Official Title: Prevention of suicide in Veterans through brief intervention and contact (VA-BIC)

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Prevention of suicide in Veterans through brief intervention and contact (VA-BIC)

Investigators

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Specific Aims/Purpose

Suicide is of grave concern in U.S. Veterans as over 6,000 Veterans die from suicide each year,[1-3] and risk is particularly high following a psychiatric hospitalization.[4-7] Several factors may contribute, including problems with engagement in care and poor social connectedness.[8-19] To address post-discharge suicide risk, the VA has implemented a comprehensive package of interventions to promote engagement in care and provide timely care. Yet, despite these efforts, suicide after psychiatric discharge remains an ongoing problem in the VA.[2] These findings highlight the need to identify new interventions and approaches to further reduce the number of Veteran suicides after psychiatric hospitalization. Notably, VA standard care does not include a targeted strategy to improve social connectedness, a key risk factor for suicide. There is a growing interest to determine whether easily scalable, mobile health (mHealth) interventions that address social connectedness can prevent suicide.

In response, we developed an intervention called Prevention of suicide: Education, Awareness, Connection, and Engagement (PEACE). PEACE is comprised of two synergistic, promising components to prevent suicide: 1) an mHealth app which aims to improve social connectedness after discharge, but has not been studied in Veterans; and 2) a manual-based intervention (Veterans Affairs Brief Intervention and Contact Program, VA BIC) that promotes engagement in care. The VA BIC is derived from the World Health Organization Brief Intervention and Contact Program (WHO BIC), an intervention with efficacy in preventing suicide after hospital discharge.[15] Our pilot work suggests that VA BIC holds promise for improving engagement in care and decreasing suicidal ideation but may not fully address social connectedness. The effect of VA BIC may be further enhanced by pairing it with an mHealth app, which focuses on social connectedness. However, neither VA BIC nor an enhanced version of VA BIC have ever been tested in the Veteran population. Thus, there is a critical need to test an enhanced version of VA BIC in Veterans before deploying this approach as a suicide prevention strategy in the VA.

My *long-term goal* is to develop a career as an independent clinical researcher with a focus on developing, testing, and improving interventions to prevent suicide in Veterans. To achieve this goal, my *overall objective* for this application is two-fold: First, I aim to obtain the skills needed to build my professional career and conduct clinical research in suicide prevention by learning how to: (1) design and adapt clinical interventions; (2) design, conduct, and manage clinical trials; and (3) perform research in patients at high risk for suicide. Second, I aim to study the efficacy of a novel, two-component intervention called PEACE. My *central hypothesis* is that PEACE will lead to greater reductions in suicidal ideation after psychiatric hospitalization, compared to standard care alone. I hypothesize that PEACE exerts its effect by improving social connectedness and engagement in care. The *rationale* for this proposal is that the results from this single-site trial will advance my knowledge in designing effective strategies to prevent suicide, which I will use to develop a future merit award proposal. To attain the overall objectives, the following *specific aims* will be pursued:

1. To identify the effect of PEACE on suicidal ideation after psychiatric hospitalization, compared to standard care alone. My *hypothesis* is that PEACE will lead to greater reductions in suicidal ideation at one, three, and six months after hospitalization, compared to standard care.

2. To identify the effect of PEACE on social connectedness and engagement in care after psychiatric hospitalization, compared to standard care alone. My *hypothesis* is that PEACE will lead to greater

improvements in social connectedness and engagement in care at one, three, and six months after hospitalization, compared to standard care.

3. To compare the effect of PEACE on suicide attempts and suicide deaths after psychiatric hospitalization compared to standard care alone. This is an exploratory analysis.

At the completion of the award period, the ***expected outcome*** is to determine the efficacy of PEACE in reducing suicidal ideation after psychiatric hospitalization and to gain insight into the effect of the intervention on social connectedness and patient engagement in care. The proposal has the potential to have a ***large impact*** on Veteran health by elucidating an effective strategy to decrease suicidal risk in a program that can eventually be disseminated throughout the VA healthcare system.

Scientific Rationale and Significance

Suicide is a major public health concern in the U.S. Suicide mortality rates in the U.S. have risen by more than 30% over the past decade (10.5 versus 14.0 per 100,000 standard population in 1999 and 2017, respectively).[1] Veterans account for a sizable proportion of all suicide deaths in the U.S., with approximately 14% of suicide deaths in the U.S. each year being attributed to a Veteran.[2] In addition, the rate of suicide in the Veteran population is more than two times that of non-Veteran U.S. adults.[2] Finally, over the past decade, the average number of suicides in Veterans who use VA services (VA users) has risen from four suicides per day in 2005 to six suicides per day in 2016.[2] Accordingly, the Department of Veterans Affairs (VA) considers suicide prevention a top clinical priority.[3]

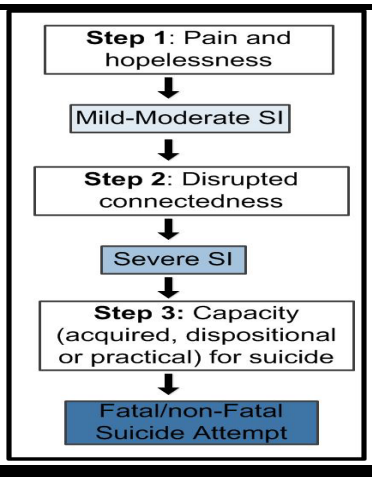
The period following a psychiatric hospitalization is one of the highest risk periods for suicide.[4-6] In fact, studies have found that the risk for suicide is the highest in the first three months after psychiatric hospitalization, and then the risk gradually decreases over time.[5,6] For example, in a large meta-analysis of 100 studies, the suicide rate in the first three months after psychiatric hospitalization was almost 100 times that of the global suicide rate (1,132 per person-years vs. 11.4 per 100,000 person-years, respectively).[6] Similarly, in a large retrospective cohort study of over 850,000 Veterans diagnosed with depression, suicide rates were the highest in the first 12 weeks after discharge from an inpatient mental health unit at 568 per 100,000 person-years.[5] This compares to a rate of 37.5 per 100,000 person-years in VA users.[7] Together, these findings indicate that targeted interventions to prevent suicide in the period following hospitalization could have a meaningful impact on overall suicide rates in VA users.

Based on current evidence, some of the most important contributing factors to post-hospitalization suicide risk include problems with engagement in care, fragmented care in the post-discharge period, and lack of social connectedness.[8-19] Riblet *et al.* conducted a retrospective review of root-cause analysis (RCA) reports of suicide occurring within seven days of discharge from a VA inpatient mental health unit in order to identify health system vulnerabilities contributing to death by suicide in the post-discharge period.[8] Among 141 RCA reports of suicide occurring within seven days of discharge, Riblet *et al.* found that RCA reports commonly cited concerns about poor engagement in post-discharge care.[8] In addition, RCA reports mentioned that many Veterans experienced lapses in their follow-up care, despite the availability of adequate mental health treatment resources within the VA.[8] Other studies in civilian populations have raised similar concerns that poor engagement in care and fragmented care contribute to suicide risk.[10-17] Furthermore, studies have suggested that lack of social connectedness with friends, family and other social supports may adversely impact the health of patients.[18-19] The finding that social connectedness plays an important role in mental health outcomes is neither new nor surprising. In fact, there is robust evidence demonstrating that lack of social connectedness (or social isolation) is a strong and reliable predictor of suicidal behavior (as well as many other adverse health outcomes).[20-22] Durkheim first introduced the concept that social forces play a role in suicidal behavior in the late 1800s.[23] Subsequently, other theories have been proposed. Notably, Joiner and Van Orden's Interpersonal Theory of Suicide (ITS) is commonly used to characterize the relationship between social connectedness and suicide risk.[24]

According to the ITS, social connectedness includes two constructs: thwarted belongingness, TB (i.e., feeling lonely, lacking reciprocally-caring relationships) and perceived burdensomeness, PB (i.e., feeling self-hatred, perceiving oneself to be a liability to others). Veterans with greater TB and PB have been shown to have more suicidal ideation.[25-26] Similarly, in a meta-analysis of 122 cross-sectional samples, Chu *et al.* found that TB and PB were significantly associated with suicidal ideation and prior suicidal behavior.[27] These findings highlight that it may be important to address social connectedness as part of the design of effective interventions to prevent death by suicide.

To address suicide risk in the period following psychiatric hospitalization, the VA has implemented a number of suicide-prevention strategies.[28-34] These interventions are intended to raise awareness about suicide prevention and promote engagement in care after hospital discharge. VA inpatient mental health teams must: 1) ensure that Veterans receive timely follow-up care after discharge; 2) encourage Veterans to complete a safety plan (a concrete list of strategies to decrease suicide risk) prior to discharge;[35] 3) encourage Veterans to include family in discharge care planning; and 4) consider placing the Veteran on the High Risk for Suicide List per VA policy. In 2016, the VA also implemented the Recovery Engagement and Coordination for Health-Veterans Enhanced Treatment (REACH VET).[36] The goal of REACH VET is to use data from health records to identify Veterans who are at higher risk for suicide. This information is then shared with their providers so that they can reach out to these Veterans and use their clinical judgement to determine whether additional interventions might be necessary. While the VA's high quality and comprehensive approach to suicide prevention has certainly been effective to some degree, poor engagement in care and fragmented care remain an important concern.[8-9] In addition, VA discharge practices are not standardized and, therefore, may vary across facilities.[37] Moreover, currently recommended discharge practices do little to promote social connectedness in the period following psychiatric hospitalization. Finally, death by suicide remains a chief concern in Veterans after psychiatric hospitalization.[4]

Figure 1. Three-Step Theory of Suicide Risk (3ST)[38] *



SI = suicidal ideation
*Based on Klonsky & May 2016[38]

A proposed conceptual model to inform the design of effective suicide prevention strategies

The 'ideation-to-action' framework is a theoretical model that is commonly used to understand suicide risk and to develop targeted strategies to prevent suicide.[38] As shown in **Figure 1**, based on the 'ideation-to-action' framework, the Three-Step Theory of Suicide (3ST) considers that there are three specific steps that put an individual at risk for suicide.[38] First, the individual must experience pain and hopelessness in order to develop mild to moderate symptoms of suicidal ideation. Pain is defined broadly and usually refers to psychological or emotional pain. Second, the individual must experience disrupted social connectedness in order for their suicidal ideation to become severe. Aligned with Joiner and Van Orden's ITS,[24] the 3ST considers that disrupted connectedness includes aspects of belongingness (TB) and burdensomeness (PB). Finally, the individual must have the capacity to make a suicide attempt. Capacity may include acquired (an increased tolerance over time to pain, injury, or death), dispositional (inborn traits), or practical (e.g., access to lethal means) capacity. According to the 3ST, suicide-prevention interventions are more likely to be effective if they treat psychological pain, increase hope, improve connectedness, and/or address capacity.[38]

A review of current evidence on suicide prevention strategies

In a review of strategies to prevent suicide following psychiatric hospitalization, we identified more than 30 published randomized control (RCT) and quasi-experimental trials of interventions in patients treated for suicide risk in a hospital or emergency room setting.[39] Approaches included: 1) brief intervention plus follow-up, 2) case management, 3) post-card interventions, 4) peer support interventions, 5) psychotherapy for suicide prevention with (or without) follow-up, 6) safety planning, 7) specialized inpatient treatment, and 8) other outreach strategies such as chain of care. Consistent with prior reviews,[30,40] we found that there is inconclusive evidence regarding the impact of most of these strategies on suicide risk following hospital or emergency room discharge. Importantly, meta-analyses highlight that there is a relative dearth of robust evidence to support that most interventions can prevent suicide, the clinical outcome of greatest interest.[41-42] For example, Milner *et al.* found in a meta-analysis of five trials of brief contact interventions that there was no significant reduction in suicide (OR 0.58, 95%CI: 0.24–1.38).[41] Conversely, Riblet *et al.* identified among 72 trials of various suicide prevention strategies that there was only one strategy that prevented death by suicide in patients discharged after a suicide attempt: the World Health Organization Brief Intervention and Contact Program (WHO BIC) (three RCTs, N = 2,028, OR: 0.20, 95% CI: 0.09–0.42).[42] The WHO BIC is a brief suicide prevention intervention that targets individuals who are being discharged from an acute care setting after a suicide attempt.[43] The WHO BIC includes a brief, personalized, suicide-prevention educational intervention before discharge, followed by regular contact after discharge. The WHO BIC incorporates aspects of motivational interviewing (MI). It is designed to: (1) educate patients about suicide risk in order to facilitate engagement in care; and (2) to provide patients with necessary support after discharge.

Opportunities for future study of WHO BIC in the Veteran population

Despite the apparent strengths of the WHO BIC as a suicide prevention strategy, the results of the WHO BIC trials have uncovered a number of key questions that require additional study. First, the WHO BIC has only been studied in low- and middle-income countries and the applicability of the findings from these trials to other populations, including U.S. Veterans, remains unclear. VA/DoD Practice Guidelines recommend that the WHO BIC should be studied in U.S. Veterans.[30] Second, while the WHO BIC trials demonstrated a significant effect on death by suicide—the clinical outcome of prime importance—these results did not extend to suicide attempts. However, the interpretation of these latter findings is limited by the fact that the WHO BIC trials did not use a more robust measure of assessment such as validated rating scales to detect suicide attempts. Therefore, it is unclear whether similar results would have been found using a validated scale, such as the Columbia Suicide Severity Rating Scale (C-SSRS). Furthermore, although the WHO BIC significantly improved suicidal ideation, the outcome was reported in a single trial (N = 139). Finally, while the WHO BIC targets engagement in care, a key contributor to post-discharge suicide risk, the WHO BIC peripherally touches upon social connectedness. Yet, there is strong evidence that lack of social connectedness with friends, family, and other social supports plays an important role in suicide risk.[20-23,25-27] This suggests a need to enhance the capacity of WHO BIC to address suicide risk by coupling it with an intervention that targets social connectedness in the period following hospitalization.

Unfortunately, there is a general lack of evidence to support that most interventions that focus on social factors (e.g., groups, psychotherapy interventions) significantly improve social connectedness or reduce suicide risk.[45-46] There is a growing interest in clarifying whether mobile health applications (mHealth) may foster social connectedness and reduce suicide risk.[47-48] mHealth is appealing because it aligns with cultural trends and is easily scalable. Furthermore, mHealth could enhance brief suicide prevention strategies, such as WHO BIC. Yet, mHealth remains in its infancy in mental health research and there is a need for clinical trials to demonstrate that mHealth can be used to mitigate suicide risk.[48] One mHealth strategy of particular interest in the area of suicide prevention research includes My3, an app that is designed to support social

connectedness in patients to prevent suicide (see Intervention Description section). To date, the promising My3 app has not been tested in a trial in Veterans.

Significance of the Proposed Research: Suicide is a chief public health problem and a central concern in the Veteran population. Despite the VA's extensive package of strategies to prevent suicide in Veterans, death by suicide remains an ongoing problem among Veterans, including VA users, and those recently discharged from VA mental health units.[2,4] In fact, suicide rates in VA users increased between 2005 and 2016 (29.7 versus 39.3 per 100,000 population, respectively).[2] Among male VA users, the suicide rate (measured in deaths per 100,000 person-years) after psychiatric hospitalization significantly rose from 234 in 2005 to 340 in 2008, and the rate has since plateaued.[4] Data on Veteran suicide occurring after 2016 has not yet been made available from the VA Office Mental Health Suicide Prevention. The lack of improvement in Veteran suicide rates highlights the critical need to identify and to test newly developed strategies to prevent suicide in Veterans. Accordingly, the VA stresses that it is imperative that clinicians and researchers tackle the problem of suicide.[3]

Therefore, my *long-term career goal* is to become an independent clinical researcher who focuses on developing, testing, and improving interventions to prevent suicide in Veterans. My *short-term goal* in this CSR&D CDA proposal is two-fold. First, I will receive the necessary mentorship and training in conducting clinical research in the area of suicide prevention. Second, I will gain practical skills in designing and adapting clinical interventions to address suicide risk. To support these goals, I have developed a novel intervention to prevent suicide in the period following psychiatric hospitalization. The intervention is called PEACE and is comprised of synergistic suicide prevention strategies including: 1) an mHealth app to improve social connectedness; and 2) a manual-based program, VA BIC, to promote engagement in care. In support of the proposal, I identified a promising mHealth app called My3, which aims to increase social connectedness in patients to prevent suicide but has not been tested in Veterans. I also developed and pilot-tested a manual-based program (VA BIC) to promote engagement in care in patients. The VA BIC is based on the WHO BIC, an intervention with efficacy in preventing suicide after hospital discharge in low- and middle-income countries.[15] In this proposal, I intend to carry my work forward by testing PEACE under randomized conditions in psychiatrically hospitalized patients at the White River Junction VA Medical Center (WRJ VAMC). I hypothesize that PEACE reduces suicide risk by decreasing suicidal ideation after psychiatric hospitalization. I hypothesize that the mechanism by which PEACE reduces suicide risk includes improving social connectedness and promoting engagement in care. My primary outcome is suicidal ideation after discharge. My secondary outcomes are social connectedness and engagement in care after discharge. I will conduct an exploratory aim to evaluate suicide attempts after discharge. My trial will provide critical insight into the effect of PEACE on suicide risk and its potential mechanisms of action. I will use these data to submit a merit award proposal during the last two years of the award period. Ultimately, through completing this proposal, I hope to build skills in designing suicide-prevention strategies that can have a substantial, positive impact on Veteran health.

Preliminary Studies

As summarized below, I have conducted preliminary work in direct support of this CSR&D CDA application. My preliminary studies serve as an integral foundation to this proposal for the following five key reasons: First, I collected information on the applicability of the WHO BIC program to the Veteran population by seeking input from psychiatrically hospitalized Veterans who will be end-users of the program. Second, I developed a manual-based intervention (VA BIC), which is adapted from the successful WHO BIC and tailored to meet the unique needs of Veterans. Third, I conducted a pilot study of VA BIC and these pilot data will be used to support the clinical trial of VA BIC described in this CSR&D CDA proposal. Finally, I identified that the VA BIC could be enhanced by combining it with a mental health app to improve social connectedness and prevent

suicide. . I have collected pilot data on the applicability of a mental health app to Veterans, including those discharged from an inpatient mental health unit.

Study 1: Veterans' perspectives on the applicability of the WHO BIC to Veterans at risk for suicide. In order to understand the applicability of the WHO BIC to Veterans, I conducted and published a qualitative study of Veterans hospitalized on the inpatient mental health unit at the WRJ VAMC.[9] The goal of the study was to elicit Veterans' perspectives, both positive and negative, on facilitators and barriers to treatment engagement after discharge. They were also asked specifically about their perception of the role of treatment engagement in reducing post-discharge suicide risks. The interview guide included open-ended questions that asked patients to comment on whether or not the components of the WHO BIC (i.e., suicide prevention education prior to discharge and regular contacts after discharge) were relevant to psychiatrically hospitalized Veterans. In addition, the interview guide included a set of open-ended questions that elicited information from patients about their attitude, subjective norm, and perceived behavioral control regarding follow-up care and suicide risk. Veterans also had opportunity to comment on positive and negative aspects of other treatment interventions such as medications, therapies, and novel approaches including technology.

I used convenience sampling to recruit patients who were hospitalized on the inpatient mental health unit at the WRJ VAMC and were deemed clinically fit to be discharged back to the outpatient setting. I conducted individual, semi-structured interviews with patients prior to discharge. The interview guide included open-ended questions that asked patients to comment on whether or not the WHO BIC was relevant to psychiatrically hospitalized Veterans. In addition, the interview guide included a set of open-ended questions that elicited information from patients about their attitude, subjective norm, and perceived behavioral control regarding follow-up care and suicide risk. I followed patients for a period of three months after discharge and evaluated continuity of care after discharge. Among 22 eligible patients, 16 patients (all men) consented to enrollment. Despite uniform high risk for suicide in psychiatrically hospitalized patients, more than half of enrolled patients (N = 10) perceived that they were at no or low future suicide risk after discharge because the current hospitalization had resolved their symptoms and future risk. Several of the patients who perceived that their future suicide risk was low experienced poorer continuity of care during the three-month follow-up. Qurashi *et al.* also found that psychiatric inpatients with lower insight scores at the time of discharge were more prone to be non-compliant with medications.[49] Therefore, targeted educational interventions at the time of discharge may be important in suicide prevention in Veterans, emphasizing a role for the WHO BIC's brief educational intervention at the time of discharge. Thirty-one percent of enrolled patients (N = 5) experienced poor continuity of care within the first three months after discharge, despite having an established follow-up care plan at the time of discharge. In fact, three of these five patients were readmitted within three months of discharge. This finding is consistent with the results of my retrospective review of RCA reports of suicides occurring within seven days of discharge from an inpatient mental health unit.[8] Here, I found that while Veterans have access to many mental health resources following hospitalization, they encounter many challenges in accessing these services, and that these factors may contribute to suicide risk after discharge. Together, my results suggest that the WHO BIC's regular contacts after discharge may be relevant and of importance in the care of Veterans who are being discharged from an inpatient mental health unit. Finally, patients responded favorably to both components of the WHO BIC. However, the patients mentioned that it was important to include Veteran-specific resources, while most (N = 15) preferred in-person visits. This suggests that while the WHO BIC may be acceptable to Veterans, it requires some adaptation prior to use in the VA system.

Study 2: Develop the VA BIC Manual-Based Intervention. As part of a two-year New England VA CDA (V1CDA) and with the support of my mentors, I developed a manual-based intervention called the VA BIC (see attached PEACE Manual). The VA BIC intervention is adapted from the successful WHO BIC program and is tailored to meet the unique needs of Veterans (based on Veteran and provider feedback). The educational materials address suicide risk in Veterans. The manual includes references to treatment resources that are

relevant to Veterans who receive their care through the WRJ VAMC. The manual includes a discussion of the safety plan. The VA BIC manual is highly structured and is comprised of standardized, scripted material to facilitate the delivery of all aspects of the intervention. The structured format of the VA BIC will facilitate eventual scaling-up of VA BIC across the VA. The manual was created with input from Veterans treated at the WRJ VAMC, the WRJ VAMC Suicide Prevention Coordinator (SPC), VA inpatient psychiatrists, and WHO-BIC methodologist, Dr. Wasserman.

Study 3: Pilot study of VA BIC. As part of a V1CDA, I piloted the VA BIC program at the WRJ VAMC inpatient mental health unit using a pre-post design. I enrolled 9 patients (8 men, 1 woman) who were hospitalized on the inpatient mental health unit, were deemed clinically stable by the inpatient team, and were awaiting discharge. The mean age of enrolled patients was 43.4 years [standard deviation (SD): 14.31)]. Patients were eligible for inclusion if they were admitted because of acute risk of self-harm. My primary aim was to assess feasibility and acceptability. My secondary aim was to gather pilot data on the impact of VA BIC on related measures of suicide risk including suicidal ideation and attempts, hopelessness, patient engagement and perceived connectedness. I created a standardized, protocol-specific electronic data capture (EDC) system to facilitate data collection of outcome measures and obtained the necessary licenses to administer several standardized instruments in this pilot study. The same data repository and similar licenses will be used in the trial that I propose to conduct as part of this proposal. I developed a fidelity scale and evaluation method to ensure that the VA BIC is properly administered (see assessments). The pilot work yielded important insights.[50] First, I was able to show the feasibility and acceptability of the VA BIC intervention. The study recruitment was acceptable, at 70% (9/13). Furthermore, I was able to retain 100% of patients in the study and obtain complete data on each enrolled patient. The patients also reported high satisfaction with the intervention as measured by the Client Satisfaction Questionnaire-8 (CSQ-8). For example, one patient reported, "*I think the study was helpful in keeping me connected as well as providing another support avenue to my repertoire...It reinforced the value of structure and purpose in my life…It was personal, but not too personal*." Second, I was able to collect pilot data on the effect of VA BIC on related measures of suicide risk. As shown in **Table 1**, patients experienced a significant reduction in suicidal ideation, as measured on the C-SSRS and Beck Scale for Suicidal ideation (BSS). In fact, BSS scores improved by a mean of 8 points; prior studies suggest that decreases of 5 points or more on the BSS is clinically relevant.[54] Hopelessness, as measured by the Beck Hopelessness Scale (BHS), also significantly improved in the first three months after discharge. While I observed that patients experienced improvements in PB and TB, as measured by the Interpersonal Needs Questionnaire-15 (INQ-15), over the three-month follow-up period, I did not find similar improvements in social support, as measured on the Medical Outcomes Social Support Survey (MOS-SSS). This discrepancy may not be surprising because the VA BIC does not address social connectedness with family, friends, or other supports. In fact, several patients aptly noted during assessments that the MOS-SSS subscales were asking about their interactions with family, friends, or other

Table 1. Impact of VA BIC on symptoms at baseline, 1 and 3 months after discharge

Measure	T0 Mean (SD)	T1 Mean (SD)	T2 Mean (SD)	ANOVA *p*
C-SSRS	3.78 (2.0)	0.89 (1.2)	0.89 (1.3)	0.01
BSS	16.11 (7.9)	9.33 (7.2)	8.00 (5.2)	<0.01
BHS	11.89 (6.4)	6.00 (3.7)	7.00 (6.1)	0.04
INQ-15 (PB)	23.40 (7.4)	15.00 (6.0)	12.22 (5.1)	0.01
INQ-15 (TB)	42.67 (11.4)	33.33 (14.9)	32.56 (8.8)	0.02
MOS-SSS (EI)	26.6 (10.2)	30.9 (7.5)	29.7 (7.3)	NS
MOS-SSS (TS)	12.8 (5.8)	15.9 (4.4)	12.4 (5.3)	NS
MOS-SSS (AS)	10.4 (4.7)	11.4 (4.2)	9.1 (4.6)	NS
MOS-SSS (PS)	8.8 (3.5)	10.4 (4.4)	8.4 (3.6)	NS
MOS-SSS (AI)	2.9 (1.3)	3.2(1.4)	2.4 (1.0)	NS

AI = Additional item; ANOVA = analysis of variance; AS = Affectionate support; EI =emotional and informational support; NS = not significant; PB = perceived burdensomeness; PS = Positive social interaction; SD = Standard deviation; TB = thwarted belongingness; TS = Tangible support; T0 = baseline; T1= 1 month; T2 = 3 months

supports, rather than healthcare professionals. These results suggest a need to enhance the VA BIC with a novel strategy, for example by including an mHealth app, that focuses on improving social connectedness.

Veterans' perspectives on the applicability of an mHealth app to Veterans at risk for suicide. I have identified a novel, mHealth strategy (My3) that aims to prevent suicide by improving social connectedness and has not been tested in Veterans. As part of my qualitative study of Veterans hospitalized on the inpatient mental health unit at the WRJ VAMC (see **Study 1**), I observed that Veterans reported an interest in the potential role of mHealth in supporting their engagement in treatment and perceived social connectedness after discharge. Most patients believed that mHealth could be helpful, and they reported they would consider using an app if it was made available to them. One patient said, "*it could [also] help my wife, who is my advocate, to feel empowered to reach out to my providers if necessary*." Another patient shared, "*I am not technology minded, but I would be willing to learn*." Yet, patients emphasized the need for autonomy in selecting their support network on the app. One patient stated, "*I only want to add my fiancée and my family, not my friends.*" Thus, it will be critical that the mHealth app can be personalized. Of note, the majority of Veterans on the WRJ VAMC inpatient mental health unit have access to mobile technology.

Research Design and Methods

Death by suicide after psychiatric hospitalization is a notable concern in the Veteran population.[4-5] Although the VA has implemented many strategies to prevent suicide in the post-discharge period, suicide remains an ongoing concern in this population.[29-34] Based on my preliminary work and available evidence, an intervention that I developed, called PEACE, may be an effective strategy to mitigate suicide risk in Veterans after psychiatric hospitalization because it addresses two key risk factors for suicide after psychiatric hospitalization: lack of social connectedness and poor engagement in care. My ***central hypothesis*** is that PEACE reduces suicide risk in Veterans in the period following psychiatric hospitalization by decreasing suicidal ideation. I also hypothesize that PEACE exerts its anti-suicidal effect by improving social connectedness and engagement in care after psychiatric hospitalization. I will conduct an exploratory aim evaluating the number of suicide attempts occurring after discharge. In this CSR&D CDA proposal, I intend to address these hypotheses by testing PEACE under randomized conditions in psychiatrically hospitalized patients. I expect that my work will result in the publication of important papers and will provide me with necessary data to support my goal of becoming an independent clinical researcher who develops, tests, and improves interventions to prevent suicide in Veterans.

Overview of Intervention and RCT Design:

As shown below in **Figure 2,** to test the aforementioned hypotheses, we propose to conduct a single-site, assessor-blinded RCT at the WRJ VAMC comparing PEACE plus standard psychiatric hospital discharge care to standard psychiatric hospital discharge care alone. The trial will enroll patients 18 years and older who are being discharged from the WRJ VAMC inpatient mental health unit (called Ground East, GE). The primary aim is to determine whether PEACE reduces suicidal ideation at one, three, and six months after psychiatric hospitalization. The secondary aim is to determine the mechanism by which PEACE exerts its anti-suicidal effect after hospitalization. An exploratory aim includes describing the number of suicide attempts after discharge.

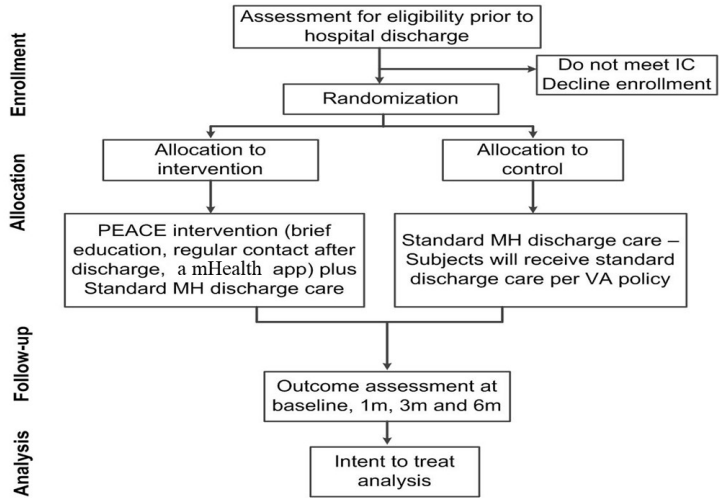
Baseline Assessment and Randomization: Prior to the start of study enrollment, allocation cards will be prepared using a fixed-block randomization scheme. These cards will be put into sealed, opaque, numbered envelopes. The box of envelopes will be stored in a locked cabinet in the study coordinator's locked office.

The study team member will meet with each eligible patient in a private room on GE at the WRJ VAMC around the time of discharge. The study team member will obtain informed consent from the patient and then administer the baseline assessments, which are described under the outcome measures (see below). The baseline visit will take approximately 90 minutes to complete. Study staff will also contact the support person the patient selected to obtain consent from this person.

After obtaining consent and completing the baseline assessments, the study coordinator will take the next numbered envelope from the box (described above) and open the envelope to determine the patient's assignment. In the event that the patient has been assigned to the intervention, the study coordinator will notify the intervention staff in order that the intervention staff can initiate the intervention. Otherwise, the patient will be informed that they have been assigned to usual care.

PEACE Intervention Description: Patients assigned to the intervention arm will receive PEACE (please see PEACE manual). The intervention can be delivered by a trained mental health staff member, such as a psychologist, mental health nurse, social worker, or psychiatrist. For simplicity sake, we will use the term "study therapist" to refer to the intervention staff member throughout the rest of this proposal and the accompanying documents.

Figure 2. Flow chart of study procedures



d=days; IC = inclusion criteria; m= months; MH = inpatient mental health; w = weeks

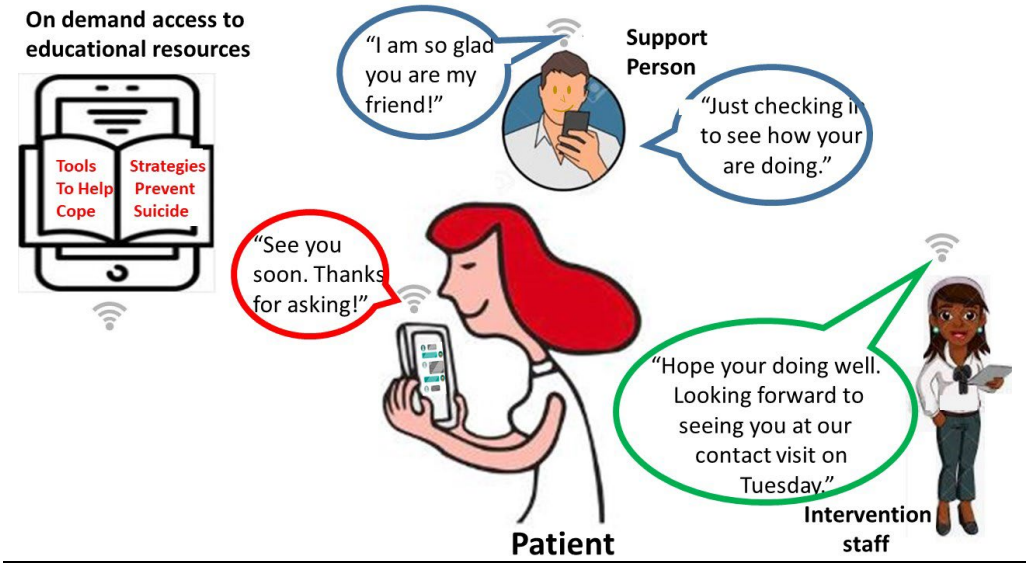
PEACE targets the needs of patients who are being discharged from a VA inpatient mental health unit after having been admitted because of acute suicide risk. Because PEACE is designed to enhance the standard hospital discharge care that patients receive as part of psychiatric hospitalization, patients assigned to PEACE will continue to have access to standard discharge care (described below). There are no restrictions on the types of treatments that patients may pursue after discharge; however, we will track the treatments that patients decide to utilize after discharge. By comparing PEACE with standard discharge care (including care provided through the Suicide Prevention Coordinator program), we hope to determine whether PEACE enhances standard discharge care. As described below, we conceptualize that the PEACE intervention consists of three synergist components that work to support the patient after discharge:

- *Brief Educational Component:* Patients receive a one-hour, one-on-one, personalized, brief educational intervention on suicide prevention. The session is performed by the study therapist and takes place on the inpatient mental health unit around the time of discharge. We anticipate that, in most cases, the patients will receive the intervention the day prior to discharge. The education is designed to meet the information needs of Veterans receiving mental health care in the VA and to address barriers to follow-up. The education includes a discussion of the patient's safety plan, draws upon MI techniques, and emphasizes self-efficacy. The sessions are highly interactive, allowing time for questions and providing patients with written materials that they can keep for future reference.
- *Seven Regular Contacts after Discharge Component*: The patients will maintain regular contact with the same study therapist for seven follow-up contacts (totaling 8 contacts including the initial Brief Educational

visit) over the course of the three months after psychiatric hospitalization. At each of these contacts, the study therapist will monitor the patient's symptoms, assess treatment adherence, review the safety plan with the patient, and, if necessary, assist the patient with engaging in care. The contacts will include the use of MI techniques. The contact sessions are systematic and structured. The contacts are designed to be highly interactive, allowing times for questions and providing patients with written materials that they can keep for future reference. Depending on the patient's preference, the contacts will be delivered via phone, VA Video Connect, or in-person in a private office on the grounds of the WRJ VAMC.

- *mHealth Component:*
- As described in the VA BIC manual, the intervention staff member directs patients to a wide variety of resources available within and outside the VA that may assist them in their recovery after discharge. One of these resources includes the My3App to help with suicide prevention in veterans. The app is a free app available for Android or iPhone and is owned and maintained by Vibrant Emotional Health, the administrator of the National Suicide Prevention Lifeline. While the My3App has been endorsed by the VA, the app has not been formally tested in Veterans and is not currently incorporated in a standard fashion in discharge care practices. The intervention staff member will introduce the app as part of the brief educational intervention and will provide formal education around the role of the app in follow-up care. The interventionist will continue to encourage use of the app at each follow-up visit.

Figure 3. How the my3 app works to support connectedness.



1) ***Behavioral health coach****:* The study therapist will educate patients on My3 during the brief educational visit and set up the app on the patient's phone. In this study, the study therapist will act in the role of behavioral health coach and therefore, in this role, their VA-issued iPhone number will be added to the patient's app. In their role as "*Coach*," the study therapist will be available to the patient between follow-up visits to answer any question and facilitate mental health treatment engagement. If My3 app were to be implemented into routine practice, the "*Coach*" would be a mental health provider (e.g., suicide prevention coordinator (SPC)).

2) ***Support network*****:** As shown in **Figure 3,** the app includes a support network that consists of a "behavioral coach' as well as up to two additional support persons. The patient will add the VA-issued cell phone number of the interventionist as their "behavioral coach."

The patient will also select up to two support persons to add to the app. The interventionist and the patient together will decide who these individuals should be. By adding these individuals to the app, the patient will have easy access to their phone numbers, which will continue to be stored in the patient's contact list. The app will also directly input the support person's phone number into the patient's keypad, facilitating a quick and easy way to call the support person. Importantly, this information is not stored within the app itself. The patient will be encouraged to reach out to their support persons throughout the study period for positive emotional support as they continue to recover after discharge. The patient can also reach out to the "behavioral coach" for support.

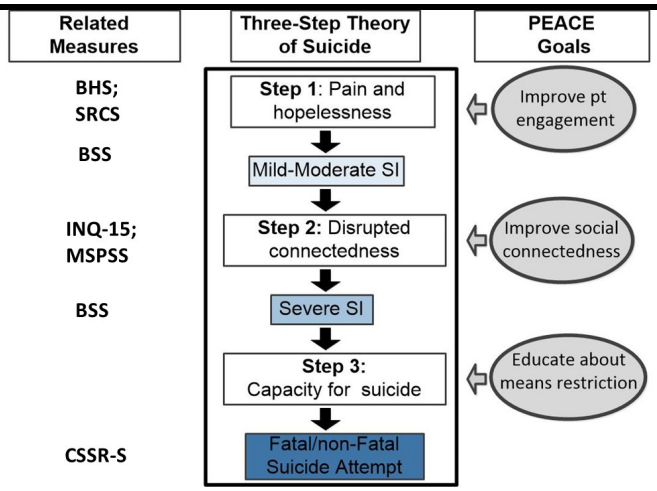
3) **Safety plan**: the patient will enter an abbreviated safety plan into the app, which will include strategies that they will use to support their well-being after discharge. The interventionist and patient will discuss this plan at follow-up contact visits and consider whether there is any need to further refine this plan. The patient may wish to share their safety plan with the two support persons they have chosen to be included on the app. This can be shared via email if the patient has the support person's email address in their contact list. Similarly to the call feature of the app, email addresses are not stored within the app itself. The app simply directs the patient to their main email app on their phone.

4) ***Educational materials*:** As shown in **Figure 3**, the patient can access educational materials related to suicide prevention on the app. These materials are standard on the app, and therefore, all patients will have access to the same material. Patients can use these interactive educational materials at any time to gain skills in supporting their mental health.

Standard Psychiatric Hospital Discharge Care: Patients assigned to the PEACE intervention as well as the control condition will receive the standard VA hospital discharge care that occurs as part of psychiatric hospitalization. VA current standard psychiatric hospital discharge care includes five core elements. First, patients and their outpatient providers are required to be involved in discharge planning. Second, patients should be offered evidence-based treatments to address their mental health symptoms. Third, the inpatient team should work with the patient to complete a safety plan prior to discharge. Fourth, the inpatient team should arrange two follow-up care visits within 30 days of discharge. Fifth, the inpatient team in conjunction with the SPC assess whether patients are appropriate to be placed on the High Risk for Suicide List. Patients who are placed on the High Risk for Suicide List receive enhanced oversight as outlined in VA policy. More recently, this enhanced care was renamed the Suicide Prevention Pathway. The SPC oversees the following elements of the Suicide Prevention Pathway: 1) The SPC reminds the mental health provider that the patient should be scheduled to be seen four times within the first 30 days following hospitalization; 2) The primary care or mental health provider is expected to tailor the patient's treatment to address his/her unique risk factors for suicide; 3) The SPC places a pop-up flag in the medical record to alert providers of the patient's high-risk status; and 4) The continued need for the patient to remain on the High Risk for Suicide List is reassessed by the SPC every three months. Of note, at the clinical discretion of the inpatient treatment team and the SPC, some patients may be assigned to the Suicide Prevention Pathway but may not meet criteria for the High Risk for Suicide List. Per VA policy, SPCs are not required to provide clinical care.

Organizing framework for PEACE's Anti-Suicidal Effect: As shown in **Figure 4** below, based on the 3ST and our pilot data,[38,50] we hypothesize that PEACE will reduce the risk for suicide after psychiatric hospitalization through the following mechanisms: First, suicide-prevention education and ongoing contact with a person at risk for suicide may help to facility continuity of care and reinforce the importance of engaging in treatment after discharge. MI may also promote self-efficacy and the ability to overcome barriers to treatment engagement. Because a person is receiving continuous mental health treatment after discharge, he/she may experience a lessening of symptoms of mental illness and, thus, a decrease in the psychic pain associated with mental illness. The 3ST suggests that a decrease in psychic pain and

Figure 4. Organizing Framework for PEACE Intervention*



*measures described in outcomes section; pt =patient

hopelessness may decrease suicide risk.[38] Second, PEACE may help patients to feel more socially connected. Because patients are more supported after discharge and experience increased social connectedness, this will also help to prevent their suicidal ideation from worsening. [20,21,22,44] Finally, because patients are better educated about means restriction as part of the brief educational intervention, patients may take steps to mitigate their practical capacity for suicide. Together, these factors may reduce the risk for suicide after psychiatric discharge.

Outcome Measures: As outlined in **Table 2**, we will use several standardized instruments to collect information on primary and secondary outcomes throughout the study. Copies of assessment tools are available in **the Assessment Manual**.

Table 2: Overview of Standardized Assessment Measures and Timing of Assessment

	Measurement Methods				Timing of Assessment			
Outcome	Instrument	Cronbach's α	Length	Time*	0M	1M	3M	6M
Diagnosis	**MINI**	**N/A**	**N/A**	**15**	**X**	**-**	**-**	**-**
Suicidal Ideation	**BSS**	**0.87 – 0.97**	**21 items**	**10**	**X**	**X**	**X**	**X**
Hopelessness	**BHS**	**0.87 – 0.93**	**20 Items**	**10**	**X**	**X**	**X**	**X**
Connectedness	**INQ-15**	**0.89 – 0.91**	**15 items**	**5**	**X**	**X**	**X**	**X**
Connectedness	**MSPSS**	**0.85 – 0.91**	**12 items**	**5**	**X**	**X**	**X**	**X**
Engagement	**SRCS**	**0.89**	**17 items**	**5**	**X**	**X**	**X**	**X**
Suicide Attempts	**C-SSRS**	**N/A**	**7 items**	**5-10**	**X**	**X**	**X**	**X**
App Engagement	**AES**	**0.839**	**7 items**	**5**	**-**	**X**	**X**	**X**
Estimated time (in minutes) to complete assessments					**60**	**50**	**50**	**50**

AES = App Engagement Scale; BHS = Beck Hopelessness Scale; BSS = Beck Scale for Suicidal Ideation; CSSR-S = Columbia Suicide Severity Rating Scale; INQ-15 = Interpersonal Needs Questionnaire-15; M = months; MINI = MINI International Neuropsychiatric Interview; MSPSS: Multidimensional Scale of Perceived Social Support; N/A = Not applicable; SRCS: The Suicide-Related Coping Scale; *Time is described in minutes

Baseline Characteristics: We will collect socio-demographic data from patient report and the electronic medical record such as age, sex, marital status and service history (e.g., branch, era, combat exposure). We will also collect diagnostic information using the MINI International Neuropsychiatric Interview (MINI), which has been validated against the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (DSM).[51] The MINI is a short, structured diagnostic interview that, on average, takes about 15 minutes to administer. We will inquire about any history of suicide attempts using the validated Columbia Suicide Severity Rating-Scale (C-SSRS).[52] The C-SSRS includes a 7-item subscale that assesses for actual and interrupted suicide attempts.

Primary Outcome (Suicidal Ideation): The primary outcome will be assessed using the Beck Scale for Suicidal Ideation (BSS).[53-54] Patients will be asked about their current suicidal ideation (i.e., past week) at assessments 1 as well as at assessments 2, 3, and 4. The BSS is a self-reported questionnaire that assesses severity of suicidal ideation. The BSS measures attitudes, behaviors, and plans to die by suicide. Each item on the BSS is scored on a scale from 0 to 2 and the first 19 of the 21 items are used to calculate a total score ranging from 0 – 38. The BSS has high reliability and is a valid measure of suicidal ideation. There is also evidence that the BSS is measurement invariant across time.[55] The BSS is widely used in clinical trials, is sensitive to clinical change, and unlike most other measures of suicidal ideation, higher scores on the BSS are associated with death by suicide. While there is no established BSS cutoff score to classify suicide risk as

high, low, or none, there is evidence that higher scores on the BSS correspond to more severe suicidal ideation.[53-54] There is evidence that an improvement of five points or more on the total BSS scores may be clinically relevant. [52]

***Secondary Outcome (Patient Engagement)*:** We will measure patient engagement in treatment at assessment 1 as well as at assessments 2, 3 and 4. Patient engagement is a complex phenomenon to measure.[69] The term 'patient engagement' encompasses various aspects of care related to a patient's motivation and intent to be an active participant in addressing their healthcare needs.[56] To date, there is no agreed-upon measure in the literature that incorporates all aspects of the experience of 'patient engagement.[56] In the field of mental health, there is some notion that 'patient engagement' should mean that a patient experiences collaborative care, feels supported during their treatment, and adopts 'good practices' or behaviors that support their overall well-being.[56-57] Therefore, only assessing whether a patient attended a mental health appointment may not adequately reflect treatment engagement. There is also evidence that symptom severity can preclude patients from engaging in care.[58] Pfeiffer *et al*. found that, despite improvements in timely outpatient follow-up after VA psychiatric hospitalization, there were no significant changes in readmission or antidepressant treatment.[59] In fact, Bernet *et al.* found that appointment intensity was higher in Veterans who reattempted suicide after discharge versus those who did not reattempt.[60] Furthermore, in reviewing our data thus far from our trial on Ground East, we have identified that our current measures of engagement may not be adequately covering a key component of patient engagement as it relates to suicide including self-efficacy around managing suicide risk. This is a key concept that is part of the VA BIC intervention. Thus, we conceptualize that engagement includes patient activation, continuity of care, and self-efficacy.

- Patient activation: Patient activation is defined as "an individual's knowledge, skill and confidence for managing their health and health care."[61-62] Individuals who demonstrate higher degrees of patient activation have been found to be more likely to engage in health-promoting behaviors and to experience better outcomes.[63] Because our trial focuses specifically on activation and related self-efficacy in avoiding suicidal behavior after discharge, we will administer the validated Suicide-Related Coping Scale (SRCS).[64] This scale includes 17 questions related to a patient's perception of their ability to cope with suicidal thoughts. Each item is assessed using a 5-point Likert scale and the measure has been developed based on two studies of suicide prevention strategies conducted within Veteran populations. The scale includes two subscales including an External Coping subscale and an Internal Coping Subscale. Both subscales have shown good acceptable internal consistency. The two factors are also sensitive to change over time. Higher scores on the scale suggest better coping.
- Continuity of care: There is some evidence that improved continuity of care may lead to better mental health outcomes.[65-66] However, a single, valid, standardized measure of continuity of care for mental health has not been described in the literature. Work by Greenberg *et al.* in Veterans who were discharged from a VA inpatient mental health unit provides sufficient evidence that three aspects of continuity of care after psychiatric hospitalization (regularity of care, continuity of treatment across organizational boundaries, and intensity of treatment) are associated with improvements in overall mental health.[67] We will use the three measures of continuity of care as validated by Greenberg *et al.* This includes:
    a) Continuity of care: Measure of whether a patient discharged from the inpatient MH unit received any MH outpatient treatment in the first month and between 1 – 3 m after discharge.
    b) Regularity of care: The number of months in the 3 m after the baseline assessment in which the patient attended at least 1 MH visit (Range 0 – 3 m), and
    c) Intensity of care: Measure of the total number of MH visits between initial entry into the

study and the last study assessment.

In addition, we will also evaluate evidence of disruptions of care including no-show and cancelled appointments. We will abstract these measures from the electronic medical record. Since it is possible that some patients may receive portions of their care outside of the VA system, we will also ask patients to self-report on non-VA care.

- Hopelessness: To gather clinical evidence of treatment engagement, we will assess hopelessness at baseline and at follow-up assessments using the Beck Hopelessness Scale (BHS). The BHS is a 20-item self-report scale that assesses hopelessness over the past seven days.[68] Patients comment on feelings about the future, loss of motivation, and future expectations. Total scores range from 0 to 20, with higher scores suggesting more hopelessness. Higher scores on the BHS are associated with increased suicide risk.[64] The BHS has good reliability and validity and is sensitive to change.[69] The psychometrics of the BHS in the Veteran population have not been studied, but the BHS has been used in other studies of the Veteran population.[70]
- ***Secondary Outcome (Connectedness):*** We defined social connectedness (or connection) as 'the extent to which an individual is socially connected [that] takes a multifactorial approach including 1) connections to others via the existence of relationships and their roles; 2) a sense of connection that results from actual or perceived support or inclusion; and 3) the sense of connection to others that is based on positive and negative qualities' (Holt-Lunstad et al 2017, page 521).[71] Social connectedness is a complex construct and the literature highlights that there is no single, ideal measure that adequately captures all aspects of this construct or can be tied directly to suicide risk.[71-76] In this setting, we chose Holt-Lunstad et al's (2017) definition of social connectedness because their work is widely recognized, their framework is comprehensive, and draws upon factors that may be tied to poor outcomes including suicide.[71] Holt-Lunstad et al 2017 (page 521) define the three domains of social connectedness as follows: 1) Structural ('the existence and interconnections among differing social ties and roles'); 2) Functional ('functions provided or perceived to be available by social relationships' including 'feelings of isolation, disconnectedness, and not belonging'); and 3) Quality ('perceptions of positive and negative aspects of social relationship'). Within each of the aforementioned domains, there are many measures to select from and some of these measures have been studied in the context of suicide risk. We were judicious in selecting two measures that we believe will enable us to tap into the domain of interest that our intervention is designed to target (i.e. functional), while not overburdening the enrolled patients with excessive measurements. We acknowledge that there is no single comprehensive and universally accepted measure of social connectedness. We will use two scales that we believe provide synergistic information about this construct. These scales both address social connectedness and have shown association with suicidal behavior. The Interpersonal Needs Questionnaire-15 (INQ-15) taps into a major component of the functional domain of social connectedness, namely perceived inclusion.[77] The INQ-15 is a 15-item self-report scale that measures thwarted belongingness and perceived burdensomeness. Thwarted belongingness measures an individual's perception that their 'fundamental need for connectedness' is left unmet (Van Orden 2012, page 198).[77] Each item is measured on a 7-point Likert scale, with higher scores suggesting lower perceived connectedness.[77] The INQ-15 has good reliability and validity in the Veteran population. Higher scores on the INQ-15 have been associated with suicide risk.[77-78] The Multidimensional Scale of Perceived Social Support (MSPSS)[79] The MSPSS also taps into a major component of the functional domain of social connectedness, namely perceived social support. he MSPSS is a 12-item self-reported scale that is designed to ask about support from several sources including friends, family and significant other. The scale has been shown to have good internal and test-retest reliability as well as good validity. There is some evidence that perceived social support as measured by the MSPSS may also be associated with

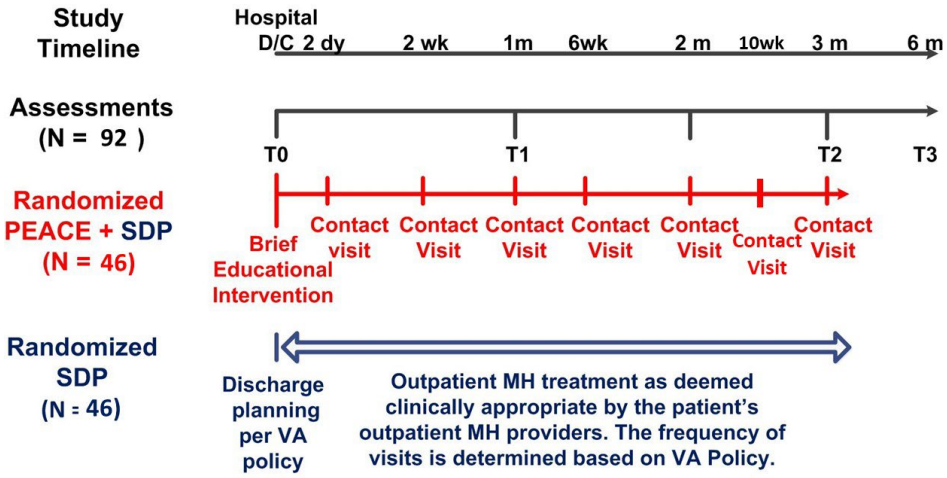
suicide risk.[80]

***Secondary Outcome (Suicide Attempts)*:** We will assess for non-fatal and fatal suicide attempts at one and three months after discharge using the C-SSRS.[52] The C-SSRS is a valid and reliable scale that includes a seven-item subscale that asks patients to self-report on actual attempts, interrupted attempts, aborted attempts, and preparatory acts or behaviors. The scale asks the assessor to document the actual and potential lethality of these behaviors. The C-SSRS is widely used in the VA. The psychometrics of the C-SSRS in Veterans is unknown. We will also review suicide behavior reports (SBR) in the electronic medical record. SBRs are required in the VA and include information on suicide attempts, suicide deaths, and other types of suicidal behaviors including interrupted attempts.[81]

Secondary Outcome (App engagement): Several measures have been selected to aid in a planned secondary analysis of the data to characterize the relationship between app engagement and outcomes in patients assigned to the intervention arm. Although mHealth is being used with increasing frequency to address various health behaviors, there is a dearth of evidence on effective methods to assess app engagement, though many approaches exist.[82-83] Therefore, we will administer the App Engagement Scale (AES) at one-, three-, and six- months. Notably, the one- and three-month AES assessment will include the period during which the patient is receiving the PEACE intervention; however, the six-month assessment will measure whether the Veteran decided to continue to use the app on their own even after the intervention period ended and the intervention staff member was removed from the social network. The AES is adapted from the end-user version of the Mobile Application Rating Scale (uMARS).[84] The AES has been studied in patients with mental health conditions, has been shown to have good internal reliability, and is strongly related to app engagement.[85]

Study Design: As shown in **Figure 5**, patients allocated to the PEACE intervention will meet with the study therapist prior to discharge. During this visit, they will receive the first intervention visit. The intervention will be delivered in a private office on GE. After discharge, patients will participate in seven regular follow-up contacts with the study therapist over a period of three months in addition to use of the My3 app. Depending on patient preference, the regular contacts will occur in a private office on the WRJ VAMC campus or the contacts will occur over the phone or VA Video Connect.

Figure 5. Timeline of Assessments and Interventions



dy = days; m = months; MH = Mental health; SDP = Standard psychiatric discharge practices; T0, T1, T2, T3 = assessment time points; wk = weeks

- All patients (including patients randomized to PEACE) will have access to standard discharge care. Furthermore, regardless of study assignment, all patients will undergo four outcome assessments including assessment 1 (baseline or study entry, occurs just prior to hospital discharge)(0M), assessment 2 (occurs one month after baseline assessment) (1M), assessment 3 (occurs three months after baseline

assessment) (3M) and assessment 4 (occurs six months after baseline assessment) (6M). These assessments will be conducted by the independent outcome assessor. The independent outcome assessor will conduct the baseline assessment in a private office on GE. We anticipate that, in most cases, assessment 1 will occur on the day before discharge. Depending on patient preference, the independent outcome assessor will conduct assessments 2, 3, and 4 in a private office on the WRJ VAMC campus, over the phone, or using VA Video Connect. The assessors will be blinded to study assignment and the patients will be instructed to not reveal their status to the assessor. All outcome variables will conform to the PhenX Common Data Elements (CDE) in order to improve our ability to compare our findings across other studies and maximize the impact of our results. The independent assessor will be blinded to study assignment. At each study visit, we will ask the assessor to guess the study assignment of the participant. We will consider that the blinding of the assessor was successful if the assessor is able to guess the assignment less than half of the time.

- Because app engagement will only be tracked in patients exposed to PEACE, we will ask that the study coordinator or study therapist (rather than the outcome assessor) administer the self-reported scale (AES) in order to avoid compromising the blinding of the outcome assessor. Quantitative measures of app engagement can be directly downloaded onto a secure server.
- As the WRJ VAMC is a rural medical center that serves a large geographic area (New Hampshire and Vermont), we anticipate that several enrolled patients will prefer phone (or VA Video Connect) over in-person follow-up. Fortunately, the assessment instruments that we selected for this study can be administered over the phone or in person. Furthermore, our decision to allow patients to participate in study follow-up by phone (or VA Video Connect) or in person is consistent with the study methods of the original WHO BIC trials.

Intervention Training, Supervision, and Fidelity: Given the systematic and structured nature of PEACE, it will be essential to maintain fidelity to the intervention and the manualized guide during the course of the trial. N.R. will train the study staff in the delivery of PEACE, then the staff will complete several practice cases. N.R. will review the staff's performance, provide feedback, and give additional training if necessary. As described above, PEACE incorporates MI techniques and N.R. has experience in delivering MI. A fidelity-rating scale for PEACE was developed for this proposed trial (see Assessment Manual). The scale is adapted from the validated Yale Adherence and Competence Scale (YACS).[86] The scale evaluates both adherence to the study protocol and the competence of the staff performing the intervention. The fidelity scale includes 15 items, of which 10 items pertain to the brief educational intervention and 5 items pertain to the regular contacts occurring after psychiatric hospitalization. The elements of the fidelity scale are based on the criteria outlined in the original WHO BIC protocol. Adherence to each of the 15 items on the scale will be rated on a 5-point scale ranging from "not at all" to "extensively."[87] A random sample of 10% of cases will be selected for fidelity rating and the investigator (N.R.) will sit in on these sessions as an observer in order to complete the rating scale. N.R. will inform the intervention staff member if further adjustments are necessary to improve and maintain fidelity.

Statistical Considerations

Statistical Analyses: To maintain blinding, the statistician who is otherwise not directly involved in the study will conduct the analysis based on the intention-to-treat principle. Below, we have outlined the specific analysis plan for assessing each of the three aims of interest of this study. As part of the analyses of the three aims, we plan to account for potential confounding. We will assess for statistically significant differences in baseline study characteristics, including age, sex, race, history of suicide attempts, mental health diagnosis, marital status, employment, recent life stressors, service history, High Risk for Suicide List status, and Suicide Prevention Pathway status between study arms using *t*-tests for continuous measures and chi-squared tests

for dichotomous variables. We will report these results using 95% confidence intervals (CI) and *P*-values. We will define statistical significance as a *P*-value < 0.05. If we identify any variables for which there are significant differences across study arms, we will control for these confounders in the analysis of the aims.

Specific Aim 1: The primary aim of the study is to determine whether PEACE plus standard psychiatric hospital discharge care reduces suicidal ideation after psychiatric hospitalization compared to standard psychiatric hospital discharge care, alone. Based on available evidence, we hypothesize that the intervention plus standard psychiatric hospital discharge care will lead to a significant reduction in suicidal ideation after psychiatric hospitalization. We believe that the effect of the intervention on suicidal ideation will be the greatest at the three-month assessment because the greatest intensity of follow-up care provided through the intervention occurs within the first three months after discharge. In order to assess whether the effect of the intervention is maintained after the intervention is discontinued, we will reassess patients at six months (i.e., three months after the intervention has been discontinued). This length of follow-up is feasible within the scope of this mentored award period and more than 50% of suicide attempts occur within six months after discharge. We will generate descriptive summary statistics (e.g., means and standard errors, medians) and graphical displays for the BSS total scores at baseline (assessment 1) and at assessments 2, 3, and 4. Aligned with evidence from the literature, we will use a hurdle model to analyze our primary outcome.[88-89] First, we will use logistic regression whereby we will treat the measure as a dichotomous outcome with zero versus nonzero values (i.e. presence or absence of any suicidal ideation). Second, we will look at the degree of suicidal ideation by using a zero-truncated over-dispersed negative binomial regression for the distribution of nonzero values. The BSS scale is a 21-item scale.[53] The first five items are intended to evaluate for the presence of any suicidal ideation. These items together get at the complex construct of suicidal ideation including passive and active suicidal ideation. As described in the literature,[89] all 5 initial items on the BSS are used to define the presence or absence of suicidal ideation (i.e. “zero” on all of the first five questions defines “no suicidal ideation present”). If suicidal ideation is present, then additional items (i.e. items 6-19) are used to evaluate the severity of suicidal ideation.

We will calculate 95% CI and *P*-values and will define a *P*-value of < 0.05 to be statistically significant. We will use the maximum likelihood ratio to account for any missing data.

Specific Aim 2: The secondary aim of our study is to determine the mechanism by which PEACE exerts its anti-suicidal effect on patients after psychiatric hospital discharge. Based on available evidence, we hypothesize that the intervention plus standard psychiatric hospital discharge care exerts an anti-suicidal effect on patients after psychiatric hospitalization by improving social connectedness and engagement in care after discharge. We will assess this aim by performing the following analyses: First, we will perform an analysis to demonstrate whether there are greater improvements in social connectedness and engagement in care over time in patients assigned to the intervention versus control condition at one, three, and six months after discharge. For continuous variables measuring patient engagement, we will generate descriptive summary statistics (e.g., means and standard errors, medians) and graphical displays for each measure at baseline (assessment 1) and atassessments 2, 3, and 4. Second, using structural equation modeling,we will calculate mean differences in scores for each of our continuous measures at the one-, three-, and six-month assessment periods, as well as the associated 95% confidence intervals and *P*-values. For the categorical measure of patient engagement, we will use chi-squared tests to compare the proportion of patients adhering to their discharge plan between the two study arms at one- month after discharge. Third, we will assess whether social connectedness and patient engagement mediate the effect of the intervention on suicidal ideation, as measured by total BSS scores. In order to conduct this analysis, we will use structural equation modeling. We will use the maximum likelihood to account for any missing data. We will calculate the associated 95% CIs and *P*-values and will define a *P*-value of 0.05 to be statistically significant.

Specific Aim 3: We plan to conduct an exploratory analysis on the number of suicide attempts (fatal and non-fatal) that occur after discharge in the intervention plus standard psychiatric hospitalization discharge care arm compared to standard psychiatric hospital discharge care, alone. While suicide deaths and suicide attempts are important clinical endpoints, this single-site trial will not be powered to detect a statistically significant effect between study arms. Furthermore, because we assume that few events will be observed in either arm, we plan to summarize our findings by providing basic descriptive statistics regarding the number of events in each arm at one-, three-, and six-month follow-ups. In the event that there are a sufficient number of suicide attempt events to perform statistical analysis, we will use a log-rank statistic to test for statistically significant differences in the proportion of suicide attempts between arms. We will use the Kaplan-Meier method to plot and compare survival curves for each arm. Specifically, we will calculate the time from the baseline assessment (assessment 1) to first suicide attempt after discharge for each study arm. Patients who are lost to follow-up or do not attempt suicide will be censored during the analysis. We will calculate hazard ratios using the Cox proportional hazards model. This approach will also enable us to adjust for baseline differences between study arms, if necessary. We plan on using these data to inform a future trial that is powered to detect an effect.

Proposed Secondary Analysis: Within the intervention group, we will conduct a secondary analysis of engagement with the mHealth app to assist further in the interpretation of our findings. Specifically, we are interested in learning about the degree to which patients assigned to PEACE interacted with app and whether differences in the degree of engagement with the app are associated with changes in social connectedness and suicidal ideation. First, we will generate descriptive summary statistics (e.g., means and standard errors, medians) and graphical displays for app engagement at one and three-month follow-up. Second, we will use generalized linear modeling to evaluate the relationship between app engagement and the primary outcome, suicidal ideation, and the secondary outcome, social connectedness.

Sample Size:

Based on a pilot RCT of the VA BIC Program in 19 patients discharged from the WRJ VAMC inpatient mental health unit (manuscript currently under review), we found that the intervention had an estimated effect size of 0.5 (Cohen's d_s) on the BSS. We see the 0.5 as a medium sized effect and consistent with effects of other psychosocial interventions. We have reason to believe that this effect size may be even higher in our trial where we will be enhancing the intervention with the addition of the mHealth app. We used these pilot data to re-calculate the required sample size for this proposed study. In doing so, we used a formula for estimating sample sizes for longitudinal designs with repeated measures as proposed by Hedeker et al (1999).[90] We assumed that the correlation of repeated measures (*p)* was 0.5 based on findings from our pilot data. Furthermore, we assumed that there were four assessment points and that the data followed a normal distribution. We made this latter assumption because our pilot data followed a normal distribution according to the Shapiro-Wilk test for normalcy. We also are assuming that the data that we collect in this proposed trial will follow a normal distribution because the data will be drawn from the same population (and the same setting) as our pilot work. As shown in **Table 3**, based on the aforementioned calculations, a sample size of 80 (40 per arm) will achieve an 80% power to detect an effect size of 0.5 (Cohen's d) or greater between arms across the study timepoints with a significance level of 5%. In our pilot study, there were no patients who dropped out, but

Table 3. Sample size estimates

Power	Alpha	*p*	n	Effect Size	Size of Effect	Intervention	Control	Intervention	Control
0.8	0.05	0.5	4	0.3	Small	109	109	120	120
0.8	**0.05**	**0.5**	**4**	**0.5**	**Medium**	**40**	**40**	**46**	**46**
0.8	0.05	0.5	4	0.6	Medium	27	27	30	30
0.8	0.05	0.5	4	0.8	Large	16	16	18	18

p = correlation of repeated measures; n = 4 timepoints; N=number
*Size of effect are based on criteria described in *Laken D 2013.*[91]

two patients had missing data at one or three-month follow-up. Conservatively, we assumed that in the proposed trial that there could be a drop out as high as 10%. This means that we will need to recruit for this proposed trial a sample size of **92** (46 per arm).

Study Population and Recruitment

The study will be conducted at the WRJ VAMC and will recruit patients hospitalized on Ground East (GE), the facility's 12-bed inpatient mental health unit. GE staff includes psychiatrists, a therapist, nursing staff, a social worker, and trainees from these disciplines. Study staff will attend daily inpatient treatment team meetings in order to identify potentially eligible patients who can be approached about study participation. The inpatient team and attending psychiatrist will make the determination as to when and whether it is clinically appropriate for study staff to approach potentially eligible patients. After approaching eligible patients, study staff will make them aware of the study and determine if they are interested in participating in the study. If patients are interested in the study, study staff will obtain informed consent using a written informed consent document prior to enrolling the patient into the study. During the course of the study, it will be impossible to blind the study therapist or patients to treatment allocation; however, the outcome assessor will remain blind to study assignment throughout the trial. Patients will be instructed during the course of the trial not to reveal their study assignment to the outcome assessor. In order to assist with study retention, reminder letters will be sent in the form of U.S. mail or a phone call, depending on patient preference.

Inclusion Criteria:

- Per the unit psychiatrist, hospitalization was due to concerns about acute risk for self-harm including suicidal ideation, suicide attempt, and/or admitting provider deemed the patient was at imminent risk for self-harm;
- Be a Veteran eligible to receive VA services;
- Be 18 years or older;
- Be able to speak English;
- Have access to a smart phone and express willingness to download the My3 app.

Exclusion Criteria:

- Unable to provide informed consent;
- We do not plan to enroll any potentially vulnerable populations including prisoners or involuntarily committed patients.

Informed Consent

Eligible participants who are interested in participating in this study will complete the informed consent process. Study staff will inform the patient about the study and provide them with the informed consent document. Patients will have the option to review the document with their doctor, family, and/or friends prior to signing if they choose. Upon signing, they will be provided with a photocopy of the document. We do not anticipate a waiting period between informing the patient of the study and obtaining informed consent, but participants may choose to wait. To ensure understanding of the study purpose and procedures, the patient will be encouraged to ask questions if there is anything they do not understand. Additionally, the informed consent document is written in easy-to-understand language to facilitate comprehension. As a result of the certificate of confidentiality, the consent form will not be uploaded to the patient's medical chart.

Risks and Side Effects:

Potential Risks

As described above, it is expected that patients may report worsening suicidal ideation or suicidal behaviors at the study assessments (i.e., assessments 1, 2, 3, and 4) regardless of whether they are assigned to the intervention or control condition. It is also possible that patients assigned to the intervention arm may report worsening suicidal ideation or suicidal behavior during an intervention visit. It is also possible that patients could be seen in the emergency room or be hospitalized because of any of these events. Thus, it is expected for the patients to continue with the study unless the patient requests to be removed from the study.

Furthermore, as outlined in our **Safety Alert Protocol**, study personnel will immediately follow the safety alert protocol in response to any reports of worsening suicidal ideation or behaviors. If necessary, patients will be connected immediately with required clinical treatment. All patients will continue to have access to standard-of-care treatment during the course of the trial regardless of study assignment. Furthermore, all patients may continue any treatments that they were receiving as part of their routine care prior to enrolling in the study.

Therapeutic Risks

During the trial, the research staff will ask patients questions about how they are feeling and their interactions with other people. Patients will be exposed to these therapeutic risks during assessments 1, 2, 3, and 4. In addition, patients assigned to the intervention condition will also be exposed to these therapeutic risks at the intervention visits (brief education visit plus seven contact visits after discharge as well as during the use of the My3app). Sometimes, patients can feel embarrassed, nervous, bored, or generally uncomfortable when they are asked to answer these types of questions. However, because there are sufficient safeguards in place to mitigate these potential risks, the overall therapeutic risk from this study to enrolled patients is very low.

Research Risk

During the course of the trial, protected health information including name, social security numbers (in order to process participant payments), phone numbers (for contact purposes), sociodemographic information (e.g. age, race), psychiatric diagnoses (e.g., Alcohol Use Disorder, Substance Use Disorder, Depression), mental health treatments received, and psychiatric symptoms (e.g., responses to standardized questionnaires) will be collected from all enrolled patients. Furthermore, the My3 app will use the patient's contact list in order to facilitate easy communication between the patient and their support network. The app does not store this information within the app, and thus, the risk of confidentiality being compromised is extremely low. As there are sufficient safeguards in place to mitigate these risks (see Protection Against Risk below), the overall research risk in this study is very low. This study will also be protected by a Certificate of Confidentiality. As a result, the consent form will not be uploaded to the patient's medical chart. Study staff will write visit notes in the patient's chart including information about the intervention as well as any relevant research or clinical information necessary for continuity of the patient's medical care.

Protection Against Risk

Study Population Safety Risk

Our target population is a high-risk population. All patients in our study will need to have been admitted psychiatrically due to suicide risk to meet enrollment criteria. We fully expect that all patients at baseline will report high suicidal ideation (and possibly a suicide attempt) that led to current admission. We expect that many patients will remain at high risk for suicide throughout the study. To maximize the safety of patients during the study, we have taken the following steps. First, we will only accept referrals for the study from the inpatient mental health team. The inpatient mental health team led by the psychiatric medical director will determine if patients are appropriate for the study. Second, we are only using trained mental health providers

as study staff assessors (and interventionist). Third, at each study assessment time point (i.e., assessments 1, 2, 3, and 4), patients will be assessed for symptoms of suicidal ideation and suicidal behavior because these are *a priori* study endpoints. Our follow-up schedule matches that recommended in the literature (Schatten 2020). In addition, for patients assigned to the intervention, patients may report worsening suicidal ideation or suicidal behavior in the context of the intervention visits or by contacting the intervention staff member by phone via the My3 app. Regardless of whether the patient is assigned to the intervention or control condition, the study staff will be ethically bound to take appropriate action if the patient is at imminent risk for self-harm. We have an established algorithm that will be used by the trained assessor to determine whether there is a safety alert based on scale scores. The **Safety Alert Protocol** outlines the process that study staff members will follow in order to ensure the safety and well-being of all enrolled patients regardless of whether they are assigned to the intervention or control condition. In the event that a safety alert is met, the research staff member will contact Dr. Natalie Riblet (or the mental health physician covering for her) or, if necessary, the patient's mental health provider. As part of this risk assessment, the assessing clinician will immediately complete a comprehensive evaluation of risk and determine the most appropriate next level of care for the patient. The next level of care may include psychiatric admission, emergency room referral, or an outpatient follow-up appointment with the patient's healthcare provider. Please see **the Safety Alert Protocol** for a full description of all safety alerts and required actions by study staff members. The safety protocol aligns with standard care approaches that are followed by all VA mental health providers at the WRJ VAMC facility.

Of note, it is possible that the patient could contact the study therapist by phone call through the My3 app relaying that he/she is doing worse or that they are experiencing worsening suicidal ideation or behaviors. We have instituted several safe-guards to ensure the safety of the patient: First, the My3 app would direct the patient's call to the study therapist's VA issued cell phone. Second, in the event that the study therapist is not available, the voicemail greeting message includes the standard required language required by all WRJ mental health providers). The standard language includes information on what the recipient should do in the event of acute safety concerns such as calling the Veterans Crisis Line. This is also the same standard language that the inpatient treatment team on Ground East shares with families/friends if they request for advice on how to manage safety risk in their loved one. In the event that the study therapist is made aware of safety concerns about the patient, the study therapist will follow standard procedures as are followed by any mental health provider who works at the WRJ VA Medical Center. This procedure includes attempting to contact the patient. If the patient cannot be located, the study therapist will reach out to the support person (and if necessary, any other contacts provided to the study staff by the patient) in order to locate the patient. Once the patient is reached, the study therapist will follow **the Safety Alert Protocol**. If the patient can't be located, the study therapist will reach out to the Suicide Prevention Coordinator to determine the next best plan of action.

Please note that the My3 app does not have any capability to send or receive text messages. The My3 App can only enable the patient to communicate with the intervention staff member through a cellular phone call.

Therapeutic Risk

Patients will be given ample time to answer questions and complete visits in order to reduce any discomfort they may experience. Patients will also be made aware that if any of the questions make them feel uncomfortable, they should feel free to mention this to the study staff member and have this concern addressed immediately. At any point during a visit, a patient can take a break or refuse to answer a question.

Research Risk

Every effort will be made to ensure that the privacy and confidentiality of the patient is maintained. All study visits will occur in a private office on the WRJ VAMC campus to ensure privacy. If a visit or assessment is

done via a phone call, the research staff will conduct the phone call in a private office. All assessments that can be collected electronically will be stored on a secure, password-protected file on a secure, local researcher server. All staff associated with the study will complete required security training prior to the start of the study in order to be permitted access to this server. Furthermore, all study staff will adhere to the required annual training (by the WRJ VAMC) necessary to maintain their access to the server. All paper copies of study-related data, including consent and HIPAA forms, will be kept in a locked file cabinet, in a locked office, dedicated to this study. Only research staff will have access to this locked cabinet

Finally, the phone numbers of the patient, the support person and the study therapist must be entered into the patient's contact list, which the My3 app will then use to facilitate a phone call. A phone number is the only reliable mechanism by which the My3 app can enable the patient to make a cellular phone call to the support network member or the intervention staff member. The intervention staff member on this study has access to a personal, VA-issued cell phone, which is in full compliance with VA security requirements and receives scheduled security updates. No phone numbers will be stored directly in the app. As stated above, the My3 App is not capable of sending or receiving text messages.

Benefits:

All patients participating in this trial will receive standard of care and will be able to continue all treatments and mental health care that they would otherwise have access to outside of the study. In addition, depending on study assignment, some patients may receive the PEACE intervention. The PEACE intervention is designed to enhance care that patients receive by helping to connect them with available mental health resources and educating them about suicide prevention after psychiatric hospitalization. Although the PEACE intervention is adapted from a successful suicide prevention strategy (WHO BIC),[32,34] it is unknown whether the PEACE intervention significantly reduces suicide risk after psychiatric hospitalization relative to standard discharge practices. The work from this proposed study will be able to more definitively address whether the PEACE intervention is an effective suicide-prevention strategy in patients following a hospitalization. This is important, given that death by suicide after hospitalization remains an important problem in the Veteran population despite the VA's multiple suicide-prevention strategies. Since the overall risks associated with this trial are minimal and the anticipated benefits and knowledge to be gained are clinically important, there is sufficient reason to conduct this study.

Protected Health Information:

We will administer several validated instruments to all enrolled patients at baseline and follow-up (one-, three- and six-month follow-ups). These instruments ask various questions related to self-harming thoughts or behavior and social connectedness. We will also ask patients to report on any non-VA healthcare utilization at one-, three- and six- month follow-ups. Demographic data and other baseline characteristics will be collected from the patient's electronic medical record at baseline. Information on VA healthcare utilization will be collected from the patient's electronic medical record at one- and three-month follow-ups. For patients assigned to the intervention arm, data on app utilization will also be downloaded from their app. All data will be collected solely for the purposes of this study. All study data will be collected using an electronic data-capture system. These data are stored on a local, secure research server that only study staff will have access to. All paper copies of study-related data, including consent and HIPAA forms, will be kept in a locked file cabinet, in a locked office, dedicated to this study. Only research staff will have access to this locked cabinet.

The My3 app will not store any PHI within the app. The app will only require access to the patient's contact list in order to facilitate a phone call between the patient and their support person.

Multi-Site Study Concerns

Not applicable

Resources Available

This project will be conducted at the WRJ VAMC. We anticipate that we will enroll up to 160 subjects over a period of four years to reach the target sample size of 92 subjects. Dr. Riblet will oversee and lead this project with the help of research staff, which includes:

- Intervention staff
- Study coordinator(s)
- A statistician
- Independent assessor(s) blinded to study arm

Of note, because this trial is occurring as part of a career development award, Dr. Riblet will receive ongoing mentorship and support from her mentorship team in conducting this trial. Her primary mentor is Dr. Bradley V. Watts who is responsible for overseeing the mentorship team..

Subject Compensation:

We will compensate each patient for each study assessment completed. Patients will receive $25 for the assessment 1; $50 for assessment 2 (one-month follow-up); $75 for assessment 3 (three-month follow-up); and $100 for assessment 4 (six-month follow-up). The maximum total compensation is $250. We chose this staggered payment schedule for two reasons: First, we are asking patients to remain in the study over the course of six months and we believe that this payment schedule will account for the additional inconvenience and burden on the patient. Second, prior studies have shown that the use of staggered payments and higher compensation improves study retention while not being coercive.[92-93] Every effort will be made to compensate participants, however, if a participant does not provide necessary information for payment purposes, study staff will initiate the following: In the event that the patient has completed all assessments and/or interventions, and has not provided the necessary information to pay them, study staff will call the patient up to five times to obtain the required information. In addition to these phone attempts, after completion of the study, study staff will mail a blank VA 10091 (Direct Deposit/Vendorization) form with instructions, envelope, and stamp for the patient to easily mail back. After five attempts to contact the patient via phone and one attempt at mailing the patient, if the patient does not provide the necessary information to be paid, we will classify this patient as "unable to be paid".

Privacy and Confidentiality:

Please see *Protection Against Risk* above.

Data and Safety Monitoring Plan

Monitoring and Interim Analysis Plan:

As described in the charter (signed by our study team), "Data and safety monitoring for this study will be provided by the Clinical Science Research and Development (CSRD) centralized Data Monitoring Committee (DMC) as described in this charter. The DMC is provided by CSRD to ensure independent oversight of the safety and integrity of the project. The DMC is an independent multidisciplinary group, whose members have collectively – through research, education, training, experience, and expertise – the requisite knowledge pertinent to the subject areas to be reviewed. Membership details are available on the CSRD website. The DMC will provide an ongoing independent evaluation of this study focused on safety and feasibility, including participant accrual and retention, adverse events monitoring, and data analyses. Meetings will be held two times per year at which time recommendations will be made to the Director of CSRD for endorsement. These

recommendations will range from approval to continue (unconditionally or with conditions to be addressed) to probation or possibly termination, if there are problems with enrollment or safety concerns."

Study Safety & Monitoring:

Enrolled patients will be monitored for any unanticipated problems or adverse events during the course of the study. Unanticipated death possibly related to research will be orally reported to VINNE immediately with a written report submitted via IRBNet within 5 business days. Possibly study-related unanticipated problems involving risk to subjects or others and deviations/non-compliance will be reported within 5 business days to VINNE. Information security or privacy incidents will be reported to the ISO or PO within one hour of discovery. We have reviewed the literature and made two important observations. First, there is little consensus on what defines adverse events including SAE and AEs in suicide research.[94-95] Suicidal behavior and worsening of mental health symptoms is nearly universal in this population[96] and rehospitalization is common.[97] As such there is a strong argument in the literature that suicidal behavior (and any related events including worsening mental health symptoms) are expected in this population in the context of research. Second, it is entirely possible that the intervention could both reduce the risk of death by suicide and increase use of inpatient and emergency services. This use of emergency and inpatient services may be protective. While our study uses standardized measures of suicidal ideation and behavior, our study does not include any standardized measures to evaluate worsening mental health conditions (e.g. depression). Because suicidal ideation is common in this population, it is fully expected that patients will report these symptoms after hospitalization and may trigger our safety alert (described above). As such, we can only reliably evaluate for patient safety events by looking at well-established clinical endpoints that may indicate worsening health state. This includes the need for higher level care (i.e. hospital admission or emergency room visit) as well as actual suicide attempts. We have also reviewed the advice from leading experts in the field of suicide research[94-95] who emphasize key challenges in classifying adverse events in a clinical trial of a population at high risk for suicide. Consistent with our thinking, these experts recommend that suicide researchers use the following definitions to identify meaningful events related to patient safety during the study follow-up period:

Study Definition of Adverse Event:

- Any inpatient hospitalization
- Any emergency room admission
- Actual suicide attempt (per reporting guidelines of the WRJ IRB (VINNE)**

Reporting of adverse events: AEs will be reported to the CSR&D DMC and the WRJ IRB (VINNE) at regularly scheduled reviews as designated by each of these entities.

Study Definition of Serious Adverse Event:

- Actual suicide attempt (per reporting guidelines by the CSR&D DMC)**
- Death, any cause

Reporting of serious adverse events: SAEs will be reported to the CSR&D DMC within 72 hours of the study team becoming aware of the incident. Furthermore, as required by the WRJ IRB (VINNE), serious adverse events will be reported to the WRJ IRB (VINNE) within 5 days of discovery if the event is determined to be both unanticipated AND may be related to the research.

***In accordance with VHA Handbook 1058.01 and the Common Rule (45 CFR 46. 103(a) and 46. 103(b), the WRJ IRB (VINNE) has determined that suicide attempts in this study are expected and should be reported as adverse events. However, per the CSR&D DMC's request, we will report suicide attempts as SAE to the DMC.*

Reasons for stopping assigned treatment and follow-up:

The following events will be considered reasons to stop assigned treatment and or follow-up of an enrolled patient: (1) death because the patient would no longer be accessible to study staff; (2) patient requests to withdraw from the study; or (3) the study investigator or the patient's mental health provider request to withdraw the patient from the study because they believe it is in the best clinical interest of the patient. In the event that the patient is assigned to the intervention, we will ask the patient if they are willing to continue with the outcome assessments but respect his/her wishes if he/she chooses to withdraw from the study.

Trial Registration Requirements

We are required by CSR&D to register this trial with the United States National Library of Medicine registry of clinical trials.

Milestones and Timelines

Gantt chart of milestones and timelines

Year of Award	Pre-Award	FY2021				FY2022				FY2023				FY2024				FY2025			
Quarter	**JIT**	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Pre-enrollment phase																					
Finalizing the study procedures																					
Finalizing the intervention manual																					
Finalizing assessment protocols																					
Finalizing fidelity measures and procedures																					
IRB submission and approval																					
DMC submission and approval																					
Study team preparation and training																					
Enrollment phase																					
Enroll 20 patients (Year 1)																					
Enroll 24 patients (Year 2)																					
Enroll 24 patients (Year 3)																					
Enroll 24 patients (Year 4)																					
Recruitment target reached																					
25% of sample enrolled (N=23)																					
50% of sample enrolled (N=46)																					
75% of sample enrolled (N=69)																					
100% of sample enrolled (N=92)																					
Data collection phase																					
Complete follow-up on 32 patients (Year 2)																					
Complete follow-up on 24 patients (Year 3)																					
Complete follow-up on 24 patients (Year 4)																					
Complete follow-up on 12 patients (Year 5)																					
Analysis phase and next steps																					
Data cleaning, analysis and interpretation of results																					
Preparation of de-identified data																					
Preparation of relevant documentation for data sharing																					
Merit award proposal for future study based on trial results																					
Drafting and publication of manuscript of findings																					

Legend: FY= Fiscal Year; IRB = Institutional Review Board; JIT = Just-in-time period; N = Number

References & Literature Cited

1. Hedegaard H, Curtin SC, Warner M. Suicide mortality in the United States, 1999 – 2017. NCHS Data Brief, no 330. Hyattsville, MD: National Center for Health Statitistics. 2018.
2. VA Office of Mental Health and Suicide Prevention. VA National Suicide Data Report, 2005-2016 Data Appendix. Available at https://www.mentalhealth.va.gov/suicide_prevention/data.asp
3. Franklin K. Preventing Veteran Suicide Is Everyone's Business American Foundation for Suicide Prevention, July 1, 2018. https://afsp.org/preventing-veteran-suicide-is-everyones-business/
4. Britton PC, Bohnert KM, Ilgen MA, et al. Suicide mortality among male veterans discharged from Veterans Health Administration acute psychiatric units from 2005 to 2010. Soc Psychiatry Psychiatr Epidemiol. 2017;52:1081 – 7.
5. Valenstein M, Kim HM, Ganoczy D, et al. Higher risk periods for suicide among VA patients receiving depression treatment: prioritizing suicide prevention efforts. J Affect Disord. 2009;112:50 – 8.
6. Chung DT, Ryan CJ, Hadzl-Pavlovic D, et al. Suicide rates after discharge from psychiatric facilities: a systematic review and meta-analysis. JAMA Psychiatry. 2017;74(7):694 – 702
7. Office of Mental Health and Suicide Prevention. VA National Suicide Data Report, 2005 – 2015. June 2018. Available at https://www.mentalhealth.va.gov/docs/data-sheets/2015/OMHSP_National_Suicide_Data_Report_2005-2015_06-14-18_508.pdf
8. Riblet N, Shiner B, Watts BV, et al. Death by suicide within one week of hospital discharge: a retrospective study of root-cause analysis reports. J Nerv Ment Dis. 2017;205:436 – 42.
9. Riblet N, Shiner B, Scott R, et al. Exploring psychiatric inpatients' beliefs about the role of post-discharge follow-up care in suicide prevention. Mil Med. 2019; 184: e91-e100.
10. Krulee DA, Hales RE. Compliance with psychiatric referrals from a general hospital psychiatry outpatient clinic. Gen Hosp Psychiatry. 1988;10:339 – 45.
11. Kurz A, Moller H. Help-seeking behavior and compliance of suicidal patients. Psychiatr Prax.1984;11:6-13.
12. Rudd MD, Joiner TE, Jobes DA, King CA. The outpatient treatment of suicidality: an integration of science and recognition of its limitations. Professional Psychology: Research and Practice. 1999;30:437 – 46.
13. Fawcett JA, Scheftner WA, Fogg L, et al. Predictive factors of post-discharge follow-up care among adolescent suicide attempters. Acta Psychiatric Scandinavica. 2001;104:31 – 6.
14. Kuramoto-Crawford SJ, Han B, McKeon RT. Self-reported reasons for not receiving mental health treatment in adults with serious suicidal thoughts. J Clin Psychiatry. 2017;78:e631 – 7.
15. Brenner LA, Barnes SM. Facilitating treatment engagement during high-risk transition periods: a potential suicide prevention strategy. Am J Public Health. 2012;102(S1):S12 – 14.
16. Van Heeringen C. The management of non-compliance with out-patient aftercare in suicide attempters: a review. Italian Journal of Suicidology. 1992;2:79 – 83.
17. Carlton PA, Deane FP. Impact of attitudes and suicidal ideation on adolescents' intentions to seek professional psychological help. J Adolesc. 2000;23(1):35 – 45.
18. Dixon LB, Holoshitz Y, Nossel I. Treatment engagement of individuals experiencing mental illness: review and update. World Psychiatry. 2016;15:13 – 20.
19. Barrett MS, et al. Early withdrawal from mental health treatment: implications for psychotherapy practice. Psychotherapy (Chicago, Ill). 2008;45(2):247 – 67.
20. Holt-Lunstad J, Robles T, Sbarra DA. Advancing social connection as a public health priority in the United States. Am Psychol 2017; 72: 517-530.
21. Fassberg MM, et al. A systematic review of social factors and suicidal behavior in older adulthood. Int J Environ Res Public Health 2012; 9: 722-745.
22. Harandi TF, Taghinasab MM, Nayeri TD. The correlation of social support with mental health: A meta-analysis. *Electron Physician*. 2017;9(9):5212–5222. Published 2017 Sep 25. doi:10.19082/5212
23. Durkheim E. Suicide: a study in sociology. The Free Press, New York 1979. Translated by John A. Spaulding and George Simpson. Edited with an introduction by George Simpson.
24. Van Orden KA, et al. The interpersonal theory of suicide. Psychol Rev 2010, 117(2): 575-600.
25. Rogers ML, Kelliher-Rabon J, Hagan CR, Hirsch JK, Joiner TE. Negative emotions in veterans relative to suicide risk through feelings of perceived burdensomeness and thwarted belongingness. Journal of Affective Disorders 2017; 208: 15-21.
26. O'Connor SS, Carney E, Jennings KW, Johnson LL, Gutierrez PM, Jobes DA. Relative impact of risk

factors, thwarted belongingness, and perceived burdensomeness on suicidal ideation in Veteran service members. Journal of Clinical Psychology 2017; 73:1360-1369.
27. Chu C, Buchman-Schmitt JM, Stanley IH, et al. The interpersonal theory of suicide: a systematic review and meta-analysis of a decade of cross-national research. Psychol Bull 2017; 143:1313-1345.
28. Veterans Health Association. High Risk for Suicide Patient Record Flag Changes. Memo, Oct. 3, 2017.
29. Bagley S, Munjas B, Shekelle P. A systematic review of suicide prevention programs for military or Veterans. Suicide Life Threat Behav. 2010;40:257 – 65.
30. The Assessment and Management of Suicide Risk Work Group. VA/DoD clinical practice guideline for the assessment and management of patients at risk for suicide. 2019. Version 2.0. https://www.healthquality.va.gov/guidelines/MH/srb/VADoDSuicideRiskFullCPGFinal5088919.pdf
31. Cross GM, Feeley WF. Department of Veterans Affairs. Memorandum: Patients at High-Risk for Suicide. 2008. Deputy Under Secretary for Health for Operations and Management (10N).
32. VHA. High Risk for Suicide Patient Record Flag Changes. Memorandum, October 3, 2017.
33. VA Deputy Under Secretary for Health for Operations and Management (VA DUSHOM). Memorandum (2017), Eliminating Veteran Suicide: enhancing acute inpatient mental health and residential rehabilitation treatment program (RRTP) discharge planning and follow-up. June 12 2017.
34. VA. Inpatient mental health services. VHA Handbook 1160.06 Transmittal Sheet. September 16, 2013. https://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=2937
35. Stanley B, Brown GK. Safety planning intervention: a brief intervention to mitigate suicide risk. Cogn Behav Pract. 2012;19:256 – 64.
36. Kessler RC, Hwang I, Hoffmire CA, et al. Developing a practical suicide risk prediction model for targeting high-risk patients in the Veterans health Administration. Int J Methods Psychiatr Res. 2017;26:e1575.
37. Taniellian T. Reducing suicide among US Veterans: implications from RAND research. Testimony presented before the House Oversight and Reform Subcommittee on National Security. May 8, 2019. Available at https://docs.house.gov/meetings/GO/GO06/20190508/109420/HHRG-116-GO06-Wstate-TanielianT-20190508-U1.pdf
38. Klonsky ED, May AM, Saffer BY. Suicide, suicide attempts, and suicidal ideation. Annu Rev Clin Psychol. 2016;12:307 – 30.
39. Riblet N, Shiner B. Prevention of suicide following psychiatric hospitalization. *In Oxford Textbook of Suicidology and Suicide Prevention: A Global Perspective (Wasserman D, Wasserman C eds).* 2nd edition. Oxford University Press Inc., New York. (in press)
40. Zalsman G, Hawton K, Wasserman D et al. (2016). Suicide prevention strategies revisited: 10-year systematic review. *Lancet Psychiatry,* 3, 646-659.
41. Milner AJ, Carter G, Pirkis J, Robinson J, Spittal MJ (2015). Letters, green cards, telephone calls and postcards: systematic and meta-analytic review of brief contact interventions for reducing self-harm, suicide attempts and suicide. *Br J Psychiatry,* 206, 184-190.
42. Riblet NBV, Shiner B, Young-Xu Y, Watts BV (2017b). Strategies to prevent death by suicide: meta-analysis of randomised controlled trials. *Br J Psychiatry,* 210, 396-402.
43. Fleischmann A, Bertolote JM, Wasserman D et al. (2008). Effectiveness of brief intervention and contact for suicide attempters: a randomized controlled trial in five countries. *Bull World Health Organ,* 86, 703-709.
44. Kleiman EM, Liu RT. Social support as a protective factor in suicide: findings from two nationally representative samples. J Affec Disord 2013; 150: 540-545.
45. Gardiner C, Geldenhuys G, Gott M. Interventions to reduce social isolation and loneliness among older people: an integrative review. Health Soc Care Community 2018; 26: 147-157.
46. Van Orden. Preventing suicide through social connectedness: overview of what we know about promoting connectedness. December 13, 2018. http://suicideprevention-icrc-s.org/sites/default/files/sites/default/files/events/18_12_13_ConnectednessSlides.pdf
47. Waytz A, Gray K. Does online technology make us more or less sociable? A preliminary review and call for research. Perspectives on Psychological Science 2018; 13: 473-491.
48. Luxton DD, June J, Chalker SA. Mobile health technologies for suicide prevention: feature review and recommendations for use in clinical care. Curr Treat Options Psych 2015; 2: 349-362.
49. Qurashi I, Kapur N, Appleby L. A prospective study of noncompliance with medication, suicidal ideation, and suicidal behavior in recently discharged psychiatric inpatients. Arch Suicide Res. 2006;10:61-67.

50. Riblet N, Shiner B, Schnurr P, et al. A pilot study of an intervention to prevent suicide following psychiatric hospitalization. *Journal of Nervous and Mental Disease 2019;* 207(12):1031-1038. doi: 10.1097/NMD.0000000000001061.
51. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 59(Suppl 20):22–33.
52. Posner K, Brown GK, Stanley B, et al. The Columbia-Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. Am J Psychiatry. 2011;168(12):1266 – 77.
53. Beck AT, Kovacs M, Weissman A. Assessment of suicidal intention: the Scale for Suicide Ideation. J Consult Clin Psychol. 1979;47:343 – 52.
54. Beck AT, Steer RA. Manual for the Beck scale for suicide ideation. San Antonio, TX: Psych Corp. 1991.
55. De Beurs DP, Fokkema M, de Groot MH, de Keijser J, Kerkhof AJFM. Longitudinal measurement invariance of the beck scale for suicide ideation. Psychiatry Research 2015; 225: 368 – 373.
56. Barello S, Graffigna G, Vegni E, Bosio C. The challenges of conceptualizing patient engagement in health care: a lexicographic literature review. The Journal of Participatory Medicine. 2014. https://participatorymedicineorg/journal/evidence/reviews/2014/06/11/the-challenges-of- conceptualizing-patient-engagement-in-health-care-a-lexicographic-literature-review/
57. Greene J, Hibbard JH, Sacks R, Overton V. When seeing the same physician, highly activated patients have better care experiences than less activated patients. Health affairs (Project Hope). 2013;32:1299 –305.
58. Magnezi R, Glasser S, Shalev H, Sheiber A, Reuveni H. Patient activation, depression and quality of life. Patient Educ Couns. 2014;94(3):432 – 7.
59. Pfeiffer PN, Ganoczy D, Zivin K, McCarthy JF, Valenstein M, Blow FC. Outpatient follow-up after psychiatric hospitalization for depression and later readmission and treatment adequacy. Psychiatr Serv. 2012;63(12):1239 – 42.
60. Bernet AC. Postdischarge behavioral health treatment and 6-month reattempt rate for Veterans hospitalized for suicide attempt. J Am Psychiatr Nurses Assoc. 2015; 21:212 – 222.
61. Hibbard J, Gilburt H. Supporting people to manage their health: an introduction to patient activation. The King's Fund. Available at https://www.kingsfund.org.uk/sites/files/field/field_publication_file/supporting-people- manage-health-patient-activation-may14.pdf
62. Hibbard JH, Mahoney ER, Stockard J, Tusler M. Development and testing of a short form of the patient activation measure. Health Serv Res. 2005;40(6 Pt 1):1918 – 30.
63. Greene J, Hibbard JH, Sacks R, Overton V, Parrotta CD. When patient activation levels change, health outcomes and costs change, too. Health affairs (Project Hope). 2015;34(3):431 – 7.
64. Stanley B, et al. The construct and measurement of suicide-related coping. Psychiatry Research 2017; 258: 189-193.
65. Hoertel N, Limosin F, Leleu H. Poor longitudinal continuity of care is associated with an increased mortality rate among patients with mental disorders: results from the French National Health Insurance Reimbursement Database. Eur Psychiatry. 2014;29(6):358 – 64.
66. Puntis S, Rugkasa J, Forrest A, Mitchell A, Burns T. Associations between continuity of care and patient outcomes in mental health care: a systematic review. Psychiatr Serv. 2015;66(4):354 – 63.
67. Greenberg GA, Rosenheck RA. Continuity of care and clinical outcomes in a national health system. Psychiatr Serv. 2005;56:427 – 33.
68. Beck AT, Steer RA. Manual for the Beck Hopelessness Scale. San Antonio, TX: Psychological Corporation. 1988.
69. Brown GK. A review of suicide assessment measures for intervention research with adults and older adults. pgs 1-57. Available at http://sbisrvntweb.uqac.ca/archivage/15290520.pdf
70. Brenner LA, Forster JE, Hoffberg AS, et al. Window to Hope: A Randomized Controlled Trial of a Psychological Intervention for the Treatment of Hopelessness Among Veterans With Moderate to Severe Traumatic Brain Injury. J Head Trauma Rehabil. 2017. doi: 10.1097/HTR.0000000000000351

71. Holt-Lunstad 2017 Holt-Lunstad J, Robles TF, Sbarra DA. Advancing social connection as a public health priority in the United States. Am Psychol. 2017; 72(6):517-530. doi: 10.1037/amp0000103. PMID: 28880099; PMCID: PMC5598785.

72. Calati et al 2019 Calati R, Ferrari C, Brittner M, et al. Suicidal thoughts and behaviors and social isolation: A narrative review of the literature. J Affect Disord. 2019; 245:653-667. doi: 10.1016/j.jad.2018.11.022. Epub 2018 Nov 7. PMID: 30445391.
73. Hare Duke 2019 Hare-Duke L, Dening T, de Oliveira D, Milner K, Slade M. Conceptual framework for social connectedness in mental disorders: Systematic review and narrative synthesis. J Affect Disord 2019;245:188-199. doi:10.1016/j.jad.2018.10.359. Epub 2018 Oct 29. PMID: 30396057.
74. Leigh-Hunt 2017 Leigh-Hunt N, Bagguley D, Bash K, Turner V, Turnbull S, Valtorta N, Caan W. An overview of systematic reviews on the public health consequences of social isolation and loneliness. Public Health 2017;152:157-171. doi: 10.1016/j.puhe.2017.07.035. Epub 2017 Sep 12. PMID: 28915435.
75. Holt-Lunstad J, Smith TB, Layton JB. Social relationships and mortality risk: a meta-analytic review. PLoS Med. 2010;7(7):e1000316. doi: 10.1371/journal.pmed.1000316. PMID: 20668659; PMCID: PMC2910600.
76. Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. Perspect Psychol Sci. 2015; 10(2):227-37. doi: 10.1177/1745691614568352. PMID: 25910392.
77. Van Orden KA, Cukrowicz KC, Witte TK, Joiner TE. Thwarted belongingness and perceived burdensomeness: construct validity and psychometric properties of the Interpersonal Needs Questionnaire. Psychol Assess. 2012;24(1):197 – 215.
78. Gutierrez PM, Pease J, Matarazzo BB, Monteith LL, Hernandez T, Osman A. Evaluating the psychometric properties of the interpersonal needs questionnaire and the acquired capability for suicide scale in Military Veterans. Psychol Assess. 2016; 28:1684 – 94.
79.
80. Zimet GD, Dahlem NW, Zimet SG, Farley GK. The Multidimensional Scale of Perceived Social Support. Journal of Personality Assessment 1988;52:30-41.Nam, EJ, Lee J-E. Mediating Effects of Social Support on Depression and Suicidal Ideation in Older Korean
81. Adults With Hypertension Who Live Alone. Journal of Nursing Research 2019; 27; pe20Hoffmire C, Stephens B, Morley S, Thompson C, Kemp J, Bossarte RM. VA Suicide Prevention Applications Network: a national health care system-based suicide event tracking system. Public Health Rep. 2016; 131:816 – 821.
82. McKay FH, Cheng C, Wright A, et al. Evaluating mobile phone applications for health behavior change: a systematic review. Journal of Telemedicine and Telecare 2018; 24: 22-30.
83. Short CE, DeSmet A, Woods C et al. Measuring engagement in eHealth and mHealth behavior change interventions: viewpoint of methodologies. Journal of Medical Internet Research 2018; 20: e292 p1-18.
84. Bakker D, Rickard N. Engagement in mobile phone app for self-monitoring of emotional wellbeing predicts changes in mental health: MoodPrism. Journal of Affective Disorders 2018; 227: 432-442.
85. Pham Q, Graham G, Carrion C et al. A library of analytic indicators to evaluate effective engagement with consumer mHealth apps for chronic conditions: scoping review. JMIR Mhealth Uhealth 2019; 7: e11941.
86. Carroll KM, Nich C, Sifry RL, et al. A general system for evaluating therapist adherence and competence in psychotherapy research in the addictions. Drug Alcohol Depend. 2000;57(3):225 – 38.
87. Borrelli B. The Assessment, Monitoring, and Enhancement of Treatment Fidelity In Public Health Clinical Trials. J Public Health Dent. 2011;71(s1):S52 – 63.
88. Comtois KA, Kerbrat AH, DeCou CR, et al. Effect of Augmenting Standard Care for Military Personnel With Brief Caring Text Messages for Suicide Prevention: A Randomized Clinical Trial. JAMA Psychiatry 2019; 1;76(5):474-483. doi: 10.1001/jamapsychiatry.2018.4530. PMID: 30758491; PMCID: PMC6495345.
89. Jobes DA, Comtois KA, Gutierrez PM, et al. A Randomized Controlled Trial of the Collaborative Assessment and Management of Suicidality versus Enhanced Care as Usual With Suicidal Soldiers, Psychiatry, 2017 80:4, 339-356, DOI: 10.1080/00332747.2017.1354607Hedeker D, Gibbons RD, Waternaux C. Sample size estimation for longitudinal designs with attrition: comparing time-related contrasts between two-groups. Journal of Educational and Behavioral Statistics 1999; 24: 70-93.
90. Laken D. Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. *Frontiers in Psychology* 2013; 4(863): 1-12.
91. Festinger DS, Marlowe DB, Dugosh KL, Croff JR, Arabia PL. Higher magnitude cash payments improve research follow-up rates without increasing drug use or perceived coercion. Drug Alcohol Depend. 2008; 96:

128 – 135.
92. Gelinas L, Largent EA, Largent JD, Cohen G, Kornetsky S, Bierer BE, Fernandez L. A framework for ethical payment to research participants. NEJM 2018; 378:766 – 771.
93. Oquendo M, Feldman S, Silverman E, et al. Variability in the definition and reporting of adverse events in suicide prevention trials: an examination of the issues and a proposed solution. Archives of Suicide Research 2011; 15: 29-42.
94. Schatten HT, Gaudiano BA, Primack JM et al. Monitoring, assessing, and responding to suicide risk in clinical research. Journal of Abnormal Psychology 2020; 129: 64-69.
95. Forte A, Buscajoni A, Fiorillo A, Pompili, Maurizio, Baldessarini RJ. Suicidal risk following hospital discharge: a review. Harvard Review of Psychiatry 2019; 27: 209-216.
96. Cepeda MS, Schuemie M, Kern D, Reps J, Canuso C. Frequency of rehospitalization after hospitalization for suicidal ideation or suicidal behavior in patients with depression. Psychiatry Res 2020; 285: 112810.