have developed a system for oversight of the proposed study and its participants. The Data and Safety Monitoring Plan for this application will begin by implementing standard procedures for day-to-day monitoring of the study. The Principal Investigator, Dr. Ranney, will be responsible for monitoring the data quality and safety. As already noted above, all research projects involving human participants at Rhode Island Hospital, including this proposed study, require approvals from the Rhode Island Hospital (RIH)/Lifespan Institutional Review Board (IRB). In addition, because of the sensitive nature of the data being collected, a Certificate of Confidentiality will be obtained for this study from the National Institute of Health (NIH).

Dr. Ranney will ensure that all relevant IRB policies, procedures and stipulations are being followed. Dr. Ranney also will be responsible for ensuring that other investigators and project staff adhere to the RIH IRB policies including the following: (1) All participants in the full Aim 2 and Aim 3 studies will understand, agree to, and sign a written assent form (and consent from parent/guardian) before participating; (2) Strict adherence to a participant's right to withdraw or refuse to answer questions will be maintained; (3) All interviews and assessments will be completely confidential and no names will be associated with the data; (4) Consent forms and identifying information will be kept separate from the actual participant data; (5) All identifying information (consents, tracking data) will be kept locked at all times and computer files will be saved with passwords; and (6) Participants will be informed in writing in the consent form on how to contact the PI, the study coordinator, and IRB office with any questions and/or concerns.

Weekly meetings with Dr. Spirito will be conducted to evaluate the progress of the trial and to review data quality, recruitment, study retention, and examine other factors that may affect outcome. Participant experiences and the rates of adverse events will also be reviewed to determine any changes in participant risk. Dr. Ranney will report any adverse events that are observed to the IRB within one week of occurrence, and to NIMH in our annual report. Serious adverse events (SAEs) will be reported to the IRB within 2 work days of our receipt of information regarding the event; if deemed to require a change in protocol, NIMH will also be notified. Reports of changes or amendments to the protocol in general must be requested first in writing to the IRB, which then will grant or deny permission to make the requested change or amendment in protocol.

Finally, if significant homicidal, suicidal, or mental health risks occur during the study period, the participant's parent(s) will be notified, as described in **14b.2. Protection against risks** (above), and evaluation by the Rhode Island Hospital crisis team will be immediately initiated to determine whether hospitalization is needed.

In the event that a research participant either withdraws from the study or the investigator decides to discontinue a research participant due to SAE, the research participant will be monitored by the investigator via ongoing status assessment until either a resolution is reached (i.e. the problem requiring hospitalization has resolved or stabilized with no further changes expected), the SAE is determined to be clearly unrelated to the study intervention, or the SAE results in death.

Independent evaluators from the Department of Emergency Medicine and the Department of Psychiatry will be incorporated into the existing Data Safety & Monitoring Board (DSMB) in the Department of Emergency

Medicine, to assist with study-specific ongoing monitoring of data. These additional members will include Dr. James Linakis (pediatric emergency physician and chair of the Lifespan IRB, Dept of EM, Brown University); and Dr. Michael J. Mello (emergency physician and researcher in the overlap between alcohol abuse and injury, Dept of EM, Brown University). This enhanced Dept of EM DSMB, as an adjunct to the IRB, will have control and independence in offering recommendation arising from participant concerns or adverse events related to our study, or stopping the study for the benefit of our participants. This DSMB will convene once yearly, and as needed, and produce a written report. This report will be sent to the Lifespan IRB as well as to the project officer at NIMH. The DSMB will review all serious or unexpected adverse events to determine any changes in participant risk and provide recommendations.

Participants will only be identified by number during review of study progress by the DSMB. In the event that confidentiality must be breached, only the PI and Primary Mentors would be informed of identifying information in order to report to the appropriate authorities or health care providers. In the event that a conflict of interest within the DSMB is identified, the DSMB will disclose the matter to the Lifespan IRB. The DSMB will provide recommendations to the PI on how to resolve the conflict of interest, and the PI will report and document the action to the Lifespan IRB.

14g. Educational Training

Since October 1, 2001, Lifespan has required that researchers and IRB members read Protecting Study Volunteers in Research (Dunn & Chadwick) and complete the related exam. This process has served as initial certification between 10/2001 and 5/2005. In June, 2005, the Office of Research Administration contracted with CITI, a Collaborative Institutional (modular) Training Initiative program, for our Human Subjects protection and HIPAA training for all research personnel. Currently this program offers our researchers a basic human subject's protection course as well as a refresher course which we require every three years. Documentation of successful completion is automatically generated and should be printed directly by the researcher. For further information regarding Lifespan's Human Subject's Protection course go to: <http://www.lifespan.org/research/IRB/MandatoryEdguidance.asp>

Additional and continuing education opportunities for clinical researchers include the Office of Research Administration newsletter that is circulated to > 900 recipients every 6 weeks. Relevant information concerning research review is available on the ORA web page at www2.lifespan.org/research/. In addition to standard institutional research information, the web page contains links to other sites such as CenterWatch, NIH, PRIM&R/ARENA.

Finally, the PI will participate in the training in the Responsible Conduct of Research detailed in Section 5, above.

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