



Suicide Prevention Interventions and Referral/Follow-up Services: A Systematic Review

EXECUTIVE SUMMARY

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PREFACE

Quality Enhancement Research Initiative's (QUERI) Evidence-based Synthesis Program (ESP) was established to provide timely and accurate syntheses of targeted healthcare topics of particular importance to Veterans Affairs (VA) managers and policymakers, as they work to improve the health and healthcare of Veterans. The ESP disseminates these reports throughout VA.

QUERI provides funding for four ESP Centers and each Center has an active VA affiliation. The ESP Centers generate evidence syntheses on important clinical practice topics, and these reports help:

- develop clinical policies informed by evidence,
- guide the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures, and
- set the direction for future research to address gaps in clinical knowledge.

In 2009, the ESP Coordinating Center was created to expand the capacity of QUERI Central Office and the four ESP sites by developing and maintaining program processes. In addition, the Center established a Steering Committee comprised of QUERI field-based investigators, VA Patient Care Services, Office of Quality and Performance, and Veterans Integrated Service Networks (VISN) Clinical Management Officers. The Steering Committee provides program oversight, guides strategic planning, coordinates dissemination activities, and develops collaborations with VA leadership to identify new ESP topics of importance to Veterans and the VA healthcare system.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP Coordinating Center Program Manager, at nicole.floyd@va.gov.

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INTRODUCTION

Suicide is the tenth leading cause of death in the United States (US), with nearly 100 suicides occurring each day and over 36,000 dying by suicide each year.¹ Among Veterans and current military, suicide is a national public health concern. Recent estimates suggest current or former military represent 20 percent of all known suicides in the US² and the rate of suicides among Veterans utilizing Veterans Health Administration (VHA) services is estimated to be higher than the general population.³ The enormity of the problem has led to several major public health initiatives and a growth in research funding for suicide prevention.⁴⁻⁷

Despite recent suicide prevention efforts, the suicide rate in the US has changed relatively little over the past 100 years.⁸ The body of research on suicide prevention approaches has been reviewed previously by Gaynes and colleagues,⁹ and Mann and colleagues,^{9,10} and recent, similar work exists in the form of draft self-harm guidelines from the National Institute for Health and Clinical Excellence (NICE) in 2011.¹¹ As requested by the Veterans Affairs (VA)/Department of Defense (DoD) Evidence Based Practice Working Group (EBPWG) on suicide prevention, we examined recent research on suicidal self-directed violence as defined by Crosby et al. 2011.¹² We update the work of Gaynes et al. and Mann et al. by systematically reviewing relevant literature that was not included in either report, and was published in 2005 through November 18, 2011. Though the focus of the report is on suicide prevention, we include as outcomes any type of suicidal self-directed violence, defined as “Behavior that is self-directed and deliberately results in injury or the potential for injury to oneself. There is evidence, whether implicit or explicit, of suicidal intent.”^{12, 13}

The key questions were:

Key Question #1. What is the effectiveness of specific interventions for reducing rates of suicidal self-directed violence in military and/or Veteran populations?

Key Question #2. What lessons can be learned from suicidal self-directed violence prevention intervention research conducted outside of Veteran or military settings that can be applied to Veteran and/or military populations?

Key Question #3. What is the effectiveness of referral and follow-up services (e.g., strategies designed to provide referrals, improve referral follow-through and attendance, etc.) for reducing rates of suicidal self-directed violence in military and/or Veteran populations?

Key Question #4. What lessons can be learned from research on suicidal self-directed violence referral and follow-up services conducted outside of Veteran or military settings that can be applied to Veteran and/or military populations?

METHODS

The VA/DoD suicide prevention Evidence Based Practice Workgroup (EBPWG) requested a systematic review of literature related to suicidal self-directed violence published since two prior reports on the topic by Mann et al. and Gaynes et al.^{9,10} The workgroup requested a review

focused on countries and populations of interest due to their similarity to US Veteran and military populations. Though a previous systematic review was conducted by Shekelle and colleagues in 2009,¹⁴ the EBPWG requested that the current review include studies of pharmacotherapy and psychotherapy interventions, which were largely excluded from this previous report; and, therefore, we used the end search date from the Mann et al. review as the starting point for the current search. We identified relevant systematic reviews and controlled trials by searching PubMed, PsycINFO, the Cochrane Database of Systematic Reviews®, and the Cochrane Central Register of Controlled Trials® from 2005 to November 18, 2011. We used suicide and related terminology, and included interventions, military, Veterans as search terms (Appendix A). We limited the search to peer-reviewed articles involving human subjects and published in the English language that were not included in the previously published systematic reviews on the topic.^{9, 10} We also report results from these two older systematic reviews, as well as results from a draft systematic review on self-harm,¹¹ comparing and combining findings across the three reports to the findings in this current report. Additional citations were identified from reference lists, consultation with content experts, and web sources. Titles, abstracts, and articles were reviewed by doctoral level investigators and project research associates trained in the critical analysis of literature; all articles were reviewed in duplicate. Quality assessment of all included primary studies and systematic reviews was performed in duplicate by investigators and research associates. We assessed study quality of systematic reviews using Oxman and Guyatt criteria.¹⁵ We assessed the risk of bias of primary studies using the tool described in version 5.1.0 of the *Cochrane Handbook for Systematic Reviews of Interventions*.¹⁶ Data on study characteristics, patient characteristics, and outcomes were extracted by trained research associates under the supervision of the Principal Investigator, a VA clinical psychologist. All data were narratively summarized.

DATA SYNTHESIS

We constructed evidence tables showing study, patient, and intervention characteristics; methodological quality; and outcomes, organized by key question, intervention type, and comparison group. We analyzed studies to compare their characteristics, methods, and findings. We graded strength of evidence based on the guidance established for the Evidence-based Practice Center (EPC) Program of the Agency for Healthcare Research and Quality (AHRQ).¹⁷ We compiled a summary of findings for each question based on qualitative and semi-quantitative synthesis of the findings. We identified and highlighted findings from VA and DoD populations.

PEER REVIEW

A draft version of this report was reviewed by eight technical experts, as well as clinical leadership. Reviewer comments were addressed and our responses were incorporated in the final report (Appendix AA).

RESULTS

We reviewed 16,518 titles and abstracts from the electronic and hand searches. Applying our inclusion/exclusion criteria eliminated studies published prior to 2005; studies that did not report suicidal self-directed violence as an outcome; studies that were not randomized controlled trials

(RCTs); and studies conducted in countries other than Australia, Canada, New Zealand, the United Kingdom, and the United States. We rejected 16,110 at the abstract level, and performed a more detailed full-text review on 408 articles. From these, we identified 38 RCTs (reported in 47 publications) and 23 systematic reviews (reported in 25 publications) that addressed at least one of the key questions.

We classified studies as pharmacotherapy interventions, psychotherapy interventions, or referral and follow-up services. We defined interventions as interventions designed to treat a condition, symptom, or behavior. Referral and follow-up services were any services that were provided to patients that were primarily designed to facilitate access to interventions rather than treat a condition, symptom, or behavior. Because many interventions include components designed to increase adherence and attendance, we classified any study describing an intervention component as an “intervention” study rather than a “referral and follow-up services” study even if it also included components of referral and follow-up services. Therefore, the studies designated as referral and follow-up services were described by the authors as solely designed to increase access to, attendance at, and adherence to other interventions not included in the study design.

Key Question #1. What is the effectiveness of specific interventions for reducing rates of suicidal self-directed violence in military and/or Veteran populations?

We found no RCTs of self-directed violence prevention interventions in military and/or VA health care settings.

Key Question #2. What lessons can be learned from suicidal self-directed violence prevention intervention research conducted outside of Veteran or military settings that can be applied to Veteran and/or military populations?

Pharmacotherapy Results

Findings from other systematic reviews with similar key questions report that pharmacotherapy findings are based on few studies with limited sample sizes, some methodological quality concerns, and short term follow-up assessment periods;⁹⁻¹¹ therefore, pharmacotherapy findings should be interpreted with caution. All three reports found that available evidence from antidepressant trials does not show a benefit for reducing suicide, but caution that rates of suicide may have been too low to detect differences. Although observational studies show a correlation between increasing prescription rates and decreasing suicide rates, this evidence is considered lower strength than evidence obtained from RCTs or meta-analyses. The three systematic reviews included different studies of antipsychotic medications. Overall, they report positive findings from trials of flupenthixol, clozapine, and fluphenazine, though caution that findings are based on small samples of patients in very few studies. Finally, the systematic reviews report different results related to mood stabilizing medications. Gaynes et al. report no reduction in suicide rates based on one trial of lithium, whereas Mann et al. and NICE report some non-significant reductions in suicide rates for patients receiving lithium.⁹⁻¹¹

Primary studies included in the current report evaluated antidepressants, atypical antipsychotics, mood stabilizers, and omega-3 supplements and reported their efficacy in prevention of suicidal self-directed violence in civilian populations. Findings from antidepressant trials in civilian populations were consistent with previous reviews on the topic, and did not provide

sufficient evidence to make a strong conclusion about the effectiveness of antidepressants in reducing suicides and suicide attempts. We identified nine trials (reported in 10 publications) that evaluated antidepressant medications. Comparisons included various combinations of antidepressant medications versus placebo,¹⁸⁻²³ one antidepressant versus another,^{24, 25} antidepressant therapy versus cognitive behavioral therapy (CBT),²³ and antidepressant therapy with and without CBT.^{19, 21, 26, 27} Many studies had no suicides in either group. Because of the short duration and low participant numbers, many of these studies would not have had the statistical power and duration of follow-up to allow the medication to effect a change in suicide rates. Therefore, they are felt to be of low strength, and are insufficient for determining the effectiveness of various combinations of antidepressant medications for reducing suicidal self-directed violence.

We found three trials that reported on the effectiveness of quetiapine (1 trial)²⁸ or adjunctive aripiprazole (2 trials in 3 publications)²⁹⁻³¹ in reducing suicide deaths. These trials were six to eight weeks in duration and none had any suicides reported during the follow-up period. The quetiapine trial reported one suicide attempt in each group (treatment and intervention). Therefore, we concluded there was insufficient evidence to determine antisuicidal benefit. Notably, the previous review by Mann and colleagues reported an antisuicidal effect of clozapine, an atypical antipsychotic medication.¹⁰

The two trials of mood stabilizers compared lithium versus valproate (2.5 years)³² and lithium versus citalopram (8 weeks).³³ These trials reported no instances of suicidal self-directed violence for the duration of either study. The previous report by Mann et al., however, found an antisuicidal effect for lithium compared to carbamazepine and amitriptyline.¹⁰ Thus, trials conducted since the Mann et al. report provided insufficient evidence to draw conclusions about the comparative effectiveness of mood stabilizers in preventing suicide attempts. One study conducted outside a country within the scope of this review was suggested for inclusion by reviewers.³⁴ This study, had it been included in our results, provided insufficient evidence for the effectiveness of lithium in prevention of suicidal self-directed violence when compared to placebo.

Finally, one trial of omega-3 fatty acid supplementation for 12 weeks did not have any suicide deaths in either group.³⁵

Psychotherapy Results

Three previously published systematic reviews on this topic all report an overall insufficient to low strength of evidence for the effectiveness of any psychotherapeutic interventions in prevention of self-directed violence.⁹⁻¹¹ In one report (NICE 2011), the authors combined findings from multiple psychotherapy studies with treatment as usual comparison groups, and describe low strength evidence of the effectiveness of these interventions in prevention of self-directed violence.¹¹ Individual psychotherapy results reported in the three reports include mixed findings related to cognitive therapies, positive findings related to Dialectical Behavior Therapy (DBT) for people with Borderline Personality Disorder, positive findings for interpersonal psychotherapy, null findings for outpatient day hospitalization, positive findings for problem-solving therapy, positive findings for psychoanalytically oriented partial day hospitalization for people with Borderline Personality Disorder, and positive findings for transference-focused psychotherapy. Notably, these results were presented in the previous reports as coming from

very few studies with small sample sizes, many methodological flaws, and short-term follow-up assessment periods, suggesting that all findings are of insufficient to low strength and should be interpreted with caution.

All psychotherapy trials meeting criteria for inclusion in this review were sufficiently heterogeneous in terms of type of treatment, duration of treatment, and population characteristics to preclude combination or quantitative comparison. Therefore, psychotherapy trials are grouped for discussion by population: those conducted in patients with Borderline Personality Disorder, recent suicide attempts, a psychotic spectrum disorder, and depression or dysthymia. The strongest evidence (moderate strength) comes from a trial of problem-solving treatment in addition to usual care versus usual care alone for patients with recent suicide attempts.³⁶ This trial showed no significant benefit of the intervention compared to usual care for the overall group of patients presenting to the hospital after engaging in self-harm behaviors; however, a significant benefit was noted for a sub-population of patients limited to people who had multiple hospitalizations for self-harm prior to the intervention. The other trials of psychotherapy provided insufficient or low strength evidence to draw definitive conclusions, often because of limitations in quality and insufficient statistical power to detect intervention effects on low base-rate outcomes of suicidal self-directed violence.

Three RCTs provided insufficient evidence to draw conclusions about prevention of suicide deaths in populations with Borderline Personality Disorder, largely because no or very few suicides occurred during the trials. One trial showed a significant reduction in suicide attempts with Mentalization Based Treatment (MBT) compared to Structured Clinical Management (SCM),³⁷ as did a trial comparing DBT with community treatment by experts.³⁸ Three other studies showed no significant benefit in suicide attempt prevention for Systems Training for Emotional Predictability and Problem Solving (STEPPS) versus treatment as usual,³⁹ CBT specific to Cluster B personality disorders versus treatment as usual,^{40, 41} or DBT versus general psychiatric management.⁴²

Few trials reported on prevention of suicide deaths as the outcome of psychotherapy interventions, and of those that did, most were insufficiently powered to detect an effect of the intervention. One study conducted a comparison among people with recent suicide attempts, self-harm incidents, or imminent risk.⁴³ This trial had several design flaws that contribute to a high potential for bias: non-randomization, baseline differences among the groups, non-blinding, and differing drop-out rates among the groups. Therefore, there was insufficient evidence to draw conclusions about the psychotherapy comparison. Two other studies of people presenting with repeat self-harm reported no suicide events in either treatment or control groups for group therapy,⁴⁴ and for intensive case management.⁴⁵ Other studies evaluated interventions in similar populations (prior suicide). A study of Attachment-Based Family Therapy versus Enhanced Usual Care showed a reduction in suicide attempts, though design flaws limit the ability to draw a firm conclusion about the results.⁴⁶ Likewise, studies comparing Collaborative Assessment and Management of Suicidality (CAMS) versus Enhanced Care As Usual (E-CAU) and skills-based intervention versus a supportive therapy control condition did not use sufficient methodological rigor to enable firm conclusions about effectiveness.^{47, 48} Notably, a study of adolescent group therapy compared to routine care resulted in fewer instances of self-harm in the routine care group indicating the possibility of iatrogenic effects in the group treatment condition; however,

design flaws in this study preclude the ability to draw firm conclusions based on the results.⁴⁹ Finally, one study compared three conditions, CBT, problem-solving therapy, and treatment as usual. This study had few patients and methodological limitations, and therefore provides insufficient evidence related to any of the interventions being investigated.⁵⁰

One study comparing CBT versus supportive counseling in patients with a psychotic spectrum disorder had an unacceptably high risk of bias because therapists were not blinded and delivered both interventions to the participants.⁵¹ Another trial compared the Improving Mood: Promoting Access to Collaborative Treatment (IMPACT) intervention (including a comprehensive depression case management and treatment component) versus usual care in people with depression or dysthymia used methods resulting in an unclear risk of bias.⁵² Each of these trials provides insufficient evidence to draw definitive conclusions about the effectiveness of the interventions.

Key Question #3. What is the effectiveness of referral and follow-up services (e.g., strategies designed to provide referrals, improve referral follow-through and attendance, etc.) for reducing rates of suicidal self-directed violence in military and/or Veteran populations?

We did not find any RCTs of suicidal self-directed violence prevention referral and follow-up services in military and/or VA health care settings.

Key Question #4. What lessons can be learned from research on suicidal self-directed violence referral and follow-up services conducted outside of Veteran or military settings that can be applied to Veteran and/or military populations?

The three previously published reports on this topic all report overall insufficient to low strength of evidence for the effectiveness of any referral and follow-up services in prevention of self-directed violence.⁹⁻¹¹ Specific findings from the three reports include positive results from studies on case management/care coordination and 24-hour contact with a mental health professional. Mixed reports of findings came from studies on emergency contact cards and postal contact. Null findings were reported from studies investigating intensive psychosocial follow-up, telephone follow-up, and video education plus family therapy. Notably, these results were presented in the previous reports as coming from very few studies with small sample sizes, many methodological flaws, and short-term follow-up assessment periods, suggesting that all findings are of insufficient to low strength and should be interpreted with caution.

Findings from primary studies included in this report include three studies of postcard interventions to decrease repeated suicidal self-directed violence, which showed mixed results.⁵³⁻⁵⁵ Two studies of Youth-Nominated Support Team (YST) interventions combined with usual care did not significantly reduce risk of suicide attempts or death in suicidal adolescents.^{56,57} One study of assertive community treatment compared with community mental health care in difficult-to-engage adults with serious mental illness showed no reduction in suicide deaths or deliberate self-harm incidents.⁵⁸ Finally, one trial of a depression care management program resulted in no significant changes in the suicide mortality rate of older adults in primary care settings.⁵⁹ However, all these studies were given low strength of evidence ratings and thus limit conclusions about the effectiveness of these interventions.