Title: Suicide Prevention for Patients with Chronic Pain

Specific Aims/Purpose: The goal of the current proposal is to ensure Problem-solving Treatment (PST) is remediating problem-solving deficits for Veterans with chronic pain and moderate suicide risk. Veterans with chronic pain and moderate suicide risk (n=60) will be randomized to receive remote-PST or remote-attentional control. We will assess problem-solving deficits through self-report, objective neuropsychological assessment and the report of the Veteran's support person (e.g., significant other, caregiver, spouse, partner, family member, friend).

Hypothesis:

Aim 1: Estimate the effect of remote-delivered PST on targets. We hypothesize that PST reduces our primary target, problem-solving deficits as assessed through (H1) self-report, (H2) objective neuropsychological assessment, (H3) caregiver report, as compared to attentional control. We hypothesize that PST reduces our secondary targets (H4) feelings of burdensomeness,[25] and (H5) feelings of not belonging[25], as compared to attentional control.

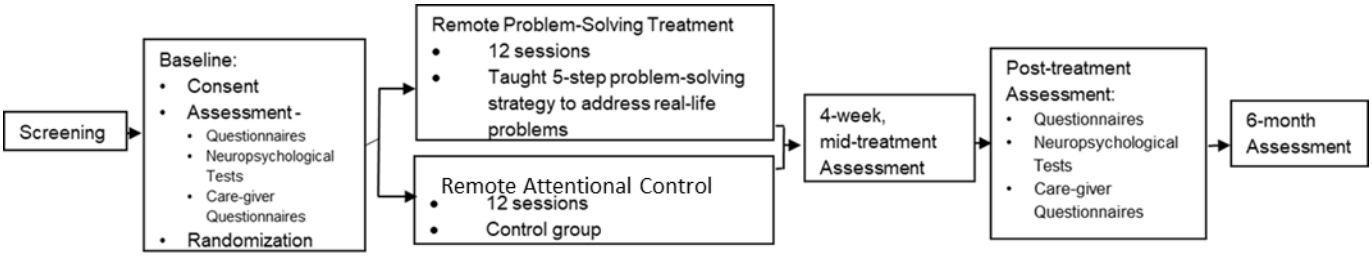
Exploratory Aim 2: Explore the effect size of PST as compared to attentional control on suicide outcomes including: (H6) intensity of suicidal ideation;[26] (H7) difficulties coping with suicidal ideation[27] and chronic pain outcomes (including (H8) chronic pain[28-30] and (H9) pain-related disability[31]).

Scientific Rationale and Significance: Every day, 120 people die from suicide – that is one person every 15 minutes.[1] Suicide prevention treatments focus on those at highest risk and are primarily delivered as mental health treatments,[2-5] and yet 70% of patients with suicide risk do not attend mental health treatment.[6] Developing treatment for patients not served by existing suicide prevention programs will improve access to care and is necessary to stop suicide.

Patients with chronic pain in the US (100 million)[7] have 2.6-times greater risk of suicide[8-11] and those on long-term opioid treatment are at even greater risk. Unfortunately, they often do not receive mental health treatment and thus do not receive suicide prevention interventions.[12] They do receive frequent healthcare for their pain[13,14] providing an unmet opportunity to integrate suicide prevention into their treatment for pain. Problem-solving Treatment (PST) is an evidence-based approach that is available where patients want to receive treatment (e.g., primary care) and is efficacious for chronic pain.[15,16] Importantly, PST targets problem-solving deficits which are known to increase risk of suicide, suggesting PST could be leveraged to reduce suicide risk. Deficits in problem-solving (an executive function used to find solutions to difficult issues)[17-19] directly increase suicidal risk because they keep patients with active suicidal ideation from generating solutions to their problems (e.g., chronic pain), other than through suicide.[3,20-22] Deficits in problem-solving also make it difficult to keep pain from impairing daily activities and social relationships. This indirectly increases suicide risk because impairment in daily activities increases feelings of burdensomeness and impairment in social relationships increases feelings of not belonging.[23] Feelings of burdensomeness and of not belonging are key theoretical pathways to suicidal behavior.[24]

Research Design and Methods: This treatment study will be a randomized controlled trial with two arms: remote Problem-solving Treatment versus remote attentional control. Up to 1,000 Veterans will be screened and up to 60 Veterans will be enrolled. Subject participation will occur over the course of

approximately 9 months; Figure 1 outlines the study methods. Additionally, we will be asking enrolled Veterans to identify their support person (e.g., significant other, caregiver, spouse, partner, family member, friend) and we will invite the identified support person to complete a questionnaire and provide their perspective on the Veteran's problem-solving ability.



Study Population Participants will consist of 60 Veterans with chronic pain and active suicide ideation. Participants will be randomized to either remote Problem-solving Treatment or remote attentional control (n=30/group). Consistent with recommendations for preliminary analyses, sample size was determined based on estimates of feasibility during the study timeframe.[90,91]

Subject Identification and Recruitment: Any Veteran who resides within the United States may be invited to participate in the study. During the phone screening, we will request verbal consent and inclusion/exclusion criteria will be evaluated. Veterans may be recruited from anywhere in the nation. Potential participants may be identified through the following: VINCI, VISTA and/or CPRS, REACH VET, the Managerial Accounting Office (MCAO), the VA Epidemiology Program, the VA Office of Public Health Gulf War Registry, the Defense Manpower Data Center (DMDC) of the Department of Defense (DoD), VADIR (Veteran Administrative DoD Identity Repository), WRIISC Clinical and Operations Databases. We may also reach out to Veterans who have both participated in recent studies and expressed interest in being contacted. We will request from VINCI, the DMDC, VADIR, the VA Epidemiology Program, and VA Office of Public Health Gulf War Registry to provide a list of Veterans who possibly meet our inclusion criteria and reside nationally. Data elements requested can include the following: name, date of birth, social security numbers, address, contact phone number(s), vital statistics, period of combat (combat pay records) and/or service medals, status of deployment.

We will also use the following methods to identify and recruit potential participants: referrals, standard mail, telephone, flyers, and advertisements. This includes: 1. planned conferences, satellite broadcasts, and other educational workshops or meetings for providers or Veterans; 2. VA facilities and affiliated ambulatory services including community-based outpatient clinics (CBOCs); 3. community locations (e.g., Home Depot); 4. Veteran-related events such as job fairs; 5. newspapers/newsletters; 6. websites relevant to Veterans (e.g., American Legions); 7. VA and Veteran-related social media; and 8. websites relevant to recruitment (e.g. clinicaltrials.gov).

In addition, we will post general information about this study on other electronic media (e.g. the WRIISC website, Office of Public Health's (OPH) website, academic affiliations websites, and other VA and Veteran-related websites. We will reach out to Veteran Service Organizations (VSO) to develop a recruitment plan. We will also inform any Veteran who walks in or contacts the WRIISC interested to participate in research opportunities about this study. This includes Veterans who are participating in other research studies at the WRIISC.

Once potential participants are identified, we will mail a recruitment letter and may follow-up approximately 1 week later with a phone call inviting them to be screened for participation. For those who express interest, we will conduct an ~25-minute telephone screening to determine eligibility (see attached – Phone Screen Script and Phone Screening Questionnaire Packet). If a Veteran is ineligible at any point during the screening process, the member of the Study Team conducting the screening will stop and inform the Veteran of this. If eligibility is unclear at the end of the screening, a member of the Study Team will inform the Veteran that he/she will call him/her back. The member of the Study Team will then consult with the PI or another member of the Study Team, review the Veteran's medical chart (if needed) and call the Veteran to let him/her know whether he/she is eligible. If the Veteran is eligible at the end of the screening, the member of the Study Team will notify the Veteran of this and offer to schedule a day and time to complete the telephone-based informed consent process. When clinically appropriate we will also reach out to Veterans' established providers at screening to communicate the patient's active suicidal ideation. (If there is an increase in C-SSRS score from screening to baseline, we will notify the Veterans' established providers of this change).

After screening eligible, we will ask Veterans to identify their support person (e.g., significant other, caregiver, spouse, partner, family member, friend). Veterans can opt out of identifying a support person and still participate in the study. Study staff will reach out to the support person via phone or mail to provide information about the study and ask if the support person is interested in participating in the study. Support person study participation is limited to filling out a questionnaire to provide their perspective on the Veteran's problem-solving ability. We will seek to over-recruit women Veterans (~30%).

Informed Consent: The consenting process for the study primarily will be conducted over the telephone and take approximately 45 minutes to complete. We are obtaining a waiver of documentation of consent for this study. A full telephone consent will be conducted with Veterans that are interested and eligible to participate. Prior to the telephone appointment during which the informed consent will be reviewed, the Veteran may be sent materials in order to review study procedures and formulate questions prior to the subsequent telephone appointment. These materials may include: a welcome letter, a confirmation letter detailing their appointment date/time, study information sheet, the baseline assessment, a copy of the written informed consent and HIPAA, provider contact forms and a revocation form. During the telephone consent procedure, the consent form will be reviewed with the Veteran. Veterans who prefer in-person consenting will be allowed to come to our site and consent in-person. Study personnel who have been specifically trained on the current protocol will obtain consent. Investigators will be available to answer any study-related questions that may arise. At the end of reviewing the informed consent and answering any questions, we will therefore ask the Veteran if he/she agrees to participate. Prior to each study component, the Veteran will be verbally told what the procedures are. Participants who express discomfort will be reminded that their participation is voluntary.

For the support people that are interested in participating, we will mail them a confirmation letter detailing their appointment date/time, a study information sheet, the baseline assessment packet, and a copy of the written informed consent and HIPAA so they can review the study procedures and formulate questions prior to their subsequent telephone appointment. We are obtaining a waiver of documentation of consent for the Veteran's support person and will ask their support person, at the end

of reviewing the informed consent and answering any questions, if she/he agrees to participate. This will take approximately 10 minutes to complete and will primarily be conducted over the phone.

Inclusion Criteria: (a) has a VA primary care provider and has had an in-person visit with a VA provider in the past year; (b) pain that is: (b1) musculoskeletal, defined as regional (joints, limbs, back, neck) or more generalized (chronic widespread pain); (b2) moderately severe, defined as a Brief Pain Inventory (BPI) intensity item score of 5 or higher for either "average" or "worst" pain in the past week; and (b3) persistent, (i.e., ≥3 months); (c) active suicidal ideation defined as scoring a 2 to 4 on the C-SSRS.

Exclusion Criteria: (a) life-threatening condition; (b) severe cognitive impairment; (c) psychotic disorder; (d) pregnant or plans to become pregnant in the next year; (e) suicide attempt in the past year or hospitalization for suicide risk in the past year.

Randomization Procedures: Since randomization may fail to ensure equivalent levels of our primary dependent variable, we will enroll Veterans in matched pairs and use an urn randomization procedure designed to maximize the equivalence of groups based on selected matching criteria [59] or "urns." Matching will be based on screening suicidal ideation intensity and problem-solving ability with members of a pair falling within +/- 20% of one another to ensure that the distribution is comparable between groups. This matching rule permits wide latitude in scores, but if a Veteran is not matched s/he will be offered Problem-solving Treatment outside of the study. We will use the computer program developed for Project MATCH to generate the randomization schedule. The study coordinator will conduct the randomization. Research investigators (including the Principal Investigator) will be blind to study assignment.

Risks and Side Effects: There is a possibility that participants may become distressed during the assessments or treatment due to the sensitive nature of the subject matter or may make statements or report behaviors indicating deteriorated psychological status unrelated to their study participation. Study personnel are trained in distressed patient management including arranging for a clinician to speak with the Veteran, if necessary. All Veterans in the study will be provided the 24-hour Veterans Crisis Line contact information.

> Problem-solving Treatment: Veterans may decide to make changes to daily activities (e.g., starting a new diet, doing physical activity, increase social activities) of their choosing. Since the activities are personalized, the exact risks are not known. If and how these changes are made is the Veteran's choice. They will be encouraged to talk with their Provider or other medical provider to minimize any risks and address any concerns. We may also contact their health care provider.
>
> Problem-solving Treatment is a known evidence-based treatment and extensive research has demonstrated no long-term risks. While we expect some participants will experience an increase in distress, this should be temporary and within a normal range of distress for the participant. A breach in confidentiality is unlikely. Overall the risk to the Veteran is minimal.
>
> Attentional control condition: Veterans are asked to identify and discuss feelings. These may include difficult emotions like embarrassment, sadness, stress, anxiety, disappointment, irritability, etc. Discussion of these emotional states may result in some Veterans experiencing increased levels of distress. Providers will remind Veterans that they do not need to discuss

anything they don't want to. Additionally, participants will be informed that our attentional control condition is **not** considered a standard treatment of care and is **not** in replacement of standard clinical care. Veterans will also be notified that there are other treatments options available to address pain and suicidal thoughts.

This attentional control has been recently used successfully as a control group in large clinical trials for suicide prevention.[92] Attentional control is thought to encompass common therapeutic factors, (e.g., therapeutic alliance, emotional support), while excluding the factors specific to the active treatment condition (e.g., skill building, use of behavior change techniques and outside practice).

Data Monitoring Plan: A three-person Data and Safety Monitoring Board (DSMB) will be recruited to oversee and monitor the safety of study participants and the validity and integrity of the research endeavor. The first meeting of the Board will establish the DSMB procedures. We plan for the board to be independent of the study and include: expert in suicide prevention, biostatistician and facility leader at the VA NJHCS (e.g., head of mental health).

It was decided that the DSMB will meet twice a year and more often as needed both with and without the investigators present. The full DSMB will determine when and if the investigators will attend. The chair of the DSMB will rotate among the three members, with each member serving as chair for one year.

Proposed DSMB Procedures: The VANJHCS IRB will be informed of the DSMB procedures - and the names of the board members - established during this initial meeting. The IRB will evaluate the monitoring procedures and recommend modifications if necessary.

Once a year, the PI will send information to the DSMB on recruitment progress (screened, declined, enrolled, excluded, medical stability considerations for inclusion/exclusion in study, active in study, lost to follow-up), treatment completion rates, serious adverse events, and rates of re-hospitalization and suicide attempts. Study personnel will maintain a running tally of this information throughout the life of the study and will report the information separately by study condition. IRB continuing review documents will also be provided to the DSMB. DSMB members will receive this material for review in advance of scheduled meetings.

The following events would be reportable to the DSMB as soon as they are recognized:

a) Serious Adverse Events (SAE) (as defined in VHA Handbooks 1058.01 & 1200.05) that are related to study procedures or occur at a rate that is at least 25% higher in one condition compared to the other.

b) New information which alters the risk: benefit ratio of participating in the study

c) Events compromising data confidentiality.

Following each meeting of the DSMB, the DSMB Chair will prepare and send a brief summary report to the PI. The report will document that: (1) a review of recruitment, data and outcomes has occurred, (2) the number, nature, and outcome of any AEs occurring during the review period, and (3) reflect the date the review took place. The report will also inform the PI of the board's conclusion with respect to study progress, any need for modification of the study protocol or operating procedures, and

approval/disapproval for the study to continue. Upon receipt of the report, the PI will be responsible for transmitting a copy of the report to the IRB.

Medical Monitor

In addition to the DSMB, the study will engage a medical monitor. The principal investigator and/or head study provider will reach out to the study monitor within 24 hours through phone and if needed encrypted email for consultation in the following situations:

- Suicide attempt
- Indication that participant has developed definite intent to carry out a suicide plan, as measured by endorsement of item 5 on Section I of the C-SSRS.
- If there is a significant increase in the severity of suicidal ideation the participant. Increased risk will include an increase of 2 points on the C-SSRS from a participant's baseline level (e.g., moving from a baseline C-SSRS score of 2 [i.e., thoughts of killing oneself without any associated method or intent] to a C-SSRS score of 4 [i.e., suicidal thoughts with some, limited intent to act on them]).
- If a participant baseline score on the C-SSRS is a 4.

We will work with the medical monitor to update these procedures as needed.

Clinical Monitoring

NIH Clinical site monitoring is conducted to ensure that the rights and well-being of human subjects are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirement(s). The main features are below.

- Monitoring for this study will be performed by NIMH Clinical Trials Operations Branch (CTOB) monitors.
- Monitoring will be conducted on-site or virtually, throughout the study, and involve targeted data verification of key data variables
- The site PI will be provided copies of monitoring reports within 10 days of visit.

Safety Plan: Our highest priority is patient safety. To develop our safety protocol, we met with the head of mental health and suicide prevention coordinators at the VA-NJHCS; we also consulted with Dr. Interian (co-investigator) who is conducting a suicide prevention trial at VA-NJHCS and Dr. Selby, a suicidologist. When interacting with a patient over the phone or VVC, the patient will provide their current address at the start of every contact. If the patient is not in a safe environment (e.g., driving), the study staff will reschedule. If at any time there is a concern the patient is in immediate risk, we will contact emergency services to perform a safety check at the patients' current location.

At screening or assessment: The C-SSRS will be administrated by study personnel. We have an established safety protocol which includes study personnel not making calls or seeing a patient on-site without at least one of the 7 mental health professionals on the floor. Additionally, staff receive twice yearly crisis intervention training. If the patient reports being in distress, a mental health provider will

conduct an immediate crisis assessment and respond using clinical judgment. This may include communicating with the patient's established providers, transferring to the VA National Suicide Prevention Hotline, or calling emergency services, if appropriate.

During treatment: Study providers will not schedule therapy sessions unless there is a backup clinician. Study providers will also obtain emergency contact info for participants (in case we need to engage participants' support person for safety), they will also compile a list of local service telephone numbers for each participant. In the event of increased suicidal ideation or risk, the study provider will conduct a comprehensive assessment. Then the study provider will use clinical judgment to ensure the patient's safety, this may include increasing calls to twice-weekly or coordinating with the suicide prevention coordinator. Any time there is a concern about immediate risk the study provider will contact emergency services. If a patient becomes too high risk to be safely treated in this setting, the study provider will work with the patient and the patient's established VA providers to consider more intensive intervention.

When a participant is withdrawn from the research for safety concerns, our team will retain clinical responsibility until continuing care is successfully transferred to the appropriate provider (e.g., emergency department, hospitalization, psychiatrist, local suicide prevention coordinator, primary care provider). The following situations will necessitate participant withdrawal from the research (but not clinical care):

- Suicide attempt
- Indication that participant has developed definite intent to carry out a suicide plan, as measured by endorsement of item 5 on Section I of the C-SSRS.
- In addition, if there is a significant increase in the severity of suicidal ideation the participant will be reviewed by an internal study safety team comprised of 3 study investigators to determine appropriateness for continued participation. Increased risk will include an increase of 2 points on the C-SSRS from a participant's baseline level (e.g., moving from a baseline C-SSRS score of 2 [i.e., thoughts of killing oneself without any associated method or intent] to a C-SSRS score of 4 [i.e., suicidal thoughts with some, limited intent to act on them]).

Data Analysis Plan: We will explore the data using scatterplot graphs and calculating the means, standard deviations, proportions, histograms, etc. to explore the distributions of the data, identify outliers and calculate correlations between variables. We will calculate the percent change from baseline for each measure. We will also calculate the effect size (Cohen's D) for the change in each arm from pre to post treatment and calculate the effect size of the change in treatment between arms. Consistent with best practices for preliminary data analysis, we will not calculate statistical significance as we are not be powered to find an effect.[90,91] The analyses will be conducted with intent to treat approach.

Best practices for determining improvement in executive functioning include using self-report, objective and support person report. While it is not expected all measures will show improvement due to variability in the assessment approaches, there should be an indication of clinically significant improvement across multiple assessments. Our preliminary data is consistent with previous research that finds PST has a moderate effect on self-report of problem-solving deficits (Cohen's D >0.22)[45,46] as

compared to control and a small effect on objective measures of problem-solving deficits (Cohen's D >0.15) as compared to control - and these are clinically significant.

We will conclude that our trial shows support for target engagement if we find a clinically significant effect size for PST as compared to control for two of the three domains (self-report Cohen's D>.22; objective neuropsychological tests Cohen's D>.15 for at least two measures; support person report Cohen's D>.22) and no domain showing support for control over PST (self-report Cohen's D>.22 in support of control; objective neuropsychological tests Cohen's D>.15 for at least two measures in support of control; support person report Cohen's D>.22 in support of control). We will also explore if there are differences in effects based on level of provider training.

If data from this study suggest converting the trial into a fully-powered clinical trial, we will consider the analyses of getting the effect size as an interim analysis to inform the planning of R01, and adjust the sample size in the R01 using the method of, for instance, sample size re-estimation approach, to appropriately adjust for the alpha level for the test at the final data analysis of the full trial.

Some of the data analysis will be completed by our collaborator at Rutgers University School of Public Health. If data needs to be physically sent to our collaborator at Rutgers University School of Public Health, a DUA will be executed prior to sending.

Benefits: There are no direct benefits to subjects. This study will enable us to learn more about treatments that may help individuals with pain and active suicide ideation. Some participants may experience improvement in pain, disability, and suicide ideation.

Protected Health Information:

Privacy and Confidentiality of Data

This is a study that involves: screening; consent review; completing a baseline assessment (questionnaires, neuropsychological battery, support person questionnaires); mid treatment assessment at the 4th week (questionnaires); post-treatment assessment (questionnaires, neuropsychological battery, support person questionnaires); and 6-month follow-up assessment (questionnaires). It also includes 12 VVC or phone sessions with a Study Provider for Veterans in Problem-solving Treatment or attentional control. To address the risk of breach of confidentiality of study data or personal information we have included a data safety and management plan:

- Data will be kept on a VA NJHCS server, \\vhaeasfpc4a.v03.med.va.gov\research\NIMH R56 Suicide-Pain Prevention. All data and study materials will be stored on a network folder. This folder will have restricted access to study personnel approved on the protocol. Data will be collected in accordance with the protocol and under supervision of qualified personnel. Data may also be placed on the VA VINCI platform for data analysis; the data will be coded. With Veterans' permission we may place their data in a VA data repository that will be created and maintained on a secure server administered by the VANJHCS Information Resource Management (IRM). Future analysis of data stored within the data repository will only happen after further Institutional Review Board and/or other applicable approvals to ensure the protection of Veterans' individual privacy.

- There exists the possible risk of loss of confidentiality. We minimize these risks by assigning participants a unique study ID that is coded and which we will use on all electronic files resulting from their participation. The "link" or key that matches the ID code with participants' personal information will be kept in an electronic study folder on the server administered by IRM in East Orange in the IRM server room with access granted only to the PI and study staff.

- In addition, all other paper documents, including forms that ask for contact information, hard copies of data, and completed questionnaires, will be kept in a locked cabinet in room 11-198.

- All recorded data from the phone sessions will be stored on the network shared folder on the secure VA server with access limited to the research team. Recordings will be obtained either directly on a VA computer or through an approved audio recording device. Before being uploaded to the server, audio recorders (if used) will be stored in a locked cabinet in Room 11-198 with access to only study team members. All digital recorders, if used, have encryption capabilities and are FIPS 140-2 validated. Once the digital recordings are uploaded onto the network folder and confirmed that the recordings are properly saved, the recordings will be immediately deleted from the digital audio recorder.

- The PI, collaborators, and study team members only will have access to the data and no confidential data will be shared with individuals outside of this team. Once a member of the study team leaves the study, s/he will no longer have access to any of the data or study folders.

Incident reporting: In the case that any digital recorders, electronic data, or hard copies of any research files are compromised (e.g., lost, theft, unauthorized access, non-compliance with security controls), the incident will be immediately reported to the PI of the study within 1 hour, the VA NJHCS Information Security Officer and Privacy Officer.

Plan for destruction/return of data: Includes the following: Study records will be destroyed in accordance with VHA RCS 10-1, and no less than 6 years past the date of study closure. All study records that are kept at the VA, including the links, will be destroyed in accordance with VHA RCS 10-1 and no less than 6 years past the date of study closure.

Qualtrics: Qualtrics is a software company for online surveys. Veterans and support persons will have the option to complete the assessments via Qualtrics. We will execute a contract to ensure Qualtrics protects our research data as required. To minimize the risk of loss of confidentiality, de-identified data will be stored on a secure server covered under a contract. Qualtrics is approved by VA TRM management group. All participant-provided electronic data will be stored temporarily on the Qualtrics servers and copies of that data will be securely transferred and stored on the VA network folder, \\vhaeasfpc4a.v03.med.va.gov\research\NIMH R56 Suicide-Pain Prevention. Qualtrics uses Transport Layer Security (TLS) encryption (also known as HTTPS) for all transmitted data and protect surveys with passwords and HTTP referrer checking. In addition, Qualtrics will go through the VA Assessment and Authorization (A&A) process to evaluate any associated risks and will be granted an Authorization to Operate (ATO).

Millisecond Inquisit Web: To objectively assess problem-solving, we will use the Inquisit Web software program developed by the Millisecond company (Millisecond software, Seattle, WA), which is a leading

provider of software for psychological testing. We will provide Veterans a unique code to use when completing the problem-solving measures - Inquisit will not collect any personally identifiable information. The link between the code and patient identifiable information will reside behind VA firewall, Inquisit will not have access to this link or any VA sensitive information. Participant-provided electronic data will be stored temporarily on Millisecond servers using their unique code. Millisecond servers reside behind firewalls and are monitored using state of the art systems for detection and prevention of various threats. Automated network security audits using the industry standard SSAE-16 method are conducted to the standards and requirements of the SANS/FBI security test, the U.S. Department of Homeland Security's published recommendations and the Payment Card Industry Data Security Standard. Millisecond encrypts all data in transit by enforcing Transport Layer Security (TLS) encryption (also known as HTTPS). Millisecond encrypts all data at rest using the industry standard AES-256 cypher. We will securely download data from Inquisit and save it on the VA network folder, \\vhaeasfpc4a.v03.med.va.gov\research\NIMH R56 Suicide-Pain Prevention. No data from us will be sent to Millisecond Inquisit Web.

Transfer of Data:

National Institute of Mental Health Data Archive (NDA) at the National Institutes of Health (NIH):

With the Veteran's and support person's permission, NIMH (study funding agency) would like the data collected from subjects to be reused later for additional research purposes. If the subject agrees, their data will be submitted to the National Institute of Mental Health Data Archive (NDA) at the National Institutes of Health (NIH). NDA is a large database where deidentified study data from many National Institute of Mental Health (NIMH) studies is stored and managed.

During and after the study, the study staff will send deidentified data to the NDA. Other researchers across the world can then request our deidentified study data for other research. Every researcher (and institutions to which they belong) who requests our deidentified study data must adhere to protocols that will keep our data safe and will not make any attempt to try to learn our subjects' identity. Experts at the NIH will review each request carefully to reduce risks to subjects' privacy.

Subjects can still participate in this research study even if he/she decides to not have their data added to the NDA. Once data is part of the NDA, we cannot take back the study data; more information about NDA is available on-line at http://nda.nih.gov. Prior to submitting data to NDA, we will obtain/ execute any necessary agreements (e.g. DUA).

Costs to Subjects: There are no costs to subjects to participate in this study. If subjects normally pay a co-pay for standard care, those payments will still be required.

Subject Compensation: Veterans may receive up to $250 for their participation in the study as follows:

- $50 for returning the completed baseline assessment packet and completing the neuropsychological tests;
- $50 for completing and returning the 4-week, mid treatment assessment;
- $75 for returning the completed post-treatment assessment questionnaire packet and completing neuropsychological tests;
- $75 for completing and returning the 6-month follow-up assessment packet.

Veteran reimbursement will take place through a mailed check, direct deposit (if established), or cash (if in-person).

The Veteran's support person will not be compensated for their completion of the questionnaires at baseline and post-treatment.

Procedure (step-by-step guidance on conducting the study):

Each session for Problem-solving Treatment and attentional control will last approximately 1 hour and can be completed either using VA Video Connect (VVC) or over the phone. Sessions will be administered by a study provider who will be a licensed and credentialed mental health provider (e.g., psychologist) or a mental health trainee (e.g., fellow) supervised by a licensed and credentialed mental health provider. Veterans who do not own a device compatible for use with tele-mental health (i.e., smart phone, tablet, or computer), or who do not wish to use their own, may be provided either a VA WRIISC owned device or a device through the VA's established loan system. A telephone may be used when necessary or if the Veteran prefers. As part of both treatment arms, study providers will check-in weekly with the patient to monitor the patient's risk and intervene if there is concern for the patient's safety (e.g., call emergency care).

Problem-solving Treatment and attentional control sessions may be audio-recorded using a digital recording device or recorded directly onto a VA computer. The recordings are to ensure that treatment is administered consistently and standardly across participants and that there is differentiation between the treatment arms.

Prior to starting a session, the Veteran will also be reminded that he/she can request for the recorder to be turned off at any time during the session. After the session, the recording will be downloaded and saved onto a secure VA server and deleted from the audio recorder. We plan to make phone calls to remind participants about their scheduled sessions and appointments.

Problem-Solving Treatment:

The remote Problem-solving Treatment teaches patients strategies to address real-life problems.[20] Sessions are once a week for approximately one hour except for the first session, which will last about two hours.

The treatment has four main goals:

1. Safety planning;
2. Problem-orientation – addressing patients' attitudinal/emotional reactions to problems;
3. Planful problem-solving – developing a logical approach to address problems;
4. Behavioral activation – encouraging regular participation in positive/pleasant activities.

Patients are provided weekly worksheets on problem-solving and will receive weekly assessments of emotional state and suicidal ideation monitoring. Throughout treatment, the study provider will guide the patient to prioritize the problems to address in the treatment:

- Problems that are contributing to increased suicide risk
- Problems caused by their chronic pain

- Problems completing their activities

Goals of the first session are to engage the patient and ensure safety. This will be accomplished by:

- Understanding the patients' goals for treatment and how their pain has influenced their daily life
- Providing education about PST
- Providing safety planning intervention
- Introducing a "Hope Toolbox" to identify strategies that instill hope.

Safety planning is an evidence-based brief intervention in which patients and study provider working together to identify triggers of suicidal ideation (e.g., a fight with spouse). The patients and study provider then identify a set of coping strategies that can be used to manage the difficult feelings that may emerge. These strategies include internal strategies (e.g., deep breathing), distracting activities (e.g., go bowling), and help-seeking behaviors (e.g., call a friend or a mental health professional). The patient and study provider also identify emergency contacts for the patient (e.g., crisis line) and ways to reduce access to means of self-harm.

The second (2^{nd}) through fourth (4^{th}) sessions of Problem-solving Treatment focus on problem-orientation. Problem-orientation refers to the way an individual is predisposed to think and feel about their problems. It is comprised of the attitudes, beliefs and expectations a person has about the likelihood of their successful problem-solving. A positive problem orientation leads to increased confidence and recognition that with adequate investment of time and effort, most problems can be addressed. To improve problem orientation, the Patient is taught to identify their "red flags" or threats to a positive problem orientation (e.g., feeling overwhelmed). They then identify strategies that will create a more positive problem orientation (e.g., relaxation exercise, positive self-talk).

In sessions five (5) through eight (8), Patients are taught a 5-step planful problem-solving approach we call S-O-L-V-E. Steps of S-O-L-V-E include:

1. **S**tate the problem and goals
2. **O**ption identification
3. **L**ist pros and cons of options
4. **V**isualize the steps
5. **E**valuate success

In sessions nine (9) through eleven (11), patients practice the entire problem-solving approach for a different problem each week with a real-life example from their actual experience.

Finally, session 12 focuses on maintenance of success and preventing backsliding. In PST, the patient solves problems that are occurring in their daily life. At the Study Provider's or PI's discretion, the treatment or protocol may vary in order to meet a Veteran's needs (e.g., changing the order of the information given, having an additional session if feasible).

<u>Attentional control:</u>

Our control will be remote attentional control which will focus on discussing weekly stressors in a supportive, non-directive way.[24]

Session content of attentional control is patient-driven, and sessions focus on emphasizing the patients' strengths, following patients' emotional affect, and building a therapeutic alliance. Participants will be asked to generate the topic they would like to discuss for the session and will be provided a new worksheet to complete between sessions noting emotional events throughout their week ("A time when I felt stressed was …") This will help identify experiences for discussion in session. These worksheets will be provided to participants.

As Veteran safety is our primary concern, if a pre-existing VA safety plan is not found in the Veteran's medical record, a safety plan will be developed collaboratively between Veteran and provider during the first session. Safety planning is an evidence-based brief intervention that identifies triggers of suicidal ideation as well as spells out a concrete set of coping strategies that can be used to manage the difficult feelings that may threaten an impending crisis. Throughout the treatment, the provider will use clinical judgment to monitor the Veterans suicidal ideation. Participants and their usual care providers will be informed that: sessions are designed to be supportive and non-directive; providers will not engage in problem-solving; and that attentional control is not a treatment for suicidal ideation. If a patient is not receiving treatment for their suicidal ideation, we will recommend treatment for suicidal ideation to the patient and their usual care provider.

Treatment Fidelity: We have planned a multi-step approach to ensuring fidelity, competence and treatment differentiation for both treatments (Table 1). We audio record each session and code ~20% for fidelity. For the attentional control we will assess for the active ingredients of this treatment (e.g., empathy) as well as identifying if there is any inappropriate drift into PST. This will enable us to ensure that active ingredients of the two treatments remain separate. Providers are highly supervised, and we intervene if there is poor adherence to treatment or low competency. We used NIH's Behavioral Change Consortium's treatment fidelity framework and Perpletchikova recommendations[65,66] on treatment integrity to guide the development of fidelity monitoring.

Table 1 – Treatment Integrity Approach

Treatment integrity procedure	**Provider treatment fidelity**	**Provider competence**	**Treatment differentiation**
Assessment of treatment integrity	Direct observation in peer supervision; therapy checklist after each session; record length of time for each session.	Direct observation in individual and peer supervision.	Direct observation in individual and peer supervision.
Accuracy of data	A random sample (20%) of collected tapes is examined, sampled across study providers, treatment phases, situations, cases and sessions.		Code the control for use of PST.
Rating integrity	Raters are highly trained; interrater reliability is assessed; multiple raters are used.		
Operational definition	Specific treatment manual with information about the theory & sequencing of techniques.		
Training of providers	Three days of didactic instruction for each treatment; listen to treatments delivered by other providers; role-play with other providers; on-going bi-weekly feedback and peer training.		
Supervision of study providers	Study providers attend twice-weekly peer & weekly individual supervision; supervision includes observation; review of adherence checklists; if a study provider fails to meet criteria s/he will receive more intensive supervision.		

Assessments: Assessments will consist of the Veterans completing questionnaires and a short battery of neuropsychological tests. Additionally, the specified support person of the Veteran will be asked to complete questionnaires. Veterans (and their support person) can complete the questionnaire packets

through Qualtrics, the U.S. mail (the packet would be mailed to the Veteran along with a pre-paid envelope to return the packet), and/or over the telephone with a member of the study team. The neuropsychological battery will be completed through Millisecond's Inquisit Web, a software package designed to administer neuropsychological measures online, as well as over the phone to administer the means-end problem-solving task. We will make a concerted effort to remind Veterans with letters and phone calls to complete and return questionnaires, and also to complete the neuropsychological battery. If needed, we will resend questionnaire packets to Veterans and/or their support person. We will also collect data from the Veterans' medical record about their diagnoses, treatments, medications.

Assessments will be completed at four time points:

- **Baseline**: questionnaire packet, neuropsychological battery, and support person questionnaire packet will be collected at the start of the study (~2 hours for questionnaire packet and neuropsychological battery; ~5 minutes for the support person questionnaire packet)
- **4-week, mid treatment**: questionnaire packet will be collected after completion of the 4th session of either Problem-solving Treatment or attentional control (~30 minutes)
- **Post-treatment**: questionnaire packet, neuropsychological battery, and support person questionnaire packet will be collected after the 12th session of either Problem-solving Treatment or attentional control (~2 hours for questionnaire packet and neuropsychological battery; ~5 minutes for the support person questionnaire packet)
- **6-month follow-up assessment**: questionnaire packet will be collected ~6 months after the 12th session of either Problem-solving Treatment or attentional control (~1 hour)

See below for Table 2, which outlines when the measures and neuropsychological tests will be administered, along with a summary of each.

Table 2 – Measures administered at each timepoint

Domain	Study Instruments	Screening	Baseline	4 week	Post Treatment	6 Months
Aim 1: Primary Outcome	Social Problem-Solving Inventory Revised [SPSI-R] *		X	X	X	X
	Neuropsych Assessment: Emotional Go No-Go		X		X	
	Neuropsych Assessment: Means-End Problem-Solving Task [MEPS]		X		X	
	Neuropsych Assessment: Iowa Gambling Task		X		X	
	Neuropsych Assessment: Stroop Test		X		X	
Aim 1: Secondary Outcome	Interpersonal Needs Questionnaire [INQ]		X	X	X	X
Aim 2: Exploratory Outcome	Columbia-Suicide Severity Rating Scale [C-SSRS]	X	X		X	X
	Suicide Ideation Questionnaire [SIQ]		X	X	X	X
	Suicide-Related Coping Scale		X	X	X	X
	Pain Disability Index [PDI]		X	X	X	X
	Brief Pain Inventory [BPI]	X	X	X	X	X
Participation Characterization and Screening Instruments	Healthcare Access [HCA]		X		X	
	Demographic * / Treatment Survey	X	X		X	
	Post-Traumatic Stress Disorder Checklist [PCL]		X		X	
	The Patient Health Questionnaire-9 [PHQ-9]		X		X	X
	Patient Health Questionnaire [PHQ-15]		X		X	X
	World Health Organization Disability Assessment Schedule [WHO-DAS 2.0]		X		X	
	MOS Social Support		X		X	
	Audit-C		X		X	
	Cognitive Failures Questionnaire		X		X	X
	Coronavirus Stressor Survey	X				
Quality of Treatment Delivery	Working Alliance Inventory [WAI]			X	X	
	Patient Global Impression of Change [PGIC]				X	
	Client Satisfaction Survey				X	
* = Veteran's support person will complete their own version						

*For Veterans' who we were unable to capture the Coronavirus Stressor Survey at baseline (due to timing of its addition to the protocol), we will attempt to capture it at a follow-up timepoint (e.g. 4 week, post treatment, or 6-month follow-up assessment).

Involvement in Alternate Treatments: Throughout the course of their participation, Veterans will be allowed to begin a new treatment, continue with current medical regiment/treatments, or make changes to their existing medical regimen. For patients not currently in mental health treatment, we will communicate the availability and appropriateness of mental health services to the patient and their established provider. Adherence to medical protocols and participation in alternate treatments will be evaluated by a questionnaire during assessments and this will be controlled for in analyses.

Communication with Other Providers: In both arms, the Veteran can continue to receive care from their established providers. This includes their primary care provider and mental health provider (if they have one). If deemed clinically appropriate by a study provider, we will reach out to the Veteran's local

providers at screening to communicate the patient's active suicidal ideation. When the Veteran consents to participate in the study, the study team will send the primary care and mental health providers a letter describing the study, letting the provider know about the patient's suicidal ideation, and inviting them to contact the study team with any questions or concerns. **The letter will additionally detail that their Veteran's participation the research study is not a replacement for standard clinical care.** During baseline, a study provider will assess suicide risk using the C-SSRS.[26] If the baseline C-SSRS score represents an increase from that at screening, the study provider will communicate this to the Veteran's established providers. If providers have any concern about Veteran safety at any point during their participation, a provider will reach out to the Veteran's local health care team. Additionally, providers will place a note in the electronic medical record after every session with the Veteran.

We will contact participants' health care providers at any time during the study if we have a concern about the Veteran's health and/or safety. For urgent matters, the study providers will call the established providers and/or send encrypted emails.

Clinical Training and Supervision: Study providers will be licensed and credentialed mental health providers (e.g., psychologist) or mental health trainees (e.g., fellows) supervised by a licensed and credentialed mental health provider. Before seeing patients, all study providers will first receive extensive training on problem-solving and attentional control. They will listen to all 12 sessions of our tailored PST and observe Dr. Nezu's problem-solving video. They then will role play the PST and attentional control. Only when it is determined that they are ready, can they communicate with their first patient. Study providers attend twice-weekly peer supervision. The WRIISC has a training program and allows psychology trainees to become study providers. Trainees will receive individual supervision. During these sessions, the team reviews audio tapes, and discusses problems and successes.

Study providers will each see equal numbers of problem-solving treatment and attentional control patients to ensure that the level of providers is balanced between the arms.

Additionally, Dr. McAndrew will lead a monthly meeting to discuss study progress, successes, difficulties and data analysis. Dr. McAndrew will meet with study personnel once a week to set goals and discuss priorities. Dr. McAndrew will meet weekly with the study coordinator (Ms. Anastasides) and head of her mental health team (Dr. Litke). Ms. Anastasides will meet daily with the research assistant to guide recruitment and study progress. Dr. Litke will provide weekly supervision for all study providers and, as needed, for administering the C-SSRS.

Minimizing Attrition: We will schedule appointments at a time most convenient for the Veteran (including evenings). We will attempt to make reminder phone calls approximately 24 hours prior to their session. It is our experience that missing sessions, no matter what the reason, often leads to attrition. Therefore, the study staff will try to call a Veteran within 24 hours if they miss a session.

Primary Outcomes:

Social Problem-Solving Inventory-Revised (SPSI-R)[70]. The SPSI-R measures problem-solving that is sensitive to change. In clinical research, the SPSI-R has been successfully used to elicit meaningful self-appraisals. The questionnaire is 52 items long. We will use the total score, as well as the 5 subscales. The

SPSI-R is internally consistent (alpha=.90) and reliable (r=.87) and has been used as an outcome of PST. Support person will also complete a version of this.

Affective Go/No Go[71]. This is a neuropsychological test that measures attention and impulse control. Inhibiting impulses is a key component of preventing impulsive behavior that can lead to suicide. Indeed, scores on the Go/No Go have been shown to predict suicidal behavior.

Means-End Problem-Solving Task[73]. The MEPS is a neuropsychological test that consists of a series of scenarios, with each one identifying the beginning and end of a story. The subject's task is to come up with the middle of the story. Stories are scored according to how many steps the patient identifies in reaching the end. This instrument captures a crucial element of problem-solving: identifying the steps (i.e., means) that will lead to goal attainment (i.e., end). This aspect of problem-solving is directly relevant to patients with pain whose limited set of identified means includes suicide. An increase in effective means generated is expected to drive reduction in suicide ideation. The MEPS has been used in suicide research and has shown that suicide attempters generate fewer relevant means than both non-suicidal psychiatric controls and non-psychiatric controls.[74]

Iowa Gambling Task[75]. The Iowa gambling task is a neuropsychological task of problem-solving. The goal of the task is to make "money". Participants are presented with four decks of cards and have to choose cards from these decks to make "money". Subjects have the opportunity to learn about the gains and losses associated with each deck in order to maximize profit. Performance on this task has been shown to change after problem-solving therapy.[76]

Emotional Stroop[77,78]. The emotional Stroop is a test of response inhibition. This is a critical skill needed to refrain from engaging in suicidal behavior.[79] Our preliminary data suggest that Stroop is responsive to change in clinical trials for suicidal behavior.

Caregiver Social Problem-Solving Inventory-Revised (SPSI)[70]. A support person of the Veteran will be identified by the patient and invited to complete the SPSI to provide their perspective of the patient's problem-solving ability.

Secondary Outcome:

Interpersonal Needs Questionnaire (INQ).[80] Feelings of burdensomeness and belongingness will be measured by the Interpersonal Needs Questionnaire (INQ). The INQ is an 18-item self-report questionnaire. Scale items have high levels of internal consistency, and findings from prior investigations have also supported the construct, convergent, and predictive validity of this measure.

Exploratory Outcome:

Columbia-Suicide Severity Rating Scale (C-SSRS).[26] The C-SSRS is the gold standard for suicide assessment and measures level and intensity of suicidal ideation, planning and preparation for suicidal behavior, and method and lethality of recent and past lifetime suicidal behavior. During assessment, this measure will be administered by study personnel. To determine eligibility, we will use the level of suicidal ideation. Patients will be eligible who have a score of 2 (have you actually had any thoughts of killing yourself?), 3 (have you been thinking about how you might do this?) or 4 (Have you had these thoughts and had some intention of acting on them?). The intensity of ideation subscale (the summed score from five

separate items on Part II of the C-SSRS; subscale range = 2-25) will be the primary dependent variable for the fully powered clinical trial. The intensity of ideation asks about the intensity of ideation in the past 6 months (e.g., the frequency, duration controllability).

Suicide Ideation Questionnaire (SIQ).[81] The SIQ is a 30-item self-report instrument designed to assess thoughts about suicide experienced during the prior month. SIQ has strong internal consistency ($\propto$ = .97) and construct validity. This measure will allow for supplementary investigation of ideation.

Suicide-Related Coping Scale.[27] The Suicide-Related Coping Scale captures an individual's perceived ability to use internal and external coping to problem-solve suicidal thoughts and urges. This measure was validated in a Veteran sample. The items in this measure capture the types of skills we expect Veterans to be able to use after learning problem-solving (i.e., "I recognize the circumstances that make me suicidal")

Pain Disability Index (PDI).[31] Is a 7-item measure of the impact of pain on daily activities and social relationships. It will be used to assess disability from pain.

Brief Pain Inventory (BPI).[28] Pain will be assessed using the BPI. The BPI is a 10-item measure of pain severity and interference. The total score is sensitive to change with 1 point considered clinically meaningful.

Self-Report Participant Characterization and Screening Instruments:

Demographic/Treatment Survey. This is a brief questionnaire designed to elicit basic demographic information including: medical conditions; treatment; sex; age; marital status; etc. Support person will also complete a version of the demographic questionnaire.

Post-Traumatic Stress Disorder Checklist (PCL).[82] The twenty item National Center for PTSD Checklist (PCL) has been updated to align with the newest PTSD criteria and will be used to assess PTSD. The PCL is a valid and reliable measure of PTSD symptoms.

The Patient Health Questionnaire-9 (PHQ-9).[83] The PHQ-9 is a 9-item self-report questionnaire that assesses the frequency of depressive symptoms over the past two weeks. The total score of the PHQ-9 has also been used as indicative of depression severity and is sensitive to clinical change.

Patient Health Questionnaire (PHQ-15).[84] The PHQ-15 measures physical symptoms. The PHQ-15 was validated on a sample of 6,000 and found to be reliable, valid and responsive to change

World Health Organization Disability Assessment Schedule (WHO-DAS 2.0).[62] The WHO-DAS measures impairment in completing daily activities and social relationships due to physical and mental health conditions. The items of the WHODAS have a factor loading on composite score of 0.82 to 0.98.

MOS Social Support.[85] The MOS Social Support measure captures perception of access to available supports. The MOS Social Support has high convergent and divergent validity in addition to excellent reliability.

Audit-C.[86] The audit-c captures alcohol abuse and is predictive of alcohol abuse problems.

Coronavirus Stressor Survey. This captures experience with COVID-19 and difficulties that have been encountered due to it.

Self-Report Measures of the Quality of Treatment Delivery:

Working Alliance Inventory (WAI) – Self.[87] The working alliance assesses the participants' perception of their relationship with their study provider. The working alliance has excellent reliability (.80) and validity.

Patients experience with treatment. We will ask patients about their experiences with treatment using a short validated satisfaction measure (8 items)[88] and the 2-item Patient Global Impression of Change[30] which asks patients about their perceived improvement during the course of treatment. These mostly analogue measures will allow us to asses if the patient perceives improvement from the treatments.

Cognitive Failures Questionnaire.[89] The cognitive failures questionnaire is a self-report measure of perceived cognitive dysfunction.

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