

## **Protocol for Phase 1 of Suicide Prevention Trials Database (SPTD)**

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Protocol Revision (1-21-2022): The protocol was amended in January 2022 to add an additional inclusion/exclusion criterion for use in article selection. A detailed description of this criterion appears in *Section VIII. Protocol Amendments* on p. 6 of this document.

### **I. Background and Objectives**

Suicide is the tenth leading cause of death in the United States,<sup>1</sup> and Veterans are 1.5 times as likely to die by suicide as nonveterans.<sup>2</sup> The rise in suicides over the past several decades has been met with a proliferation in research on the treatment and prevention of suicidal ideation (i.e., thoughts of suicidal self-directed violence) and suicidal behavior (i.e., suicidal self-directed violence). Healthcare systems, including the Veterans Health Administration (VHA), have made suicide prevention one of their top clinical priorities.

Increasingly, health, research, policy, and legislative stakeholders need timely, accurate, and detailed information on the evidence supporting effectiveness and potential harms of suicide prevention approaches. Given the vast number of prevention modalities (e.g., psychotherapy, psychopharmacology, complementary and integrative health approaches, etc.) that have been studied, and the tremendous diversity in participant and study characteristics, it is difficult to compile and synthesize findings in a timely manner. Efforts to systematically catalog and synthesize suicide prevention data have included systematic reviews,<sup>3,4</sup> clinical practice guidelines<sup>5,6</sup> and clinical trial registries such as ClinicalTrials.gov. Even these high-quality, systematic approaches can fall short if the set of evidence necessary to address a specific stakeholder question has not been recently searched, compiled, and synthesized. Additionally, guidelines and systematic reviews provide some information about suicide prevention trials, but not about all trials, and not all in one place.

The objective of the Suicide Prevention Trials Database (SPTD) is to identify studies of suicide prevention interventions and abstract detailed study-level data in a standardized manner into a publicly accessible database. The abstracted data and methods documents (including a detailed data dictionary and replicable search strategy) will also be publicly available and can be used for future systematic reviews or clinical practice guidelines, for identifying research gaps, and as an information resource for clinicians, patients, policymakers, and family members. This protocol outlines the activities for Phase 1 of the SPTD development.

## II. Phase 1 Guiding Question

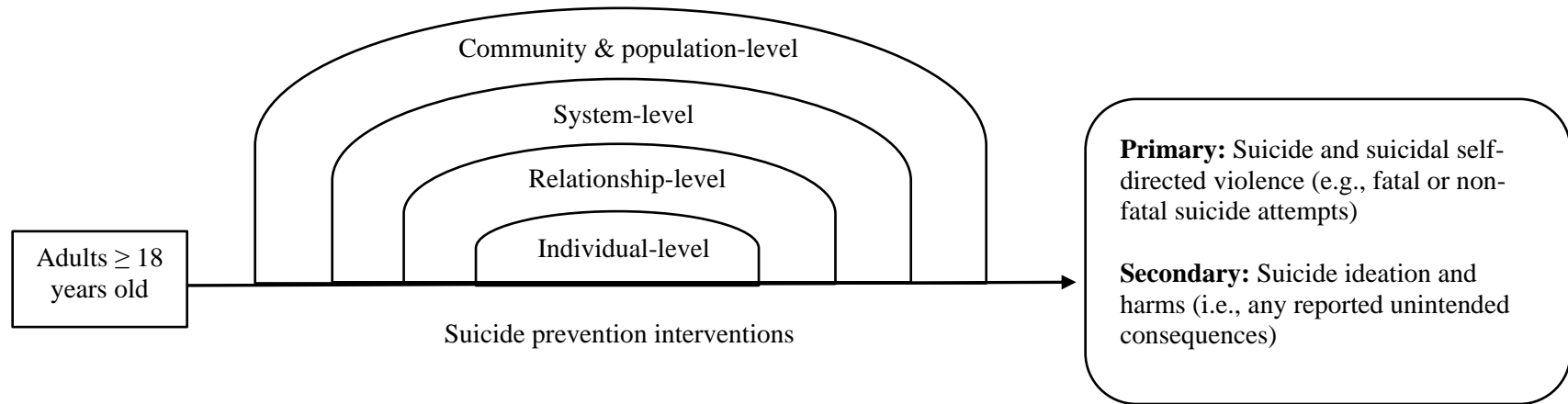
**Guiding Question #1:** What are the characteristics (Population, Interventions, Comparators, Outcomes, Timing, Settings, and Study Design) of randomized controlled trials (RCTs) examining individual, relationship, system, community, and population-level suicide prevention interventions?

- **Population:**
  - Adults ( $\geq 18$  years old)
- **Interventions:**
  - Interventions from studies whose primary aim is preventing suicidal ideation, suicide, or suicidal self-directed violence
- **Comparators:**
  - Any comparator, including another intervention, usual care, or no intervention
- **Outcomes:**
  - Primary: Suicide and suicidal self-directed violence (i.e., fatal or non-fatal suicide attempts)
  - Secondary: Suicide ideation and harms (i.e., any reported unintended consequences such as medication side effects)
- **Timing:**
  - No limitation on study duration or length of follow-up
- **Settings:**
  - No limitation on study setting
- **Study Design:**
  - Randomized controlled trials (RCTs)

## III. Phase 1 Conceptual Framework

Figure 1 depicts the guiding question within the context of the PICOTS inclusion and exclusion criteria presented in Table 1. The figure illustrates that the SPTD will include RCTs of suicide prevention interventions delivered to adults, and data will be organized by the four levels of the socio-ecological framework (i.e., individual-level, relationship-level, system-level, and/or community & population-level). The outcomes of interest will include suicide and suicidal self-directed violence, suicidal ideation, and harms.

**Figure 1. Conceptual Framework for Phase 1 of Suicide Prevention Trials Database (SPTD)**



## IV. Phase 1 Methods

### Criteria for Inclusion/Exclusion of Studies

Detailed inclusion and exclusion criteria for the guiding question are listed in Table 1 and are consistent with the PICOTS above.

**Table 1. Phase 1 Inclusion and exclusion criteria**

	<b>Inclusion Criteria</b>	<b>Exclusion Criteria</b>
Population	Adults ( $\geq 18$ years old) <ul style="list-style-type: none"><li>• Will accept studies where average age of participants is <math>\geq 18</math></li></ul>	Children and adolescents ( $< 18$ years old)
Interventions	Interventions from studies whose primary aim is preventing suicidal ideation, suicide, or suicidal self-directed violence	Interventions from studies whose primary aim is not preventing suicidal ideation, suicide or suicidal self-directed violence
Comparators	No limitations applied (e.g., another intervention; usual care; no intervention)	None
Outcomes	<b>Primary:</b> Studies must report on suicide or suicidal self-directed violence (e.g., fatal or non-fatal suicide attempts) to be included  <b>Secondary:</b> Suicide ideation and harms (e.g., any reported unintended consequences such as medication side effects) are additional outcomes of interest	Studies that do not report the primary outcome will be excluded
Timing	Any study duration and length of follow-up	None
Settings	All	None
Study Design	Randomized controlled trials	Non-randomized controlled studies, before-after studies, narrative reviews, cross-sectional studies, qualitative studies, editorials, and commentaries.  Selected systematic reviews will be considered as reference sources for studies to be reviewed for possible inclusion; however, data will be abstracted from individual studies, rather than from systematic reviews.
Publication Language and Dates	English language articles 1980 to present	Non-English language articles Unpublished data Publication date prior to 1980

### Literature Search Strategies

We will review reference lists from the 2005 systematic review<sup>7</sup> and 2021 updated systematic review<sup>8</sup> on suicide prevention interventions by Mann and colleagues to identify eligible RCTs published from 1980 to 2019. We will also search for RCTs published after the search conducted by Mann and colleagues (i.e., from 2020-2021) using the search strategy in Appendix A.

Literature Databases: MEDLINE, Cochrane Central Register of Controlled Trials (CCRCT), the Cumulative Index to Nursing and Allied Health Literature (CINAHL®), SCOPUS, and PsycINFO®.

Hand Searching: Reference lists of additional, recent, high-quality systematic reviews or meta-analyses will be reviewed to identify studies eligible for inclusion.

Experts: We will also consult with experts in the field to identify potentially relevant studies.

### **Article Selection**

The PICOTS described in Section II and criteria in Table 1 will be used to determine eligibility for inclusion and exclusion of abstracts. Titles, abstracts, and full-text articles will be retrieved and reviewed independently for eligibility by two investigators. At the abstract level, any citation considered potentially eligible for inclusion by one reviewer will be retrieved for full-text review. At the full text level, disagreements will be resolved by consensus of the team of investigators.

### **Data Abstraction and Data Management**

After studies are screened and determined to meet inclusion criteria, data will be abstracted into a piloted data extraction template by one investigator. Data elements that will be abstracted include study design, setting, country, sample size, eligibility criteria, participant characteristics, intervention characteristics, eligible results, and sources of funding. Mean, standard deviation, effect size, and other statistics and results will be abstracted from each study for included outcome variables. A detailed table of anticipated data elements to be extracted appears in Appendix B. All study data will be verified for accuracy and completeness by a senior investigator. A record of studies excluded at the full-text level with reasons for exclusion will be maintained.

### **Data Synthesis**

Data will be abstracted into a detailed evidence table. Characteristics of included studies, such as number of publications by year, study sample size, proportion of studies enrolling community versus military populations, and distribution of studies by intervention type will be synthesized qualitatively.

### **Grading the Strength of Evidence (SOE) for Major Comparisons and Outcomes**

Strength of evidence will not be assessed.

### **V. Additional Phase I Work**

In Phase 1, we also will build a data extraction template for non-randomized, controlled studies and pilot test it with 10 exemplar studies.

## VI. References

1. Curtin SC, Warner M, Hedegaard H. Increase in Suicide in the United States, 1999-2014. *NCHS Data Brief*. 2016(241):1-8.
2. Department of Veterans Affairs, Office of Mental Health and Suicide Prevention. 2021 National Veteran Suicide Prevention Annual Report. September 2021. Retrieved September 29, 2021 from <https://www.mentalhealth.va.gov/docs/data-sheets/2021/2021-National-Veteran-Suicide-Prevention-Annual-Report-FINAL-9-8-21.pdf>.
3. O'Neil ME, Peterson K, Low A, et al. Suicide Prevention Interventions and Referral/Follow-Up Services: A Systematic Review. In: *VA Evidence-based Synthesis Program Reports*. Washington (DC): Department of Veterans Affairs (US); 2012.
4. Nelson HD, Denneson LM, Low AR, et al. Suicide Risk Assessment and Prevention: A Systematic Review Focusing on Veterans. *Psychiatr Serv*. 2017;68(10):1003-1015.
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6. Department of Veterans Affairs and Department of Defense. 2013 VA/DoD clinical practice guideline for assessment and management of patients at risk for suicide. Washington, DC: U.S. Department of Veterans Affairs. Retrieved on June 10, 2021 from [https://www.healthquality.va.gov/guidelines/MH/srb/VADODCP\\_SuicideRisk\\_Full.pdf](https://www.healthquality.va.gov/guidelines/MH/srb/VADODCP_SuicideRisk_Full.pdf).
7. Mann JJ, Apter A, Bertolote J, et al. Suicide prevention strategies: a systematic review. *Jama*. 2005;294(16):2064-2074.
8. Mann JJ, Michel CA, Auerbach RP. Improving Suicide Prevention Through Evidence-Based Strategies: A Systematic Review. *Am J Psychiatry*. 2021;178(7):611-624.

## VII. Plans for Future Phases

In future phases of the SPTD project, the study team will evaluate the risk of bias of Phase 1 included studies using a standardized tool. The PICOTS may also be expanded in future phases to include additional populations (e.g., adolescents) or study designs (e.g., non-randomized, controlled studies). Decisions on the expansion of the PICOTS will be made in consultation with operational partners and technical experts.

## VIII. Summary of Protocol Amendments

If the study team needs to amend the protocol, we will give the date of each amendment, describe the change, and provide rationale in this section. Changes will not be incorporated into the protocol.

Protocol Amendment #1 (1-21-22): Due to the large number of eligible RCTs identified in Phase 1's article selection process, an additional inclusion/exclusion criterion was added to the Phase 1 protocol. During Phase 1, we will only include RCTs in which individual participants are the unit of randomization. Cluster-RCTs in which the unit of randomization is the provider, clinic, community, or city will be excluded. These cluster-RCTs will be included in Phase 2 of the project.

## IX. Technical Experts

The TEP is a multi-disciplinary panel of methodological and content experts that will provide input on key aspects of the development of the SPTD. TEP members will represent a wide

range of perspectives on suicide prevention interventions (e.g., pharmacologic, nonpharmacologic, complementary and integrative health interventions; community- or population-level interventions; means safety approaches). TEP members will be recruited based on significant contributions to the suicide prevention literature, clinical expertise, and leadership in the field.

SPTD leadership expects there to be disagreements between TEP members and perceives this to be part of a healthy scientific discourse. Decisions on methodologic approaches for searching for and determining eligibility of studies for inclusion, and the elements of each included study that will be abstracted in this work will not necessarily represent the views of individual technical or content experts.

Members of the TEP must disclose financial conflicts of interest and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Technical Experts and those who present with potential conflicts may be retained. SPTD leadership will work to balance, manage, or mitigate any potential conflicts of interest identified.

## **X. Public Review**

A draft report summarizing the results of Phase 1 of this project will be posted for public comment. The study team will review public comments, make needed changes to the report, and summarize these changes as well as the rationale for why changes were made in the final report.

## **XI. SPTD Team Disclosures**

SPTD core team members must disclose financial conflicts of interest and any other relevant business or professional conflicts of interest.

## **XII. Role of the Funder**

This project is funded by a service directed research award to Dr. Denneson and Dr. O'Neil from VA Clinical Science Research & Development (Award # SDR-SPTD-20S). CSR&D is responsible for tracking SPTD project progress, reporting requirements, and reviewing any requests related to modifications. The authors of the report are responsible for its content. The views expressed in this report are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States government.

## APPENDIX A. SEARCH STRATEGIES

### Planned MEDLINE (PubMed) Search Strategy

("automutilat\*"[Title/Abstract] OR "auto mutilat\*"[Title/Abstract] OR "auto mutilat\*"[Title/Abstract] OR "parasuicid\*"[Title/Abstract] OR "selfdestruct\*"[Title/Abstract] OR "self destruct\*"[Title/Abstract] OR "self destruct\*"[Title/Abstract] OR "self directed violence"[Title/Abstract] OR "selfharm\*"[Title/Abstract] OR "self harm\*"[Title/Abstract] OR "self harm\*"[Title/Abstract] OR "Selfhatred"[Title/Abstract] OR "Self-hatred"[Title/Abstract] OR "Self-hatred"[Title/Abstract] OR "selfimmolat\*"[Title/Abstract] OR "self immolat\*"[Title/Abstract] OR "self immolat\*"[Title/Abstract] OR "selfinflict\*"[Title/Abstract] OR "self inflict\*"[Title/Abstract] OR "self inflict\*"[Title/Abstract] OR "selfinjur\*"[Title/Abstract] OR "self injur\*"[Title/Abstract] OR "self injur\*"[Title/Abstract] OR "selfmutilat\*"[Title/Abstract] OR "self mutilat\*"[Title/Abstract] OR "selfpoison\*"[Title/Abstract] OR "self poison\*"[Title/Abstract] OR "self poison\*"[Title/Abstract] OR "suicid\*"[Title/Abstract] OR ("suicide, completed"[MeSH Terms] OR "suicide, attempted"[MeSH Terms] OR "self injurious behavior"[MeSH Terms] OR "suicidal ideation"[MeSH Terms] OR "suicide"[MeSH Terms])) AND ("prevention and control"[MeSH Subheading] OR "risk reduction behavior"[MeSH Terms] OR "crisis intervention"[MeSH Terms] OR "hotlines"[MeSH Terms] OR "safety management"[MeSH Terms] OR "tertiary prevention"[MeSH Terms] OR "secondary prevention"[MeSH Terms] OR "primary prevention"[MeSH Terms] OR "preventive psychiatry"[MeSH Terms] OR ("prevent\*"[Title/Abstract] OR "control\*"[Title/Abstract] OR "reduc\*"[Title/Abstract] OR "manag\*"[Title/Abstract])) AND "adult"[MeSH Terms] AND ("groups"[Title/Abstract] OR "trial"[Title/Abstract] OR "randomly"[Title/Abstract] OR "drug therapy"[MeSH Subheading] OR "placebo"[Title/Abstract] OR "randomized"[Title/Abstract] OR "controlled clinical trial"[Publication Type] OR "randomized controlled trial"[Publication Type]) AND 2020/01/01:3000/12/31[Date - Entry]

This search strategy will be adapted for the syntax and controlled vocabulary for the following bibliographic databases: CCRCT, CINAHL<sup>®</sup>, SCOPUS, and PsycINFO<sup>®</sup>.



## APPENDIX B. ANTICIPATED DATA ABSTRACTION ELEMENTS

Data elements that we expect to extract from each eligible study appear below.

**Table 2. Anticipated data elements to be abstracted**

<b>Data Category</b>	<b>Data elements to be abstracted</b>
Study identification	First author and year of publication; citation; PubMed and ClinicalTrials.gov identifiers; funding source
Study characteristics	Country; study site type (e.g., VA, DoD, civilian); clinical/community setting; study design; subgroup analysis reporting; study class (individual, relationship, system, and/or community/population-level)
Suicide risk definition	Suicide risk category (e.g., indicated, selected, universal, other); definitions of suicide risk used for study inclusion (e.g., ideation severity level, prior attempt status)
Population characteristics	Number of participants; % of participants in active-duty military/veteran/community; % reintegrating Veterans; % homeless; mean age; gender; race; ethnicity; % with comorbid Post-Traumatic Stress Disorder, depression, substance use disorder, and other associated comorbidities
Study and intervention description	Number of participants randomized to each intervention; intervention name, description, dose/session length, frequency, and duration; intervention completion/adherence definition and % meeting criteria
Suicide-related outcomes: measures and analysis	Suicidal ideation severity outcome measure name; suicidal behavior type and method for assessment; method for handling missing data; statistical analysis type (e.g., ITT) and method; variables adjusted for in primary outcome analysis
Suicide-related outcomes: within-group comparison	Number of participants assessed; mean measure score; measure change; within-group effect size for continuous outcomes; risk-related change
Suicide-related outcomes: between-group comparison	Score difference, effect size, and risk-related change
Harms	Rates of any reported unintended consequences