A Novel Cognitive Remediation Intervention Targeting Poor Decision-Making and Depression in Veterans at High Risk for Suicide: A Safe, Telehealth Approach During the COVID-19 Pandemic

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2a. RESEARCH PLAN

1. Background and Significance

The prevention of suicide and treatment of those at greatest risk remains a top priority for the VA. The proposed study will advance knowledge in rehabilitation research by determining whether a novel cognitive remediation intervention aimed at improving decision-making and cognitive control deficits is feasible for Veterans at high risk for suicide. This work relates to several RR&D priority areas. Specifically, it examines: (1) a telehealth intervention for suicide prevention during a global pandemic with social-distancing restrictions, which has been shown to increase suicide rates.[17] Additionally, it investigates (2) a suicide prevention intervention (adapted cognitive remediation (CR); CR+Bridging) that is innovative in its use with Veterans diagnosed with major depressive disorder (MDD) and suicidal behavior (SB), which has not been done previously. The intervention not only provides this population of Veterans with skills-based training, it provides a recovery-oriented approach to targeting the neurocognitive factors increasing their risk of engaging in suicidal behavior with an added focus on them making functional gains (e.g., treatment response, social connectedness, quality of life). It aims to not only enhance/potentiate current mental health treatment for these Veterans by improving the neurocognitive skills required to make gains in conventional psychotherapies in which Veterans with MDD participate (e.g., Cognitive Behavioral Therapy, Dialectical Behavior Therapy), it also aims to provide new targets for suicide prevention and intervention in Veterans with MDD. It has been argued that Veterans are particularly vulnerable during COVID-19 due to the many parallels that exist between this global pandemic and past wartime service conflicts (e.g., separation from family, shortages of food/medical supplies, loss of control and routine, frequent media mention of mortality).[18] This intervention, delivered via telehealth in a group-therapy format, also provides a way to investigate the impact of "social-distancing" amongst this vulnerable population during a global pandemic and aims to protect against the distress and social isolation symptoms that may be experienced by Veterans.

While neurocognitive deficits have been identified as key risk factors for suicidal behavior in MDD[19] and are also associated with the recency of a suicide attempt,[20] little work has examined neuro-based interventions that target the neurocognitive mechanisms underlying suicidal behavior in Veterans with MDD. Further, conventional treatments target mood symptoms and their accompanying thoughts and behaviors, not neurocognitive symptoms. As such—in line with NIMH's move to prioritize "experimental therapeutics"[21]—the field remains in dire need of novel interventions that address these neurocognitive targets.

1.A. Neurocognitive Deficits in MDD and Suicidal Behavior**.** An emerging literature now has identified two executive functioning deficits that may be specific to MDD patients with a history of suicide attempts.[5, 6] *These difficulties include two functions associated with the prefrontal cortex (PFC): (1) disadvantageous values-based decision-making/problem-solving, associated with ventral/medial regions of the PFC and (2) impaired cognitive control abilities (e.g., repetitive negative thinking), which draw from multiple processes (e.g., cognitive inhibition, error monitoring, cognitive flexibility, working memory) and are primarily modulated by the dorsolateral PFC and the anterior cingulate cortex.*[22] Jollant and colleagues[23] have laid out a model of suicidal behavior that elucidates how these deficits interact with depression at the time of suicidal behavior, resulting in suicidal behavior. See **Figure 1.A**. Vulnerable individuals exhibit trait-like difficulty with value-based decision-making/problem-solving skills, as reflected by tendencies to strongly value particular life events (e.g., social signals of rejection) that lead to an intense/prolonged negative state. Difficulty controlling this response—manifested as a ruminative mode of thinking (poor cognitive control)—combined with difficulty assigning adequate value to the consequences of strategies for escaping the negative response, limits their ability to consider alternatives to suicidal behavior. Notably, these cognitive deficits accompanying the depressive state are associated with risk of psychological pain, suicidal ideas, and impaired functioning, all of which factor together to increase the likelihood of suicidal behavior.

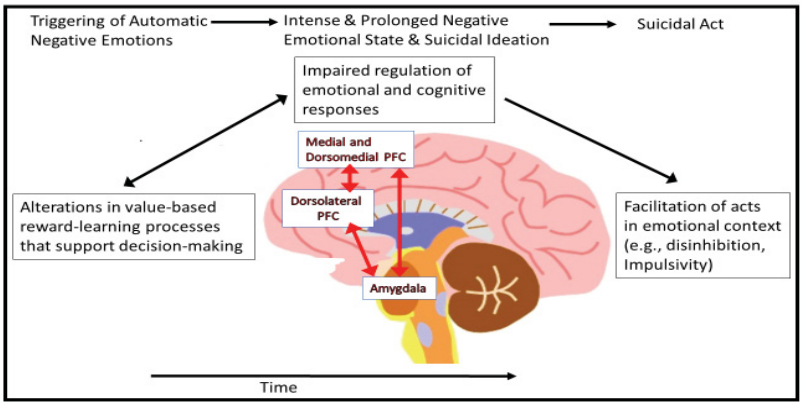

Fig. 1.A. Neuropsychological Model of Suicidal Behavior (Jollant et al 2011[23]).

1.B. Significance and Innovation. The goal of this intervention is to foster recovery in Veterans experiencing depression and suicidal symptoms and help re-integrate them into their family, community, and society. There

is a dearth of research on treatment interventions for suicidal Veterans and a lack of evidence-based treatment interventions that target both suicide prevention and recovery. **This application is novel in that it constitutes the first implementation of this intervention in Veterans with MDD and SB.**

There is evidence that cognitive problems, including cognitive control difficulties (e.g., repetitive negative thinking/rumination), are frequent residual symptoms following remission of depression. Yet, cognitive remediation techniques for improving executive functioning weaknesses are not sufficiently targeted by or incorporated into current forms of treatment for depression.[24] Thus, it is not surprising that existing forms of treatment for depression show limited to no effects on the debilitating executive functioning problems frequently experienced by individuals diagnosed with depression. Further, reduced cognitive functioning is known to predict non-response to treatment of the depressive disorder and functional impairment, along with lower quality of life.[25, 26, 27] This application proposes an open label pilot study of a group-format clinical intervention integrating cognitive remediation and Bridging sessions that aim to improve poor decision-making, weak cognitive control, and depression symptoms in Veterans at high risk for suicide (i.e. Veterans with a history of a suicide attempt in the past year). Cognitive control and decision-making, the two cognitive skills shown to put individuals with MDD at increased risk of suicide,[5, 6] are exercised during the initial part of each session, followed immediately by Bridging sessions. During the Bridging sessions, explicit connections are made between the cognitive skills acquired during sessions and the application of those skills to everyday life situations and stressors, consequently promoting generalization and transfer for increased adaptive and successful functioning in daily life. This short-term 10-week (20 sessions) intervention is designed to be a helpful adjunctive treatment that will complement ongoing VA TAU (psychotherapy) while also providing virtual peer connections (group telehealth therapy) during COVID-19 when key social ties have been put at risk due to physical-distancing restrictions. Close communication and feedback to the Veteran's primary psychiatric outpatient team will be provided.

1.C. Telehealth During the Time of COVID-19. Given mandated social-distancing policies to prevent the spread of COVID-19 and ongoing concern regarding virus transmission months after the initial submission of this project, the bi-weekly CR+Bridging intervention will be conducted via telehealth. Under normative circumstances, the CR+Bridging intervention would be conducted in person. However, with consistent and ongoing support and guidance from Dr. Medalia and Ms. Nicholas, those aspects have been adapted for telehealth, an additional novel feature of the current study. This format not only serves to protect the health of the patients and increase social connections for a certain population of individuals shown to benefit from maximizing support from a range of social ties,[28] it also aims to increase patient engagement and decrease no-show rates. However, the assessments (see **Table 3.D**) at the various timepoints: pre- **(Baseline)**, post-intervention **(Week 10)** and follow-up **(Week 20)** will be administered in person and abiding by strict COVID-19 safety precautions (e.g., health screening on day prior and day-of visit, temperature check, socially distanced throughout visit, sanitization of all testing materials and furniture before, during, and after each visit).

2. Preliminary Work

2.A. Suicide Prevention Randomized Clinical Trial (RCT). The PI (Dr. Hazlett) has extensive research experience working with high-risk suicidal individuals (both Veterans and civilians). She has published >20 papers on borderline personality disorder and MDD, including a RCT examining Dialectical Behavior Therapy (DBT) in Veterans at high risk for suicide with her colleague, Dr. Goodman (Co-I on this study).[29, 30] The RCT was funded by the Department of Defense and involved DBT (12-months) and 18-month follow-up in suicidal Veterans at the JJPVAMC (PI: Goodman). PI Hazlett also received a supplemental grant (MPIs: Hazlett & Goodman) that involved a rigorous clinical assessment and psychophysiology component. The results indicated that affective startle modulation (non-verbal psychophysiological measures of emotion processing mediated by the amygdala) is exaggerated during unpleasant picture processing in Veterans at high risk for suicide (i.e. multiple attempters) and shows promise as a predictor of a future suicide attempt.[30] For the RCT component, we consented 368 Veterans and 324 completed the clinical assessments. Approximately 59% of the sample completed the 6-month DBT trial and 51% were retained at the 12-month follow-up. Over 100 Veterans participated in the supplement study.[30] This underscores our ability to recruit and retain a large sample size of Veterans at risk for suicide and conduct a treatment trial in this population. The proposed pilot study will recruit the majority of Veterans from the PI's current VA Merit examining the neurobiology of suicidal behavior using MRI. To date, we have recruited >200 Veterans for this Merit study and of those, ~100 met our stringent criteria and received extensive clinical assessments, neurocognitive assessments, and a MRI scan. We will also recruit outpatients, if necessary. Dr. Haznedar (Co-I), a full-time psychiatrist in the Psychiatry OPD Care Center at the JJPVAMC will facilitate recruitment.

2.B. Prior Work in Cognitive Remediation in Veterans with Serious Mental Illness. We have a track record of successfully conducting a CR plus social skills training (SST) group intervention in Veterans with serious mental illness (SMI) at the JJPVAMC.[31] We studied 19 Veterans with schizophrenia in an 8-week trial of CR+SST and also obtained structural MRI scans. The results indicated that Veterans with schizophrenia demonstrated statistically significant improvement on MATRICS Consensus Cognitive Battery[32] scores for reasoning/problem solving and verbal learning following the CR+SST intervention. Additionally, Veterans with schizophrenia also improved on a social cognition task (Movie for the Assessment of Social Cognition[33]) and there was a trend for improvement on a measure of functional skills outcome (UCSD Performance-Based Skills Assessment[34]). Baseline MRI measurement of white matter integrity (i.e. fractional anisotropy; FA) in the superior longitudinal fasciculus also predicted improvements in visual-spatial working memory while overall baseline FA predicted improvements in social cognition. Importantly, the Veterans were highly engaged with excellent attendance (mean attendance: 79% and *no dropouts during the treatment)* across cohorts (mean cohort size was 4 participants, range: 3-6 which is in line with the proposed group size of 6). Although a small sample size, significant results were observed and indicate that the proposed study, which also involves CR in Veterans who are also outpatients with SMI, is highly feasible.

2.C. Cognitive Remediation in Depression. Dr. Medalia (Co-I) has extensive clinical and research experience developing and implementing CR therapies for individuals with SMI, including MDD. As Clinical Director of Cognitive Health Services for the largest mental health system in the U.S., she continues to advance research on techniques of neuropsychological rehabilitation in individuals with psychiatric disorders so that they can be effective and functional in daily life. Dr. Medalia's work examining psychiatric outpatients, including many who had been diagnosed with depression, shows significant improvement in attention skills and work-related behavior after participating in Neuropsychological Educational Approach to Cognitive Remediation (NEAR, termed CR plus "Bridging" session, CR+Bridging; total of 26 hours, 1-hour session/week).[35] Her work with acute psychiatric inpatients, the majority of whom carried a diagnosis of MDD, also demonstrated effects; the experimental group exhibited greater improvement in verbal problem solving and on measures of ability to cope with their symptoms and the requirements of daily living.[36] She has also contributed significantly to work establishing the feasibility and acceptability of CR+Bridging in research and clinical settings.[37] *A highly novel aspect of the proposed study is to begin to examine CR+Bridging in Veterans at high risk for suicide.*

3. Research Design and Methods

3.A. Neuropsychological Educational Approach to Cognitive Remediation (NEAR, termed CR+Bridging). This study proposes to use the Neuropsychological Educational Approach to Cognitive Remediation (NEAR[10] as an adjunct to usual treatment) developed by Dr. Alice Medalia (Consultant on this SPiRE application; see letter of support) to target the cognitive control and decision-making/problem-solving deficits associated with suicidal behavior in MDD. CR+Bridging is a manualized treatment program (group format) based on empirically-supported principles of learning and motivation. It is a recovery-oriented rehabilitation approach that provides a focus on cognitive skills but does so by taking into account the social-emotional variables which impact and interact with "thinking" throughout the day. The sessions consist of computerized executive functioning (EF) exercises, followed immediately by a Bridging group to discuss effective strategies for transferring the EF skills exercised to real-life situations. NEAR has been shown to be effective in other psychiatric populations, including schizophrenia and bipolar disorder.[38] It results in significant improvement in attention/executive functioning skills, including problem-solving[36, 39] and cognitive control.[40] These remediation effects have been shown to persist for at least four months post intervention and translate to improvements in symptoms, real-world problem solving, social functioning, and occupational functioning.[38]

CR+Bridging stands out from other CR programs that have been criticized for lack of transfer to everyday skills because it augments each EF training session with the Bridging group. The Bridging group takes a meta-cognitive approach to helping patients improve their cognitive skills and daily functioning for more long-term effects. It does so by: (1) teaching them about/bringing self-awareness to their own cognitive control, decision/making, and emotion regulation skills (e.g., they learn how to regulate their emotions elicited by the task context, which simulates the process of regulating such emotions during daily stressors) utilized during the computer exercises. The Bridging session subsequently: (2) builds on that self-awareness to promote the simulation, practice, and implementation of effective strategies for employing effective cognitive control, decision-making, and emotion-regulation skills in personalized, real-life situations and stressors. These situations and stressors primarily include those that trigger depression symptoms and accompanying thoughts of rumination on SB. *Given the demonstrated utility of CR+Bridging for helping individuals with MDD manage their illness and restore the skills needed for living successfully in the community,*[7, 8, 9] *the proposed work (1) aligns with the goals of VA RR&D in developing "interventions which will enable Veterans with psychologically*

disabling conditions to function more fully in society" and (2) may provide new targets for suicide prevention/ intervention. With supervision and support from Dr. Medalia and Ms. Nicholas, each session follows the CR+Bridging format and is tailored to address the specific cognitive control and decision-making/problem solving deficits linked to suicidal behavior in this patient population. The widely used computerized exercises utilized during the initial portion of each session are modeled after those proven to be effective at improving cognitive control and decision-making/problem-solving skills in psychiatric populations with weakness in those areas.[41, 42] The Bridging session that immediately follows each cognitive training session involves consistent practice of learned cognitive control and problem-solving strategies, ultimately enabling patients to exert better control over emotion regulation processes in stressful situations. Each session involves the following: (1) Use of password to enter telehealth platform; (2) Verify confidentiality/privacy with all patients; (3) Check-in regarding status of each patient's technology and print log/journal; (4) Check-in with patients regarding their mood; (5) Share screens depicting their computer-based cognitive training and initiate use of exercises; (6) Break; (7) Quit all members' sharing of screens and initiate Bridging session to promote transfer of skills learned in context of computer-based training to a broader set of real-world scenarios; (8) Complete log/journal and list tasks for next session. See **Table 3.A** for brief summary of content for each active learning plan/session. See **Appendix 4** for Individual Session Log and examples of Bridging Group content.

Table 3.A. Bridging Session Content.

Week/Session #	Targeted Cognitive Skills	Transfer to Daily Functioning Skills in Bridging Session
1/Sessions 1 & 2	Session 1: (a) Introduce CR+Bridging as a meta-cognitive program ("thinking about thinking"), identify/define the target cognitive skills and why, when, and how they will learn to use them to improve their daily functioning, define patient goals for treatment; (b) Introduce computer-based exercises. Session 2: Selective & sustained attention: Part 1	Session 1: (a) Provide psychoeducation on the relationship between depression and cognition; (b) Discuss neuroplasticity, the brain's ability to learn, and draw explicit "bridges"/links between the computer-based exercises and how they relate to real-world use of cognitive strategies to improve cognitive control and problem-solving difficulties in daily life, particularly during times of distress. Session 2: Discussion and practice of strategies to manage external distractions (e.g., auditory, visual), including those that trigger and/or result from stress.
2/Sessions 3 & 4	Selective & sustained attention: Part 2	Discussion and practice of strategies to overcome emotional and cognitive distractors.
3/Sessions 5 & 6	Selective & sustained attention: Part 3	Continued practice of strategies to overcome emotional and cognitive distractors.
4/Sessions 7 & 8	Flexible attention: Part 1	Discussion and practice of strategies for "switching" from one thought/behavior to more adaptive thoughts/behaviors, which will consequently facilitate problem-solving.
5/Sessions 9 & 10	Flexible attention: Part 2	Continued practice of strategies for "switching" from one thought/behavior to more adaptive thoughts/behaviors, which will consequently facilitate problem-solving.
6/Sessions 11 & 12	Problem solving: Part 1	Discussion/practice of problem-solving strategies. Focus: describing the problem, goals, and obstacles.
7/Sessions 13 & 14	Problem solving: Part 2	Discussion/practice of problem-solving strategies. Focus: brainstorming solutions, evaluating the possible outcomes/consequences, and selecting a solution to try.
8/Sessions 15 & 16	Problem solving: Part 3	Discussion/practice of problem-solving strategies. Focus: developing a plan to implement solution and breaking it down into manageable steps.
9/Sessions 17 & 18	Problem solving: Part 4	Discussion/practice of problem-solving strategies. Focus: trying the solution and evaluating again. Is the problem solved? If not, try a new solution or solutions.
10/Sessions 19 & 20	Problem solving: Part 5	Review and continued practice of cognitive control and problem-solving skills across multiple contexts/situations.

3.B. Procedure. Patients will be recruited through an ongoing VA Merit Study (PI: Hazlett) at the JJPVAMC, *"Neurobiology of affective instability in Veterans at Low and High Risk for Suicide"* that already has in place recruitment and assessment procedures for diagnosis. To date, the PI has recruited and screened >200 Veterans for this Merit study and ~100 of them met the stringent study criteria and received structured clinical interviews and MRI scans. The proposed study leverages support from the parent study for recruitment, as the Veterans have already been screened and diagnosed. See **Human Subjects** and **Appendix 2**.

3.C. Participants. *Inclusion criteria.* Age 18-60; U.S. Veteran; primary diagnosis of MDD and history of suicide attempt in the past year; elevated score (>1SD above the normal mean) on rumination measure (Ruminative Response Scale;[43] see **Table 3.D**, below); based on the Columbia-Suicide Severity Rating Scale (C-SSRS)[44]:

current suicidal ideation (either passive, i.e. "wish to be dead") or active ideation but with no intent to act on it immediately and no specific plan; and currently in psychotherapy treatment as usual (TAU) at the JJPVAMC. We will include women and aim for the sample to be 30% women. *Exclusion criteria.* Current substance use disorder; history of traumatic brain injury; neurological disorder, or other medical confound; compromised intellectual abilities (WASI[45] FSIQ<70). *We will enroll six Veterans in each group and conduct six 10-week intervention cycles for a total sample of 36 Veterans.* See **Appendix 3** for Enrollment Table.

3.D. Clinical, Cognitive, Social, and Adaptive Functioning Assessments and Schedule. Patients referred from Dr. Hazlett's current VA Merit study will already have been screened/diagnosed using the Structured Clinical Interview for DSM-5 Disorders (SCID),[46] Structured Interview for DSM-5 Personality Disorders (SCID-PD),[47] and the C-SSRS.[44] We use the SCID-PD given our interest and prior work in borderline personality disorder (BPD), and because many high-risk Veterans meet criteria for BPD, e.g., see [30]**.** These three assessments will be reviewed for any interested participants once they have consented for the current study. Additionally, the Ruminative Response Scale[43] will be administered during the screening process to determine whether they meet the study inclusion criteria for poor cognitive control problems (see **3.C.** *Inclusion*). Participants will be enrolled in the intervention and undergo assessments (**Table 3.D**) at the various timepoints: pre- **(Baseline)**, post-intervention **(Week 10)** and follow-up **(Week 20)** to be administered in person and abiding by strict COVID-19 safety precautions (e.g., health screening on day prior and day-of visit, temperature check, socially distanced throughout visit, sanitization of all testing materials and furniture before, during, and after each visit).

Following baseline assessments, Veterans will participate in the CR+Bridging sessions (2x/week for 10 weeks; i.e. 20 sessions) via telehealth with a clinical neuropsychologist (Dr. Goldstein/Co-I, who will administer all treatment sessions and train MIRECC Advanced Psychology Fellows on the intervention). Dr. Haznedar (Co-I) will conduct all clinical assessments blind to the patients' progress in the CR+Bridging sessions.

Table 3.D. Clinical, Cognitive, Social, Adaptive Functioning Assessment Schedule. Primary outcome variables are **bold** font.

Assessment:	**Domain**	**Baseline (Pre-Tx)**	**Week 10 (Post-Tx)**	**Week 20 (Follow-Up)**
Demographics	Demographics	X		
Structured Clinical Interview for DSM-5 Disorders[46]	Diagnostic	X		
Structured Clinical Interview for DSM-5 Personality Disorders[47]	Diagnostic	X		
Columbia-Suicide Severity Rating Scale (C-SSRS)[44]	Diagnostic	X	X	X
Ruminative Response Scale[43]	Rumination	X	X	X
Cognitive Remediation Fidelity Scale[10]	Fidelity		X	
Patient and Therapist Satisfaction Questionnaire (see Appendix 5)	Feasibility/Acceptability		X	X
Intrinsic Motivation Inventory[48]	Motivation	X	X	
Revised Helping Alliance Questionnaire[49]	Therapeutic Alliance		X	
Iowa Gambling Task[11-12] (with alternate decks)	Problem-solving	X	X	X
Tower of Hanoi[50] (with parallel versions)	Problem-solving	X	X	X
Stroop Test[51] (with parallel versions)	Cognitive inhibition	X	X	X
Go/No-Go[52] (with parallel versions)	Motor inhibition	X	X	X
Naming Test/Neuropsychological Assessment Battery,[14] Form 1 & 2 (Control test; not expected to change with intervention)	Naming/Control test	X	X	X
Montgomery-Ashberg Depression Rating Scale[13]	Depression	X	X	X
The Personal & Social Performance Scale[2]	Social	X	X	X
The Work & Social Adjustment Scale[3]	Social, Occupational	X	X	X
Questionnaire for assessing the impact of the COVID-19 pandemic and accompanying mitigation efforts on older adults[15]	Impact of COVID-19	X	X	X
Longitudinal Interval Follow-up Evaluation Range of Impaired Functioning Tool, LIFE-RIFT[16]	Functional impairment	X	X	X

3.E. CR+Bridging Training, Fidelity, Acceptability, and Feasibility. Members of our research team (Drs. Medalia and Goodman) have extensive experience developing psychosocial interventions in civilian and Veteran samples and establishing their fidelity. CR+Bridging training will include weekly supervision of Dr. Goldstein with Dr. Medalia or Ms. Nicholas and a modified version of the Cognitive Remediation Fidelity Scale[10] (see **Appendix 6**) will be employed to assess fidelity to the manual. Dr. Medalia will also oversee implementation of supplementary measures of potential moderators of the intervention (e.g., motivation for treatment and baseline sets of work habits,[48] quality of therapeutic relationships[49]).

Acceptability will be examined via survey responses (see **Appendix 5**) completed by the patients and therapist at the completion of the intervention and follow-up (Weeks 10 and 20). Feasibility will be measured in

several ways. This includes: (1) ease of implementation—operationalized as less than 60 hours per cycle from start/preparation through intervention delivery until conclusion of follow-up assessment; (2) recruitment, attendance, and retention (operationalized as >75% successful recruitment and 75% attend >15 sessions); and (3) training and fidelity of therapist to CR+Bridging will be conducted at Week 10 (see **Appendix 6**).

3.F. Timeline. As shown in **Table 3.F**, the CR+Bridging open trial will be conducted with six groups (each group including six Veterans for the 10-week intervention) during months 4-16 with Week 10/Post-tx and Week 20/Follow-up sessions conducted during months 8-21. Data collection will be completed in month 21, followed by data analysis. Manuscript writing and CSR&D Merit Award RCT application submission will occur during months 23-24. A potential limitation that may impact the success of this project is recruitment of Veterans during this challenging time of COVID-19. However, a strength of the proposed clinical intervention study is that it involves telehealth, making it more appealing to participants and less prone to high no-show rates.

Table 3.F. Study Timeline. **Year:**	1	1	1	1	1	1	1	1	1	1	1	1	2	2	2		2	2	2	2	2	2	2	2	2
Month:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15		16	17	18	19	20	21	22	23	24
Train staff/Obtain IRB approval:	x	x	x																						
Conduct open trial: Group # Note: Each group includes 6 Veterans/patients: 6 groups x 6 = 36 (total)				1	1	1 & 2	2	2	3	3	3 & 4	4	4	5 & 6	5 & 6		5 & 6									
Conduct baseline/pre-tx assessments:			x		x			x		x			x												
Week 10/post-tx & 20/follow-up assessments:								x	x	x	x	x	x	x	x		x	x	x	x	x	x			
Data entry/analysis:				x	x	x	x	x	x	x	x	x	x	x	x		x	x	x	x	x	x	x	x	x
Submit papers and RCT VA Merit Award																								x	x

3.G. Statistical Approach. *Rationale for Proposed Sample Size (which applies to all aims):* We used data from a similar CR study in civilians[53] to determine our sample size. Hamilton Depression Rating Scale (self-report measure that includes the same symptoms as the clinician-administered MADRS[13] which we will use in the proposed study) scores from pre- and post-CR intervention from Naismith et al[53] were used to provide estimates of change in depression severity that we can apply to the MADRS. Using a sample size of 22 achieves 90% power to detect a mean of paired differences of 3.2 with an estimated standard deviation of 4.35 for differences and with a significance level of 0.05 using a two-sided paired t-test. For the current pilot study, we will enroll 36 Veterans in the intervention and we conservatively anticipate up to 40% attrition. This means that even with only 22 completers, we will still be well-powered for the proposed analyses.

Aim 1: *Sample size:* Definitive conclusions about the efficacy of the CR+Bridging intervention cannot be made based on this pilot study's findings. We plan to use the data collected to: (1) calculate power for a larger confirmatory study and (2) examine acceptability and feasibility data. We plan to submit a VA Merit application that will involve a rigorous RCT to determine efficacy of this novel intervention.

Analysis: We will calculate descriptive statistics, e.g., means, standard deviations, minimum, maximum for continuous measures (e.g., CR+Bridging treatment fidelity ratings, retention), as well as count and frequencies for categorical measures (e.g., attendance). We will be able to compare these descriptive statistics to published rates of recruitment, engagement, and attendance of similar type interventions.

Aim 2: *Sample Size:* Using a two-sided paired t-test to compare MADRS[13] before and after for each subject, for 90% power at a 5% level of significance and assuming a decrease in MADRS with a range of standard deviations from 1 to 10, we can detect a mean paired difference of -0.7 to -6.5 for 22 Veterans.

Analysis: MADRS[13] and Iowa Gambling Task (IGT[11, 12]) scores are the primary outcome variables here. For all of the study completers, each outcome measure will be compared initially between Baseline and Week 10 (pre- vs. post-intervention) by paired t-test. As a secondary analysis, all outcome measures in Table 3.D will be compared this way as well. Correction for multiple comparisons will be performed using a Holm's correction.

For exploratory analyses, outcome variables that reach significance for Pre-tx/Baseline vs. Post-tx/Week 10 comparisons will also be analyzed across all three time points (Baseline, Week 10, Week 20/Follow-up) using a linear mixed-effects model with unstructured correlation between time points.

Missing data will be assumed to be missing at random and handled accordingly by multiple imputation. All statistical tests will be 2-tailed with alpha=0.05.

Aim 3: *Sample Size:* This aim is exploratory. We will utilize the same sample size as shown in the sample size section and acknowledge that we may be underpowered for these analyses.

Analysis: Each outcome measure (e.g., QAICPOA[15], LIFE-RIFT[16]) will be compared initially between Baseline and Week 10 by a paired t-test and if either show significance, then they will be compared across all three time points using the same mixed-effects model analysis as described in Aim 2.