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Advancing Suicide Intervention Strategies for Teens (ASSIST): study protocol for a multisite randomised controlled trial

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ABSTRACT

Introduction Brief interventions that reduce suicide risk following youth's experience with acute care due to suicidality are needed.

Methods and analysis The study will use a three-arm randomised controlled trial designed to test the effectiveness of the Safety Planning Intervention with structured follow-up (SPI+) and the Collaborative Assessment and Management of Suicidality (CAMS) compared with enhanced usual care. The primary outcomes measure will be suicidal events, defined as death by suicide, attempted suicide, preparatory acts toward imminent suicidal behaviour or suicidal ideation resulting in a change in emergency evaluation or inpatient admission. Secondary measures will be the number of suicide attempts and severity of suicidal ideation. The experimental interventions, SPI+ and CAMS, consist of up to eight sessions over approximately 8 weeks that are designed to manage (SPI+) or treat (CAMS) patient-identified 'drivers' of suicidal thoughts and behaviours. Mechanisms and moderators of change will be evaluated to understand treatment impacts.

Ethics and dissemination This study has been approved by the Seattle Children's Institutional Review Board and is monitored by external agencies including the University of Washington Institute for Translational Health Sciences, and a National Institute of Mental Health (NIMH)-appointed Data Safety and Monitoring Board. Trial results will help establish evidence towards safe and effective treatment strategies for youth transitioning from acute to outpatient care due to a suicidal crisis. The data will be shared with the NIMH Data Archives and disseminated through publications and conferences.

Trial registration number NCT05078970.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Randomised controlled trial designed to maximise and balance internal and external validity.
⇒ Internal validity strategies include single-blind assessment, adherence review of treatment conditions and a minimisation randomisation strategy.
⇒ External validity is maximised by using real-world settings and practicing clinicians from two paediatric hospitals.
⇒ The study seeks to recruit participants that reflect the communities that the paediatric hospitals serve, however, this may not generalise to other populations.
⇒ Due to power, the experimental interventions will not be compared with one another, but to treatment as usual.

INTRODUCTION

Suicide is the second leading cause of death among adolescents in the USA, and despite prevention efforts, the past two decades have seen notable increases in youth suicide deaths. Suicidal thoughts and behaviours (STBs) increase dramatically during adolescence, with recent survey data suggesting 3.3 million adolescents reported serious thoughts of suicide in the past year, and 892 000 youth attempted suicide.[1] STBs represent a major public health problem; they are recurrent, lead to substantial healthcare utilisation and increase risk for death by suicide.

There is a paucity of interventions that are considered 'well-established' for reducing adolescent suicide risk. The only psychotherapy approach with replicated effects for reducing STBs is full-model dialectical behaviour therapy (DBT).[2–4] Additional intervention options to promote long-term outcomes are needed. While efforts have been made to improve access to DBT, the fact remains that even with DBT, many youths drop out of treatment and report ongoing STB even after an initial course of treatment.[5] Evidence in support of other promising treatment approaches (eg, cognitive behavioral therapy, mentalisation, attachment-based family therapy) is emerging, with a recent meta-analysis suggesting that interventions with a strong family component and with

multiple treatment sessions were associated with a significant reduction of ideation and suicide attempts, as opposed to studies with weak family involvement and/or single session interventions.[5 6] However, this meta-analysis finding is complicated by the fact that several family therapy trials and meta-analyses[7 8] have not demonstrated reductions in key STB outcomes compared with usual care (UC) or non-directive supportive therapy. Consequently, there is a pressing need to have a scientific evaluation of common elements that characterise quality improvement for suicide-specific healthcare including brief interventions which provide: (1) direct prioritisation of STB in therapy, (2) continuous risk assessment and patient monitoring on suicide risk indicators and (3) safety planning.[9] Two brief interventions have been piloted with adolescents and are well-established with adults—the Safety Planning Intervention with follow-up (SPI+) and the Collaborative Assessment and Management of Suicidality (CAMS).

SPI+[10–12] has demonstrated efficacy in reducing suicide attempts and greater treatment engagement compared with UC for military and veteran populations. Pilot feasibility and acceptability in adolescent settings with adolescents has also been demonstrated.[13–15] SPI has six key steps to achieve a personalised prevention plan: (1) identify personalised warning signs for a suicidal crisis, (2) determine internal coping strategies that distract from STB, (3) identify supportive people and social settings that can distract from STB, (4) identify the adults who can help provide support during a suicidal crisis, (5) list mental healthcare and urgent care contacts to use for professional care during a suicidal crisis and (6) identify ways to make the environment safer through reducing access to lethal means. Contacts continue to help support risk assessment, durability of the SPI and connection to treatment. An additional follow-up component (+) includes weekly telephone calls to a review of mood, assessment of suicide risk, problem solving, safety plan use and linkage engagement to outpatient care. The use of SPI+ with adolescent populations has also demonstrated high levels of acceptability, feasibility and is likely effective as youth in pilot SPI+ intervention trials report higher self-efficacy to refrain from suicidal behaviour (d=0.25), higher readiness for treatment (d=0.52) and use of safety plan (d=0.26) compared with those in treatment as usual.[13]

CAMS is an efficacious, suicide-focused intervention framework to reduce suicidal ideation.[16] CAMS guides clinicians to engage, assess, and treat STBs providing a structure to deliver the common elements of suicide-focused treatment.[16] CAMS is designed to enhance the therapeutic alliance and increase motivation in a joint effort to effectively engage the patient to collaboratively target and treat the suicidal risk. The structure of CAMS has broad appeal and scalability as clinicians can continue to use their own theoretical approach to treat the patient-identified 'drivers' of STBs identified through the CAMS framework, making the approach amenable to broader uptake by clinicians. Replicated trials demonstrate that CAMS used with adults is associated with improvements in overall symptom distress, rapid reduction in suicidal ideation and changes in the ability to manage suicidal thoughts and behaviors while maintaining behavioral stability (ie, suicide cognitions; ratio of wish to live vs wish to die ratings; implicit associations with suicide) over the course of clinical care.[17–19] Further, individuals treated with CAMS report higher satisfaction, better treatment retention and reduced medical healthcare utilisation compared with enhanced treatment as usual.

Pilot work with CAMS for adolescents is also promising. The psychometric validation of the Suicide Status Form (SSF)—the core CAMS assessment tool—indicates that it is valid for use with adolescents and does not need to be adapted or modified for this age group.[20] In addition, our preliminary data indicate that CAMS is an effective and efficient intervention for reducing adolescent suicide risk.[21] Specifically, in our sample of suicidal adolescents aged 13–17, 54.5% of youth resolved their STBs in 8 weeks, similar to the response rates obtained in adult populations and other well-established interventions for self-injury (ie, in the adolescent DBT trial 54.2% of youth had no injury at the end of the intervention).[20] The importance of this study is further underscored given that CAMS and SPI+ interventions have been deployed with adolescents in response to clinical need, without a large-scale, controlled trial to evaluate their effectiveness with youth and guide widespread practice.

Aims

The overall objective of this three-arm randomised controlled trial (RCT) is to evaluate the clinical effectiveness of SPI+ and CAMS compared with UC among adolescents aged 11–17 years admitted to acute care for STBs. SPI+ and CAMS encourage suicide-specific management elements and linkage to care. In addition to targeting STB following discharge, these treatments may provide a framework for the transitional services needed following acute-phase treatment to promote adherence to clinical recommendations, continuity of care and reduce suicide risk over a 1-year period. The primary outcomes investigated will be suicidal events (death by suicide, attempted suicide, preparatory acts toward imminent suicidal behaviour or suicidal ideation resulting in an emergency or inpatient care) as well as the differential impact of the interventions on STBs. Table 1 outlines the aims and primary endpoints. We will evaluate target engagement resulting in reduced STBs and explore moderating effects for adolescents. Based on extant literature, SPI+ is hypothesised to result in increased self-efficacy, whereas CAMS is hypothesised to reduce suicide-specific attentional biases.

METHOD

Design

This is a phase two, three-arm RCT to evaluate the impact effectiveness of two interventions compared with UC.

Table 1 Primary aims and endpoints

Objectives	Endpoints	Justification for endpoints
Primary		
Test the relative effectiveness of two interventions SPI+ and CAMS compared with usual care.	Suicidal events at 12 months	The primary outcome is suicidal events which includes death by suicide, attempted suicide, preparatory acts toward imminent, suicidal behaviour or suicidal ideation resulting in an emergency evaluation as measured by the C-SSRS.
Evaluate if SPI+ is superior to CAMS in decreasing suicide attempts over 1 year.	Suicide attempts at 12 months as measured by the C-SSRS	To provide a more fine-grained analysis of impact on specific suicide risk outcomes, we have selected these two outcomes based on initial data with adults.
Evaluate if CAMS is superior to SPI+ in decreasing suicidal thoughts over 1 year	Suicidal thoughts at 12 months as measured by Suicidal Ideation Questionnaire, Jr	
Analyse the mechanisms of change	Suicidal events at 12 months	
Exploratory		
Analyse the moderators of treatment response	Suicidal events at 12 months	

*C-SSRS: Columbia Suicide Severity Rating Scale
CAMS, Collaborative Assessment and Management of Suicidality; SPI+, Safety Planning Intervention with follow-up.

Participants will be randomised in a 1:1:1 ratio to (1) SPI+, (2) CAMS or (3) enhanced UC. Figure 1 highlights the study design. Study start and end dates are 9 August 2021 to 31 July 2026.

Participants

Youth

A total of 306 youth, ages 11–17, who have been admitted to acute care (defined as emergency, inpatient medical or inpatient psychiatric care) due to STB at Seattle Children's or Nationwide Children's academic medical centres will be enrolled for the study. To be eligible, youth must also have a past-month Suicidal Ideation Questionnaire-Jr. (SIQ-JR) score ≥31 (clinical cut-off), consent/assent to study procedures and have a parent/guardian/caregiver willing to consent and participate. Youth are excluded if medical record review indicates the presence of psychosis, intellectual disability, autism spectrum disorder, eating disorder with unstable vitals, limited English proficiency that would interfere with the ability to complete study assessments, or unwillingness to participate.

For planning purposes, we propose randomising 306 youth participants with 102 randomised per treatment group. Power estimates were generated with the PROC POWER in SAS V.9.4. The sample size in the present design was selected to achieve power of 0.80 for the primary treatment effect on suicidal events (Hypothesis 1). Data form is count. Our first power calculation is based on comparison of CAMS/SPI+ compared with UC on any suicidal event. We estimate that a sample selected for STB in acute care settings at baseline will have an approximate 45% rate of suicidal events over the following year. In addition, we consider a 50% reduction in suicidal events to be a clinically meaningful reduction, as well as a benchmark that recent behavioural interventions for suicide have achieved.[4] Using Stroup's formula for count data,[22] power calculations are based on using a negative binomial model to account for overdispersion (overdispersion factor set to 0.13), we use the mean of events in UC per McCauley and colleagues with a mean post-baseline of 5.9. With the overdispersion parameter set to 0.13, the variance is approximately doubled the mean; therefore violating the equidispersion assumption of standard Poisson models. We cautiously set a 20% reduction in mean suicidal events for CAMS or SPI+. Stroup's power formula yields 93% power with an alpha=0.025.[22] Accounting for up to 20% missing data/attrition, we will still have up to 86% power.

Clinicians

Clinicians are mental health providers from Seattle Children's or Nationwide Children's hospital settings. To be eligible, clinicians must provide behavioural health services to youth, attend a 3-hour training and weekly consultation meetings. Clinicians provided informed consent when they agreed to participate. Adherence was measured in both CAMS and SPI+ conditions for the first session for a clinician and a random selection of subsequent sessions. Clinicians may only provide treatment in one intervention arm to reduce contamination between conditions. The modality of the first session is requested to be in-person, and follow-up sessions can occur remotely or in-person depending on family and clinician preference.

Outcome measures

Table 1 outlines the primary outcomes for study aims. The online supplemental appendix outlines the assessment

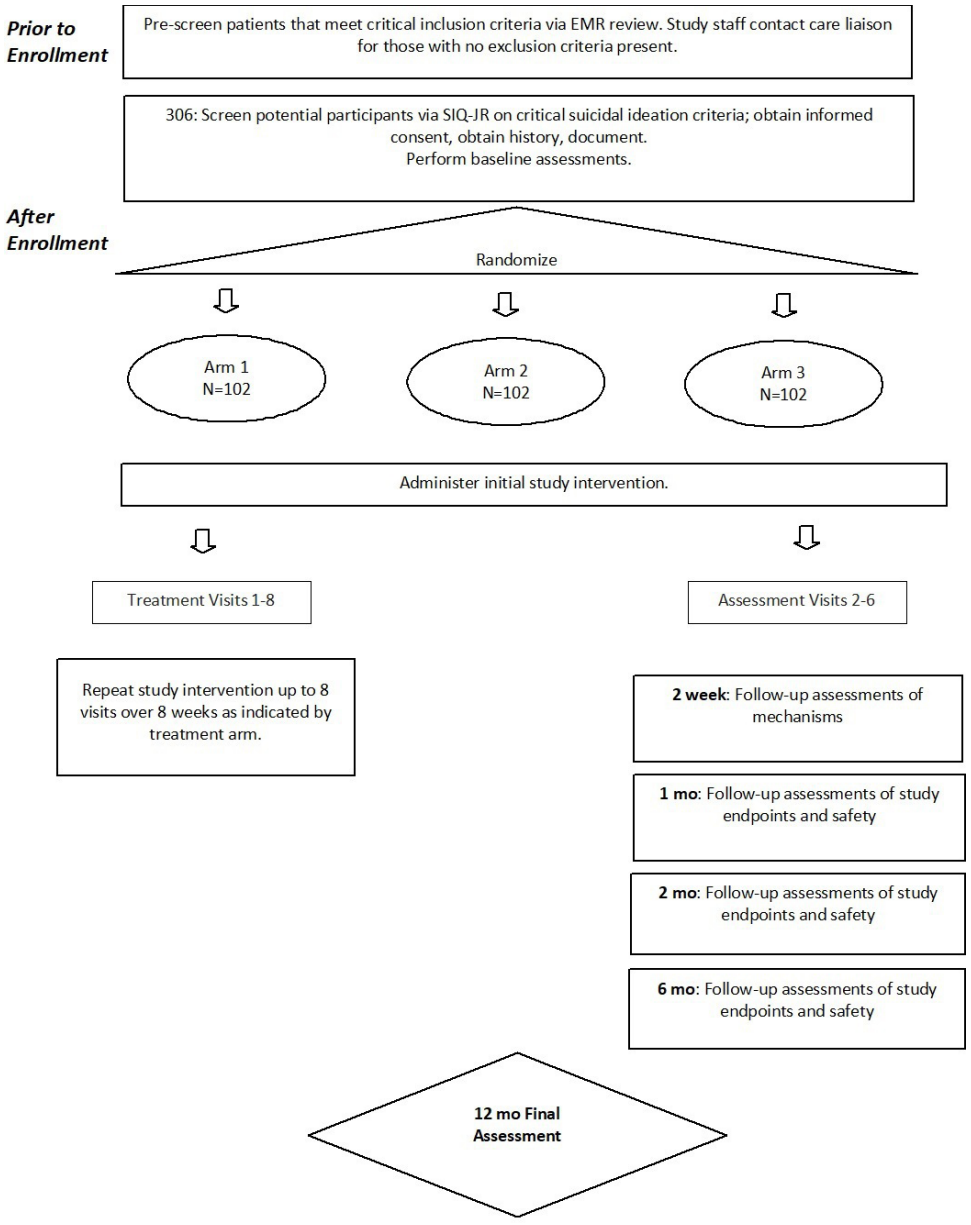

Figure 1 ASSIST study flow. ASSIST, Advancing Suicide Intervention Strategies for Teens; SIQ-JR, Suicidal Ideation Questionnaire-Jr.

schedule. Assessments were selected based on their use in prior clinical trials focused on youth with STBs.[4 15 23] Youth complete assessments related to STBs, service satisfaction and utilisation, arousal (sleep, attentional biases), social processes (social experiences, problem solving, self-efficacy), substance use and psychological functioning. Caregivers complete information regarding their perceptions of their child's STBs, psychological functioning, service satisfaction and utilisation. Clinicians report on their experience with the interventions. At the 1-year follow-up, electronic medical record is reviewed for acute care admissions for youth during the 1-year study period.

Interventions

Interventions begin within 2 weeks following discharge from acute care. Youth can receive outside concomitant care as needed. Table 2 highlights the components of the three interventions.

Intervention #1: SPI+

SPI+ is focused on how acute suicidal crises wax and wane over time. At times of acute risk, a pre-specified and individualised plan identifies the internal warning signs that serve as a reminder for patients to use the safety plan. SPI+ strategies focus on patient's narrative of a recent suicidal crisis and identifying coping strategies and resources that are most likely to reduce suicide risk. The brief structured intervention is conducted in six key steps as outlined in the introduction. Youth in this condition will be offered weekly follow-up, with a minimum of four sessions and a maximum of eight sessions. The initial SPI+ session is 90 min and subsequent follow-ups are scheduled for up

Table 2 Treatment components

Intervention components	SPI+	CAMS	Usual care
Assessment			
Idiographic assessment approach	Personal experience of a suicidal crisis	SSF Core Assessment	Epidemiological risk factors
Intervention			
Intervention structure	4–8 sessions with Safety Plan Form	4–8 sessions with Suicide Status Form	Unstructured
Intervention plan	Identify warning signs, coping strategies, social and professional resources, lethal means safety to mitigate acute suicide risk	Structured treatment around patient-identified drivers	Locally adapted crisis prevention/safety plan and referral list
Discontinuation criteria	Connection to ongoing care is established and patient has attended one appointment	Three consecutive sessions of low STB, management of any low STB if present, and low self-reported risk for future suicide	No defined criteria
Connection to care	Included on safety plan, barriers addressed at each visit	Explicitly outlined in treatment plan and strategies	Referral list provided

CAMS, Collaborative Assessment and Management of Suicidality; SPI+, Safety Planning Intervention with follow-up; STB, suicidal thoughts and behaviours.

to 30 min on a weekly basis. The goal is to create a safety plan that patients will use to reduce risk when suicidal crises emerge. Parents are also included during the safety planning session with a focus on sharing the safety plan and preparing parents, with input from the adolescent, for how they may support the adolescent in implementing the safety plan and are included in lethal means counselling (ie, step 6). Following the creation of the safety plan, follow-up sessions are conducted in person or by telehealth. These sessions focus on brief risk assessment and mood check, review and revision of the safety plan and facilitation of treatment engagement. Follow-up sessions end when the person indicates that they would no longer prefer to have sessions or they are connected to ongoing care.

Intervention #2: CAMS

CAMS is based around a model of STBs which states that adolescents become suicidal in response to overwhelming psychological pain, and treatment identifies and targets the drivers of suicide as the primary focus of assessment and intervention.[16] The SSF is used as a means for deconstructing the functional utility of STBs, to better assess, treatment plan and track ongoing risk. CAMS strategies focus on collaborative deconstruction and treatment of the patient-defined drivers, which are the problems that make suicide compelling to the patient and uses a problem-focused treatment approach to address the drivers as they relate to suicide. Participants will be assigned to CAMS for a minimum of four sessions and a maximum of eight sessions. This timeframe, based on initial data from our pilot work with adolescents and emerging adults (ages 18–25[24]), suggests that a subset of participants resolve their STBs in 6–8 sessions. There is a published manual in its second edition that has been evaluated with adult populations. CAMS initial sessions are 90 min and subsequent individual sessions will be provided weekly for 50 min. The treatment has an assessment framework driven by the SSF that helps the clinician collaboratively identify, engage, conceptualise and treat the drivers of STBs within a problem-solving framework in an outpatient setting. Treatment strategies that target drivers of STBs allow clinicians flexibility and do not require a clinician to shift their theoretical orientation beyond adopting ongoing measurement feedback via the SSF and driver-focused care. The CAMS Stabilisation Support Plan is used to engage parents in a supportive role. A treatment responder is defined as three consecutive sessions of low STBs, management of any low STBs if present and low self-reported risk for future suicide, indicating a minimum of four sessions to meet resolution and may be offered up to eight sessions. Sessions can occur in person or via telehealth.

Intervention #3: enhanced UC

Participants in this group will be studied as they proceed through treatment in the acute care setting and follow the intervention plan laid out in the discharge summary, per usual protocols at each facility. In both settings, the elements of typical care include a modified version of the Stanley & Brown safety plan. At Seattle Children's this includes crisis prevention planning, which outlines potential triggers from parent and youth perspective, skills to use and people and places to call in a crisis, as well

as referral to ongoing behavioural health treatment. At Nationwide Children's, the modifications to the Stanley and Brown template include addition of school setting for several steps of the safety plan. Neither site routinely uses the risk curve to elucidate the personal narrative of suicidality and cue the use of the safety plan. The study does not alter UC but tracks recommendations, contacts and care through questionnaires the family completes, as well as medical record review, in order to understand the impact of the experimental conditions in relation to typical services. If high risk is noted during research assessment, management strategies may include connection to higher levels of care. Recent meta-analyses suggest value in understanding UC, as gains are made by many youths in reducing STBs.[6]

Procedures

Screening

Screening via medical record review confirms elevated Ask Suicide Questions[25] (administered as part of routine care) and suicidal crisis resulting in acute care as determined by the attending provider in the admission note. Youth can be approached while they are in acute care after the care team determines that youth will be discharged to home. Youth complete the SIQ-JR[26] to confirm eligibility. Following screening for eligibility, consent/assent meetings with the caregiver and youth are conducted.

Assessment

Adolescents and their parents will complete six assessments over a 12-month period. After the consent meeting, youth and caregivers complete the baseline assessment. Following baseline assessment, a 2-week assessment will help identify early response, and mediation effects, 1-month assessment is the early end of treatment, 2 months corresponds with the longest treatment, and two longer-term follow-ups are planned at 6 and 12 months. Youth are provided an incentive in the form of a gift card totalling $200 over the six assessments. Parents are also provided incentives totalling $70 over the year of assessments. The assessments are a combination of questionnaires entered directly by participants into Research Electronic Data Capture, interview and Death/Suicide Implicit Association Task. Follow-up assessments are conducted by assessors who are blind to the assigned treatment condition. If a treatment condition is revealed to an assessor, the assessment is conducted by a different assessor who has remained blind to treatment assignment for the participants' duration in the study. Interview assessments will be recorded for quality assurance and reliability, with 10% of interviews reviewed by a certified assessor. Certification is obtained by completing the training and conducting two interviews that are in 100% agreement with a gold standard rater.

Randomisation

Youth are the target of randomisation and randomisation scheme is 1:1:1 to the three conditions. Randomisation is done within 48 hours of completing the baseline assessment. A minimisation random assignment procedure is based on the Fortran programme RAND.F (4/17/09) by Kevin Cain designed for the Behavioral Research Treatment Center of University of Washington and adapted by author (RG) to be specific to this study's needs. Randomisation is done within site by study staff/treatment coordinators and will be used to match subjects on five variables: (1) medication management status (yes or no); (2) sex; (3) age (young <15; older ≥15); (4) suicide attempt history (no suicide attempt; one or more suicide attempts) and (5) source of recruitment (inpatient or emergency care). This minimisation random strategy for assignment to condition was developed specifically for research studies where the number of matching criteria is large for the number of subjects in a study. In contrast to stratified randomisation, which aims for equal numbers of subjects in each treatment for every possible combination of the prognostic variables, the minimisation method restricts its aim to equalising treatment numbers at the different levels of each variable taken separately. The minimisation technique is an adaptive randomisation which changes the allocation probability according to the progress and position of the study. And considering the imbalance of the prognostic factors. The system generates a running log of the respective stratification variable responses and blinded treatment assignment (only available to specific study personnel) in ASCI format. Monitoring of balance as well as inspection of discernable patterns is made periodically (ie, monthly).

The algorithm is based on an overall imbalance score which measures how far out of balance (within strata) the study is for a given set of random assignments in line with the minimisation method outlined by Pocock.[27] Thus, there is still a random seed per randomisation with which the respective allocation assignment is dependent. The more out of balance an allocation becomes the weighted comparison to the random seed weighs more heavily on the imbalanced arm but still is dependent on the random seed with the 'potential' to still randomise in the out-of-balance direction.

Analytic framework

For our primary examination of youth treatment effectiveness based on suicidal events across conditions over a 1-year follow-up period, mixed models of change over the six time points (Week 0, Week 2/early response, 1 month/mid-treatment, 2 months/post-treatments, 6 months and 12 months) will be conducted separately for each outcome. Mixed models are preferred for longitudinal designs because they allow for individual estimates of change and have robust power in the presence of missing data and attrition. We will use Generalised linear mixed-effects models as our modelling framework.

With the multisite design, we will control for site in all analyses. Stratification variables will be included in the model. Sensitivity analyses will be conducted both including and excluding these covariates. As far as other

covariates, any baseline demographics or clinical measures that significantly differ across the intervention arms will be included as covariates. Potentials include outside treatment/services, medication and demographics such as sexual and gender minority status, ethnicity and sex.

The mixed model framework we propose will be extended to accommodate the count data through a negative binomial. Our primary assumption is that the outcome distribution will be Poisson/Negative Binomial and the change over time will be piecewise. Within Aim 1 for suicidal events, assuming linear change and a two-level model with timepoint nested within participant, the fitted combined model will be:

$$\begin{aligned} log\left(Y_{ij}\right) = \; & \pi_{00} + \pi_{01} tx1_i + \pi_{02} tx2_i + \pi_{10} \\ & \times time_{ij} + \pi_{11} tx1_i \times time_{ij} + \pi_{12} tx2_i \\ & \times time_{ij} + r_{0i} + r_{1i} time_{ij} + e_{ij} \end{aligned}$$

where Y_{ij} is the count per patient at the jth assessment per the Columbia Suicide Severity Rating Scale (C-SSRS). The significance of π_{11} and π_{12} will assess the statistical significance of CAMS and SPI+ to UC respectively in the rate of change over time in the log-counts. Examination of the distribution over time and per arm will be performed. We may need to model the counts as binary (none vs any), ordinal (using ordinal ranges), zero-inflated if there is a preponderance of 0 responses. If the response is treated as counts, fitted distribution will consist of Poisson, negative binomial, generalised Poisson to accommodate equidispersion, overdispersion and underdispersion of the response.

The same approach will be used for suicidal attempts, assuming linear change and a two-level model, the fitted combined model will be:

$$\begin{aligned} log\left(Y_{ij}\right) = \; & \pi_{00} + \pi_{01} tx1_i + \pi_{02} tx2_i + \pi_{10} \times time_{ij} + \pi_{11} tx1_i \\ & \times time_{ij} + \pi_{12} tx2_i \times time_{ij} + r_{0i} + r_{1i} time_{ij} + e_{ij} \end{aligned}$$

where Y_{ij} is the count per patient at the jth assessment per the C-SSRS. The significance of π_{11} and π_{12} will assess the statistical significance of CAMS and SPI+ to UC respectively in the rate of change over time in the log-counts.

Within Aim 1 for suicidal ideation, assuming linear change and a two-level model, the fitted combined model will be:

$$\begin{aligned} Y_{ij} = \; & \pi_{00} + \pi_{01} tx1_i + \pi_{02} tx2_i + \pi_{10} \times time_{ij} + \\ & \pi_{11} tx1_i \times time_{ij} + \pi_{12} tx2_i \times time_{ij} + r_{0i} + r_{1i} time_{ij} + e_{ij} \end{aligned}$$

where Y_{ij} is the total score of the SIQ-JR per patient at the jth assessment. The significance of π_{11} and π_{12} will assess the statistical significance of CAMS and SPI+ to UC respectively in the rate of change over time in ideation.

The primary analyses will be conducted with the intent to treat sample. Planned modified analyses will also be conducted with those who received at least one session of an intervention. As a sensitivity analysis, we will examine the Complier Average Causal Effect focused on those participants who received at least one session as planned as 'treatment received'. Potential moderator effects of race/ethnicity, sex, gender identity, age, substance use and sleep quality will be exploratory. Moderators will be determined by significant interaction with intervention by extending mixed models executed for Aim 1. When analyses involving a continuous moderator are significant, we will probe these by estimating and contrasting estimates of the impact of a 1SD increase in the continuous predictor. Clinical interpretation of the impact of the potential moderators will be based on risk ratios (RRs) for count outcomes and estimated change in suicidal events. For the predictors, the impact is quantified overall, whereas, for moderators, the impact is quantified within each intervention. Moderation effects involve both treatment and time, which is the three-way interaction of treatment, time and the moderator. Models for each outcome and each moderator will be tested separately. Post hoc probing of simple effects will follow for all significant three-way interactions using the methods described by Preacher and colleagues.[28] Mediation analyses will use casual mediation model called the marginal mediation model,[29 30] which does not require the assumption of sequential ignorability, and which connects the common mediation parameters to causal parameters.[31] The marginal mediation model produces the significance of the multiplicative paths from (a) intervention to the outcome (path c), (b) intervention to the posited mediator (path a) and (c) the mediator to outcome (path b), controlling for intervention under the marginal mediation model referred to as the natural indirect effect (NIE). 'Path c' corresponds to the controlled direct effect (CDE) of the intervention on the outcome after the mediator is introduced into the model. As described by Vander Weele,[30] the CDE and NIE account for the direct and indirect effects, respectively, while addressing the sequential ignorability violation. The mediators evaluated for each intervention are suicide-related coping as measured by the Suicide Related Coping Scale and implicit associations as measured by the Death/Suicide Implicit Association Task. Mediators are measured at baseline, 2-week, 1-month and 2-month assessments. Outcome variable for analyses of mediation will be suicidal events at 12 months.

Patient and public involvement

Patient, caregiver and clinician feedback was used in the trial design for the selection of interventions due to feedback around feasibility, acceptability and likely impact. Preliminary feedback on use of both SPI+ and CAMS from clinicians and families support feasibility and acceptability of both interventions. Adolescents and their parents view SPI+ favourably, with high ratings of satisfaction (ie, M=3.59 out of four for adolescents and M=3.71 out of four for parents; 13). Similarly, preliminary work on implementation of CAMS with adolescents supports the feasibility of this approach, with a mean satisfaction score of 3.8 (SD) on a 4-point Peabody Satisfaction with Services Scale.[20] Responses from clinicians (n=15) who were trained and used CAMS with at least one patient indicate that the majority found CAMS easy

to incorporate into their practice, and felt their patients benefited from using the CAMS framework for a suicide-specific treatment. Additionally, clinicians who completed measures of acceptability, feasibility and appropriateness indicated a high degree of satisfaction with the CAMS framework (acceptability M=4.60 on a scale of 1–5, with 5 indicating extremely acceptable, feasibility=4.27 and appropriateness=4.73; with no clinicians endorsing lower than 4 ratings on these items). Both interventions have preliminary data supporting feasibility, acceptability and impact with adolescent populations from the perspective of youth, caregivers and clinicians.

ETHICS AND DISSEMINATION

The primary ethical issues revolve around the primary outcomes also being the key safety indicators for the trial. This study has a NIMH-appointed Data Safety and Monitoring Board to review safety events for the trial. Adverse events include breach of confidentiality, evidence of coercion to participants, non-suicidal self-injury (NSSI), suicidal ideation with intent, method and/or plan (identified during a follow-up interview assessment) resulting in referral to a crisis resource for further assessment via crisis line or emergency evaluation. Serious adverse events include death, suicide attempt and inpatient hospitalisation. In addition, assessors have an obligation to respond to safety concerns as they emerge and each site has a specific protocol to review assessments, connect to crisis resources as needed and document actions taken. A second key dilemma is around discontinuation of the experimental interventions. For research purposes, there is a preferred limit to the number of the sessions[8]; however, procedures for elevated suicide risk during termination may extend treatment length for purposes of safety. Data quality and trial procedures are also monitored by external monitoring agreement with University of Washington Institute for Translational Health Sciences. Major protocol changes will be documented in clinicaltrials.gov.

This study's dissemination plan includes data sharing with the NIMH Data Archives, presentations and manuscript development to share results with other investigators. Further, dissemination efforts will focus on providing information to key centres of influence (families, healthcare systems and academicians) about (1) the effectiveness of two interventions on suicide outcomes and (2) the mechanisms that were responsible for reduced suicidality STBs in each intervention. Expected audiences to benefit from this research primarily include other researchers and clinicians, particularly those focused on adolescent suicide-specific intervention development, those interested in improving the care suicidal adolescents receive and implementation scientists interested in sustainability and treatment integrity. We will also include public involvement in our dissemination plan through our Family Advisory Boards.

We recognise there are limitations to evaluating interventions against UC given the significant heterogeneity in this condition. We include a UC comparison group given UC is the most established approach to evaluating an incremental gain in experimental conditions and recent meta-analyses suggest that UC demonstrates an impact on STBs.[6] To understand the heterogeneity and similarities across conditions we propose coding each condition's contents to characterise the dose of condition-specific therapeutic strategies.

We have prioritised the most urgent questions about how to most efficiently reduce STBs, at the expense of other important questions of moderation, differentiation of intervention effects on NSSI and implementation. Although an important predictor of STBs, NSSI is not the target of either SPI+or CAMS. We will however, with careful attention to participant burden, collect data on NSSI. We hope that following the execution of these prioritised aims, additional proposals will address these important questions with the guidance of the results of the initial aims we prioritised.

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REFERENCES

1 Substance Abuse and Mental Health Services Administration. Key substance use and mental health indicators in the United States: results from the 2021 National Survey on Drug Use and Health. HHS publication no.Pep22-07-01-005, NSDUH series H-57). 2022.
2 Mehlum L, Tørmoen AJ, Ramberg M, *et al*. Dialectical behavior therapy for adolescents with repeated suicidal and self-harming behavior: a randomized trial. *J Am Acad Child Adolesc Psychiatry* 2014;53:1082–91.
3 Mehlum L, Ramberg M, Tørmoen AJ, *et al*. Dialectical behavior therapy compared with enhanced usual care for adolescents with repeated suicidal and self-harming behavior: outcomes over a one-year follow-up. *J Am Acad Child Adolesc Psychiatry* 2016;55:295–300.
4 McCauley E, Berk MS, Asarnow JR, *et al*. Efficacy of dialectical behavior therapy for adolescents at high risk for suicide: a randomized clinical trial. *JAMA Psychiatry* 2018;75:777–85.
5 Ougrin D, Tranah T, Stahl D, *et al*. Therapeutic interventions for suicide attempts and self-harm in adolescents: systematic review and meta-analysis. *J Am Acad Child Adolesc Psychiatry* 2015;54:97–107.
6 Kothgassner OD, Robinson K, Goreis A, *et al*. Does treatment method matter? A meta-analysis of the past 20 years of research on therapeutic interventions for self-harm and suicidal Ideation in adolescents. *Borderline Personal Disord Emot Dysregul* 2020;7:9.
7 Cottrell DJ, Wright-Hughes A, Collinson M, *et al*. Effectiveness of systemic family therapy versus treatment as usual for young people after self-harm: a pragmatic, phase 3, multicentre, randomised controlled trial. *Lancet Psychiatry* 2018;5:203–16.
8 Harris LM, Huang X, Funsch KM, *et al*. Efficacy of interventions for suicide and self-injury in children and adolescents: a meta-analysis. *Sci Rep* 2022;12:12313.
9 Zima BT, Murphy JM, Scholle SH, *et al*. National quality measures for child mental health care: background, progress, and next steps. *Pediatrics* 2013;131 Suppl 1:S38–49.
10 Micol VJ, Prouty D, Czyz EK. Enhancing motivation and self-efficacy for safety plan use: incorporating motivational interviewing strategies in a brief safety planning intervention for adolescents at risk for suicide. *Psychotherapy (Chic)* 2022;59:174–80.
11 Stanley B, Brown GK. Safety planning intervention: a brief intervention to mitigate suicide risk. *Cognitive and Behavioral Practice* 2012;19:256–64.
12 Stanley B, Brown GK, Brenner LA, *et al*. Comparison of the safety planning intervention with follow-up vs usual care of suicidal patients treated in the emergency department. *JAMA Psychiatry* 2018;75:894–900.
13 Czyz EK, King CA, Biermann BJ. Motivational interviewing-enhanced safety planning for adolescents at high suicide risk: a pilot randomized controlled trial. *J Clin Child Adolesc Psychol* 2019;48:250–62.
14 Stanley B, Brown G, Brent DA, *et al*. Cognitive-behavioral therapy for suicide prevention (CBT-SP): treatment model, feasibility, and acceptability. *J Am Acad Child Adolesc Psychiatry* 2009;48:1005–13.
15 Brent DA, Greenhill LL, Compton S, *et al*. The treatment of adolescent suicide attempters study (TASA): predictors of suicidal events in an open treatment trial. *J Am Acad Child Adolesc Psychiatry* 2009;48:987–96.
16 Jobes DA. *Managing suicidal risk: a collaborative approach*. Second Edition. Guilford Publications, 2016: 290.
17 Comtois KA, Jobes DA, S. O'Connor S, *et al*. Collaborative assessment and management of Suicidality (CAMS): feasibility trial for next-day appointment services. *Depress Anxiety* 2011;28:963–72.
18 Jobes DA. Clinical assessment and treatment of suicidal risk: a critique of contemporary care and CAMS as a possible remedy. *Practice Innovations* 2017;2:207–20.
19 Swift JK, Trusty WT, Penix EA. The effectiveness of the collaborative assessment and management of suicidality (CAMS) compared to alternative treatment conditions: a meta-analysis. *Suicide Life Threat Behav* 2021;51:882–96.
20 Adrian MC, Blossom J, Anderson A, *et al*. Collaborative assessment and management of suicide with adolescents: results from an open trial [under review]. 2023.
21 Brausch AM, O'Connor SS, Powers JT, *et al*. Validating the suicide status form for the collaborative assessment and management of suicidality in a psychiatric adolescent sample. *Suicide Life Threat Behav* 2020;50:263–76.
22 Stroup WW. PROC GLIMMIX as a teaching and planning tool for experiment design. *SAS Glob Forum* 2016.
23 Diamond GS, Kobak RR, Krauthamer Ewing ES, *et al*. A randomized controlled trial: attachment-based family and nondirective supportive treatments for youth who are suicidal. *J Am Acad Child Adolesc Psychiatry* 2019;58:721–31.
24 Pistorello J, Jobes DA, Gallop R, *et al*. A randomized controlled trial of the collaborative assessment and management of suicidality (CAMS) versus treatment as usual (TAU) for suicidal college students. *Arch Suicide Res* 2021;25:765–89.
25 Horowitz LM, Bridge JA, Teach SJ, *et al*. Ask suicide-screening questions (ASQ): a brief instrument for the pediatric emergency department. *Arch Pediatr Adolesc Med* 2012;166:1170–6.
26 Reynolds WM. *Suicidal ideation questionnaire: professional Manual*. Psychological Assessment Resources, 1988.
27 Pocock SJ. *Clinical trials a practical approach*. New York, NY: John Wiley & Sons, 1983.
28 Preacher KJ, Curran PJ, Bauer DJ. Computational tools for probing interactions in multiple linear regression, multilevel modeling, and latent curve analysis. *Journal of Educational and Behavioral Statistics* 2006;31:437–48.
29 VanderWeele TJ. Explanation in causal inference: developments in mediation and interaction. *Int J Epidemiol* 2016;45:1904–8.
30 VanderWeele T. *Explanation in causal inference: methods for mediation and interaction*. New York City, NY: Oxford University Press, 2015: 729.
31 Imai K, Keele L, Tingley D. A general approach to causal mediation analysis. *Psychol Methods* 2010;15:309–34.