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The Marine Suicide Prevention and Intervention REsearch (M-SPIRE) study: A randomized clinical trial investigating potential treatment mechanisms for reducing suicidal behaviors among military personnel

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ABSTRACT

Suicides within the U.S. Armed Forces remain elevated. Brief cognitive behavioral therapy for suicide prevention (BCBT) has demonstrated preliminary efficacy as a psychotherapeutic intervention that reduces suicide attempts among U.S. Army Soldiers. The generalizability of BCBT's effects in other military groups and its underlying mechanisms of action remain unknown, however. The Marine Suicide Prevention and Intervention REsearch (M-SPIRE) study is designed to test the efficacy of BCBT for the prevention of suicide attempts among active duty U.S. Marines with recent suicidal ideation or attempts and to identify potential mechanisms of change contributing to BCBT's effects. In this protocol paper, we describe M-SPIRE's rationale and methods with a particular emphasis on measuring treatment fidelity and BCBT's hypothesized mechanisms of action.

1. Introduction

Suicides among members of the U.S. Armed Forces have doubled over the past decade, with the largest increases occurring in the Army and Marines. In 2017, 34.9% of Marines who died by suicide and 49.8% who made a nonfatal suicide attempt accessed mental health services in the months preceding these behaviors [1], implicating a potentially important role for improved mental health treatments. Cognitive behavioral therapies (CBTs) have garnered the most empirical support and are associated with significant reductions in suicidal behaviors [2]. Among U.S. military personnel, brief CBT for suicide prevention (BCBT; [3], a 12-session outpatient treatment, has been shown to reduce suicide attempts by 60% as compared to treatment as usual [4]. However, BCBT's within-group effects on suicidal thoughts and other psychological symptoms (e.g., depression, hopelessness, anxiety) are comparable to those of treatment as usual, consistent with patterns observed in other suicide-focused treatments using similar procedures [5–8]. Given these findings, reductions in suicidal behaviors are likely influenced by change processes other than suicidal thoughts and psychiatric symptoms.

Although the mechanisms accounting for CBT's effect on suicidal behaviors remain unknown [3,9,10], two processes are hypothesized: cognitive flexibility and emotion regulation [11]. Cognitive flexibility refers to the ability to switch between thinking about one concept to another, and to think about multiple concepts simultaneously [12], whereas emotion regulation refers to the ability to delay or inhibit one's spontaneous responses, especially those inconsistent with one's goals [13]. Both cognitive flexibility and emotion regulation are targeted in CBTs for suicide prevention, but the effect of CBT on these processes among high risk individuals has never been tested.

BCBT's efficacy for reducing suicide attempts among U.S. military personnel is supported in a single trial with active duty Army personnel [4]. The current study plans to expand the generalizability of the initial results by testing the intervention in a population of active duty Marines. The first aim of the Marine Suicide Prevention and Intervention REsearch (M-SPIRE) study is to replicate previous findings supporting BCBT's efficacy for preventing suicide attempts among treatment-seeking active duty Marines. We hypothesize that Marines receiving BCBT will be significantly less likely to attempt suicide during the two-year follow-up period than those randomized to an active control condition. The second aim of M-SPIRE is to explore potential psychological and neurocognitive mediators of BCBT's effects. Further, we hypothesize that Marines randomized to BCBT will demonstrate significant improvements in cognitive flexibility and emotion regulation—measured via a combination of self-report, computerized behavioral, and psychophysiological methods—and that the effect of BCBT on reducing sui-

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cide attempts will be mediated by improvements in these processes. The purpose of this protocol paper is to summarize the study's methodology, focusing on treatment fidelity and incorporation of hypothesized mediators.

2. Study design and procedures

This study uses a 2-arm parallel randomized controlled trial (RCT) design to compare the efficacy of BCBT to an active comparator, present centered therapy (described in Section 2.6). Eligible participants are active duty U.S. Marines reporting suicide ideation with intent to die within the past week and/or a suicide attempt within the past month. Blinded assessments are conducted at 3-month intervals post-treatment for 2 years. This study has been registered with ClinicalTrials.gov (identifier: NCT03769259).

2.1. Study site, participants, and personnel

This study is conducted in the outpatient mental health clinic located at Naval Medical Center Camp Lejeune (NMCCL), North Carolina. NMCCL serves approximately 150,000 military personnel, dependents, and retirees each year on an inpatient and outpatient basis. Participants include 210 active duty Marines meeting eligibility criteria (see Section 2.5). Potentially eligible Marines are referred to research staff by NMCCL mental health clinicians as part of routine outpatient mental health care or as part of their discharge plan from inpatient hospitalization. In addition, research staff participate in departmental requirements and attend weekly clinic and discharge planning meetings in order to identify Marines that may be eligible for participation while allowing for as much consistency with other clinical procedures at NMCCL as possible. Study personnel meet with referred Marines in the outpatient mental health clinic to complete informed consent procedures, answer questions about the study, and complete all baseline assessments.[1] The total estimated completion time for baseline assessment and procedures is 3 h.

Independent evaluators and clinicians hold either a masters or doctorate degree in a licensable mental health discipline. All evaluators and clinicians are not affiliated with NMCCL but are hired employees of the principal investigator's institution.

2.2. Inclusion and exclusion criteria

Marines meet inclusion criteria if they are (1) active duty, (2) 18 years of age or older, (3) report suicidal ideation with intent to die during the preceding week, which is confirmed through responses to the Scale for Suicide Ideation (SSI [16]; e.g., score of five or higher; See Section 2.3.2) or a past-month suicide attempt, defined as a deliberate, potentially injurious behaviors in which there is at least some intent to die as a result of the behavior. (Suicide attempts may or may not result in physical injury or tissue damage. [14]) Eligibility on the basis of suicidal ideation and/or attempt is confirmed by responses to the Self-Injurious Thoughts and Behaviors Interview-Revised (SITBI-R; [49]; See Section 2.3.1). Additional inclusion criteria include (4) the ability to speak and understand the English language, and (5) the ability to complete the informed consent process. The only exclusion criterion is having a medical or psychiatric condition that precludes the ability to understand or provide written informed consent (e.g., psychosis, mania, acute intoxication). Marines excluded from participation from the study due to impaired mental status at the time of informed consent may be enrolled in the study at a later date if they subsequently meet eligibility criteria (e.g., manic state or psychosis resolves). Marines expecting to leave military status (e.g., separation, retirement), deploy, or change stations within 90 days of enrollment are also be excluded from participating in the study in order to ensure that they receive the entire treatment. The exclusion criteria are minimal in order to maximize the heterogeneity of the sample and, by extension, increase generalizability to outpatient mental health clinics.

2.3. Outcome assessments

The timeline of assessments for key study variables is summarized in Table 1. Key variables (suicidal ideation and suicide attempts, confirmed by the SSI and SITBI-R; See Sections 2.3.1. and 2.3.2) are assessed at baseline prior to randomization and at 3-month intervals for 2 years postbaseline. Baseline assessments are conducted in person by research staff. During active treatment, Marines also complete self-report measures at the start of each therapy session, scheduled approximately once per week, using a secure web-based survey data collection system. Marines who have received treatments from NMCCL are accustomed to completing similar measures as part of routine monitoring.

During follow-up assessment procedures, independent evaluators blinded to participants' study condition contact each Marine through phone or email in order to schedule appointments to complete follow-up clinical interviews and to send a secure online link to the follow-up measures. At baseline, all Marines provide their phone number, email and mailing addresses, and contact information for a trusted individual that may be contacted in case the Marine cannot be reached in order to schedule therapy sessions or follow-up assessments. The blinded assessor will attempt to contact Marines through each of these methods, if needed, in order to minimize attrition at follow-up. The blinded assessor will schedule a time of the participant's choosing in order to minimize burden and further reduce any potential participant attrition. Additionally, study personnel on site at NMCCL contact Marines to complete follow-up behavioral and psychophysiological measures in person. See Table 1 for a listing of measures and timing of administration for the study. Follow-up procedures including only clinical interviews and self-report measures are anticipated to be completed in a maximum of 1 h, while those also including behavioral and psychophysiological assessment procedures are anticipated to be completed in a maximum of one and a half hours.

2.3.1. Primary outcome: Suicide attempts

Our primary method for assessing the incidence and characteristics of suicide attempts defined in Section 2.2 (e.g., lethality, motivations) is the Self-Injurious Thoughts and Behaviors Interview-Revised (SITBI-R; [49]), a clinician-administered interview that assesses lifetime history and features of various suicide-related and self-injurious thoughts and behaviors. The SITBI-R is an empirically-supported method for distinguishing different types of self-directed violence and is included as a recommended measure in the NIMH PhenX Toolkit (https://www.phenxtoolkit.org). The SITBI-R is supplemented by medical record review to identify potential suicide attempts unreported by participants during their assessments as well as for participants lost to follow-up. Medical record review includes a search for ICD-10 self-injury diagnostic codes, review of procedure codes, and review of medical record documentation. Suicide deaths are handled as suicide attempts with fatal outcomes.

2.3.2. Secondary outcome: suicidal ideation

Suicidal ideation is assessed using the Scale for Suicide Ideation (SSI; [16], a 21-item self-report measure assessing thoughts and attitudes about suicide, as well as steps taken to prepare for a suicide attempt, that have occurred within the past week. The SSI is included as a recommended measure in the NIMH PhenX Toolkit.

[1] Due to COVID-19 restrictions mandated by NMCCL, all treatment and in-person assessments were postponed in March 2020 and have since been lifted. Marines receiving treatment when these restrictions were imposed were transferred to an on-site provider, per NMCCL policy.

Table 1
Study scales, constructs measured, and timeline of administration for all patients enrolled in M-SPIRE.

Scale	Construct	BL	3 mo	6 mo	9 mo	12 mo	15 mo	18 mo	21 mo	24 mo
Primary Outcomes:										
Self-Injurious Thoughts and Behaviors Interview-Revised	Suicide attempts									
Review of medical records	Suicide attempts									
Secondary Outcomes:										
Scale for Suicide Ideation	Suicidal ideation									
Hopelessness Scale	Suicidogenic cognitions									
Suicide Cognitions Scale	Suicidogenic cognitions									
Meaning in Life Questionnaire	Suicidogenic cognitions									
Cognitive Flexibility Inventory	Cognitive flexibility									
Suicide Implicit Association Task	Cognitive flexibility									
Dot Probe Task	Cognitive flexibility									
Difficulties in Emotion Regulation Scale Short	Emotion regulation									
Heart Rate Variability	Emotion regulation									
Monetary Choice Questionnaire	Emotion regulation									
Covariates:										
Patent Health Questionnaire - 9	Psychological symptoms									
Insomnia Severity Index	Psychological symptoms									
PTSD Checklist	Psychological symptoms									
Brief Reasons for Living Inventory	Psychological symptoms									
Composite International Diagnostic Interview	Psychiatric diagnosis									
Working Alliance Inventory Short Revised	Patient perceptions of clinicians									
Credibility Expectancy Questionnaire	Patient perceptions of treatment									
Post-Treatment Health Interview	Changes in military status									

2.3.3. Secondary outcomes: process variables and mechanisms of change

The hypothesized mechanisms of change, cognitive flexibility and emotion regulation, are assessed using a multitrait, multimethod approach (see Table 2). Suicidogenic cognitions (commonly referred to as the suicidal belief system [17]; will be assessed using three self-report methods. First, the Beck Hopelessness Scale (BHS; [18]) assesses the intensity of negative beliefs about the future. Second, a revised version of the Suicide Cognitions Scale (SCS [19]; will assess thoughts, beliefs, and perceptions that maintain suicidal thoughts and facilitate the emergence of suicidal behavior. Third, the Meaning in Life Questionnaire (MLQ; [20] measures the extent to which respondents perceive their lives to be meaningful and the strength of their desire to find something meaningful about life.

Cognitive flexibility is assessed using both self-report and behavioral methods. First, the Cognitive Flexibility Index (CFI; [21] is a 20-item self-report measure that assesses the respondent's perceived ability to identify alternatives and to control one's thinking. Second, the Suicide Implicit Association Task (S-IAT; [22], is a 20-min computer-administered reaction time task that measures implicit cognitive bias towards death and suicide. In the S-IAT, patients are directed to classify stimuli presented at the center of the computer screen (e.g., “alive”, “suicide”) into concept (“suicide”, “not suicide”) and attribute categories (“me”, “not me”). Reaction times to each stimulus are recorded in milliseconds and analyzed using a standardized scoring algorithm. Scores have been shown to be strongly correlated with a diminished desire to live. Third, the dot probe task [23] is a computer-administered task that measures reaction time to target probes that replace neutral words (e.g., table) as compared to reaction time to target probes that replace suicide-related words (e.g., kill), negative words (e.g., frown), and positive words (e.g., happy). Subjects are presented with a target probe, then press a button to denote its location on the computer screen. Faster reaction times to targets replacing suicide-related words compared to those replacing neutral words indicates the presence of a suicide-related attentional bias.

Table 2
Treatment components and procedures contained within BCBT and PCT.

Treatment Procedure/Component	BCBT	PCT
Suicide risk screening	X	X
Narrative assessment	X	
Crisis response plan/safety plan	X	X
Means safety counseling	X	X
Weekly monitoring of suicide risk, symptoms	X	X
Psychiatric symptom management	X	X
Psychoeducation: suicide as symptom of mental illness		X
Psychoeducation: suicide as deficit in self-regulation	X	
Emotion regulation skills training	X	
Cognitive restructuring skills training	X	
Relapse prevention task	X	

Emotion regulation is assessed using self-report and behavioral methods. First, the Difficulties in Emotion Regulation Short Form (DERS-SF [24]; is an 18-item self-report measure that assesses the respondent's perceptions about how they respond to emotional distress. Second, the Monetary Choice Questionnaire (MCQ [25]; is a 27-item self-report measure that assesses response inhibition, specifically by assessing the respondent's preference for smaller rewards that are immediately available over larger rewards that are available only after a delay. Third, heart rate variability (HRV) is assessed while individuals are engaged in the S-IAT and dot probe task at NMCCL during baseline and specific follow-up assessment periods. Disposable Ag-Agn Cl electrodes will be attached to participants' right and left pectoral muscles, and electrocardiogram (ECG) data will be sampled at 1000 Hz and recorded continuously throughout the protocol on a Biopac MP36 data acquisition system (Biopac Systems, Goleta, CA). Participants will be instructed to complete a task of selecting a preference between pairs of scenic pictures for a 5-min baseline, after which they will participate in the dot probe task and S-IAT while ECG is concurrently recorded. Heart rate (HR) and HRV indices will be averaged across the 5-min baseline, as well as across the various conditions on the dot probe and S-IAT task. In addition to the S-IAT, the dot probe task is administered in-person at NMCCL during baseline and at three and 12 months postbaseline.

2.3.4. Covariates

Assessed covariates include psychological symptoms, psychiatric diagnosis, and demographic variables. Self-reported psychological symptoms include depression, assessed with the Patient Health Questionnaire 9-item depression subscale (PHQ-9 [26]; subjective sleep quality, assessed with the Insomnia Severity Index (ISI [27]; symptoms of post-traumatic stress disorder (PTSD), assessed with the PTSD Checklist (PCL [28]; and reasons for living, assessed with the Brief Reasons for Living Inventory (BRFLI; [29]. Psychiatric diagnosis is assessed using the Composite International Diagnostic Interview (CIDI), which has

been validated for use with military personnel [30]. Patient perceptions of the treatments and their clinicians are assessed using the Credibility Expectancy Questionnaire (CEQ [31]; and the Working Alliance Inventory-Short Revised (WAI-SR; [32]. Finally, change in military status (e.g., retirement, administrative separation, discharge) and treatment utilization is assessed using a semi-structured interview developed by the investigators and used in previous clinical trials.

2.4. Treatment conditions

Participants are randomized to receive one of two treatments: BCBT or present centered therapy (PCT). PCT is selected as the control condition instead of treatment as usual because multiple studies of CBT for suicide prevention, including BCBT, have already demonstrated superiority as compared to treatment as usual. The mechanisms and processes of change in CBT remain unknown, however, because the use of treatment as usual as a comparator limits the ability to investigate these variables. PCT is also considered an empirically supported treatment for posttraumatic stress disorder and depression, and is associated with reductions in suicidal ideation [33,34]. Including an active comparator known to reduce psychological symptom severity therefore enables us to determine if observed reductions in suicidal behaviors are attributable to the procedures used in BCBT and the mechanisms and change processes specifically hypothesized by BCBT. The specific components and procedures used in BCBT and PCT are summarized in Table 2.

All participants also have access to treatment services available to all Marines seeking care at NMCCL (e.g., psychiatric medication management, couples' counseling, emergency services, group therapy). These services are offered by military mental health professionals with appropriate credentials. Prior to enrolment in the study, Marines receive services including suicide risk screening using the Columbia Suicide Severity Rating Scale [35], receipt of information about the Military Crisis Line, safety planning, and enrollment in caring contacts and outreach from the Marine Intercept Program (MIP), all of which are recommended components of standard care for suicidal patients [36].

2.4.1. Brief cognitive behavioral therapy (BCBT)

BCBT is a 12-session treatment designed to reduce the probability of suicidal behavior by targeting two hypothesized mechanisms of action: cognitive flexibility and emotion regulation. The treatment is divided into three sequential phases that focus on emotion regulation skills training (phase 1), cognitive flexibility skills training (phase 2), and relapse prevention (phase 3). During phase 1 (approximately 5 sessions), clinicians conduct a narrative assessment of the most recent suicidal episode or suicide attempt, provide a cognitive-behavioral conceptualization, collaboratively develop an individualized crisis response plan (CRP), develop treatment goals, and begin emotion regulation skills training. During phase 2 (approximately 5 sessions), clinicians teach cognitive restructuring techniques to reduce suicidogenic beliefs and assumptions that maintain suicidal thoughts and increase the risk for suicidal behaviors (e.g., hopelessness, perceived burdensomeness, self-hatred). During phase 3 (approximately 2 sessions), the clinician repeatedly conducts a relapse prevention task wherein the patient imagines and recounts the events and internal experiences (e.g., thoughts, emotions, physiological responses) that led up to their index suicidal episode while also imagining and describing themselves using skills learned during treatment to reduce their distress and avoid suicidal behavior. This task is repeated for hypothetical future stressful situations. The BCBT manual and fidelity checklists are published [3].

2.4.2. Present centered therapy (PCT)

PCT is an active control condition frequently used as a comparison condition in psychotherapy trials to control for the nonspecific common factors of psychological treatment, such as active listening, emotional validation, psychoeducation, and symptom management [37]. The hypothesized mechanisms of change in PCT are its focus on psychoeducation about the patient's current symptoms, identifying and changing current maladaptive behavior patterns, and use of problem-solving strategies to change these behaviors [38,39]. Patients record the daily problems they encounter in diary or journal, which is brought to each session and reviewed collaboratively with the clinician. Non-specific problem-solving skills are then discussed in order to address these problems. PCT prohibits clinician behaviors that are active components of cognitive-behavioral interventions such as cognitive restructuring and emotion regulation skills training (e.g., relaxation, mindfulness), and does not assign skills practice to be completed outside of session. To further distinguish PCT from BCBT, participants receiving PCT receive psychoeducation that conceptualizes suicidal thoughts and behaviors as a result of mental illness (e.g., depression), and suicidal thoughts and behaviors can be reduced by decreasing symptoms of mental illness. In this condition clinicians and Marines do not develop a CRP. Instead, clinicians inquire whether Marines have completed a safety plan with NMCCL personnel before enrolling in the study, which is part of the medical center's protocol for military personnel experiencing thoughts of suicide or who have recently attempted suicide. Marines who report that they did not complete a safety plan or have misplaced or forgotten its contents are provided with a blank safety planning form used at the medical center and are encouraged to fill it out independently in order to prevent administration of treatment components present in BCBT (e.g., CRP).

2.5. Randomization

Eligible Marines are randomized to either the PCT or BCBT condition using stratified blocks of six or eight participants based on gender and suicide attempt history (i.e., no previous suicide attempts, one previous suicide attempt, two or more previous suicide attempts). The randomization scheme is computerized to minimize alteration or manipulation by research members and is managed by a research coordinator who is not involved in treatment or follow-up assessment procedures. To control for clinician effects, randomization occurs at the participant level. See Fig. 1 for the CONSORT diagram depicting anticipated participant allocation and flow through the study.

2.6. Training, supervision, and monitoring of study personnel

All study personnel participate in a 3-day training workshop focused on study procedures and core competencies for assessing and managing suicide risk. Independent evaluators and clinicians additionally completed a multiday training focused on the administration and scoring of the SITBI and SSI. Finally, clinicians complete a 2-day training workshop focused on BCBT and a 2-day workshop focused on PCT. These workshops were designed to be of equal length, and both included didactic instruction, video demonstrations, and supervised role-play with feedback.

All interviews and therapy sessions in both conditions are audio recorded for the purposes of supervision and interview/treatment fidelity monitoring by study investigators. At the outset of the study, 100% of interviews and therapy sessions are reviewed to ensure fidelity. Fidelity checklists used in this and the previous BCBT trial are published [3]. After clinicians demonstrate sufficient fidelity on two consecutive cases with each treatment protocol, fidelity monitoring reduces to no less than 20% of randomly-selected sessions. If a clinician's fidelity ratings fall below 85% for either treatment, no additional participants are assigned to them until they are retrained and can demonstrate acceptable fidelity. Clinicians also participate in weekly supervision sessions with members of the investigative team to review cases and receive feedback on recorded sessions. In addition, study therapists are supervised by on-site licensed clinical staff who are credentialed at NMCCL, in accordance with medical center protocol and state regula-

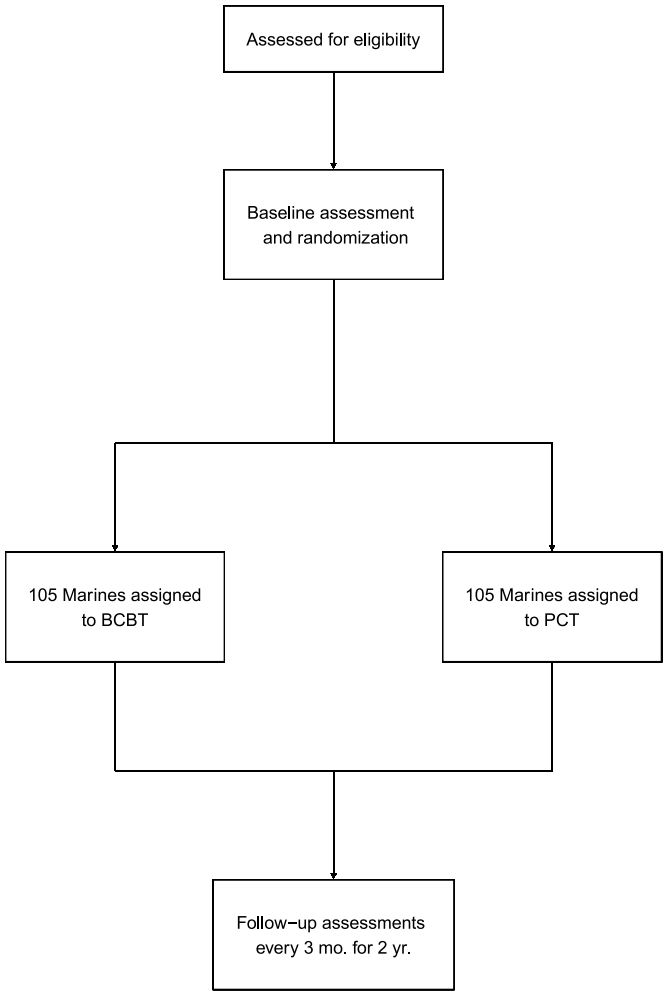

Fig. 1. Planned participant flow through the study.

tions. Independent evaluators record all interviews for monitoring by study investigators using a similar supervision schedule wherein 100% of interviews will initially be reviewed until fidelity and reliability are demonstrated, after which the number of audio recordings will be reduced to a randomly selected subsample comprising 20% of all interviews.

2.7. Planned statistical analyses

Prior to beginning planned analyses, data will be examined to determine the need for scale transformations (e.g., log, reciprocal) to normalize distributions and reduce variance heterogeneity. All analyses are conducted consistent with the intent to treat principle, wherein all available data from all participants will be included, regardless of missingness or attrition.

To determine if Marines randomized to BCBT are significantly less likely to attempt suicide during the 2-year follow-up, we will employ survival analyses for time-to-event data. The overall test of differences between the two intervention groups is accomplished using the hazard ratio derived from the Cox regression, and the log-rank and Wilcoxon statistics derived using the Kaplan-Meier method. Proportional hazard survival regression are also used to explore between-group differences using demographic and baseline characteristics as covariates. In addition to our primary analysis, we will conduct a secondary analysis focused on the broader spectrum of suicide-related behaviors, including suicide attempts, interrupted attempts, aborted attempts, and preparatory behaviors. This secondary analysis will be conducted to determine if treatment effects on suicide attempts, which result in injury or the potential for injury, are similar to (or different from) treatment effects on other risky behaviors that do not involve the potential for injury.

To determine if Marines randomized to BCBT demonstrate significantly larger improvements in secondary outcomes and hypothesized process variables, a series of longitudinal generalized mixed effects regression models will be conducted. Treatment group, time, and the treatment-by-time interaction are entered as independent variables. Separate models will be constructed for each of the secondary outcomes and process variables. Covariance structures are selected by comparing likelihood criteria (e.g., Akaike's Information Criteria), though the autoregressive structure is well-suited for such analyses. Finally, to test the hypothesis that BCBT's effect on reduced suicide attempts will be mediated by improvements in these process variables, a series of mediation analyses [40] with 10,000 bootstrapped samples will be conducted. The intervention group is entered into the models as the independent variable, suicide attempt is entered as the dependent variable, and each process variable is entered as a mediator variable. Type I error inflation due to multiple comparisons is handled by adjusting for the false discovery rate[41].

2.7.1. Handling missing data

Due to the study's longitudinal design, missing data and attrition are anticipated. To assess the potential impact of missing data on our results, Little's test of missingness will be conducted prior to data analyses to assess if data are missing at random. If data are not missing at random, full information maximum likelihood estimation is used. If missingness are non-ignorable, we will use random effects pattern-mixture modeling to determine the extent to which missingness influences longitudinal results.

2.7.2. Power analysis

To estimate the minimum sample size required for this study, we conducted power analyses for our first hypothesis (i.e., BCBT will be associated with a significant reduction in suicide attempts) using the PROC POWER procedure in SAS 9.4 assuming a 20% attrition rate, 80% power, and a one-tailed $p < .05$. Estimated suicide attempt rates from the previous BCBT trial among U.S. Soldiers are 14% in BCBT versus 40% in TAU [4]; similar rates have been observed in other trials of CBT [42] and Dialectical Behavioral Therapy (DBT; [6,43]. We therefore estimated that 20–30% of the participants in BCBT would make at least one suicide attempt during follow-up. To estimate the suicide attempt rate in PCT, we also considered the results of previously published studies. Multiple clinical trials of CBT and DBT indicate these treatment are associated with an approximate 50% reduction in suicide attempts as compared to treatment as usual [4,6,42,43], although the results of a recent meta-analysis suggested a more conservative risk reduction of 25%, suggesting an estimated suicide attempt rate in the comparator ranging from 25 to 50%. An important and unique consideration for the present study was the fact that all Marines, regardless of treatment assignment, could receive caring contacts as part of the Marine Intercept Program (MIP). Caring contacts have been shown to reduce the incidence of suicidal behaviors across multiple populations including U.S. military personnel [44,45,46], and could lead to lower than expected attempt rates across both treatment arms. We therefore considered a range of possible attempt rates in BCBT and PCT (see Table 3), and determined that a total sample size of 210 Marines (n = 105 per arm) was sufficient to detect between-group differences under most conditions, even conditions with low rates of suicide attempts (i.e., 10% in BCBT vs. 20% in PCT).

Regarding secondary outcomes, we used Hedeker's RMASS2 power software for mixed effects longitudinal models (available for download at hedeker.people.uic.edu/ml.html) assuming a 5% attrition rate per time point based on attrition rates observed in the previous efficacy trial of BCBT in active duty Army personnel [4], and an autoregressive

Table 3
Minimum sample sizes and expected number of suicide attempts for Hypothesis 1, assuming 80% power, 20% attrition, and one-tailed $p < .05$

BCBT vs. TAU	N	Expected no. of attempts
10% vs. 40%	34	9
15% vs. 40%	54	16
20% vs. 40%	90	27
10% vs. 30%	66	14
15% vs. 30%	130	30
20% vs. 30%	312	79
10% vs. 20%	204	32
15% vs. 20%	960	168

correlation structure for longitudinal data (i.e., adjacent scores will be more strongly correlated than scores that are spaced farther apart). With these assumptions, a sample size of $N = 210$ provides sufficient power to detect a medium-sized between groups mean difference when the magnitude of autocorrelation ranges from 0.25 to 0.75 and only less than one-third of all planned data points are available.

2.7.3. Planned interim analyses

Basing our power analysis on conservative estimates could result in a much larger number of participants being enrolled than necessary. This could extend the length of the trial needlessly and, in the case of a larger treatment effect, could result in participants continuing to receive a less effective treatment for a potentially life-threatening condition. To mitigate the risk of continuing the trial for longer than necessary, a series of interim analyses are therefore planned using the alpha spending function [47] for time-to-event data, which establishes thresholds for interim analyses based on the number of observed events rather than the number of enrolled participants. With a total sample of $N = 210$, the estimated 10% versus 20% suicide attempt rates would yield a total of 32 expected suicide attempts during the trial (i.e., 11 in BCBT and 21 in PCT). Based on this expected event rate, interim analyses are conducted when a total of 20, 27, and 29 suicide attempts have occurred, which approximates 60%, 75%, and 90% of the expected suicide attempts across both treatments.

When these thresholds are reached, trial data are temporarily frozen while the interim analysis is conducted by an independent statistician who is blind to treatment assignment. The trial stopping rule is calculated using the alpha spending function with one-sided O'Brien-Fleming type boundaries [47], which applies a greater alpha penalty for earlier interim analyses. If the alpha boundary has been reached, the statistician informs the principal investigator that the criterion for early trial termination has been reached, at which point the database is permanently frozen and the trial is stopped. If the alpha boundary has not been reached, the statistician informs the principal investigator to continue the trial and the data is unfrozen, but no information about the resulting p-value, observed effect size, or overall trend is shared with the principal investigator.

3. Discussion

As suicides in the U.S. military have risen, there has been increased interest in identifying and testing efficacious, time-limited treatments that can be readily used in military settings. BCBT has demonstrated preliminary efficacy as a psychotherapeutic intervention for reducing suicide attempts among active duty Army Soldiers [4], but its efficacy has not yet been examined in other military samples like the Marine Corps, a branch of service that has also experienced an especially large increase in suicides. M-SPIRE is therefore aimed at replicating the results of this earlier study of BCBT, thereby providing critical information about the generalizability of earlier findings to a broader military population.

Another knowledge gap involves the mechanisms and change processes that underlie BCBT's effects on suicide attempts. Although suicide-focused treatments like CBT and DBT reduce suicide attempt rates, the reductions in psychological symptoms and other indicators of mental illness observed in these treatments are comparable in size to those observed in treatment as usual [4,6,8,42,43], a pattern that implicates mechanisms other than symptom severity. Based on the results of laboratory-based psychological and neural research, cognitive flexibility and emotion regulation have been identified as possible mechanisms of action [11]. M-SPIRE is the first suicide-focused clinical trial to incorporate psychophysiological assessment methods to explore the potential role of these hypothesized mechanisms. Because this study involves an active and well-described comparator instead of treatment as usual, the present trial is uniquely positioned to test this hypothesis and provide critical new information about why and how the risk of suicidal behaviors can be reduced in psychological treatments. M-SPIRE may therefore help to isolate the procedures and components of psychological treatments that have the greatest impact on suicidal behaviors, a much-needed area of further research [48] that could significantly advance the care of at-risk military personnel.

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