# Internet and Mobile Interventions for Adults with PTSD and Their Family Members

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#### **PREFACE**

The VA Evidence Synthesis Program (ESP) was established in 2007 to conduct timely, rigorous, and independent systematic reviews to support VA clinicians, program leadership, and policymakers improve the health of Veterans. ESP reviews have been used to develop evidence-informed clinical policies, practice guidelines, and performance measures; to guide implementation of programs and services that improve Veterans' health and wellbeing; and to set the direction of research to close important evidence gaps. Four ESP Centers are located across the US. Centers are led by recognized experts in evidence synthesis, often with roles as practicing VA clinicians. The Coordinating Center, located in Portland, Oregon, manages program operations, ensures methodological consistency and quality of products, engages with stakeholders, and addresses urgent evidence synthesis needs.

Nominations of review topics are solicited several times each year and submitted via the <u>ESP website</u>. Topics are selected based on the availability of relevant evidence and the likelihood that a review on the topic would be feasible and have broad utility across the VA system. If selected, topics are refined with input from Operational Partners (below), ESP staff, and additional subject matter experts. Draft ESP reviews undergo external peer review to ensure they are methodologically sound, unbiased, and include all important evidence on the topic. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. In seeking broad expertise and perspectives during review development, conflicting viewpoints are common and often result in productive scientific discourse that improves the relevance and rigor of the review. The ESP works to balance divergent views and to manage or mitigate potential conflicts of interest.

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#### **Operational Partners**

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

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#### **Disclosures**

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The findings and conclusions in this document are those of the author(s) who are responsible for its contents and do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. The final research questions, methodology, and/or conclusions may not necessarily represent the views of contributing operational and content experts. No investigators have affiliations or financial involvement (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.



#### **KEY FINDINGS**

- ▶ Internet and mobile interventions may have small to negligible benefits on posttraumatic stress disorder (PTSD) and depression outcomes for military Veterans and service members (low strength of evidence [SOE]). Findings are based on mostly randomized controlled trials (RCTs) of internet-based cognitive behavioral therapy (iCBT) that varied in comparison condition, treatment duration, and level of facilitation. Studies had notable methodological limitations and inconsistent results.
- ► Internet and mobile interventions may have small to moderate short-term benefits on PTSD and depressive symptoms for civilian populations, but do not appear to be long lasting (low SOE).
- ➤ Symptom improvement appeared to be largest for interventions with greater provider facilitation, compared with interventions with minimal or no provider support.
- ▶ It is unclear whether internet and mobile interventions for caregivers and family members of adults with PTSD improve stress, coping, or mental health symptoms (low SOE). Only 5 studies were identified and effectiveness differed across studies.
- Gaps to address in future research include whether increased levels of direct therapeutic involvement with trauma-focused iCBTs increases the effectiveness of treatments in military populations. Future studies might also explore whether internet and mobile resources have a beneficial role in supporting the established VA clinical pathway for PTSD, for example to improve treatment adherence or facilitate at-home activities that reinforce principles and practices introduced during in-person therapy.

Approximately 10% of United States (US) military Veterans experience posttraumatic stress disorder (PTSD) at some point in their lifetime. Untreated PTSD is associated with significant functional impairment, high rates of psychiatric and medical comorbidities, substance misuse, and death by suicide. PTSD is treatable for many people, and the Department of Veterans Affairs (VA) and Department of Defense (DoD) have invested significant resources in developing and broadly implementing clinical pathways that incorporate effective therapeutic approaches. However, despite these considerable advancements in trauma-focused care, most Veterans with PTSD still do not access and benefit from PTSD treatments.

Virtual treatments, in which a provider delivers evidence-based therapies via synchronous telehealth, are now largely considered equivalent to in-person therapy for PTSD. Self-guided, asynchronous PTSD treatments that use the internet or mobile phone applications have also become available in recent years. These interventions—which are offered with varying levels of therapeutic support but are generally lower intensity than conventional in-person therapies—have the potential to expand access to effective PTSD treatments to anyone with internet access or a smartphone.

Internet and mobile interventions have also been developed to provide a more accessible means of support to family members and caregivers of adults with PTSD, who often experience psychological distress, caregiver burden, and diminished well-being.

#### **CURRENT REVIEW**

The aim of this review is to synthesize the available evidence on the effectiveness of internet and mobile interventions for individuals with PTSD and family members or caregivers of individuals with PTSD.

Primary outcomes of interest were PTSD and depression symptom severity, and a sufficiently large number of studies were identified in Veterans or active-duty service members to allow for reporting of these outcomes separately for military and civilian populations. We were also interested in intervention and study methodological characteristics that may influence intervention effects on PTSD and depression symptom severity. These characteristics were 1) intervention modality, 2) level of facilitation, 3) intervention duration, 4) presence or absence of a written exposure component, 5) outcome assessment method, and 6) comparison group type.

Sixty primary studies met eligibility criteria, including 36 RCTs, 1 non-randomized trial, 1 cohort study, and 22 pre-post studies. Most studies were conducted in individuals with PTSD, and evidence from comparative studies (k = 36) was prioritized over evidence from pre-post studies in this population. All available evidence was considered for interventions conducted among family members and caregivers.

Most comparative studies of internet and mobile interventions for adults with PTSD were conducted in the US, and 13 were enrolled Veterans or military Service members. Most studies evaluated internet-based CBT (iCBT) interventions, though there was considerable variation across studies in the proportion of participants meeting diagnostic criteria for PTSD; the intervention modality, duration, and level of facilitation; and in the type of comparison conditions and outcomes assessed.

Thirty-two studies assessed the effectiveness of internet or mobile interventions on PTSD symptoms immediately post-treatment (31 RCTs, 1 cohort; total N = 2,237). Of these, 21 studies were conducted in civilian populations (total N = 1,655) and 11 in military populations (Veterans or active-duty service members; total N = 582). Results of meta-analyses of these studies indicate differential effectiveness of internet and mobile interventions for PTSD for civilian and military populations. Interventions may be moderately effective in reducing PTSD and depression severity in civilians, immediately post-treatment. In comparison, military populations may experience small to negligible benefits from treatments. For both populations, no treatment effects were evident at shorter and longer-term follow-up periods. We have low confidence in findings (low strength of evidence) because of study methodological limitations and moderate inconsistency in effects across studies.

Five studies (2 RCTs, 3 pre-post studies) on internet and mobile interventions for family members or caregivers of adults with PTSD were identified. Four studies evaluated internet interventions, and 1 evaluated an app-based intervention. All studies were conducted among intimate partners or family members or Veterans, military service members, or first responders with PTSD. Studies reported on a variety of outcome measures. Four outcomes that were reported by at least 2 studies were included in our synthesis: caregiver burden, depression, anxiety, and quality of life. Across treatments and outcomes, there was limited evidence of any consistent treatment effects. Most studies had high risk of bias and the strength of evidence across outcomes was low.

Military Veterans and service members may experience small to negligible benefits on PTSD and depressive symptoms from self-guided, asynchronous PTSD treatments. Civilians may experience moderate benefits at post-treatment, but these gains do not appear to be sustained. Consequently, the

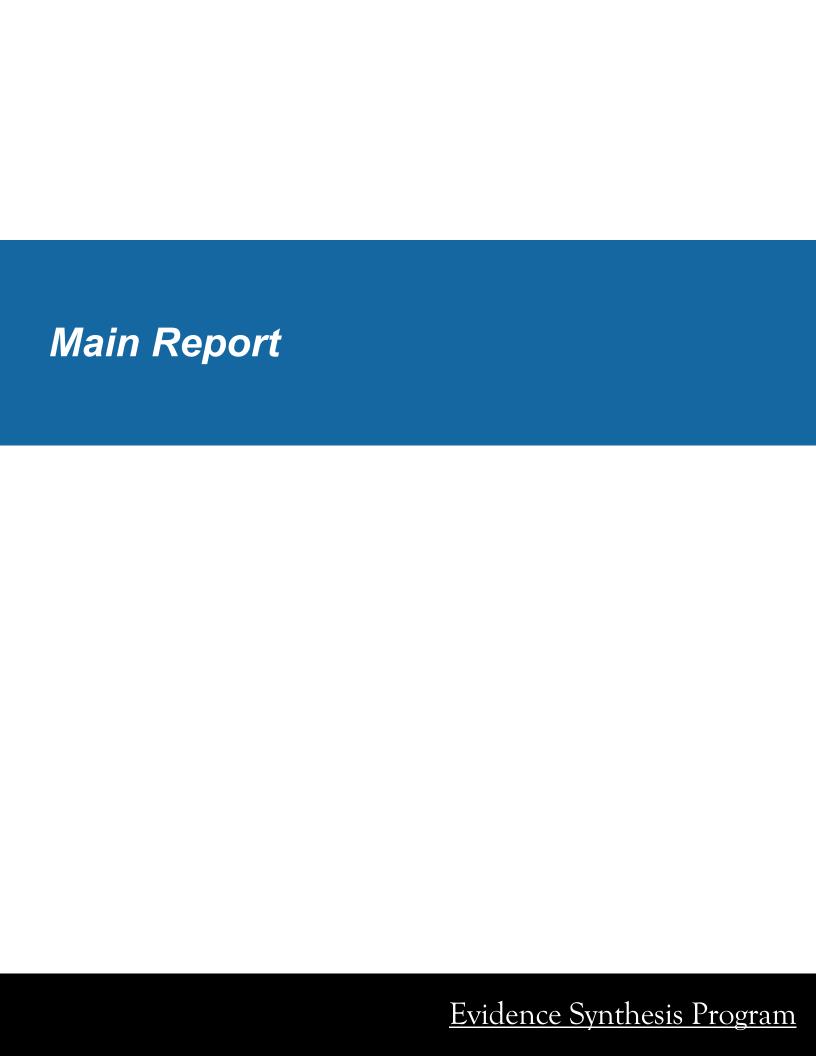
available evidence does not currently support internet and mobile interventions as an effective treatment for military populations with PTSD. Based on a small evidence base, internet and mobile interventions do not appear to benefit family members of adults with PTSD.

Examining intervention characteristics that may influence effectiveness suggests that the level of facilitation could be a key factor in the effectiveness of internet and mobile interventions for PTSD. Future research should examine whether greater direct therapeutic involvement with trauma-focused iCBTs increases the effectiveness of treatments for military populations. Future studies might also explore whether internet and mobile resources have a beneficial role in supporting the established VA clinical pathway for PTSD, for example to improve treatment adherence or facilitate at-home activities that reinforce principles and practices introduced during in-person therapy.

#### ES Table. Summary of Evidence

| Outcome  | Evidence                   | Findings  |
|--|----------------------------|---|
| Posttraumatic stress disorder  |                            |   |
| PTSD symptom severity at PT  | 31 RCTs and 1 cohort study | Low SOE: Internet and mobile interventions for PTSD may improve PTSD symptom severity at post-treatment among civilians but may have no effect among Veteran/military populations.                      |
| PTSD symptom severity at 1-3 months  | 18 RCTs                    | Low SOE: Internet and mobile interventions for PTSD may have no effect on PTSD symptom severity 1-3 months post-treatment.  |
| PTSD symptom severity at 4+ months   | 5 RCTs                     | Low SOE: Internet and mobile interventions for PTSD may have no effect on PTSD symptom severity 4+ months post-treatment.   |
| Clinically significant PTSD symptom improvement from PT to 3 months          | 9 RCTs and 1<br>NRT        | Low SOE: Internet and mobile interventions may increase the odds of clinically meaningful PTSD symptom improvement among civilian but not military populations.   |
| No longer meeting PTSD criteria, recovered, or remission from PT to 3 months | 10 RCTs                    | Low SOE: Internet and mobile interventions for PTSD may increase the odds of recovery, remission, or no longer meeting PTSD diagnostic criteria.  |
| Reliable improvement or change from PT to 3 months                           | 5 RCTs and 1 cohort study  | Low SOE: Internet and mobile interventions for PTSD may increase the odds of reliable symptom improvement or change.  |
| Depression   |                            |   |
| Depression symptom severity at PT  | 19 RCTs and 1<br>NRT       | Low SOE: Internet and mobile interventions for PTSD may have a small effect on depression symptom severity at post-treatment among civilians but may have no effect among Veteran/military populations. |
| Depression symptom severity at 1-3 months                                    | 10 RCTs                    | Low SOE: Internet and mobile interventions for PTSD may have no effect on depression symptom severity 1-3 months post-treatment.  |

Abbreviations. NRT=non-randomized trial; PT=post-treatment; TSD=posttraumatic stress disorder; RCT=randomized controlled trial; SOE=strength of evidence.



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## **ABBREVIATIONS TABLE**

| Definition  |  |  |  |
|---|--|--|--|
| Clinician-Administered PTSD Scale                                 |  |  |  |
| Clinician-Administered PTSD Scale for DSM-5                       |  |  |  |
| Cognitive behavioral therapy                                      |  |  |  |
| Confidence interval   |  |  |  |
| Couple Helping Overcome PTSD and Enhance Satisfaction             |  |  |  |
| Department of Defense   |  |  |  |
| Diagnostic and Statistical Manual of Mental Disorders - version 5 |  |  |  |
| Impact of Events Scale  |  |  |  |
| Impact of Events Scale - Revised                                  |  |  |  |
| Internet-based cognitive behavioral therapy                       |  |  |  |
| Key Question  |  |  |  |
| Mini International Neuropsychiatric Interview                     |  |  |  |
| Non-randomized trial  |  |  |  |
| Organisation for Economic Co-operation and Development            |  |  |  |
| Odds ratio  |  |  |  |
| Primary Care PTSD Screen  |  |  |  |
| PTSD Checklist for DSM-5  |  |  |  |
| PTSD Checklist – Civilian version                                 |  |  |  |
| PTSD Checklist – Military version                                 |  |  |  |
| PTSD Checklist – Specific version                                 |  |  |  |
| Posttraumatic Stress Diagnostic Scale                             |  |  |  |
| Prolonged exposure  |  |  |  |
| Prediction interval   |  |  |  |
| Posttraumatic Symptom Scale – Interview version                   |  |  |  |
| Posttraumatic Symptom Scale – Self-report                         |  |  |  |
| Posttraumatic stress  |  |  |  |
| Posttraumatic stress disorder                                     |  |  |  |
| Randomized controlled trial                                       |  |  |  |
| Standardized mean difference                                      |  |  |  |
| Short messaging service   |  |  |  |
| Strength of evidence  |  |  |  |
| Treatment as usual  |  |  |  |
| Traumatic Event Scale   |  |  |  |
| United Kingdom  |  |  |  |
| Department of Veterans Affairs                                    |  |  |  |
| Veterans Affairs – Community Reinforcement and Family Training    |  |  |  |
| Veterans Health Administration                                    |  |  |  |
| Written exposure therapy  |  |  |  |
|   |  |  |  |



#### **BACKGROUND**

Approximately 10% of United States (US) military Veterans experience posttraumatic stress disorder (PTSD) at some point in their lifetime, with nearly one-quarter of Veterans reporting significant posttraumatic stress (PTS) symptoms. Untreated PTSD is associated with significant functional impairment, high rates of psychiatric and medical comorbidities, substance misuse, and death by suicide. Veterans with PTSD engage in high levels of healthcare utilization and pursue disability compensation at a high rate. Individual face-to-face trauma focused treatments, to include traumafocused cognitive behavioral therapies (CBT) and eye movement desensitization and reprocessing (EMDR), have been identified as the most effective treatments for PTSD and are considered first-line treatments. The Department of Veterans Affairs (VA) and Department of Defense (DoD) have invested significant resources in developing and broadly implementing clinical pathways that incorporate effective therapeutic approaches. Routine screening and access to evidence-based treatment for PTSD are now standard practices across all VA medical facilities. However, despite these considerable investments in care, the majority of the military population (Veterans and military service members) with PTSD do not access and benefit from PTSD treatments.

Increasing access to effective PTSD treatments is a high priority for the VA and DoD. Veterans endorse several obstacles that may prevent them from engaging in PTSD treatment such as shame and stigma, fear of social consequences, and logistical challenges. <sup>15–17</sup> Virtual treatments for PTSD that offer more flexible treatment delivery options with reduced provider requirements have the potential to overcome many of these barriers, especially given Veterans' receptivity to home-based telehealth options. <sup>17,18</sup> Over the past 2 decades several types of technology-assisted treatments for PTSD have been developed and tested. <sup>19</sup> Internet and mobile interventions have also been developed to support family members and caregivers of adults with PTSD who often experience psychological distress and caregiver burden related to their relationship. <sup>20</sup> These interventions aim to overcome similar access barriers to improve family member/caregiver wellbeing.

Virtual treatments, in which a provider delivers evidence-based therapies via synchronous telehealth, are now largely considered equivalent to in-person therapy for PTSD. Self-guided, asynchronous PTSD treatments that use the internet or mobile phone applications (apps) have also become available in recent years. These interventions, which differ in level of therapeutic support but are generally lower intensity than conventional in-person therapy, have the potential to expand access to effective PTSD therapies to anyone with the internet or a smartphone.

Internet treatments are generally structured interventions that deliver therapeutic content over the internet with varying levels of provider guidance.<sup>23</sup> Recent reviews indicate that internet-based cognitive behavioral therapies (iCBTs) may be more effective in reducing PTSD symptoms relative to waitlist conditions.<sup>24</sup> Although iCBTs are generally rated favorably by participants, high dropout rates present a limitation to these treatments.<sup>25</sup> Mobile mental health apps use smartphone technology to offer self-directed or remotely facilitated therapeutic content.<sup>26</sup> The evidence supporting these newer treatment approaches is mixed. Two recent reviews evaluating apps for the treatment of PTSD detected no significant benefits of these interventions relative to a control comparison,<sup>27,28</sup> while a more recent review detected a small effect of stand-alone, smartphone-based mental health apps.<sup>29</sup>

There is considerable variation among existing internet and mobile interventions in terms of treatment modality used (*ie*, delivered over the internet, an app, or SMS), the content and duration of the treatment, the extent and nature of facilitation, and the targeted population of the treatment. Studies

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also differ in whether they compare interventions to no treatment (waitlist or treatment as usual), active control conditions, or in-person therapy. Examining how these factors impact treatment effectiveness can help inform implementation considerations. Given the potential benefits and broad accessibility of internet and mobile interventions for PTSD, the aim of this review is to synthesize available evidence on the effectiveness of internet and mobile interventions (with asynchronous therapist-guided or self-guided content and resources) for adults with PTSD and their family members or caregivers.



#### **METHODS**

#### REGISTRATION AND REVIEW

A preregistered protocol for this review can be found on the PROSPERO international prospective register of systematic reviews (<u>CRD42023471333</u>). A draft version of this report was reviewed by external peer reviewers; their comments and author responses are located in the <u>Appendix</u>.

#### **KEY QUESTIONS AND ELIGIBILITY CRITERIA**

The following key questions (KQs) were the focus of this review:

| Key Question<br>1 | Are internet and mobile interventions with asynchronous therapist-guided or self-guided content and resources designed to improve PTSD symptom severity and/or self-management effective for improving PTSD symptoms and other mental health symptoms among adults with a diagnosis of PTSD?            |
|-------------------|---|
| Key Question<br>2 | Are internet and mobile interventions with asynchronous therapist-guided or self-guided content and resources designed to enhance coping and symptom management skills for family members and caregivers of adults with PTSD effective for improving stress, mental health symptoms, and coping skills? |

#### Eligibility Criteria

Study eligibility criteria are shown in the table below. We included studies where a substantial portion of the sample (about half, at minimum) met criteria for probable PTSD, as defined by the study. For studies meeting these criteria, we used a best-evidence approach and prioritized evidence from randomized controlled trials (RCTs) and cohort studies, when available.

| Population   | KQ1: Adults diagnosed with PTSD using a validated clinician-administered or self-report PTSD instrument.   |
|--------------|--|
|              | KQ2: Family members and caregivers of adults diagnosed with PTSD.  |
| Intervention | KQ1: Internet and mobile interventions with asynchronous therapist-guided or self-guided content and resources designed to improve PTSD symptom severity and/or self-management. Interventions may address mental health or medical comorbidities, provided the intervention includes components to address PTSD symptoms. |
|              | KQ2: Internet and mobile interventions with asynchronous therapist-guided or self-guided content and resources designed to enhance coping and symptom management skills of family members and caregivers of adults with PTSD.  |
|              | For both KQs, therapist guidance associated with the internet or mobile intervention cannot exceed 5 hours. There are no restrictions on the number of interactions with a therapist or the length of the program, and interventions may be delivered alone or in conjunction with other psychological interventions.      |
| Comparator   | Alternate intervention, treatment as usual, waitlist control, post-intervention (pre-post studies).  |
| Outcomes     | KQ1: Mental health symptom severity, functioning/quality of life. KQ2: Stress or mental health symptom severity, coping skills.  |
| Setting      | We will include studies conducted in the US or comparable countries (OECD member countries).   |
| Study Design | Any comparative or pre-post studies will be eligible, but we may prioritize more rigorous designs in our synthesis.  |



#### SEARCHING AND SCREENING

To identify articles relevant to the key questions, a research librarian searched Ovid MEDLINE, PsycINFO, PTSDPubs, and the Cochrane Central Register of Controlled Trials through October 2023 using terms for *PTSD* and *internet and mobile interventions* (see <u>Appendix</u> for complete search strategies). Additional citations were identified from clinicaltrials.gov and hand-searching reference lists of relevant systematic reviews. English-language titles, abstracts, and full-text articles were independently reviewed by 2 investigators, and disagreements were resolved by consensus.

#### DATA ABSTRACTION AND RISK OF BIAS ASSESSMENT

Effect information and population, intervention, and comparator characteristics were abstracted from all included studies. When needed effect information was reported only in plots or other graphics, we abstracted data using the WebPlotDigitizer tool (<a href="https://apps.automeris.io/wpd/">https://apps.automeris.io/wpd/</a>). Data abstraction was first completed by 1 investigator and checked by another. The internal validity (risk of bias) of each included study was rated using the Cochrane Risk of Bias 2.0 tool for randomized controlled trials and the ROBINS-I tool for non-randomized studies. Internal validity ratings were completed independently by 2 investigators. Disagreements were resolved by consensus or discussion with a third reviewer (see <a href="https://apps.automeris.io/wpd/">Appendix</a> for risk of bias ratings).

#### **SYNTHESIS**

Available evidence was synthesized using a best-evidence approach,<sup>32</sup> prioritizing findings from RCTs and cohort studies over pre-post studies. Findings were organized by key question, outcome, and outcome assessment timing (immediately post-treatment, 1-3 month follow-up, or longer-term follow-up). For KQ1, PTSD and depression symptom severity were primary outcomes, and we did not conduct strength of evidence assessment on other outcomes. Although not originally planned, a sufficiently large number of studies were identified in Veterans or active-duty service members to allow reporting of primary outcomes separately for military and civilian populations.

We were also interested in intervention and study methodological characteristics that may influence intervention effects on PTSD and depression symptoms severity. These characteristics were 1) intervention modality (internet, app, or SMS/text message), 2) level of facilitation, 3) intervention duration, 4) presence or absence of a written exposure component (CBT-based interventions only), 5) outcome assessment method (clinician-administered or self-reported measure), and 6) comparison group type (active control, in-person therapy, minimal contact, intervention without exposure component, intervention without guidance, psychoeducation only, treatment as usual, or waitlist control). Level of facilitation was categorized as *none* (reminders or technical support only), *minimal support* (guidance/feedback on writing assignment or homework and/or other minimal unstructured support), or *direct facilitation* (provider directly delivers some aspect of intervention). Intervention duration was categorized as *brief* (1 week or less or a single session), *moderate* (2-5 weeks), *long* (6 weeks or longer), or *self-guided timeline*. Virtually all interventions used CBT or were informed by CBT principles, so it was not feasible to compare effects of CBT and non-CBT interventions.

Between-group differences in PTSD and depression symptom severity at each assessment point were represented as bias-adjusted standardized mean differences (SMDs; Hedges' g). Several included studies also reported the proportion of patients with clinically significant PTSD symptom improvement; the proportion who recovered, were in remission, or no longer met PTSD diagnostic

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criteria; and/or the proportion with reliable PTSD symptom improvement or change. Odds ratios (ORs) were used to quantify between-group differences in these outcomes.

Effect estimates for primary outcomes were synthesized with hierarchical random-effects models, given that many studies reported multiple measures of the same construct and/or assessed the same outcome at multiple time points (even after subgrouping effect estimates into the assessment timeframes described above). Models assumed a correlation of 0.7 between measures of the same outcome construct and 0.9 between assessment time points (*ie*, autocorrelation). Cluster-robust confidence intervals and degrees of freedom calculated using the Satterwaithe approximation were used for models of dependent effect estimates. Conventional random-effects models were used when included studies each contributed a single effect estimate. Regardless of modeling approach, analyses with fewer than 10 studies incorporated the Knapp-Hartung method or comparable adjustment to standard errors. Meta-regression models used to investigate moderation by intervention and study characteristics included all effect estimates regardless of assessment time point, accounting for dependencies among estimates in the same fashion as main analyses. Meta-analyses were conducted using the *metafor*<sup>33</sup> package for R (R Foundation for Statistical Computing, Vienna, Austria).

Between-study variation in effects (heterogeneity) was estimated using restricted maximum-likelihood estimation, and in moderation analyses, the amount of heterogeneity was allowed to differ across study subgroups. For all analyses, heterogeneity is presented as 95% prediction intervals (PIs). Prediction intervals describe the likeliest range of true effects (*eg*, true differences in PTSD symptoms between groups) across studies and provide an estimate of the magnitude and direction of effects that would be found in future studies similar to those included in a synthesis.<sup>34</sup> A PI encompassing effects similar to the overall estimate suggests limited heterogeneity, whereas a PI that includes effects in the same direction as the overall estimate but that vary widely in magnitude (*ie*, small to large benefits) suggests moderate heterogeneity. If a PI encompasses effects that range widely in both magnitude and direction, then substantial heterogeneity is likely present. Prediction intervals were evaluated alongside forest plots to reach conclusions about whether effect estimates in a given analysis were consistent, moderately inconsistent, or highly inconsistent.

#### Strength of Evidence

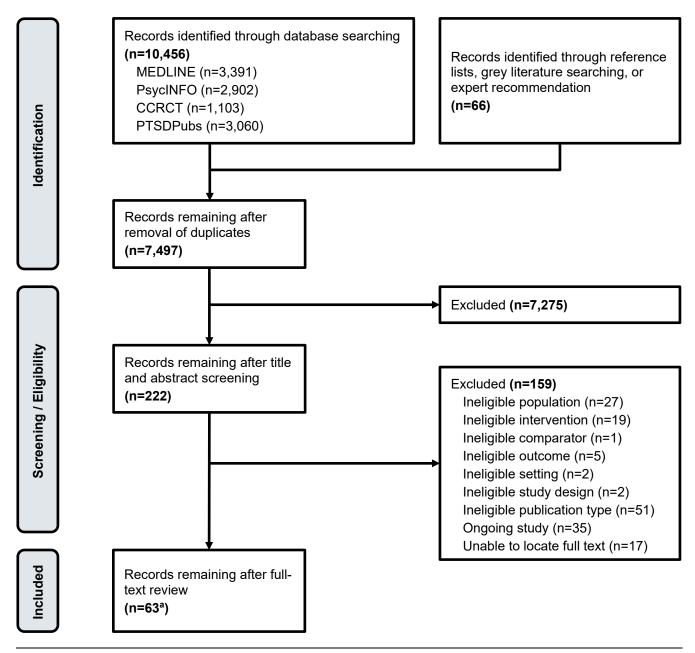
After synthesizing available evidence, we rated the strength of evidence based on the methodology and risk of bias of available studies, the consistency and certainty of findings, and the directness of outcomes (whether reported outcomes are relevant to patients and providers). For this review, we applied the following general algorithm: *high strength* evidence consisted of multiple trials with low risk of bias, consistent and precise findings, and clinically relevant outcomes; *moderate strength* evidence consisted of multiple trials with low to unclear risk of bias, consistent and precise findings, and clinically relevant outcomes; *low strength* evidence consisted of a single trial, or multiple small trials, with unclear to high risk of bias, inconsistent or imprecise findings, and/or outcomes with limited clinical relevance; and *insufficient* evidence consisted of a single trial with unclear or high risk of bias.



#### **RESULTS**

#### LITERATURE FLOW DIAGRAM

The literature flow diagram summarizes the results of the study selection process. A full list of excluded studies is provided in the <u>Appendix</u>.



Notes. a 60 primary studies in 63 records.

Abbreviations. CCRCT=Cochrane Central Register of Controlled Trials.





#### **OVERVIEW OF INCLUDED STUDIES**

Our search identified 222 potentially relevant articles after deduplication and title and abstract screening. We included 60 primary studies (in 63 publications) meeting eligibility criteria: 36 RCTs, 1 non-randomized trial, 1 cohort study, and 22 pre-post studies. We prioritized evidence from comparative studies, and did not include pre-post studies in our synthesis, except for pre-post studies on family members/caregivers, where few comparative studies were available. Characteristics of prioritized studies are shown in Table 1. We identified 35 underway studies (see <u>Appendix</u>).

#### **PTSD Studies**

Of the studies prioritized for synthesis (N = 36), 34 were RCTs,  $^{36-69}$  1 was a non-randomized trial,  $^{70}$ and 1 was a cohort study.  $^{71}$  Most were conducted in the US (N = 22), with the remaining studies conducted in Sweden (N = 4), the Netherlands (N = 3), Australia (N = 3), Canada (N = 1), Germany (N = 4)= 1), and the UK (N = 2). Sample sizes ranged from 20-196 (median = 63). Two-thirds of the studies had predominately female samples. Of the studies that reported on race or ethnicity (N = 23), all but 3<sup>48,59,60</sup> had predominately White samples. Thirteen studies<sup>36,42,44,51,54,55,58</sup>—61,65–67 were conducted with US Veterans or military Service members. Among these, 10 studies 36,42,51,54,55,59,61,65-67 were conducted exclusively among Veterans and 7<sup>36,51,55,59,65–67</sup> were conducted exclusively among Veterans enrolled in Veterans Health Administration (VHA) care or recruited from VHA health care settings. The proportion of study participants meeting criteria for a PTSD diagnosis or probable/provisional PTSD diagnosis was 100% in 21 studies, between 75-99% in 5 studies, and between 48-74% in 8 studies (exact proportions were not reported for 2 studies). PTSD diagnostic status was determined by a structured clinical interview using the gold standard Clinician-Administered PTSD Scale (CAPS) in 9 studies. Most studies used a version of the PTSD Checklist (PCL) to establish a provisional PTSD diagnosis, with cut-off scores varying across studies. Other measures used included the Mini International Neuropsychiatric Interview (MINI), the Posttraumatic Symptom Scale (interview or selfreport version; PSS-I or PSS-SR), and the revised Impact of Events Scale (IES-R).

Most studies (N = 30) evaluated internet interventions, 5 studies $^{47,52,61,62,66}$  evaluated mobile app interventions, and a single study<sup>39</sup> evaluated a text messaging (SMS) intervention. Most interventions were CBT-based (N = 32), and 18 studies specifically evaluated a trauma-focused CBT. Among civilian studies, 14 evaluated a trauma-focused CBT; among military studies, 4 studies tested a trauma-focused CBT. In the military trials, trauma-focused CBT interventions were either based on prolonged exposure (PE)<sup>60,61</sup> or written exposure. Other interventions were based on executive function training (N = 3)<sup>42,45,54</sup> or goal setting (N = 1). Over half of studies (21) investigated long-duration interventions (6 or more weeks); moderate-duration interventions (2-5 weeks) were examined in 6 studies and brief interventions (1 week or less or a single session) in 5 studies. Interventions used a self-guided timeline in 4 studies. Fifteen studies evaluated interventions that included provider guidance and/or feedback, and 6 studies evaluated interventions with some direct facilitation (*ie*, delivery of intervention content) by a provider. The remaining studies (N = 15) evaluated self-guided interventions with no provider involvement other than reminders and/or technical support. Provider involvement was primarily asynchronous in 8 studies, primarily synchronous in 5 studies, and a combination of both in 7 studies.

Nineteen studies compared an intervention to an alternative intervention. For example, an intervention may have been compared to the same intervention without 1 or more components (*eg*, with and without therapist guidance) or to psychoeducation. Two studies<sup>41,60</sup> compared the intervention to

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synchronous in-person therapy. Other comparators included a waitlist (N = 13), treatment as usual (TAU; N = 3), and minimal contact (*ie*, phone monitoring or assessments only; N = 2).

PTSD symptom severity was most often assessed with a version of the PCL (PCL-M, N = 5; PCL-C, N = 5; PCL-5, N = 14; PCL-S, N = 1). Other measures used included the CAPS-5 (N = 4), PDS (N = 2), IES/IES-R (N = 7), PC-PTSD (N = 1), PSS-SR (N = 1), PSS-I (N = 3), and TES (N = 1). In addition to symptom severity, 10 studies reported on clinically significant improvement, 10 studies reported on remission, recovery, or no longer meeting PTSD criteria, and 6 studies reported on reliable improvement or change. Other mental health outcomes reported by more than 1 study included depression (N = 23), generalized anxiety (N = 16), alcohol use (N = 6), somatic symptoms (N = 3), and psychological distress (N = 2). Drug use, stress, panic disorder symptoms, social phobia/social anxiety symptoms, anger, and moral injury-related distress were each reported by a single study. Quality of life outcomes were reported by 10 studies, and 8 studies reported outcomes related to functioning.

Common methodological limitations of RCTs were small sample sizes, low treatment adherence, limited information on randomization and co-interventions, lack of blinding of participants and outcome assessors, and analyses that did not include all randomized participants. Common methodological limitations of non-randomized studies were low treatment adherence, a high degree of missing data, lack of information on co-interventions, and use of analyses that do not account for potential confounders.

#### Family Member/Caregiver Studies

Among studies evaluating interventions for family members or caregivers of adults with PTSD (Key Question 2; N = 5), 2 were  $RCTs^{72,73}$  and 3 were pre-post studies. The Four of these studies were conducted among spouses or intimate partners and  $1^{73}$  was conducted among family members. All studies were conducted among intimate partners/family members of Veterans, military service members, or first responders. Four studies were conducted in the US, and 1 was conducted in Canada. Sample sizes ranged from 12-200 (median = 27). All studies had entirely or predominately female samples. Among the 4 studies that reported on race or ethnicity, all had predominately White samples. Three studies required that the patient with PTSD screen positive for probable PTSD using a self-report measure.

Four studies evaluated internet interventions, and 1 study<sup>73</sup> evaluated an app-based intervention. One RCT<sup>72</sup> and 1 pre-post study<sup>75</sup> evaluated VA-CRAFT, an internet intervention that includes safety planning and psychoeducation on PTSD symptoms, self-care, communication skills, and supporting the Veteran in considering treatment options and while engaged in care. The RCT compared the intervention with a minimal contact control (*ie*, reminders only), and the pre-post study evaluated VA-CRAFT with additional coaching. Two pre-post studies<sup>74,76</sup> evaluated Couple HOPES, a cognitive behavioral conjoint treatment that includes psychoeducation, communication skills training, and dyadic interventions to address behavioral avoidance, emotional numbing, and cognitions that underlie PTSD and relationship problems. Both studies included coaching. The final study<sup>73</sup> was an RCT comparing a group with access to PTSD Family Coach, an app that includes psychoeducation, stress management tools, self-assessments, and information on connecting to additional resources, to a psychoeducation-only app.

VA-CRAFT and Couple HOPES were categorized as long interventions, and PTSD Family Coach was completed on a self-guided timeline. Two studies<sup>72,73</sup> (PTSD Family Coach and the VA-CRAFT RCT) evaluated self-guided interventions with no provider involvement other than reminders or technical

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support. The remaining 3 studies evaluated interventions that included provider guidance and/or feedback. In 1 of these studies<sup>75</sup> the provider involvement was primarily synchronous, and the other 2 studies<sup>74,76</sup> included a combination of synchronous and asynchronous provider involvement. Relevant outcomes assessed included depression symptoms (N = 4), anxiety symptoms (N = 3), caregiver burden (N = 3), and quality of life (N = 3).

Like studies of adults with PTSD, common methodological limitations of RCTs evaluating interventions for family members or caregivers of adults with PTSD included small sample sizes, low treatment adherence, lack of information on the randomization process, high rates of missing data, and lack of intent-to-treat analyses. Pre-post studies were limited by low treatment adherence, lack of accounting for potential confounders in analyses, lack of information on co-interventions, and high levels of missing data.



**Table 1. Characteristics of Included Studies** 

| Study                                 | Sample<br>Size<br>Follow-Up | Study<br>Design | Population % Probable PTSD   | Intervention<br>Characteristics<br>Modality                        | Comparator                             | Outcomes Assessed   |
|---------------------------------------|-----------------------------|-----------------|--|--|--|---|
| PTSD studies                          |                             |                 |  |  |  |   |
| Acosta 2017 <sup>36</sup>             | N=162<br>3 mos              | RCT             | OEF/OIF/OND Veterans<br>with hazardous alcohol<br>use or substance misuse<br>79% | Self-guided iCBT<br>Internet                                       | TAU                                    | PTSD symptom severity, PTSD treatment response, alcohol use, drug use, quality of life                          |
| Allen 2022 <sup>37</sup>              | N=49<br>3 mos               | RCT             | Adults<br>100%   | Guided iCBT<br>Internet  | Waitlist                               | PTSD symptom severity, PTSD remission, psychological distress, depression, anxiety                              |
| Andersson<br>2021 <sup>38</sup>       | N=64<br>40 wks              | RCT             | Adults with prior IPV and current at least moderate mental health problems 57.1% | Guided iCBT<br>Internet  | Waitlist                               | PTSD symptom severity, PTSD treatment response, PTSD remission, depression, anxiety, quality of life            |
| Bedard-Gilligan<br>2022 <sup>39</sup> | N=109<br>8 wks              | RCT             | Adults reporting heavy episodic drinking 100%                                    | CBT + framing<br>SMS   | Kind attention<br>messages             | PTSD symptom severity, alcohol use, anxiety, depression   |
| Bedford 2023 <sup>40</sup>            | N=71<br>1 mo                | RCT             | University students and community members NR                                     | Safety Behavior<br>Elimination for<br>Traumatic Stress<br>Internet | Modifiable<br>Behavior<br>Intervention | PTSD symptom severity   |
| Bisson 2022 <sup>41</sup>             | N=196<br>44 wks             | RCT             | Adults<br>100%   | Guided trauma-focused iCBT Internet                                | In-person<br>trauma-focused<br>CBT     | PTSD symptom severity, PTSD remission, depression, anxiety, alcohol use, quality of life, functional impairment |
| Clausen<br>2019 <sup>42</sup>         | N=21<br><i>PT</i>           | RCT             | Male combat Veterans<br>who served since OIF<br>60%                              | Executive function training Internet                               | Placebo training                       | PTSD symptom severity, depression   |
| de Kleine<br>2019 <sup>43</sup>       | N=107<br>6 mos              | RCT             | Adults with a history of IPV 100%  | Self-guided cognitive bias modification training Internet          | Placebo training                       | PTSD symptom severity, depression   |



| Study                             | Sample<br>Size<br>Follow-Up | Study<br>Design | Population % Probable PTSD                                       | Intervention<br>Characteristics<br>Modality                      | Comparator                                   | Outcomes Assessed  |
|-----------------------------------|-----------------------------|-----------------|--|--|--|--|
| Engel 2015 <sup>44</sup>          | N=80<br>18 wks              | RCT             | Recently deployed military Service members and Veterans 100%     | Nurse-guided iCBT<br>(DESTRESS)<br>Internet                      | TAU  | PTSD symptom severity, depression, anxiety, somatic symptoms, functioning  |
| Fonzo 2019 <sup>45</sup>          | N=84<br><i>PT</i>           | RCT             | Adults<br>94%  | Cognitive/affective remediation training <i>Internet</i>         | Placebo training                             | PTSD symptom severity  |
| Gawlytta<br>2022 <sup>46</sup>    | N=25<br>12 mos              | RCT             | Patients after intensive care for sepsis and their spouses 73.5% | Guided iCBT<br>Internet  | Waitlist                                     | PTSD symptom severity, PTSD treatment response, PTSD remission, psychological distress, health-related quality of life |
| Hensler<br>2022 <sup>47,77</sup>  | N=179<br><i>PT</i>          | RCT             | Adults 55.3%   | PTSD Coach<br><i>App</i>   | Waitlist                                     | PTSD symptom severity, PTSD treatment response, PTSD remission, depression, somatic symptoms, functional disability    |
| Hirai 2020 <sup>48</sup>          | N=149<br>3 mos              | RCT             | Undergraduate students 56.3%                                     | Emotion-focused expressive writing intervention Internet         | Fact-focused expressive writing intervention | PTSD symptom severity, PTSD remission  |
| Ivarsson<br>2014 <sup>49</sup>    | N=62<br>1 yr                | RCT             | Adults<br>100%   | Guided iCBT<br>Internet  | Waitlist                                     | PTSD symptom severity, PTSD treatment response, PTSD remission, depression, anxiety, quality of life                   |
| Knaevelsrud<br>2007 <sup>50</sup> | N=96<br>3 mos               | RCT             | Adults<br>70%  | Guided iCBT (Interapy) Internet                                  | Waitlist                                     | PTSD symptom severity, depression, anxiety, functioning  |
| Krupnick<br>2017 <sup>51</sup>    | N=34<br>12 wks              | RCT             | OIF/OEF/OND Veterans<br>100%                                     | Guided trauma-focused iCBT writing intervention (WIRED) Internet | TAU  | PTSD symptom severity, depression, alcohol abuse   |
| Kuhn 2017 <sup>52</sup>           | N=120<br>3 mos              | RCT             | Adults<br>92.5%  | PTSD Coach<br>App  | Waitlist                                     | PTSD symptom severity, PTSD treatment response, depression, psychosocial functioning                                   |



| Study                             | Sample<br>Size<br>Follow-Up | Study<br>Design | Population % Probable PTSD                         | Intervention<br>Characteristics<br>Modality            | Comparator                               | Outcomes Assessed  |
|-----------------------------------|-----------------------------|-----------------|--|--|--|--|
| Lange 2003 <sup>53</sup>          | N=184<br>6 wks              | RCT             | Adults<br>90%                                      | Guided iCBT (Interapy) Internet                        | Waitlist                                 | PTSD symptom severity, PTSD treatment response, depression, anxiety, somatic symptoms                              |
| Larsen 2019 <sup>54</sup>         | N=29<br>1 mo                | RCT             | Veterans<br>100%                                   | Active emotional working memory training Internet      | Placebo training                         | PTSD symptom severity, PTSD treatment response, depression, anxiety, stress, negative affect                       |
| <b>Lehavot 2021</b> <sup>55</sup> | N=102<br>6 mos              | RCT             | Women Veterans<br>100%                             | Guided iCBT<br>(DESTRESS)<br>Internet                  | Phone<br>monitoring                      | PTSD symptom severity, PTSD treatment response   |
| Lewis 2017 <sup>56</sup>          | N=42<br>3 mos               | RCT             | Adults<br>100%                                     | Guided trauma-focused iCBT Internet                    | Waitlist                                 | PTSD symptom severity, depression, anxiety, alcohol use, functional impairment                                     |
| Littleton 2016 <sup>57</sup>      | N=87<br>3 mos               | RCT             | Women college students with rape-related PTSD 100% | Guided iCBT (From<br>Survivor to Thriver)<br>Internet  | Access to psychoeducation website        | PTSD symptom severity, depression, anxiety   |
| Litz 2007 <sup>58</sup>           | N=45<br>4 mos               | RCT             | Service members 100%                               | Guided iCBT<br>(DESTRESS)<br>Internet                  | Supportive counseling                    | PTSD symptom severity, depression, anxiety   |
| McCall 2023 <sup>70</sup>         | N=163<br>8 wks              | NRT             | Public safety personnel NR                         | Guided iCBT<br>Internet                                | Wellbeing course                         | PTSD symptom severity, PTSD treatment response, depression, anxiety, panic symptoms, social phobia symptoms, anger |
| McGuire<br>2023 <sup>59</sup>     | N=48<br>PT                  | RCT             | Veterans of Iraq or<br>Afghanistan<br>100%         | Self-guided goal setting intervention (MOVED) Internet | Online assessments only                  | PTSD symptom severity, moral injury-<br>related distress, quality of life  |
| McLean<br>2021 <sup>60</sup>      | N=40<br>6 mos               | RCT             | Active-duty Service members and Veterans 100%      | Prolonged exposure<br>Internet                         | In-person<br>present-centered<br>therapy | PTSD symptom severity, depression, functioning   |
| McLean<br>2022 <sup>61</sup>      | N=93<br>6 wks               | RCT             | Veterans<br>100%                                   | Self-management app<br>(Renew)<br><i>App</i>           | Waitlist                                 | PTSD symptom severity  |



| Study                                 | Sample<br>Size<br>Follow-Up | Study<br>Design | Population % Probable PTSD                                   | Intervention<br>Characteristics<br><i>Modality</i>          | Comparator                                    | Outcomes Assessed  |
|---------------------------------------|-----------------------------|-----------------|--|---|---|--|
| Miner 2016 <sup>62</sup>              | N=49<br>1 mo                | RCT             | Adults<br>100%   | PTSD Coach App  | Waitlist                                      | PTSD symptom severity, PTSD treatment response                                       |
| Morabito<br>2023 <sup>63</sup>        | N=51<br>1 mo                | RCT             | University students and community members 100%               | Tonic immobility-<br>focused<br>psychoeducation<br>Internet | Health education only                         | PTSD symptom severity  |
| Nieminen<br>2016 <sup>64</sup>        | N=56<br><i>PT</i>           | RCT             | Women with traumatic childbirth 100%                         | Guided trauma-focused iCBT Internet                         | Waitlist                                      | PTSD symptom severity, depression, anxiety, quality of life                          |
| Possemato 2011 <sup>65</sup>          | N=31<br><i>PT</i>           | RCT             | Veteran primary care patients 48.4%                          | Self-guided written emotional disclosure Internet           | Time<br>management<br>narratives              | PTSD symptom severity, quality of life   |
| Possemato 2016 <sup>66</sup>          | N=20<br>PT                  | RCT             | Veteran primary care patients 100%                           | Clinician-supported<br>PTSD Coach<br><i>App</i>             | Self-managed<br>PTSD Coach                    | PTSD symptom severity, PTSD treatment response, depression, quality of life          |
| Possemato 2019 <sup>67</sup>          | N=30<br>12 wks              | RCT             | Veteran primary care patients with hazardous alcohol use 60% | Peer-supported iCBT<br>Internet                             | Self-managed<br>iCBT                          | PTSD symptom severity, alcohol use, quality of life                                  |
| Spence 2011 <sup>68</sup>             | N=44<br>PT                  | RCT             | Adults<br>100%   | Guided iCBT<br>Internet                                     | Waitlist                                      | PTSD symptom severity, PTSD remission, depression, anxiety, psychosocial functioning |
| Spence 2014 <sup>69</sup>             | N=125<br>3 mos              | RCT             | Adults<br>86%  | Guided iCBT with exposure Internet                          | iCBT without exposure                         | PTSD symptom severity, PTSD remission, depression, anxiety                           |
| Wiltsey<br>Stirman 2021 <sup>71</sup> | N=51<br><i>PT</i>           | Cohort          | Adults<br>100%   | Cognitive Processing<br>Therapy<br>Internet                 | Talkspace as usual (propensity score-matched) | PTSD symptom severity, PTSD treatment response                                       |
| Family member                         | /caregiver stu              | dies            |  |   |   |  |
| Crenshaw<br>2023 <sup>74</sup>        | N=27<br>1 mo                | Pre-<br>post    | Romantic partners of military members,                       | Guided cognitive-<br>behavioral conjoint                    | NA  | Depression, anxiety, anger, alcohol misuse, quality of life, functioning             |



| Study                                  | Sample<br>Size<br>Follow-Up | Study<br>Design | Population % Probable PTSD                              | Intervention<br>Characteristics<br>Modality                             | Comparator                | Outcomes Assessed  |
|--|-----------------------------|-----------------|---|---|---------------------------|--|
|  |                             |                 | Veterans, and first responders with PTSD                | treatment (Couple<br>HOPES)   |                           |  |
|  |                             |                 | NA  | Internet  |                           |  |
| Erbes 2020 <sup>72</sup>               | N=46<br><i>PT</i>           | RCT             | Spouses or intimate partners of Veterans with PTSD  NA  | Self-guided family<br>outreach training (VA-<br>CRAFT)<br>Internet      | NA                        | Caregiver burden, general mental<br>health symptoms and distress, quality<br>of life |
| Kuhn 2023 <sup>75</sup>                | N=12<br>PT                  | Pre-<br>post    | Spouses and intimate partners of Veterans with PTSD NA  | Coach-guided family outreach training (VA-CRAFT) Internet               | NA                        | Depression, anxiety, caregiver burden  |
| <b>Morland 2023</b> <sup>76</sup>      | N=15<br><i>PT</i>           | Pre-<br>post    | Romantic partners of<br>Veterans with PTSD<br><i>NA</i> | Guided cognitive-<br>behavioral conjoint<br>treatment (Couple<br>HOPES) | NA                        | Depression, quality of life  |
| van Stolk-<br>Cooke 2023 <sup>73</sup> | N=200<br><i>PT</i>          | RCT             | Adult family members of veterans with PTSD NA           | PTSD Family Coach App   | Psychoeducation -only app | Caregiver burden, stress, depression, anxiety, self-efficacy                         |

Notes. Bold font indicates studies conducted among Veterans and/or military service members .

Abbreviations. CBT=cognitive behavioral therapy; DESTRESS=Delivery of Self Training and Education for Stressful Situations; HOPES=Helping Overcome PTSD and Enhance Satisfaction; iCBT=internet-based cognitive behavioral therapy; IPV=interpersonal violence; MOVED= Moral Elevation Online Intervention for Veterans Experiencing Distress Related to PTSD and Moral Injury; NA=not applicable; NR=not reported; NRT=non-randomized trial; OEF=Operation Enduring Freedom; OIF=Operation Iraqi Freedom; OND=Operation New Dawn; PT=posttreatment; PTSD=posttraumatic stress disorder; RCT=randomized controlled trial; SMS=short messaging service; TAU=treatment as usual; VA-CRAFT=Veterans Affairs—Community Reinforcement and Family Training; WIRED=Warriors Internet Recovery & Education.



# **KEY QUESTION 1: INTERNET AND MOBILE INTERVENTIONS FOR ADULTS WITH PTSD**

#### **PTSD Outcomes**

Thirty-two studies  $^{36-40,42-44,46-58,60-64,66-71}$  assessed the effectiveness of internet or mobile interventions on PTSD symptoms immediately post-treatment (31 RCTs, 1 cohort; total N = 2,237). Of these, 21 studies were conducted in civilian populations (total N = 1,655) and 11 in military populations (Veterans or active-duty service members; total N = 582). Among civilians, internet or mobile interventions may result in moderate post-treatment improvements in PTSD symptom severity (SMD = 0.42, 95% CI [0.18, 0.67]; number of effect sizes  $[N_{es}] = 34$ ). However, intervention effects among military populations may be small to negligible (SMD = 0.10, 95% CI [-0.11, 0.30];  $N_{es} = 12$ ). For both populations, we have low confidence in findings (low SOE) because of study methodological limitations and moderate inconsistency in effects across studies.

Eighteen RCTs<sup>36,39–41,43,44,48,51,54–58,60,63,65,67,69</sup> reported PTSD symptom severity outcomes at short-term follow up (1-3 months; total N=1,228). Nine of these studies were carried out in military populations (total N=470). Among civilians, overall improvement in PTSD symptom severity was smaller and no longer statistically significant compared with immediately post-treatment (SMD = 0.24, 95% CI [-0.18, 0.65];  $N_{es}=20$ ). Intervention effects remained small to negligible for Veterans or active-duty service members (SMD = 0.10, 95% CI [-0.13, 0.33];  $N_{es}=11$ ). Five RCTs<sup>41,43,55,58,60</sup> (total N=388) also reported outcomes at long-term follow up (4 to 11 months), and when pooled, no intervention effect on PTSD symptom severity was apparent (SMD = -0.06, 95% CI [-0.45, 0.33];  $N_{es}=6$ ). This result includes evidence from both civilian and military populations because of the small number of studies. Based on this evidence, internet or mobile interventions may have no effect on PTSD symptom severity among civilian or military populations at 1-3 months or 4+ months after treatment. We have low confidence in these findings based on study methodological limitations, imprecision, and moderate inconsistency.

Comparatively few trials reported on the proportion of participants with clinically meaningful PTSD symptom improvement, reliable change, or recovery/remission after the intervention (ranging from 6 to 13 trials per outcome). Results could be disaggregated by military or civilian status only for clinically meaningful PTSD symptom improvement. Based on available evidence, internet and mobile interventions may increase odds of clinically meaningful PTSD symptom improvement post-treatment among civilian but not military populations. Interventions may improve odds of recovery, remission, or no longer meeting diagnostic criteria and reliable symptom improvement or change, but it is unclear whether this benefit differs between civilian and military populations. Our confidence in these findings is low based on study methodological limitations, imprecision, and substantial inconsistency.

Compared with control participants, civilian participants receiving the intervention had greater odds of clinically meaningful PTSD symptom improvement post-treatment (OR = 1.97, 95% CI [0.80, 4.83]; k = 6,  $N_{es} = 7$ ), though this difference was nonsignificant. Odds of clinically meaningful improvement also favored the intervention among Veterans or active-duty service members (OR = 1.36, 95% CI [0.52, 3.58]; k = 4,  $N_{es} = 7$ ), but the difference was much smaller in magnitude compared with civilians and also nonsignificant. Not accounting for military or civilian status, participants who received the intervention also had significantly greater odds of recovery, remission, or no longer meeting diagnostic criteria (OR = 2.27, 95% CI [1.24, 4.17]; k = 13,  $N_{es} = 13$ ) and reliable symptom improvement or change (OR = 3.92, 95% CI [1.46, 10.54]; k = 6,  $N_{es} = 8$ ).



Figure 1. Differences in PTSD Symptoms Immediately Post-Treatment

| N            | Duration  | Outcome  | SMD [95% CI]   |
|--------------|---|--|--|
|              |   |  |  |
|              |   |  |  |
| 71           | Rrief   | PCL-5  | <u> </u>   |
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| 42           | Long  | CAPS-5   | <del>                                 </del>   |
| 42           | Long  | PCL-5  | <del> </del>   |
| 51           | Long  | PSS-I  | <del>  ■</del>   |
| 150          | Long  | PCL-5  | <del>  ■  </del>   |
| 56           | Long  | TES  | <del> </del>   |
| 56           | Long  | IES-R  | <u> </u>   |
| 42           | Long  | PCL-C  | <u> </u>   |
| 125          | Long  |  | <b>├─ड</b> ं-ं-  |
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|              |   |  |  |
| 179          |   | PCL-5  | <b>├─┼≣──┤</b>   |
| 120          | Self-guided   | PCL-C  | <del>                                     </del>   |
| 49           | Self-guided   | PCL-C  | <del>                                     </del>   |
|              |   |  |  |
| 47           | Madavata  | DOL E  | 4 -  |
|              |   |  | <b>——</b>  |
|              |   |  |  |
|              |   |  |  |
|              |   |  |  |
| 29           | Moderate  | PCL-5  | <del> </del>   |
| 162          | Long  | PCL-M  | <u> </u>   |
|              | Long  |  | <u> </u>   |
|              | Long  |  | <del>                                     </del>   |
|              |   |  | <u> </u>   |
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| 20           | Long  | PCL-IVI  | The state of the s |
|              |   |  |  |
| 20           | Long  | PCL-S  | <b>├</b>   |
| 93           | Self-guided   | PCL-5  | <u> </u>   |
| 5% CI [-0.11 | , 0.30], 95% PI [-0.  | 11, 0.30])   | <b>-</b>   |
|              |   |  |  |
|              |   |  | Favors Control Favors Intervention   |
|              |   |  | Favors Control Favors Intervention   |
|              | 71 107 71 71 71 71 71 71 46 34 95 95 101 101 40 64 64 62 42 42 51 150 56 56 42 125 125 125 46 179 120 49 47 57 5% CI [0.18, | 71 Brief 107 Brief 71 Brief 72 Brief 73 Brief 74 Brief 75 Moderate 95 Moderate 95 Moderate 95 Moderate 101 Moderate 101 Moderate 101 Moderate 102 Long 103 Long 104 Long 105 Long 107 Self-guided 108 Self-guided 109 Self-guided 100 Self-guided 100 Self-guided 100 Self-guided 101 Long 102 Long 11 Long 12 Long 13 Long 14 Long 15 Long 16 Long 17 Long 17 Long 18 Lon | 71 Brief PSS-SR 71 Brief PSS-SR 71 Brief PCL-5 intrusion 71 Brief PCL-5 neg. cognitions 71 Brief PCL-5 avoidance 71 Brief PCL-5 reg. cognitions 71 Brief PCL-5 arousal 71 Brief PCL-5 arousal 71 Brief PCL-5 arousal 71 Brief PCL-5 avoidance 72 Brief PCL-5 73 Moderate IES-R intrusions 74 Brief PCL-5 75 Moderate IES-R avoidance 75 Moderate IES avoidance 76 Long PDS 77 Brief PCL-C 78 Avoidance 79 Brief PCL-C 79 Brief PCL-C 70 Brief PCL-C 70 Brief PCL-C 71 Brief PCL-5 71 Brief PCL-5 72 Brief PCL-5 73 Brief PCL-5 74 Long PCL-C 75 Brief PCL-5 75 Long PSS-I 75 Long PSS-I 75 Long PSS-I 75 Long PSS-I 75 Long PCL-5 76 Long PCL-5 77 Belf-guided PCL-C 77 Belf-guided PCL-C 78 Brief PCL-5 79 Belf-guided PCL-C 79 Belf-guided PCL-C 79 Belf-guided PCL-C 70 Brief PCL-S 70 Moderate PCL-5 71 Moderate PCL-5 71 Moderate PCL-5 71 Moderate PCL-5 72 Brief PCL-5 73 Brief PCL-5 74 Moderate PCL-5 75 Moderate PCL-5 75 Moderate PCL-5 76 CI [0.18, 0.67], 95% PI [-0.63, 1.48])  |



Abbreviations. CAPS=Clinician-Administered PTSD Scale; CAPS-5=Clinician-Administered PTSD Scale for DSM-5; CI=confidence interval; IES=Impact of Events Scale; IES-R=Impact of Events Scale – Revised; PCL-5=PTSD Checklist for DSM-V; PCL-C=PTSD Checklist – Civilian version; PCL-M=PTSD Checklist – Military version; PCL-S=PTSD Checklist – Specific version; PDS=Posttraumatic Stress Diagnostic Scale; PI=prediction interval; PSS-I=Posttraumatic Stress Symptom Scale – Interview version; PSS-SR=Posttraumatic Symptom Scale – Self-report; SMD=standardized mean difference; TES=Traumatic Event Scale.

#### **Depression Outcomes**

Intervention effects on depression symptoms followed a similar pattern to effects on PTSD symptoms. Twenty trials  $^{37-39,42-44,47,49-54,56-58,64,66,69,70}$  evaluated the effectiveness of internet or mobile interventions on depression symptoms immediately post-treatment (19 RCTs, 1 NRT; total N=1,458). Of these, 6 trials were conducted in military populations (total N=171). Based on this evidence, internet and mobile interventions may result in small post-treatment improvements in depression symptoms among civilians (SMD = 0.28, 95% CI [0.04, 0.53];  $N_{es}=17$ ), but may not result in post-treatment symptom improvements among Veterans or active-duty service members (SMD = -0.03, 95% CI [-0.36, 0.30];  $N_{es}=6$ ). Based on 11 studies,  $^{39,41,43,44,51,54,56-58,69}$  internet and mobile interventions may have no effect on depression symptom severity 1-3 months after treatment among both civilians (SMD = 0.07, 95% CI [-0.41, 0.55]; k=7,  $N_{es}=7$ ) and military populations (SMD = -0.11, 95% CI [-0.41, 0.20]; k=4,  $N_{es}=5$ ). We have low confidence in findings on depression outcomes due to study methodological limitations and inconsistency in effects across studies.

#### Variation in Intervention Effects

Results of subgroup analyses based on intervention and methodological characteristics are shown in Table 2. These results are informative about potential sources of variation in intervention effects on PTSD and depression symptom severity but should be interpreted with caution because they are based on all available evidence regardless of time point and military or civilian status. Results of moderation analyses were not considered in overall conclusions about intervention effectiveness or strength of evidence judgments.

Subgroup analyses suggest that a potential source of variability in intervention effectiveness is delivery modality. As shown in Table 2, comparable-magnitude improvements in PTSD symptoms were observed for both internet interventions and mobile interventions. In contrast, the overall effect for SMS-based interventions was negligible or potentially negative based on results from a single trial of 2 independent cohorts.<sup>39</sup> Another apparent source of variability in effects is the level of facilitation. Interventions that used direct facilitation appeared to have the largest effect on PTSD symptoms. Interventions with guidance or feedback only had a somewhat smaller overall effect, while the pooled effect estimate for interventions that offered no facilitation (*ie*, reminders or technical support only) was small to negligible. Intervention effects did not appear to differ based on intervention duration (brief, moderate, long, or self-guided timeline) or whether the intervention incorporated written exposure elements.

Regarding study methodological characteristics, observed intervention effects were similar regardless of whether a clinician-administered or self-reported outcome measure was used (Table 2). Observed effects strongly favored interventions when compared with a completely inactive condition like waitlist control. Effects were considerably smaller against another active treatment condition (excluding inperson therapy). As noted above, 2 studies<sup>41,60</sup> compared an internet treatment to an evidence-based inperson therapy. One of these was a large RCT<sup>41</sup> (N = 139) that compared iCBT to face-to-face CBT among civilians in the United Kingdom (UK) National Health Services, finding that the internet





intervention was non-inferior on PTSD outcomes at post-treatment.  $^{41}$  The second study  $^{60}$  was a small feasibility study (N = 40) on treatment-seeking military service members and Veterans that found no difference in post-treatment PTSD symptoms between web-based PE and face-to-face present-centered therapy.

Table 2. Subgroup Analysis Results for PTSD and Depression Symptom Severity

|  | PTSD  | Depression  |
|--|---|---|
|  | SMD [95% CI]  | SMD [95% CI]  |
| Modality                                   |   |   |
| Internet                                   | $0.34 [0.14, 0.54] (k = 28, N_{es} = 74)$                   | $0.22 [0.02, 0.42] (k = 18, N_{es} = 32)$                     |
| Арр  | $0.31 [-0.06, 0.68] (k = 5, N_{es} = 5)$                    | $0.33$ [-0.78, 1.44] ( $k = 2$ , $N_{es} = 2$ )               |
| SMS/text message                           | -0.12 [-9.88, 9.64] $(k = 1, N_{es} = 4)^a$                 | $-0.24$ [-8.99, 8.50] ( $k = 1$ , $N_{es} = 4$ ) <sup>a</sup> |
| Facilitator Involvement <sup>b</sup>       |   |   |
| Direct facilitation                        | $0.60$ [-0.12, 1.32] ( $k = 6$ , $N_{es} = 15$ )            | $0.31 [-0.58, 1.20] (k = 4, N_{es} = 8)$                      |
| Minimal support                            | $0.35 [0.02, 0.67] (k = 14, N_{es} = 30)$                   | $0.26$ [-0.03, 0.55] ( $k = 10$ , $N_{es} = 15$ )             |
| None (reminders or technical support only) | 0.18 [-0.04, 0.40] $(k = 13, N_{es} = 37)^a$                | $0.05 [-0.35, 0.44] (k = 7, N_{es} = 15)^a$                   |
| Duration                                   |   |   |
| Brief                                      | $0.33 [-0.05, 0.71] (k = 5, N_{es} = 20)$                   | $0.27 [0.01, 0.54] (k = 1, N_{es} = 3)$                       |
| Moderate                                   | $0.37 [-0.44, 1.17] (k = 5, N_{es} = 12)^a$                 | $0.19 [-0.76, 1.13] (k = 4, N_{es} = 8)^a$                    |
| Long                                       | $0.29 [0.04, 0.55] (k = 20, N_{es} = 47)$                   | $0.14$ [-0.06, 0.35] ( $k = 14$ , $N_{es} = 25$ )             |
| Self-guided timeline                       | $0.29 [-0.14, 0.72] (k = 4, N_{es} = 4)$                    | $0.33 [-0.78, 1.44] (k = 2, N_{es} = 2)$                      |
| Written Exposure                           |   |   |
| CBT + written exposure                     | $0.39 [0.05, 0.73] (k = 13, N_{es} = 38)$                   | $0.26$ [-0.09, 0.62] ( $k = 8$ , $N_{es} = 12$ )              |
| CBT only                                   | 0.28 [0.06, 0.51] ( $k = 19$ , $N_{es} = 41$ ) <sup>a</sup> | $0.18 [-0.11, 0.46] (k = 11, N_{es} = 23)^a$                  |
| Outcome Assessment                         |   |   |
| Clinician-administered                     | $0.24 [-0.40, 0.88] (k = 6, N_{es} = 12)$                   | <del>_</del>  |
| Self-reported                              | $0.31 [0.13, 0.49] (k = 32, N_{es} = 71)^a$                 | _   |
| <b>Comparison Condition</b>                |   |   |
| Active Control                             | $0.18 [-0.13, 0.50] (k = 11, N_{es} = 33)^a$                | $0.03 [-0.47, 0.53] (k = 6, N_{es} = 14)^a$                   |
| In-person therapy                          | $-0.48$ [-5.67, 4.71] ( $k = 2$ , $N_{es} = 7$ )            | $-0.12$ [-0.52, 0.29] ( $k = 1$ , $N_{es} = 2$ )              |
| Minimal contact                            | $0.15 [-0.53, 0.83] (k = 1, N_{es} = 3)$                    | <del>_</del>  |
| No exposure                                | $-0.24$ [-0.26, -0.22] ( $k = 1$ , $N_{es} = 4$ )           | $0.05 [0.03, 0.06] (k = 1, N_{es} = 2)$                       |
| No guidance                                | $0.30$ [-2.96, 3.57] ( $k = 2$ , $N_{es} = 3$ )             | $-0.10$ [-0.97, 0.78] ( $k = 1$ , $N_{es} = 1$ )°             |
| Psychoeducation                            | $0.58 [0.44, 0.72] (k = 1, N_{es} = 2)$                     | $-0.27$ [-0.50, -0.04] ( $k = 1$ , $N_{es} = 2$ )             |
| Treatment as usual                         | $0.15 [-0.61, 0.90] (k = 3, N_{es} = 8)$                    | $-0.16$ [-1.18, 0.86] ( $k = 2$ , $N_{es} = 5$ )              |
| Waitlist                                   | $0.63 [0.36, 0.88] (k = 13, N_{es} = 23)$                   | $0.50 [0.27, 0.72] (k = 9, N_{es} = 12)$                      |

*Notes*. <sup>a</sup> Bedard-Gilligan 2022 reports results for 2 independent waves. <sup>b</sup> McLean 2022 (*N* = 93) combined 2 active conditions into a treatment group and is not included in subgroup analysis. <sup>c</sup> Reported SMD (*d*) and estimated 95% CI from single trial with *no guidance* comparison condition (Possemato 2016).

Abbreviations. Nes=number of effect sizes included in analysis; SMD=standardized mean difference (g).





#### Other Outcomes

Other outcomes of interest reported on by more than 1 study included generalized anxiety symptom severity, alcohol use, psychological distress, somatic symptoms, quality of life, and functioning. We did not conduct a meta-analysis or assess strength of evidence for these outcomes, but, overall, findings were mixed across studies.

Fifteen studies<sup>37–39,41,44,49,50,54,56–58,64,68–70</sup> reported on anxiety symptom severity (Table 3). Of these, 12 studies were conducted among civilian populations and 3 with Veteran or military populations. No studies were conducted exclusively among Veterans receiving VHA care. Among the civilian studies, 1 trial<sup>41</sup> that compared iCBT to face-to-face CBT found that improvements in generalized anxiety symptoms in the iCBT group were non-inferior to the face-to-face CBT group. Four other civilian trials that compared iCBT to a waitlist condition found significant improvements on anxiety severity at post-treatment favoring iCBT. <sup>49,50,56,68</sup> The 3 trials conducted with Veterans and/or military service members found non-significant improvements on anxiety severity at posttreatment relative to an active comparator. <sup>44,54,58</sup>

Five RCTs<sup>36,39,41,51,56,67</sup> reported on alcohol use/misuse outcomes (Table 4). Three of these studies<sup>36,39,67</sup> evaluated interventions that targeted alcohol misuse in addition to PTSD and required that participants endorse alcohol misuse. Three studies were conducted among Veterans receiving VHA care; the remaining 2 studies were conducted among civilians. Outcomes varied and results were mixed across trials and were not consistent across comparator types.

Two RCTs<sup>37,46</sup> conducted among civilians reported on psychological distress; neither found that CBT-based internet interventions for PTSD improved psychological distress symptoms at post-treatment compared to waitlist. Three RCTs reported on somatic symptoms; 2 evaluated internet interventions<sup>44,53</sup> and 1 evaluated an app-based intervention.<sup>47</sup> One RCT<sup>53</sup> conducted among civilians comparing an internet intervention to waitlist found a large effect at post-treatment, but the study was rated high risk of bias. The other 2 studies, including 1 study<sup>44</sup> conducted among Veterans and military service members, did not find evidence of an effect on somatic symptom severity.

Ten RCTs<sup>36,38,41,46,49,59,64–67</sup> reported on quality-of-life outcomes (Table 5). Five of these studies were conducted among Veterans receiving VHA care; the remaining 5 studies were conducted among civilians. Results were mixed across trials and were not consistent across comparator types.

Eight RCTs<sup>41,44,47,50,52,56,60,68</sup> reported on outcomes related to functioning (Table 6). Two studies were conducted among Veterans and military service members; the remaining studies were conducted among civilians. Results were mixed across trials and were not consistent across comparator types. Five trials conducted among civilians reported some positive effect of internet or mobile interventions for PTSD on functioning, but neither trial conducted among Veterans and military service members found a significant effect of the intervention on functioning outcomes.



Table 3. Effects of Internet and Mobile Interventions for PTSD on Anxiety Symptom Severity

| Study<br>Follow-Up                             | N   | Intervention and Comparator   | Anxiety Outcomes   |
|--|-----|---|--|
| Internet intervention                          | าร  |   |  |
| Allen 2022 <sup>37</sup><br><i>PT</i>          | 40  | iCBT compared to waitlist   | No significant difference between groups in change in GAD-7 score from pre- to post-treatment (F2, 73.49 = $0.47$ , $p = 0.63$ ); between group effect size ( $g$ [95% CI] = $0.26$ [47, .98]).      |
| Andersson 2021 <sup>38</sup><br>PT             | 64  | iCBT compared to waitlist   | No significant group differences at PT: iCBT group mean (SD) = 15.62 (11.33); waitlist group mean (SD) = 20.70 (12.5).   |
| Bisson 2022 <sup>41</sup> 44 weeks             | 160 | iCBT compared to in-<br>person CBT                                    | iCBT was non-inferior to face-to-face CBT at 8 weeks ( $d$ [95% CI] = 0.10 [- $\infty$ , 0.41]) but inconclusive at 44 weeks ( $d$ [95% CI] = 0.47 [- $\infty$ , 0.78]).                             |
| Engel 2015 <sup>44</sup> 12 weeks              | 58  | iCBT compared to TAU  | No significant difference between groups in change in PHQ anxiety score at PT, 6-week, or 12-week follow-up.   |
| Ivarsson 2014 <sup>49</sup><br><i>PT</i>       | 62  | iCBT compared to waitlist   | Significant time by treatment interaction effects for BAI score favoring iCBT group at PT: Cohen's <i>d</i> [95% CI] = 0.60 [0.04, 1.13].  |
| Knaevelsrud<br>2007 <sup>50</sup><br><i>PT</i> | 95  | iCBT compared to waitlist   | Significant time by treatment interaction effects for BSI anxiety score favoring iCBT group at PT: F = 10.73; <i>p</i> < .001.   |
| Larsen 2019 <sup>54</sup><br>1 month           | 29  | Active emotional working memory training compared to control training | No significant difference between groups in change in DASS anxiety score from pre- to post-treatment or 1-month follow-up.   |
| Lewis 2017 <sup>56</sup> 1 month               | 42  | iCBT compared to waitlist   | At PT there was a significant difference in BAI score between groups favoring the iCBT group (between-group mean difference [95% CI] = 13.40 [-19.91, -6.35]. These differences remained at 1 month. |
| Littleton 2016 <sup>57</sup><br>PT             | 51  | iCBT compared to psychoeducational website                            | No significant difference between groups in change in FDAS score from pre- to post-treatment ( $b = 8.62$ , SE = 5.71, $p = 0.139$ , $d = 0.46$ ).   |
| Litz 2007 <sup>58</sup><br>4 months            | 31  | iCBT compared to supportive counseling                                | No significant differences between groups in BAI score in ITT analyses; between group effect sizes ( $d$ ) = 0.40 at PT, $d$ = 0.54 at 3 months, $d$ = 1.01 at 6 mos.                                |
| McCall 2023 <sup>70</sup><br>PT                | 150 | iCBT compared to well-being course                                    | No significant difference between groups in change in GAD-7 score ( $\chi^2$ = 2.9, $p$ = .166) from pre- to post-treatment.   |
| Nieminen 2016 <sup>64</sup><br>PT              | 56  | iCBT compared to waitlist   | No between group effect for BAI score ( <i>d</i> [95% CI] = .18 [-0.34, .071])   |
| Spence 2011 <sup>68</sup><br>PT                | 42  | iCBT compared to waitlist   | iCBT group had significantly lower PT GAD-7 scores than the control group at PT (F1,39 = 4.62, $p$ < .04), with a moderate between-group effect ( $d$ [95% CI] = 0.55 [-1.03, 3.00].                 |



| Study<br>Follow-Up                               | N   | Intervention and Comparator                                    | Anxiety Outcomes   |
|--|-----|--|--|
| Spence 2014 <sup>69</sup> 3 months               | 125 | iCBT with exposure<br>compared to iCBT<br>without exposure     | No evidence of significant differential changes from baseline to PT or 3 months between groups in GAD-7 scores (F2, 123 = 0.8, $p$ = 0.451); PT between-group effect size ( $d$ [95% CI] = 0.24 [-0.11, 0.59], 3-month between-group effect size ( $d$ [95% CI] = -0.04 [-0.39, 0.31]) |
| SMS interventions                                |     |  |  |
| Bedard-Gilligan<br>2022 <sup>39</sup><br>1 month | 109 | CBT-based SMS intervention compared to kind attention messages | Wave 1: Change in DASS anxiety score not significantly different between groups at PT (B[SE] = 0.16 [0.17]) and 1 month (B[SE] = 0.10 [0.31])  Wave 2: Reduction was greater in the CBT group at PT (B[SE] = -0.61 [0.20], $p < .05$ ) but not at 1 month (B[SE] = -0.68 [0.36]).      |

Notes. **Bold** font indicates studies conducted among Veterans and/or military service members. Abbreviations. BAI=Beck Anxiety Inventory; BSI=Brief Symptom Inventory; CI=confidence interval; DASS=Depression Anxiety Stress Scale; FDAS=Four Dimensional Anxiety Scale; GAD-7=Generalized Anxiety Disorder-7; iCBT=internet-based cognitive behavioral therapy; ITT=intent-to-treat; PDSS-SR=Panic Disorder Severity Scale Self-Report; PHQ=Patient Health Questionnaire; PT=post-treatment; SE=standard error; SIAS-6=Social Interaction Anxiety Scale; SMS=short messaging service; SPS-6=Social Phobia Scale; TAU=treatment as usual.



Table 4. Effects of Internet and Mobile Interventions for PTSD on Alcohol Use Outcomes

| N   | Intervention and Comparator   | Alcohol Use Outcomes   |
|-----|---|--|
| ıs  |   |  |
| 162 | iCBT compared to<br>TAU   | iCBT group reported significantly greater declines in % heavy drinking days vs TAU at PT on the TLFB (difference $[\pm SE] = -1.80 \pm 0.79$ ; $p < 0.05$ ), with effects maintained at 3 months (difference $[\pm SE] = 1.89 \pm 1.33$ ). Differences between groups in % drinking days were non-significant at PT and 3 months.  |
| 160 | iCBT compared to in-<br>person CBT                                      | On the AUDIT, iCBT was non-inferior to in-person CBT at 8 weeks ( $d$ [95% CI] = 0.15 [- $\infty$ , 0.32]) and 44 weeks ( $d$ [95% CI] = 0.13 [- $\infty$ , 0.35]).  |
| 31  | iCBT compared to TAU  | No significant time by treatment interaction effects for AUDIT score. AUDIT scores increased for both groups.  |
| 42  | iCBT compared to waitlist   | No significant differences in AUDIT scores between groups at PT (between-group mean difference [95% CI] = 2.13 [-6.02, 1.63]) or at 1 month.   |
| 20  | Peer-supported iCBT compared to self-managed iCBT                       | No between group differences were observed using the TLFB at PT for drinking days ( <i>d</i> [95% Cl] = .13 [59, .84] or heavy drinking days ( <i>d</i> [95% Cl] = .17 [55, .89]).   |
|     |   |  |
| 109 | CBT-based SMS<br>intervention compared<br>to kind attention<br>messages | Wave 1: Change in drinks per week <sup>a</sup> was not significantly different between groups at PT (B [SE] = 0.11 [0.21]) and 1 month (B [SE] = -0.01 [0.40]). Among participants with at least 1 heavy drinking episode, reductions in HED <sup>b</sup> were greater for the treatment group at PT (B [SE] = -0.60 [1.29]) and 1 month (B [SE] = -0.67 [1.28]).  Wave 2: Change in drinks per week was not significantly different between groups at PT (B [SE] = -0.28 [0.16]) and 1 month (B [SE]) = -0.03 [0.25]). Changes in HED were not significantly different between groups at PT (B [SE] = - |
|     | 162<br>160<br>31<br>42  | Comparator  Iss  162 iCBT compared to TAU  160 iCBT compared to inperson CBT  31 iCBT compared to TAU  42 iCBT compared to waitlist  20 Peer-supported iCBT compared to self-managed iCBT  109 CBT-based SMS intervention compared to kind attention   |

Notes. Bold font indicates studies conducted among Veterans and/or military service members.

Abbreviations. AUDIT= Alcohol Use Disorders Identification Test; CBT=cognitive behavioral therapy; CI=confidence interval; HED=heavy episodic drinking; iCBT=internet-based cognitive behavioral therapy; PT=post-treatment; SE=standard error; SMS=short messaging service; TAU=treatment as usual; TLFB=Timeline Follow Back.



<sup>&</sup>lt;sup>a</sup> Drinks per week assessed using the Daily Drinking Questionnaire; <sup>b</sup> Heavy episodic drinking assessed using the National Institute on Alcohol Abuse and Alcoholism Recommended Alcohol Questions.

Table 5. Effects of Internet and Mobile Interventions for PTSD on Quality of Life

| Study<br>Follow-Up                          | N   | Intervention and Comparator  | Quality of Life Outcomes  |
|---|-----|--|---|
| Internet intervention                       | าร  |  |   |
| Acosta 2017 <sup>36</sup> 3 months          | 162 | iCBT compared to<br>TAU  | There was no significant effect of treatment on WHOQOL-BREF scores over time.   |
| Andersson 2021 <sup>38</sup><br>PT          | 64  | iCBT compared to waitlist  | No significant group differences in QOLI scores at PT: iCBT group mean (SD) = 0.56 (1.92); waitlist group mean (SD) = 0.07 (1.57).  |
| Bisson 2022 <sup>41</sup> 44 weeks          | 160 | iCBT compared to in-<br>person CBT   | On the EQ-5D-5L, iCBT was non-inferior to in-person CBT at 8 weeks ( $d$ [95% CI] = 0.09 [- $\infty$ , 0.33]) and borderline non-inferior at 44 weeks ( $d$ [95% CI] = 0.22 [- $\infty$ , 0.50]).   |
| Gawlytta 2022 <sup>46</sup><br>PT           | 34  | iCBT compared to waitlist  | No association between score changes on the EQ-5D-5L and iCBT with effect size $(95\% \text{ CI}) = 0.25 (-0.42, 0.93)$ .   |
| Ivarsson 2014 <sup>49</sup><br>PT           | 62  | iCBT compared to waitlist  | Significant time by treatment interaction effects on the QOLI favoring iCBT group at PT (Cohen's <i>d</i> [95% CI] = 0.53 [-0.02, 1.06]).   |
| <b>McGuire 2023</b> <sup>59</sup> <i>PT</i> | 36  | Internet goal setting intervention compared to minimal contact                         | At PT, the treatment group reported a medium, significant increase in the physical (Cohen's $d = 0.71$ ) and psychological domains (Cohen's $d = 0.74$ ) of the WHOQOL-BREF but no changes in the social or environmental domains. Participants in the control group reported no significant changes in any of the domains. |
| Nieminen 2016 <sup>64</sup><br>PT           | 56  | iCBT compared to waitlist  | No between group effect at PT for QOLI ( <i>d</i> [95% CI] =07 [59, .45]) or EQ-5D-5L ( <i>d</i> [95% CI] =07 [59, .48]).   |
| Possemato<br>2011 <sup>65</sup><br>PT       | 26  | iCBT (written<br>emotional disclosure)<br>compared to time<br>management<br>narratives | On the SF-12, iCBT group did not have significantly larger increases in physical health-related QOL ( $p = 0.96$ ) or mental health-related QOL ( $p = 0.62$ ) at PT compared to control participants.  |
| Possemato 2019 <sup>67</sup>                | 20  | Peer-supported iCBT compared to self-managed iCBT                                      | No between-group differences were observed at PT on the WHOQOL-BREF for psychological QOL ( <i>d</i> [95% CI] = .34 [39, 1.06] or social QOL ( <i>d</i> [95% CI] = .13 [59, .84]).  |
| App-based interventions                     |     |  |   |
| Possemato 2016 <sup>66</sup>                | 20  | Clinician-supported<br>PTSD Coach<br>compared to self-<br>managed PTSD<br>Coach        | Group by time effect sizes for changes in psychological QOL and social QOL on the WHOQOL-BREF were medium ( $d = .59$ ) and large ( $d = 1.46$ ), respectively.   |

Notes. **Bold** font indicates studies conducted among Veterans and/or military service members.

Abbreviations. Cl=confidence interval: FQ-5D-5I = FuroQol 5-dimension 5-level: iCBT=internet-h

Abbreviations. CI=confidence interval; EQ-5D-5L= EuroQol 5-dimension 5-level; iCBT=internet-based cognitive behavioral therapy; PT=post-treatment; PTSD=posttraumatic stress disorder; QOL=quality of life; QOLI=Quality of Life Inventory; SF-12=12-Item Short Form Health Survey; TAU=treatment as usual; WHOQOL-BREF=World Health Organization Quality of Life – Brief.



Table 6. Effects of Internet and Mobile Interventions for PTSD on Functioning

| Study<br>Follow-Up                      | N   | Intervention and<br>Comparator  | Functioning Outcomes   |  |
|---|-----|---|--|--|
| Internet interventio                    | ns  |   |  |  |
| Bisson 2022 <sup>41</sup> 44 weeks      | 160 | iCBT compared to in-<br>person CBT                                    | On the WSAS, iCBT was non-inferior to in-person CBT at 8 weeks ( $d$ [95% CI] = -0.14 [- $\infty$ , 0.13]) but inconclusive at 44 weeks ( $d$ [95% CI] = 0.24 [- $\infty$ , 0.53]).                    |  |
| Engel 2015 <sup>44</sup> 12 weeks       | 58  | iCBT compared to<br>TAU   | Group by time interaction on the SF-36 was non-significant at all time points.   |  |
| Knaevelsrud<br>2007 <sup>50</sup><br>PT | 95  | iCBT compared to waitlist   | On the SF-12, group by time pre-post effect size change favored the iCBT group for mental health functioning (F=5.95, $p < .05$ ), but the effect was not significant for physical health functioning. |  |
| Lewis 2017 <sup>56</sup><br>1 month     | 42  | iCBT compared to waitlist   | At PT, there was a significant difference between groups on the SDS (between-group mean difference [95% CI] = 9.36 [-13.56, -3.93]). These differences remained at 1 month.                            |  |
| McLean 2021 <sup>60</sup><br>6 months   | 25  | Web prolonged exposure compared to in-person present-centered therapy | Group by time interaction was not significant for either the mental or physical component scores of the VR-12.   |  |
| Spence 2011 <sup>68</sup><br><i>PT</i>  | 42  | iCBT compared to waitlist   | iCBT group did not have significantly lower PT SDS scores than waitlist ( <i>d</i> [95% CI] = 0.62 [-2.38, 4.85]).   |  |
| App-based interventions                 |     |   |  |  |
| Kuhn 2017 <sup>52</sup><br><i>PT</i>    | 120 | PTSD Coach compared to waitlist                                       | PTSD Coach condition had greater improvement on the B-IPF than waitlist (F[1, 117] = 7.63, $p$ = .007, $d$ = 0.51).  |  |
| Hensler 2022 <sup>47</sup><br>PT        | 179 | PTSD Coach compared to waitlist                                       | PTSD Coach condition had greater improvement on the WHODAS than waitlist (B = -5.39, SE = 2.49, 95% CI = -10.28, -0.50, $t$ (301.83) = -2.17, $p$ = 0.031; Cohen's $d$ = -0.27).                       |  |

Notes. **Bold** font indicates studies conducted among Veterans and/or military service members. Abbreviations. B-IPF=Brief Inventory of Psychosocial Functioning; CBT=cognitive behavioral therapy; CI=confidence interval; iCBT=internet-based cognitive behavioral therapy; PT=post-treatment; SDS=Sheehan Disability Scale; SF-12=12-Item Short Form Health Survey; SF-36= 36-Item Short Form Health Survey; TAU=treatment as usual; VR-12=Veteran's RAND 12-item Health Survey; WHODAS=World Health Organization Disability Assessment Schedule; WSAS=Work and Social Adjustment Scale.



# KEY QUESTION 2: INTERNET AND MOBILE INTERVENTIONS FOR FAMILY MEMBERS AND CAREGIVERS OF ADULTS WITH PTSD

Five studies  $^{72-76}$  were included that evaluated an intervention for family members or caregivers of adults with PTSD (2 RCTs, 3 pre-post studies; total N = 300). Three different family interventions were identified across the included studies: 2 internet interventions (VA-CRAFT, Couple HOPES) and 1 mobile intervention (PTSD Family Coach). The 2 RCTs were conducted on VA-CRAFT (comparator was waitlist control) and PTSD Family Coach (comparator was psychoeducation app). Four of the studies were conducted in the US and 1 in Canada; all the trials were conducted among intimate partners/family members of Veterans, military Service members, or first responders.

Studies reported on a variety of outcome measures. Four outcomes that were reported by at least 2 studies were included in our synthesis: caregiver burden, depression, anxiety, and quality of life. Across treatments and outcomes, there appeared to be little to no benefit of interventions on most outcomes. Most studies had high risk of bias and the strength of evidence across outcomes was low.

#### Caregiver Burden

It is unclear whether internet and mobile interventions reduce caregiver burden symptoms for family members of adults with PTSD. Our confidence in this finding is low based on study methodological limitations and inconsistent findings across studies. Three studies  $^{72,73,75}$  (2 RCTs and 1 pre-post; N = 258) assessed the effectiveness of an internet (2 studies) or mobile intervention (1 study) on caregiver burden symptoms at post-treatment (Table 7). Two studies  $^{72,75}$  evaluated the same internet intervention (VA-CRAFT). Caregiver burden symptoms improved in the first study relative to a waitlist control group (RCT, N = 46), $^{72}$  but no improvements were detected in the second study (pre-post; N = 12). $^{75}$  One RCT $^{73}$  (N = 200) that evaluated an app-based intervention did not detect any improvement in caregiver burden relative to an education-only app comparator.

Table 7. Effects of Internet and Mobile Interventions for Family Members of Adults with PTSD on Caregiver Burden

| Study<br>Follow-Up                          | N   | Intervention and Comparator                                | Caregiver Burden Outcomes   |  |
|---|-----|--|---|--|
| Internet interventio                        | ns  |  |   |  |
| Erbes 2020 <sup>72</sup><br><i>PT</i>       | 46  | VA-CRAFT compared to waitlist                              | Large treatment effect for intervention group at PT (F[1, 12] = 9.31, eta <sup>2</sup> = 0.20, $p < .01$ ).     |  |
| Kuhn 2023 <sup>75</sup><br><i>PT</i>        | 12  | Guided VA-CRAFT (pre-post)                                 | No significant change in CBS scores from baseline to PT $(d = -0.02, p = .942)$ .                               |  |
| App-based interventions                     |     |  |   |  |
| Van Stolk-Cooke<br>2023 <sup>73</sup><br>PT | 200 | PTSD Family Coach app compared to psychoeducation-only app | No significant treatment by time interaction for CBS scores at PT ( $d$ [95% CI] = 0.1 [-0.2, 0.4], $p$ = .45). |  |

Abbreviations. CBS=Caregiver Burden Scale; CI=confidence interval; PT=posttreatment; PTSD=posttraumatic stress disorder.

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### Depression

Internet and app-based interventions for family members of adults with PTSD may have no effect on depression symptoms. Though findings were consistent across studies, our confidence in this finding is low based on high risk of bias of all studies. Four studies (1 RCT and 3 pre-post; N = 254) assessed the effectiveness of an internet (3 studies)<sup>74–76</sup> or mobile intervention (1 study)<sup>73</sup> on depression symptoms at post-treatment (Table 8). Across studies, there were no improvements detected on depressive symptoms at post-treatment.

Table 8. Effects of Internet and Mobile Interventions for Family Members of Adults with PTSD on Depression

| Study<br>Follow-Up                          | N      | Intervention and Comparator   | Depression Outcomes   |
|---|--------|---|---|
| Internet intervention                       | ns     |   |   |
| Crenshaw 2023 <sup>74</sup><br>1 month      | 27     | Couple HOPES (prepost)  | No improvement on PHQ-9 from baseline to PT ( $g$ [95% CI] = 0.42 [-0.02, 0.87]) or baseline to 1-month ( $g$ [95% CI] = 0.38 [-0.41, 1.18]). |
| Kuhn 2023 <sup>75</sup><br><i>PT</i>        | 12     | Guided VA-CRAFT (pre-post)  | No change in PHQ-9 scores from baseline to PT ( $d = 0.32$ , $p = .364$ ).  |
| Morland 2023 <sup>76</sup><br>PT            | 15     | Couple HOPES (prepost)  | No change in PHQ-9 scores from baseline to PT ( $g = -0.20$ , $p = .142$ ).   |
| App-based interver                          | ntions |   |   |
| Van Stolk-Cooke<br>2023 <sup>73</sup><br>PT | 200    | PTSD Family Coach<br>app compared to<br>psychoeducation-only<br>app | No significant treatment by time interaction for PHQ-8 scores at PT ( $d$ [95% CI] = -0.0 [-0.3, 0.3], $p$ = .93).                            |

Abbreviations. CI=confidence interval; iCBT=internet-based cognitive behavioral therapy; PHQ-8=8-item Patient Health Questionnaire; PHQ-9=9-item Patient Health Questionnaire; PT=posttreatment; PTSD=posttraumatic stress disorder.

### Anxiety

Internet and mobile interventions for family members of adults with PTSD may have no effect on anxiety symptom severity. Though findings were consistent across studies, our confidence in this finding is low based on high risk of bias of all studies. Three studies (1 RCT and 2 pre-post; N = 239) assessed the effectiveness of internet (2 studies)<sup>74,75</sup> or mobile interventions (1 study)<sup>73</sup> on anxiety symptoms (Table 9). No significant benefits were detected across treatments.

Table 9. Effects of Internet and Mobile Interventions for Family Members of Adults with PTSD on Anxiety

| Study<br>Follow-Up                        | N | Intervention and Comparator | Anxiety Outcomes  |
|---|---|-----------------------------|---|
| Internet interventions                    |   |                             |   |
| Crenshaw 2023 <sup>74</sup> 27<br>1 month |   | Couple HOPES (prepost)      | No improvement on GAD-7 from baseline to PT ( $g$ [95% CI] = 0.17 [-0.19, 0.51]) or baseline to 1-month follow-up ( $g$ [95% CI] = 0.52 [-0.06, 1.10]). |

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| Study<br>Follow-Up                   | N  | Intervention and Comparator                                | Anxiety Outcomes   |
|--------------------------------------|----|--|--|
| Kuhn 2023 <sup>75</sup><br><i>PT</i> | 12 | Guided VA-CRAFT (pre-post)                                 | No change in PROMIS-SF anxiety scores from baseline to PT ( $d = 0.08$ , $p = .822$ ).                             |
| App-based interventions              |    |  |  |
| 2023 <sup>73</sup> app compared      |    | PTSD Family Coach app compared to psychoeducation-only app | No significant treatment by time interaction for GAD-7 scores at PT ( $d$ [95% CI] = -0.1 [-0.4, 0.2], $p$ = .55). |

Abbreviations. CI=confidence interval; GAD-7=Generalized Anxiety Disorder-7; iCBT=internet-based cognitive behavioral therapy; PT=posttreatment; PROMIS-SF=Patient-Reported Outcomes Measurement Information System – Short Form; PTSD=posttraumatic stress disorder.

### Quality of Life

It is unclear whether internet interventions for family members of adults with PTSD improve quality of life. Our confidence in this finding is low based on study methodological limitations and inconsistent findings across studies. Three studies  $^{72,74,76}$  (1 RCT and 2 pre-post; N = 88) assessed the effectiveness of internet-based interventions on quality of life (Table 10). One pre-post study  $^{74}$  (*Couple HOPES*) detected improvement in quality of life from baseline to PT, but not from baseline to 1-month follow-up. No significant benefits were detected in the 2 other trials.  $^{72,76}$ 

Table 10. Effects of Internet and Mobile Interventions for Family Members of Adults with PTSD on Quality of Life

| Study<br>Follow-Up                     | N   | Intervention and Comparator   | Quality of Life Outcomes   |
|--|-----|-------------------------------|--|
| Internet intervention                  | ons |                               |  |
| Crenshaw 2023 <sup>74</sup><br>1 month | 27  | Couple HOPES (prepost)        | Significant improvement in QOL on the WHOQOL from baseline to PT ( $g$ [95% CI] = 0.56 [0.10, 1.02]), but not from baseline to 1-month follow-up ( $g$ [95% CI] = 0.61 [-0.04, 1.26]).             |
| Erbes 2020 <sup>72</sup><br>PT         | 46  | VA-CRAFT compared to waitlist | No significant difference between groups at PT on the WHOQOL-BREF for psychological QOL (F[1, 12] = 2.00, eta <sup>2</sup> = 0.05) or relationship QOL (F[1, 12] = 1.18, eta <sup>2</sup> = 0.03). |
| Morland 2023 <sup>76</sup> PT          | 15  | Couple HOPES (pre-<br>post)   | No change in BBQ scores from baseline to PT ( $g = -0.05$ , $p = .326$ ).  |

Abbreviations. BBQ= Brunnsviken Brief Quality of Life Scale; CI=confidence interval; iCBT=internet-based cognitive behavioral therapy; PT=posttreatment; QOL=quality of life; WHOQOL=World Health Organization Quality of Life; WHOQOL-BREF= World Health Organization Quality of Life – Brief.



## DISCUSSION

Self-guided, asynchronous PTSD treatments that utilize internet or mobile phone technology have developed rapidly over the past 2 decades. These treatments can be delivered remotely to patients and require variable therapeutic support, potentially expanding access to PTSD treatments for adults with PTSD and their caregivers. The current systematic review examined the effectiveness of internet and mobile interventions for adults with PTSD. Primary outcomes were analyzed separately for civilian and military (Veterans or active-duty service members) populations. The effectiveness of internet and mobile interventions for caregivers and family members of adults with PTSD was also evaluated.

Our primary results indicated differential effectiveness of treatments for civilian and military populations. Internet and mobile interventions may be moderately effective in reducing PTSD and depression severity in civilians, immediately post-treatment. In contrast, military populations treated with internet or mobile interventions experienced small to negligible benefits. For both populations, no treatment effects were evident at shorter and longer-term follow-up periods. Based on available evidence, internet and mobile interventions may increase the odds of clinically meaningful PTSD symptom improvement post-treatment among civilian but not military populations. We have low confidence in these findings based on study methodological limitations, imprecision, and moderate inconsistency.

Findings that internet and mobile interventions for PTSD may have limited benefits in military populations are consistent with prior research that has shown that PTSD can be less responsive to treatment in military populations compared with civilians. However, differences in study designs and intervention characteristics limit our ability to make strong conclusions about the effectiveness or ineffectiveness of the interventions among Veterans and active duty military personnel. Future studies might explore whether internet and mobile resources have a beneficial role in supporting the established VA clinical pathway for PTSD, for example to improve treatment adherence or facilitate at-home activities that reinforce principles and practices introduced during in-person therapy.

We further explored how intervention and study factors may impact treatment effectiveness. Research has shown that integrating therapist involvement in digital interventions increases treatment effectiveness. Our results are consistent with this finding and indicated that direct facilitation had the largest benefits on treatment outcomes, followed by minimal facilitation. Interventions with no active provider support showed the least benefit for both depression and PTS severity. In one large civilian trial (N = 196), trauma-focused iCBT with a high level of direct therapeutic support (avg of 3.5 hours/participant) was non-inferior to an established face-to-face PTSD treatment for treatment-naïve patients. Exploring the appropriate level of therapeutic support (who and how much) is an important consideration in any implementation effort and should take into account the targeted population and anticipated reach of the intervention, desired effectiveness, and available health system resources.

Trauma-focused CBT treatments for PTSD are recommended as first-line treatments in clinical practice guidelines based on the current evidence. Only 4 of the 13 included studies on a military sample evaluated a trauma-focused CBT. Two of these were based on PE<sup>60,61</sup> and 2 utilized approaches based on written exposure therapy (WET). Most of these studies included a small sample size and had high drop-out rates or low treatment engagement rates. Across all 4 studies, there were nonsignificant differences on PTSD severity between treatment arms at post-treatment. In comparison, over 60% of the civilian studies evaluated a trauma-focused CBT. In addition to written exposure paradigms, these treatments also included several iCBT interventions that incorporated multiple

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trauma-focused treatment components (*ie*, in vivo and imaginal exposure; cognitive restructuring, grounding and relaxation exercises). Our subgroup analyses did not show that inclusion of written exposure contributed to improved treatment effectiveness, but there are other relevant trauma-focused treatment components worth exploring in future research. Given the promising effects of iCBT in civilians, future studies on military populations may benefit from incorporating similar treatment approaches. Further, none of the trauma-focused CBTs in the military population incorporated direct therapist involvement. Based on the promising results of civilian studies that incorporated direct facilitation with trauma-focused CBT interventions, future military trials may want to investigate whether increasing levels of provider involvement impacts treatment retention and effectiveness. Examining the cost-effectiveness of increasing provider support relative to offering traditional face-to-face trauma-focused treatments would need to be a consideration.

Treatment benefits were largest when interventions were compared with a completely inactive condition like waitlist control, and small to negligible when compared to more active treatment condition. An exception to this finding was the previously mentioned study in which iCBT with a high level of therapeutic support demonstrated non-inferiority to in-person PTSD treatment. Treatment effects were also larger against lower-intensity comparator interventions (*eg*, psychoeducation). Internet and online interventions may still play a role in increasing treatment access for those patients who are unable or unwilling to engage in a trauma-focused treatment. Future studies should explore whether internet or mobile PTSD interventions have an impact on the care pathway for patients at different levels of treatment engagement.

It is unclear whether internet and mobile interventions for caregivers and family members of adults with PTSD improve any mental health outcomes. Only 5 studies were identified and included that evaluated an internet or mobile intervention for caregivers or family members of an adult with PTSD. We examined 4 different outcomes that were assessed in at least 2 of the studies: caregiver burden, depression, anxiety, and quality of life. There was some indication that treatments may reduce caregiver burden and improve quality of life, but findings were inconsistent across individual trials. Given the study limitations, inconsistent findings across outcomes, and unknown precision, we have low confidence in these findings.

#### Limitations

There are several limitations to this review that are worth noting. Many of the included studies were small pilot trials testing the feasibility and acceptability of the online intervention and were likely inadequately powered to detect all but the largest treatment effects. There were only 4 military studies that evaluated a trauma-focused CBT, and these treatments were based on specific trauma treatments. Thus, we are unable to conclude whether our findings would generalize to other forms of trauma-focused iCBT interventions. Most studies used self-assessments to determine PTSD status and treatment outcomes rather than clinician-administered measures. Inclusion criteria in many studies did not require a full PTSD diagnosis and so the included sample often included participants with subthreshold PTSD symptoms. Although most studies included Veterans in their samples, a substantial proportion of participants were treatment-seeking White females, which may limit the applicability of findings to the VA population.



### **FUTURE RESEARCH**

Recommendations for future research on internet and mobile interventions for PTSD include the following:

- Evaluate whether trauma-focused iCBTs that integrate direct therapeutic support increase treatment retention and effectiveness for military populations. Examining the cost-effectiveness of increasing provider support relative to offering traditional face-to-face trauma-focused treatments would need to be a consideration.
- Examine whether iCBTs may be differentially effective for specific military populations. For instance, do internet interventions for treatment-naïve veterans with less complex symptom presentations demonstrate better results?
- Explore whether internet and mobile resources have a beneficial role in supporting the established VA clinical pathway for PTSD, for example to improve treatment adherence or facilitate at-home activities that reinforce principles and practices introduced during in-person therapy.
- Characterize factors that influence Veteran engagement in internet and mobile interventions, such as technology literacy or internet access, and evaluate strategies to maintain adherence.
- Evaluate the appropriate level of therapeutic training and specific competencies necessary for providers to successfully support patient engagement in iCBTs.
- Examine components of internet and mobile interventions to identify whether certain traumafocused CBT interventions have a greater influence on treatment outcomes.

### CONCLUSIONS

Internet and mobile interventions for PTSD have the potential to expand access to PTSD treatments for adults with PTSD and their caregivers. The current review examined the effectiveness of these digital treatments and explored treatment factors that may impact implementation considerations. Results indicated that civilians may experience moderate benefits from these interventions at post-treatment, but military populations experience small to negligible benefits on PTSD and depression outcomes. Treatment effects for both populations are not sustained at shorter and longer-term follow-up periods. Consistent with previous research, level of facilitation could be a key factor in the effectiveness of internet and mobile interventions for PTSD. Internet and mobile interventions do not appear to benefit family members of adults with PTSD. Currently, available evidence does not support the use of internet and mobile interventions as a replacement for first-line, in-person treatments for PTSD. Future studies could explore whether internet and mobile resources have a beneficial role in supporting the established VA clinical pathway for PTSD, including whether they improve treatment engagement for Veterans who are unable or unwilling to engage in trauma-focused therapies.



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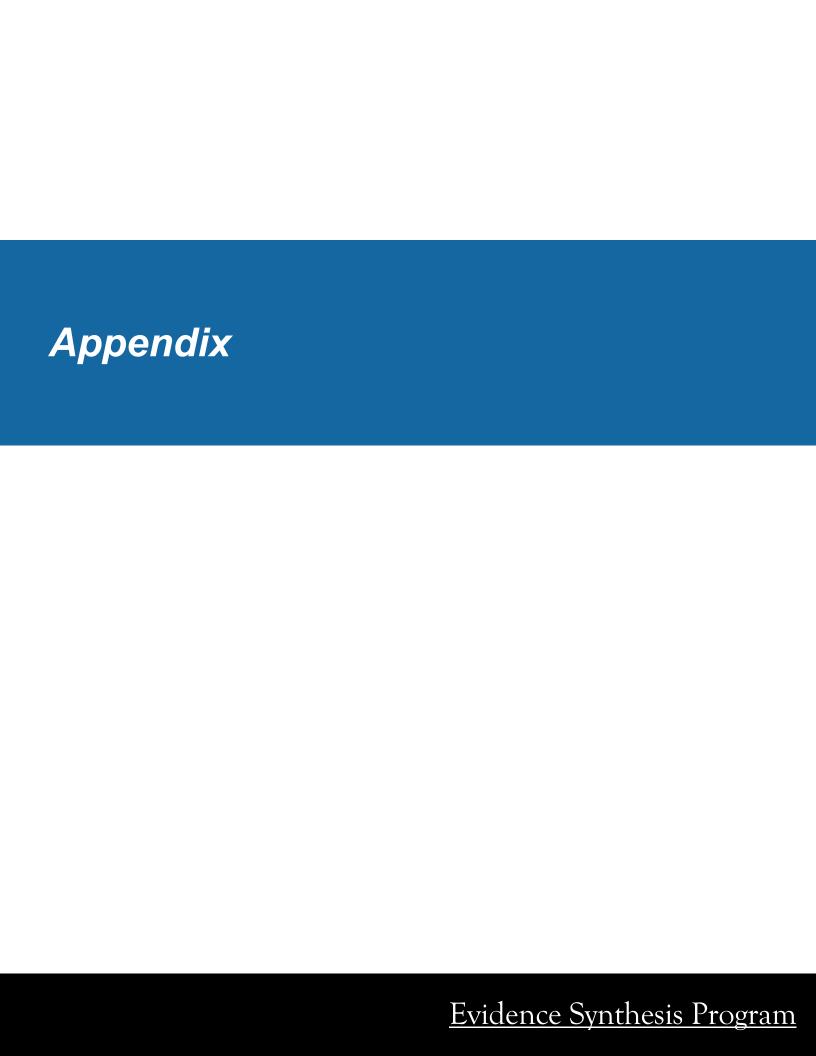


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# **SEARCH STRATEGIES**

| Search Date: 10/04/23   |   | Search Statement   | Results |
|---|---|--|---------|
| MEDLINE  Ovid MEDLINE(R) and  | 1 | Stress Disorders, Post-Traumatic/ or (((post-trauma* or posttrauma) adj3 (disorder* or neuros* or psychos* or stress* or symptom*)) or PTSD).ti,ab,kw.   | 61613   |
| Epub Ahead of Print, In-<br>Process, In-Data-Review<br>& Other Non-Indexed<br>Citations and Daily 1946<br>to October 03, 2023 | 2 | exp Telemedicine/ or Therapy, Computer Assisted/ or Internet/ or Internet-Based Intervention/ or exp Cell Phone/ or Mobile Applications/ or (electronic health or ehealth or e-health or digital health or mobile health or mhealth or m-health or ecounsel* or e-counsel* or etherap* or e-therap* or computer* or phone* or mobile* or internet* or online* or web-based or web-deliver* or app or apps or app-based or app-deliver* or application-based or application-deliver* or text or texting or text-based or text-deliver* or asynchronous).ti,ab,kw. | 1050854 |
|   | 3 | 1 and 2  | 4141    |
|   | 4 | (adolescen* or child* or infant* or pediatric* or paediatric* or PICU).ti,ab,kw.   | 2385079 |
|   | 5 | 3 not 4  | 3447    |
|   | 6 | limit 5 to English language  | 3391    |
| <b>PsycINFO</b> 1967 to September   | 1 | Posttramatic Stress Disorder/ or (((post-trauma* or posttrauma) adj3 (disorder* or neuros* or psychos* or stress* or symptom*)) or PTSD).ti,ab,id.   | 59114   |
| Week 4 2023   | 2 | exp Computer Assisted Therapy/ or Internet/ or exp Mobile Devices/ or exp Mobile Applications/ or (electronic health or ehealth or e-health or digital health or mobile health or mhealth or m-health or ecounsel* or e-counsel* or etherap* or computer* or phone* or mobile* or internet* or online* or web-based or web-deliver* or app or apps or app-based or app-deliver* or application-based or application-deliver* or text or texting or text-based or text-deliver* or asynchronous).ti,ab,id.  | 390142  |
|   | 3 | 1 and 2  | 3854    |
|   | 4 | (adolescen* or child* or infant* or pediatric* or paediatric* or PICU).ti,ab,id.   | 959997  |
|   | 5 | 3 not 4  | 3086    |
|   | 6 | limit 5 to English language  | 2902    |
| CCRCT: Cochrane<br>Central Register of  | 1 | MeSH descriptor: [Stress Disorders, Post-Traumatic] this term only   | 3701    |
| Controlled Trials   | 2 | (((post-trauma* or posttrauma*) NEAR/3 (disorder* or neuros* or psychos* or stress* or symptom*)) or PTSD):ti,ab,kw  | 8502    |
| Issue 10 of 12, October 2023  | 3 | #1 or #2   | 8502    |
|   | 4 | MeSH descriptor: [Telemedicine] explode all trees  | 4293    |
|   | 5 | MeSH descriptor: [Therapy, Computer-Assisted] this term only   | 1480    |
| •   | 6 | MeSH descriptor: [Internet] this term only   | 5193    |
| •   | 7 | MeSH descriptor: [Internet-Based Intervention] this term only  | 568     |
| •   | 8 | MeSH descriptor: [Cell Phone] explode all trees  | 3166    |
|   | 9 | MeSH descriptor: [Mobile Applications] this term only  | 1601    |



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# STUDIES EXCLUDED DURING FULL-TEXT SCREENING

| Citation  | Exclude Reason                 |
|---|--------------------------------|
| ACTRN12606000401550. The efficacy of an Internet-based therapy (Interapy) for posttraumatic stress: a randomized controlled trial. Published online September 13, 2006. https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12606000401550  | Ineligible publication type    |
| ACTRN12610000988055. The PTSD Program: a randomized controlled trial of an internet based education program for post-traumatic stress disorder. Published online November 16, 2010.   | Ineligible publication type    |
| https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12610000988055  |                                |
| ACTRN12611000951954. Sino-Swiss Internet-based intervention for Posttraumatic Stress Disorder project. Published online May 9, 2011. <a href="https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02433400/full">https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02433400/full</a>                                    | Ineligible setting             |
| ACTRN12611000989943. A comparison of Internet-based Cognitive Behavioural Therapy for Posttraumatic Stress Disorder with and without exposure: a randomized controlled trial. Published online September 16, 2011. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01835812/full   | Ineligible publication type    |
| ACTRN12616000956404. Internet-based intervention for Posttraumatic Stress Disorder (PTSD) in soldiers: exploring mechanisms of treatment outcome. Published online July 20, 2016. <a href="https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=370924">https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=370924</a> | Ineligible publication type    |
| Allen AR, Newby JM, Smith J, Andrews G. Internet-based cognitive behavioural therapy (iCBT) for posttraumatic stress disorder versus waitlist control: study protocol for a randomised controlled trial. Trials. 2015;16(101263253):544.  | Ineligible publication type    |
| Alon Y, Azriel O, Pine D, Bar-Haim Y. A randomized controlled trial of supervised remotely-delivered attention bias modification for posttraumatic stress disorder. Psychological Medicine. 2022.   | Ineligible intervention        |
| Bahena S. Efficacy of a mobile application among a sample of veterans with symptoms of post-traumatic stress disorder. Dissertation Abstracts International: Section B: The Sciences and Engineering. 2016;77(2-B(E)):No-Specified.   | Full text<br>unavailable       |
| Barrett MC. Beta-testing of an interactive multimedia computer program of exposure therapy for PTSD. Dissertation Abstracts International: Section B: The Sciences and Engineering. 2019;80(8-B(E)):No-Specified.   | Ineligible<br>comparator       |
| Bartel A. Examining change in objective and subjective neurocognitive performance following a randomized online trauma intervention. 2021;82.   | Full text<br>unavailable       |
| Bauer A, Amspoker AB, Fletcher TL, et al. A Resource Building Virtual Care Programme: improving symptoms and social functioning among female and male rural veterans. European journal of psychotraumatology. 2021;12(1):1860357.   | Ineligible<br>intervention     |
| Bedford LA, Dietch JR, Taylor DJ, Boals A, Zayfert C. Computer-Guided Problem-Solving Treatment for Depression, PTSD, and Insomnia Symptoms in Student Veterans: A Pilot Randomized Controlled Trial. Behavior therapy. 2018;49(5):756-767.   | Ineligible<br>population       |
| Belleville G, Lebel J, Ouellet MC, et al. Resilient - An online multidimensional treatment to promote resilience and better sleep: a randomized controlled trial. 2019;64:S214-S215.  | Ineligible<br>publication type |
| Belleville G, Ouellet M-C, Bekes V, et al. Efficacy of a Therapist-Assisted Self-Help Internet-Based Intervention Targeting PTSD, Depression, and Insomnia Symptoms After a Disaster: A Randomized Controlled Trial. Behavior therapy. 2023;54(2):230-246.  | Ineligible population          |
| Benight CC, Shoji K, Yeager CM, Weisman P, Boult TE. Predicting Change in Posttraumatic Distress Through Change in Coping Self-Efficacy After Using the My Trauma Recovery eHealth Intervention: Laboratory Investigation. JMIR mental health. 2018;5(4):e10309.  | Ineligible<br>population       |



| Citation  | Exclude Reason              |
|---|-----------------------------|
| Berkel DN. A randomized controlled trial of a brief online mindfulness intervention for PTSD and chronic pain. Dissertation Abstracts International: Section B: The Sciences and Engineering. 2022;83(11-B):No-Specified.   | Full text<br>unavailable    |
| Bisson JI, Kitchiner NJ, Lewis C, Roberts NP. Guided, internet-based interventions for post-traumatic stress disorder. The lancet Psychiatry. 2023;10(8):577-579.   | Ineligible publication type |
| Bomyea J. Evaluating the effect of a novel cognitive training program on ptsd symptoms. Dissertation Abstracts International: Section B: The Sciences and Engineering. 2015;75(12-B(E)):No-Specified.   | Full text<br>unavailable    |
| Bragesjo M, Arnberg FK, Sarnholm J, Olofsdotter Lauri K, Andersson E. Condensed internet-delivered prolonged exposure provided soon after trauma: A randomised pilot trial. Internet interventions. 2021;23(101631612):100358.  | Ineligible<br>population    |
| Brief DJ, Rubin A, Keane TM, et al. Web intervention for OEF/OIF veterans with problem drinking and PTSD symptoms: a randomized clinical trial. Journal of consulting and clinical psychology. 2013;81(5):890-900.  | Ineligible population       |
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## **UNDERWAY STUDIES**

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## **RISK OF BIAS ASSESSMENTS**

# RANDOMIZED CONTROLLED TRIALS (ROB-2)

| Trial Name or<br>Author Year | Bias from randomization process  | Bias from deviation<br>from intended<br>interventions<br>(Assignment)                                 | Bias from deviation<br>from intended<br>interventions<br>(Adherence)  | Bias from<br>missing<br>outcome data  | Bias in measurement of outcome   | Bias in selection of reported result   | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|------------------------------|--|---|---|---|--|--|---|
| Acosta 2017                  | Some concerns  | Low   | High  | Some concerns   | High   | Low  | High  |
|                              | Permuted block randomization based on diagnoses. Allocation concealment not described. No significant baseline differences between groups. | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | 38.3% of treatment group completed all modules. Greater # lost to follow-up in treatment group than TAU only group. Analysis included all randomized participants. Both groups had access to usual VA primary care services and groups did not differ in amount of care received. Psychotropic medication use not reported. | All randomized participants included in analysis (ITT), but methods of handling missing data not described.   | Combination of clinician-administered and self-report measures that rely on participant report of symptoms. Participants were not blind to group assignment and comparison condition was inactive. Outcome measurement did not differ between groups. Validated outcome measures used. | Primary outcomes<br>specified in<br>protocol were<br>reported.   |   |
| Allen 2022                   | Low  | Low   | Some concerns   | Some concerns   | High   | Some concerns  | High  |
|                              | 1:1 random allocation conducted by an independent individual. No significant baseline differences between groups.                          | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | 66.7% of treatment group completed all modules. Similar # withdrawals between groups. Both groups could not be currently receiving PTSD treatment and had to have stable medication regimen. Psychotropic medication use not reported.  | ITT analysis does not include participants who withdrew or didn't complete baseline assessment (4 in treatment group, 5 in waitlist). Missing data handled with model-based imputation (maximum likelihood estimation). | Outcomes were self-<br>report measures.<br>Participants were not<br>blind to group<br>assignment and<br>comparison condition<br>was inactive. Outcome<br>measurement did not<br>differ between groups.<br>Validated outcome<br>measures used.  | 6-month outcomes<br>not reported;<br>some secondary<br>outcomes of<br>interest not<br>reported (Sheehan<br>Disability Scale,<br>WHODAS-II) |   |



| Trial Name or<br>Author Year | Bias from<br>randomization<br>process   | Bias from deviation<br>from intended<br>interventions<br>(Assignment)   | Bias from deviation<br>from intended<br>interventions<br>(Adherence)  | Bias from<br>missing<br>outcome data   | Bias in measurement of outcome   | Bias in selection of reported result                   | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|------------------------------|---|---|---|--|--|--|---|
| Andersson 2021               | Low   | Low   | High  | Low  | High   | Some concerns  | High  |
|                              | Computer-generated randomization conducted by an independent individual. No baseline differences reported.  | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention.   | 18.8% of treatment group completed all modules. 15.6% dropout in treatment group and 3.1% in control group. Both groups could not be currently receiving psychological treatment. Psychotropic medication use not reported. | All randomized participants included in ITT analyses. Missing data handled with model-based imputation.  | Combination of clinician-administered and self-report measures that rely on participant report of symptoms. Participants were not blind to group assignment and comparison condition was inactive. Outcome measurement did not differ between groups. Validated outcome measures used. | No protocol<br>identified                              |   |
| Berdard-Gilligan<br>2022     | High  | Low   | Some concerns   | Unclear  | Some concerns  | Some concerns  | High  |
|                              | Randomization was likely appropriate and concealed, but baseline symptoms on the primary outcomes significantly differed in Wave 1 suggesting different levels of sx severity between groups. | Intervention groups were similar (only the content of the texts differed) and it is unclear whether participants were notified or aware of group assignment. No reported deviations from intended intervention. | Co-interventions was just included as a binary outcome and there was not exclusion criteria about current treatments.   | A small number of participants were not included in analysis. Investigators did not provide details about these participants or why they were not analyzed.                                  | condition was used.<br>Outcome measurement   | The study was not pre-registered.                      |   |
| Bedford 2023                 | Low   | Low   | Low   | Low  | Some concerns  | Low  | Some concerns   |
|                              | Computer-generated randomization within the online survey system. No baseline differences reported.   | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention.   | Single session intervention; appears all participants completed the session. No information provided on receipt of concurrent therapy. 53.3 % reported taking psychotropic medications, but % for each group not provided.  | 23.7% int. vs<br>27.3% control<br>without follow-up<br>assessment. All<br>randomized<br>participants<br>included in ITT<br>analyses. Missing<br>data handled with<br>multiple<br>imputation. | Outcomes were self-<br>report measures. Participants were not<br>blind to group<br>assignment, but active<br>comparison condition<br>was used. Outcome<br>measurement did not<br>differ between groups.<br>Validated outcome<br>measures used.   | Outcomes<br>specified in<br>protocol were<br>reported. |   |



| Trial Name or<br>Author Year | Bias from<br>randomization<br>process   | Bias from deviation<br>from intended<br>interventions<br>(Assignment)                                 | Bias from deviation<br>from intended<br>interventions<br>(Adherence)   | Bias from<br>missing<br>outcome data   | Bias in measurement of outcome  | Bias in selection of reported result                   | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|------------------------------|---|---|--|--|---|--|---|
| Bisson 2022                  | Low   | Low   | Some concerns  | Low  | Some concerns   | Low  | Some concerns   |
|                              | Computer-generated allocation sequence conducted by a data manager who emailed allocation to the trial manager. Control group had higher level of education.  | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | 79.4% of participants in the iCBT-TF group and 55.6% in the face-to-face CBT-TF group met the a priori definition of full adherence, but definitions of adherence were different for each group. Both groups could not be currently receiving psychological treatment and had to have stable medication regimen. Psychotropic medication use not reported. | 71-74% completed follow-up. All randomized participants included in ITT analyses. Missing data handled with multiple imputation. | Combination of clinician-administered and self-report measures that rely on participant report of symptoms. Participants were not blind to group assignment, but an active comparison condition was used. Outcome measurement did not differ between groups. Validated outcome measures used. | Outcomes<br>specified in<br>protocol were<br>reported. |   |
| Clausen 2019                 | High  | Low   | Some concerns  | High   | Some concerns   | Low  | High  |
|                              | First 13 participants were randomly assigned by the lab manager (unclear method). Other research staff were blind to allocation sequence. Last 7 participants were assigned to treatment group (not randomly). Baseline differences not reported. | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | 57% in intervention group and 50% in placebo group received full training. Required stable dose of antidepressant or sleep medications (2 PTSD participants reported stable dose of antidepressants). No information on concurrent therapy.  | Completer<br>analysis<br>(analyses did not<br>include<br>withdrawals; 42%<br>int. and 50%<br>control).                           | Outcomes were self-<br>report measures.<br>Participants were not<br>blind to group<br>assignment, but active<br>comparison condition<br>was used. Outcome<br>measurement did not<br>differ between groups.<br>Validated outcome<br>measures used.   | Outcomes<br>specified in<br>protocol were<br>reported. |   |
| De Kleine 2019               | Some concerns   | Low   | Low  | Some concerns  | Some concerns   | Some concerns  | Some concerns   |
|                              | Computer- generation randomization within the online platform. The active group was significantly older than the control group and  | Participants blinded to group allocation. No reported deviations from intended intervention.          | 97% completed all treatment sessions. The number of participants receiving traumafocused therapy or psychotropic   | 61% active vs. 72% control had data at 6 months. All randomized participants were included in analyses, but unclear handling     | Outcomes were self-<br>report measures.<br>Participants appear to<br>have been blind to<br>group assignment and<br>an active comparison<br>condition was used.<br>Outcome measurement   | Unable to access trial registration                    |   |



| Trial Name or<br>Author Year | Bias from randomization process  | Bias from deviation<br>from intended<br>interventions<br>(Assignment)                                 | Bias from deviation<br>from intended<br>interventions<br>(Adherence)   | Bias from<br>missing<br>outcome data   | Bias in measurement of outcome   | Bias in selection of reported result                   | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|------------------------------|--|---|--|--|--|--|---|
|                              | reported less exposure to trauma during childhood and less violence/physical assault in adulthood.                                   |   | medications did not differ between groups.   | of missing data in<br>ITT analysis.  | did not differ between<br>groups. Validated<br>outcome measures<br>used.   |  |   |
| Engel 2015                   | Low  | Low   | Some concerns  | Low  | High   | Some concerns  | High  |
|                              | Centrally conducted random permuted blocking scheme. Does not state how sequence was generated. No significant baseline differences. | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | 35% of the treatment group completed all logins. Excluded individuals actively engaged in traumafocused treatment or with an unstable medication regimen. Psychotropic medication use not reported.                                  | 82.% had complete data. No difference in missing data between groups. All randomized participants included in ITT analyses. Missing data handled with model-based imputation.                    | Outcomes were self-<br>report measures. Participants were not<br>blind to group<br>assignment and<br>comparison condition<br>was inactive. Outcome<br>measurement did not<br>differ between groups.<br>Validated outcome<br>measures used. | No protocol<br>identified.                             |   |
| Erbes 2020                   | Some concerns  | Low   | Some concerns  | Some concerns  | High   | Low  | High  |
|                              | Details of sequence<br>generation/allocation<br>concealment not<br>reported. Baseline<br>differences not<br>reported.                | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | 56% of participants in the treatment group completed the entire course. Initiation of mental health care was an aim of the study/outcome of interest: 36% treatment group vs. 21% control. Psychotropic medication use not reported. | Completer analysis; 5 (11%) randomized participants not included in analyses (2 treatment group participants that did not initiate the treatment, 3 participants missing data at posttreatment). | Outcomes were self-<br>report measures. Participants were not<br>blind to group<br>assignment and<br>comparison condition<br>was inactive. Outcome<br>measurement did not<br>differ between groups.<br>Validated outcome<br>measures used. | Outcomes<br>specified in<br>protocol were<br>reported. |   |
| Fonzo 2019                   | Low  | Low   | Some concerns  | Some concerns  | High   | Low  | High  |
|                              | Computer-generated random sequence; allocation was concealed prior to randomization of each participant. No                          | Participants blinded to group allocation. No reported deviations from intended intervention.          | Rates of adherence to completing the minimal adequate dose were 77% in the active arm and 75% in the control arm. Participants could not be currently engaged in   | 35% of total<br>sample dropped<br>out. All<br>randomized<br>participants<br>included in<br>analysis; missing<br>data handled with  | Combination of clinician-administered and self-report measures that rely on participant report of symptoms. Participants were blind to group assignment and an   | Outcomes<br>specified in<br>protocol were<br>reported. |   |



| Trial Name or<br>Author Year  | Bias from randomization process  | Bias from deviation<br>from intended<br>interventions<br>(Assignment)  | Bias from deviation<br>from intended<br>interventions<br>(Adherence)   | Bias from<br>missing<br>outcome data   | Bias in measurement of outcome   | Bias in selection of reported result                   | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|-------------------------------|--|--|--|--|--|--|---|
|                               | significant baseline<br>differences.   |  | psychotherapy and, if<br>on antidepressant<br>medications, had to be<br>on a stable regimen.<br>Psychotropic<br>medication use not<br>reported.  | model-based imputation.  | active comparison condition was used, but assessors administering the CAPS were not blind to group assignment. Outcome measurement did not differ between groups. Validated outcome measures used.             |  |   |
| Gawlytta 2022                 | Low  | Low  | Some concerns  | Low  | Some concerns  | Low  | Some concerns   |
|                               | Computer-generated random sequence; performed centrally by an independent individual. Duration of mechanical ventilation among ventilated patients greater in treatment group. | Participants blinded to group allocation. No reported deviations from intended intervention.                         | Treatment adherence unclear. Excluded patients with ongoing therapeutic treatment. Psychotropic medication use not reported.   | Up to 15% missing data. All randomized participants included in ITT analyses. Missing data handled with multiple imputation.   | Outcomes were self-<br>report measures.<br>Participants were blind<br>to group assignment.<br>Outcome measurement<br>did not differ between<br>groups. Validated<br>outcome measures<br>used.                  | Outcomes<br>specified in<br>protocol were<br>reported. |   |
| Hensler 2022;<br>Hensler 2023 | Low  | Some concerns  | Some concerns  | Low  | High   | Low  | High  |
|                               | Computer-generated allocation sequence; sequence generated by an external statistician; allocation concealed from research team. Baseline differences not reported.            | Blinding of participants not feasible. At follow-up, 4 participants on the waitlist reported having used PTSD Coach. | 19% participants with access to the app stated that they had not used PTSD Coach. 7 participants (app access=4; waitlist=3) reported using a self-management app other than PTSD Coach. Participants started psychological treatment (app access=10; waitlist=10), changed their medication (app access=8; waitlist=10), or started a new medication (app access=10; waitlist=8). 26 people sought professional help | 77-85% had complete data. All randomized participants included in ITT analyses. Missing data handled with multiple imputation. | Outcomes were self-report measures. Participants were not blind to group assignment and comparison condition was inactive. Outcome measurement did not differ between groups. Validated outcome measures used. | Outcomes<br>specified in<br>protocol were<br>reported. |   |



| Trial Name or<br>Author Year | Bias from randomization process   | Bias from deviation<br>from intended<br>interventions<br>(Assignment)  | Bias from deviation<br>from intended<br>interventions<br>(Adherence)   | Bias from<br>missing<br>outcome data  | Bias in measurement of outcome  | Bias in selection of reported result | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|------------------------------|---|--|--|---|---|--------------------------------------|---|
|                              |   |  | related to their trauma (app access=17; waitlist=9).   |   |   |                                      |   |
| Hirai 2020                   | Some concerns   | Some concerns  | Some concerns  | High  | Some concerns   | Some concerns                        | High  |
|                              | Only states that participants were randomly assigned. No significant baseline differences.  | Unclear whether participants were blind to group assignment (interventions were similar). No reported deviations from intended intervention. | 34% of participants never started the first writing session. 48% completed intervention and follow-up assessments (only completers were analyzed). Cointerventions not reported.                                       | Completer<br>analysis; only<br>includes 48% of<br>participants<br>randomized.   | Outcomes were self-<br>report measures. Unclear whether participants were blind to group assignment, but active comparison condition was used. Outcome measurement did not differ between groups. Validated outcome measures used.            | No protocol identified.              |   |
| Ivarsson 2014                | Low   | Low  | Some concerns  | Low   | High  | Some concerns                        | High  |
|                              | Computer-generated randomization sequence; randomization conducted by an independent individual. No significant baseline differences. | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention.  | 68% completed a minimum dose as defined by investigators. 22.6% of intervention group and 29% of waitlist were taking psychotropic medication at baseline. Excluded participants with ongoing psychological treatment. | Response rate<br>87%. All<br>randomized<br>participants<br>included in<br>analysis; missing<br>data handled with<br>model-based<br>imputation.  | Outcomes were self-<br>report measures.<br>Participants were not<br>blind to group<br>assignment and<br>comparison condition<br>was inactive. Outcome<br>measurement did not<br>differ between groups.<br>Validated outcome<br>measures used. | No protocol identified.              |   |
| Knaevelsrud 2007             | Some concerns   | Low  | Some concerns  | Low   | High  | Some concerns                        | High  |
|                              | Computer-<br>generation<br>randomization;<br>allocation<br>concealment not<br>described. No<br>significant baseline<br>differences.   | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention.  | 16% did not complete treatment (dropped out), but no information provided on adherence. Participants could not be receiving treatment elsewhere. Psychotropic medication use not reported.                             | 84% completed follow-up. Analyses included all randomized participants, but missing data was handled with simple imputation of baseline scores. | Outcomes were self-<br>report measures.<br>Participants were not<br>blind to group<br>assignment and<br>comparison condition<br>was inactive. Outcome<br>measurement did not<br>differ between groups.  | Unable to access trial registration. |   |



| Trial Name or<br>Author Year | Bias from<br>randomization<br>process   | Bias from deviation<br>from intended<br>interventions<br>(Assignment)                                 | Bias from deviation<br>from intended<br>interventions<br>(Adherence)  | Bias from<br>missing<br>outcome data  | Bias in measurement of outcome   | Bias in selection of reported result | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|------------------------------|---|---|---|---|--|--------------------------------------|---|
|                              |   |   |   |   | Validated outcome measures used.   |                                      |   |
| Krupnick 2017                | High  | Low   | High  | High  | High   | Some concerns                        | High  |
|                              | No detail provided on sequence generation or allocation concealment methods. Intervention group had significantly lower baseline intrusion and hyperarousal symptoms, and lower PCL total scores than those in the TAU group. | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | No information provided on adherence to intervention. 4 TAU pts began and 1 completed a course of CPT during the course of the study. The average number of psychosocial treatment sessions was 2.44 for TAU and 0.78 for intervention group. Antidepressant medication use was similar between groups. | 25% in treatment group and 67% of TAU who completed the baseline assessment completed the follow-up assessment. ITT analyses included participants who completed the baseline assessment (did not include 3 randomized participants). Missing data was handled with model-based imputation. | Outcomes were self-report measures. Participants were not blind to group assignment and comparison condition was inactive. Outcome measurement did not differ between groups. Validated outcome measures used.   | No protocol identified.              |   |
| Kuhn 2017                    | Low   | Low   | Some concerns   | Low   | High   | Some concerns                        | High  |
|                              | Computer-generated randomization sequence; randomization conducted by the study coordinator. Significant baseline differences in psychosocial functioning scores only.  | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | Intervention was access to the app; do not report how many participants in the intervention group used the app. Participants could not currently be in PTSD treatment. Psychotropic medication use not reported.  | 82% int. and 90% control responded at 3 months. All randomized participants included in ITT analyses. Missing data handled with multiple imputation.  | Outcomes were self-report measures. Participants were not blind to group assignment and comparison condition was inactive. Outcome measurement did not differ between groups. Validated outcome measures used with exception of PTSD coping self-efficacy. | No protocol identified.              |   |
| Lange 2003                   | Low   | Low   | Some concerns   | High  | High   | Low                                  | High  |
|                              | Computer-generated randomization sequence. Allocation   | Blinding of participants<br>not feasible. No<br>reported deviations                                   | 36% in intervention group did not complete treatment; no additional   | Only treatment completers were asked to complete  | Outcomes were self-<br>report measures.<br>Participants were not   | Outcomes specified in                |   |



| Trial Name or<br>Author Year | Bias from randomization process  | Bias from deviation<br>from intended<br>interventions<br>(Assignment)   | Bias from deviation<br>from intended<br>interventions<br>(Adherence)   | Bias from<br>missing<br>outcome data   | Bias in measurement of outcome  | Bias in selection of reported result  | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|------------------------------|--|---|--|--|---|---|---|
|                              | concealment not<br>described. No<br>significant baseline<br>differences.                             | from intended intervention.   | information provided on<br>adherence. Participants<br>could not currently be in<br>treatment elsewhere.<br>Psychotropic<br>medication use not<br>reported.   | follow-up assessment; 28% of randomized participants did not have follow-up data. Repeated main analysis with ITT sample (all participants randomized); missing data was handled with simple imputation of baseline values.  | blind to group<br>assignment and<br>comparison condition<br>was inactive. Outcome<br>measurement did not<br>differ between groups.<br>Validated outcome<br>measures used.   | protocol were reported.   |   |
| Larsen 2019                  | Some concerns  | Some concerns   | Some concerns  | High   | Some concerns   | Low   | High  |
|                              | Only states that participants were randomly assigned. No significant baseline differences.           | Appears that participants were blind to group assignment (interventions were similar). No reported deviations from intended intervention. | 72% of randomized participants overall were treatment completers (completed at least 80% of training sessions). There was no difference between groups on average number of completed training sessions. All but 3 participants (all in intervention group) were receiving other treatments. 3 participants in each group had a notable change in treatment status during the study. | Only treatment completers were asked to complete follow-up assessment; 28% of randomized participants did not have follow-up data. Repeated main analysis with ITT sample (all participants randomized); missing data was handled with simple imputation of baseline values. | Outcomes were self-report measures. Participants appear to have been blind to group assignment and an active comparison condition was used. Outcome measurement did not differ between groups. Validated outcome measures used. | Outcomes<br>specified in<br>protocol were<br>reported.                                      |   |
| Lehavot 2021                 | Low  | Low   | Some concerns  | Low  | High  | Some concerns   | High  |
|                              | Design paper specifies computer-generated randomization sequence. Baseline differences not reported. | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention.                                     | The intervention group had a lower proportion of treatment completers than the phone monitoring group (76% vs 96%); completion defined as >50% sessions. Participants  | Over 80% randomized completed all follow-up assessments. Analyses included all randomized participants (ITT);  | Outcomes were self-<br>report measures.<br>Participants were not<br>blind to group<br>assignment and<br>comparison condition<br>was inactive. Outcome<br>measurement did not  | Secondary<br>outcomes<br>specified were not<br>reported<br>(depression,<br>quality of life) |   |



| Trial Name or<br>Author Year | Bias from randomization process   | Bias from deviation<br>from intended<br>interventions<br>(Assignment)                                 | Bias from deviation<br>from intended<br>interventions<br>(Adherence)   | Bias from<br>missing<br>outcome data  | Bias in measurement of outcome   | Bias in selection of reported result | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|------------------------------|---|---|--|---|--|--------------------------------------|---|
|                              |   |   | could not be currently in<br>treatment; had to have<br>stable dose of<br>medications.<br>Psychotropic<br>medication use not<br>reported.   | missing data<br>handled with<br>model-based<br>imputation.  | differ between groups.<br>Validated outcome<br>measures used.  |                                      |   |
| Lewis 2017                   | Low   | Low   | Some concerns  | Low   | High   | Some concerns                        | High  |
|                              | Randomization sequence generated by an independent statistician. Allocation was concealed with sealed, opaque envelopes. Baseline differences not reported.                     | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | 36% in treatment group completed all 8 modules, 72% completed more than half. Participants could not be currently in treatment; had to have stable dose of medications. Psychotropic medication use not reported.  | 71% in treatment group and 81% in waitlist completed post-treatment assessment. Analysis includes all randomized participants (ITT); missing data handled with multiple imputation. | Combination of clinician-administered and self-report measures that rely on participant report of symptoms. Participants were not blind to group assignment and comparison condition was inactive. Outcome measurement did not differ between groups. Validated outcome measures used. | No protocol identified.              |   |
| Littleton 2016               | Some concerns   | Low   | High   | Some concerns   | High   | Some concerns                        | High  |
|                              | Randomization<br>sequence generated<br>with a computerized<br>coin flip. No<br>information provided<br>on allocation<br>concealment. No<br>significant baseline<br>differences. | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | 16% randomized did not complete baseline assessments and log in to program at least once. 16% in treatment group completed the entire program. Participants could not be currently in treatment; had to have stable dose of medications. Psychotropic medication use not reported. | 43% of treatment group and 29% of control group did not have follow-up data. ITT analyses was conducted; missing data were handled with multiple imputation.                        | Outcomes were self-report measures. Participants were not blind to group assignment and comparison condition was inactive. Outcome measurement did not differ between groups. Validated outcome measures used.   | No protocol identified.              |   |
| Litz 2007                    | Some concerns   | Low   | Some concerns  | Some concerns   | Some concerns  | Some concerns                        | Some Concerns   |
|                              | Details of sequence generation and allocation   | Blinding of participants<br>not feasible. No<br>reported deviations                                   | 73% completed treatment; no additional information on  | 31% of participants overall did not   | Combination of clinician-administered and self-report  | No protocol identified.              |   |



| Trial Name or<br>Author Year | Bias from randomization process   | Bias from deviation<br>from intended<br>interventions<br>(Assignment)                                 | Bias from deviation<br>from intended<br>interventions<br>(Adherence)  | Bias from<br>missing<br>outcome data   | Bias in measurement of outcome  | Bias in selection of reported result  | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|------------------------------|---|---|---|--|---|---|---|
|                              | concealment not<br>described. No<br>significant baseline<br>differences.  | from intended intervention.   | adherence provided. Participants could not be currently in treatment; had to have stable dose of medications. Psychotropic medication use not reported.   | complete post-<br>treatment<br>assessment. ITT<br>analysis<br>conducted, but<br>ITT group is not<br>defined; missing<br>data handled with<br>model-based<br>imputation.  | measures that rely on participant report of symptoms. Participants were not blind to group assignment, but an active comparison condition was used. Outcome measurement did not differ between groups. Validated outcome measures used.   |   |   |
| McGuire 2023                 | Low   | Low   | Some concerns   | High   | High  | Some concerns   | High  |
|                              | Computer-generated randomization sequence. Study staff remained blind to sequence until assignments were made. No significant baseline differences. | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | 63% completed all 8 sessions in the treatment condition. Veterans were not excluded if they were currently enrolled in other treatments; no information on outside treatment reported.  | Completer analysis; 67% in intervention group and 83% in control group were included in analyses. Handling of missing data not described.  | Outcomes were self-<br>report measures.<br>Participants were not<br>blind to group<br>assignment and<br>comparison condition<br>was inactive. Outcome<br>measurement did not<br>differ between groups.<br>Validated outcome<br>measures used.   | No protocol identified.   |   |
| McLean 2021                  | Some concerns   | Low   | Some concerns   | High   | Some concerns   | Low   | High  |
|                              | Block randomization; methods of sequence generation and allocation concealment not described. Baseline differences not reported.                    | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | 42% in web-PE and 81% in face-to-face control group completed all 10 sessions, but the number of sessions completed was not significantly different between groups. Excluded participants currently engaged in evidence-based treatment for PTSD. Psychotropic medication use not reported. | 53% lost to follow-up in web-PE group at post-treatment, 48% of face-to-face control. Unclear whether analyses include all randomized participants, Ns not provided; handling of missing data not described. Design paper states that all participants who provide any | Combination of clinician-administered and self-report measures that rely on participant report of symptoms. Participants were not blind to group assignment, but an active comparison condition was used. Outcome measurement did not differ between groups. Validated outcome measures used. | Not all secondary<br>outcomes<br>specified in design<br>paper reported,<br>but primary<br>outcomes are<br>reported. |   |



| Trial Name or<br>Author Year | Bias from randomization process  | Bias from deviation<br>from intended<br>interventions<br>(Assignment)                                 | Bias from deviation<br>from intended<br>interventions<br>(Adherence)  | Bias from<br>missing<br>outcome data   | Bias in measurement of outcome  | Bias in selection of reported result  | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|------------------------------|--|---|---|--|---|---|---|
|                              |  |   |   | outcome data will be included.   |   |   |   |
| McLean 2022                  | Some concerns  | Low   | Some concerns   | Low  | High  | Low   | High  |
|                              | Computer-generated randomization sequence. Randomization conducted by study RA; allocation concealment unclear. Baseline differences not reported.                             | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | There was a bug that caused one app feature to crash and was corrected halfway through the study. All received the intervention except 1 in app alone group. Unclear adherence to intervention. Co-interventions not reported.                          | 23% app alone,<br>6% app +<br>support, 19%<br>waitlist lost to<br>follow-up at<br>posttreatment. All<br>randomized<br>participants<br>included in<br>analyses (ITT);<br>missing data<br>handled with<br>model-based<br>imputation. | Outcomes were self-report measures. Participants were not blind to group assignment and comparison condition was inactive. Outcome measurement did not differ between groups. Validated outcome measures used.                                | Not all secondary<br>outcomes<br>specified in design<br>paper reported,<br>but primary<br>outcomes are<br>reported. |   |
| Miner 2016                   | Some concerns  | Low   | Some concerns   | Low  | High  | Some concerns   | High  |
|                              | Methods of sequence generation and allocation concealment not described. No significant baseline differences.  | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | No participants in treatment group reported never using the app; further adherence information not provided (intervention was access to the app only). Participants could not currently be in PTSD treatment. Psychotropic medication use not reported. | 8% in app group and 13% in waitlist did not complete posttreatment assessment. All randomized participants included in ITT analyses. Missing data handled with multiple imputation.  | Outcomes were self-<br>report measures.<br>Participants were not<br>blind to group<br>assignment and<br>comparison condition<br>was inactive. Outcome<br>measurement did not<br>differ between groups.<br>Validated outcome<br>measures used. | No protocol identified.   |   |
| Morabito 2023                | Some concerns  | Low   | Low   | Some concerns  | Some concerns   | Some concerns   | Some concerns   |
|                              | Randomization sequence generated with random number table; allocation concealment not described. Greater # of Hispanic participants in control group; higher baseline negative | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | 1 participant in the treatment group and 2 in the control group did not complete the intervention (defined as spending more than 2.5 SDs less than mean time). Stable medication regimen required; no information                                       | Excluded 3 participants who did not complete the intervention and 2 with impairing drug use during the intervention (10% of randomized participants).  | Outcomes were self-<br>report measures.<br>Participants were not<br>blind to group<br>assignment, but active<br>comparison condition<br>was used. Outcome<br>measurement did not<br>differ between groups.                                    | PANAS, TIQ,<br>LEC, PTCI not<br>mentioned in trial<br>registry. Guilt<br>mentioned in<br>registry but not<br>paper. |   |



| Trial Name or<br>Author Year | Bias from randomization process  | Bias from deviation<br>from intended<br>interventions<br>(Assignment)                                 | Bias from deviation<br>from intended<br>interventions<br>(Adherence)   | Bias from<br>missing<br>outcome data  | Bias in measurement of outcome  | Bias in selection of reported result   | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|------------------------------|--|---|--|---|---|--|---|
|                              | affect in treatment group.   |   | on other ongoing treatment.  | Missing data<br>handled with<br>model-based<br>imputation.  | Validated outcome measures used.  |  |   |
| Nieminen 2016                | Low  | Low   | Some concerns  | Some concerns   | High  | Some concerns  | High  |
|                              | Computer-generated randomization sequence; randomization conducted by independent individual. No significant baseline differences.   | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | In treatment group, 54% completed all 8 weeks of treatment and 67% completed at least four modules. Excluded individuals currently participating in psychotherapy. Required stable medication regimen. Psychotropic medication use not reported. | 64% int. vs 96% control completed interview. 86% int. vs 96% control completed questionnaire. Flow diagram shows drop-outs excluded from analysis, but table shows ITT with missing data imputed. | Outcomes were self-report measures. Participants were not blind to group assignment and comparison condition was inactive. Outcome measurement did not differ between groups. One of the self-report PTSD scales is preliminarily validated.      | No protocol identified.  |   |
| Possemato 2011               | Some concerns  | Low   | Some concerns  | Some concerns   | Some concerns   | Some concerns  | Some concerns   |
|                              | Methods of sequence generation and allocation concealment not described. Intervention group participants were significantly more likely to be separated or divorced than control participants. | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | All intervention group participants completed all 3 writing sessions. 1 in intervention group and 4 in control group sought outside treatment.   | Excluded 5 participants who received other treatment during the study period from ITT analyses. Unclear handling of missing data.   | Outcomes were self-<br>report measures.<br>Participants were not<br>blind to group<br>assignment, but active<br>comparison condition<br>was used. Outcome<br>measurement did not<br>differ between groups.<br>Validated outcome<br>measures used. | No protocol<br>identified.   |   |
| Possemato 2016               | Some concerns  | Low   | Some concerns  | Low   | Some concerns   | Some concerns  | Some concerns   |
|                              | Methods of sequence generation and allocation concealment not described. Baseline differences present  | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | All participants completed every treatment session & fidelity to treatment was high among clinicians delivering the treatment. Participants in the cliniciansupported group had  | Missing data handled with multiple imputation. All participants in the cliniciansupported group and 80% in the  | Outcomes were self-<br>report measures.<br>Participants were not<br>blind to group<br>assignment, but active<br>comparison condition<br>was used. Outcome<br>measurement did not<br>differ between groups.  | Unclear whether outcome assessors were blind to group assignment. Outcomes were self-report measures and participants were |   |



| Trial Name or<br>Author Year | Bias from<br>randomization<br>process  | Bias from deviation<br>from intended<br>interventions<br>(Assignment)                                 | Bias from deviation<br>from intended<br>interventions<br>(Adherence)  | Bias from<br>missing<br>outcome data   | Bias in measurement of outcome   | Bias in selection of reported result  | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|------------------------------|--|---|---|--|--|---|---|
|                              | in social QOL<br>scores.   |   | more days of app use compared to the self-managed group, but full usage data was not available. Participants could not be currently in mental health treatment; had to have stable dose of medications.  Psychotropic medication use not reported.  | self-managed<br>group completed<br>the posttreatment<br>assessment. ITT<br>analysis included<br>all randomized<br>participants.  | Validated outcome measures used.   | not blind to group<br>assignment.<br>Validated outcome<br>measures used.  |   |
| Possemato 2019               | Some concerns  | Low   | Some concerns   | High   | Some concerns  | Low   | High  |
|                              | Permuted block randomization; no information on methods of sequence generation or allocation concealment. No significant baseline differences. | Blinding of participants not feasible. No reported deviations from intended intervention.             | Participants in both conditions completed an average of 11 modules, but more participants completed at least 1 module in the peer support group than the self-managed group (93% vs 73%). Fidelity of peer support specialists appears to have been moderate. Participants could not be currently in mental health treatment; had to have stable dose of medications. Psychotropic medication use not reported. | Only included participants who competed follow-up assessment in analysis; did not include 33% of randomized participants. Missing data from included participants was handled with model-based imputation. | Outcomes were self-report measures. Participants were not blind to group assignment, but active comparison condition was used. Outcome measurement did not differ between groups. Validated outcome measures used. | Outcomes<br>specified in<br>protocol were<br>reported (except<br>that a different<br>version of the PCL<br>was used). |   |
| Spence 2011                  | Low  | Low   | Low   | Some concerns  | High   | Some concerns   | High  |
|                              | Computer-generated randomization sequence, conducted by an independent individual. No significant baseline differences.                        | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention. | 78% in treatment group<br>completed all lessons.<br>Participants could not<br>already be receiving<br>CBT; required stable<br>medication regimen.<br>Psychotropic   | Two control group<br>participants (10%)<br>did not begin<br>treatment and<br>were not included<br>in analyses. 9% in<br>treatment group<br>did not complete  | Outcomes were self-<br>report measures.<br>Participants were not<br>blind to group<br>assignment and<br>comparison condition<br>was inactive. Outcome<br>measurement did not                                       | No protocol identified.   |   |



| Trial Name or<br>Author Year | Bias from randomization process   | Bias from deviation<br>from intended<br>interventions<br>(Assignment)                                      | Bias from deviation<br>from intended<br>interventions<br>(Adherence)  | Bias from<br>missing<br>outcome data  | Bias in measurement of outcome  | Bias in selection of reported result  | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|------------------------------|---|--|---|---|---|---|---|
|                              |   |  | medication use not reported.  | posttreatment questionnaire. All participants who started treatment were included in analyses. Missing data were handled with simple imputation of baseline scores. | differ between groups.<br>Validated outcome<br>measures used.   |   |   |
| Spence 2014                  | Some concerns   | Low  | Low.  | Low.  | High  | Some concerns   | High  |
|                              | No details of randomization process provided. Non-exposure group was significantly older. | From protocol it appears that participants were blinded. No reported deviations from intended intervention | High rates of treatment completion; all participants started at least 1 lesson. 73% int. vs. 79% control completed all lessons. | High rates of<br>assessment<br>completion.<br>Analysis used<br>appropriate<br>methods to<br>handle missing<br>data.   | Combination of clinician-administered and self-report measures that rely on participant report of symptoms. Participants were blind to group assignment and an active comparison condition was used, but assessors administering the CAPS were not blind to group assignment. Outcome measurement did not differ between groups. Validated outcome measures used. | Protocol includes<br>PCL-C as an<br>outcome measure;<br>not reported in<br>publication. |   |
| van Stolk-Cooke<br>2023      | Some concerns   | Low  | High  | High  | Some concerns   | Low   | High  |
|                              | No details of randomization process provided. Baseline differences not reported.          | Blinding of participants<br>not feasible. No<br>reported deviations<br>from intended<br>intervention.      | Small percentage of patients used the app once. No information on co-interventions provided.                                    | High rates of missing data. Analysis were appropriate to handle missing data, but given the high rates unclear how reliable it is.                                  | Outcomes were self-<br>report measures.<br>Participants were not<br>blind to group<br>assignment, but active<br>comparison condition<br>was used. Outcome<br>measurement did not<br>differ between groups.<br>Appears not all   | Outcomes<br>specified in<br>protocol were<br>reported.                                  |   |



| Trial Name or Author Year | Bias from randomization process | Bias from deviation<br>from intended<br>interventions<br>(Assignment) | Bias from deviation<br>from intended<br>interventions<br>(Adherence) | Bias from<br>missing<br>outcome data | Bias in measurement of outcome         | Bias in selection of reported result | Overall risk of bias<br>(Low, Some concerns,<br>High) |
|---------------------------|---------------------------------|---|--|--------------------------------------|--|--------------------------------------|---|
|                           |                                 |   |  |                                      | measures used were validated measures. |                                      |   |

Abbreviations. CBT=cognitive behavioral therapy; iCBT=internet-based cognitive behavioral therapy; ITT= intent to treat; LEC=Life Events Checklist for DSM-5; PANAS=The Positive and Negative Affect Schedule Scale; PCL= PTSD Checklist; PTCI=Posttraumatic Cognitions Inventory; PTSD=posttraumatic stress disorder; PCL-C=PTSD Checklist – Civilian Version; QoL=quality of life; TAU=treatment as usual; TIQ=therapy impact questionnaire; webPE=web-prolonged exposure.



## NONRANDOMIZED COMPARISON STUDIES (ROBINS-I)

| Study Name or<br>Author Year | Bias due to confounding  | Selection bias   | Bias in classification of interventions  | Bias due to<br>departures from<br>intended<br>interventions   | Bias due to measurement of outcomes  | Bias due to<br>missing data   | Bias in the selection of reported results   | Overall risk of bias<br>(Low, Moderate,<br>Serious, Critical, No<br>Information) |
|------------------------------|--|--|--|---|--|---|---|--|
| McCall 2023                  | Low  | Low  | Unclear  | Unclear   | Unclear  | Unclear   | Low   | Unclear  |
|                              | Non-randomized preference trial. Prospective clients of an online iCBT service for public service personnel who reported clinically significant PTSD symptoms were offered choice of treatment.  | Intervention<br>groups were<br>clearly defined,<br>prior to<br>participants<br>receiving<br>treatment. | 69% of participants accessed at least 4/5 lessons. Completion rates were similar for both groups. Excluded participants currently receiving another psychological treatment. No information on psychotropic medication use provided. | Unclear whether outcome assessors were blind to group assignment, but outcomes were self-report measures and participants were not blind to group assignment. | No significant differences between groups at baseline except for depression symptom severity. Unclear whether this difference was controlled for in analyses.  | Posttreatment assessments were completed by 65% of randomized participants. Participants who started the intervention were included in analyses (92%). Missing data was handled with multiple imputation. | Primary outcomes and most secondary outcomes specified in protocol were reported. Publication is preliminary results of ongoing study and states that remaining data will be published in the future. |  |
| Wiltsey Stirman<br>2021      | Low  | Low  | Unclear  | Unclear   | Unclear  | Unclear   | Unclear   | Unclear  |
|                              | Open trial participants were Talkspace clients with probable PTSD at intake. Only included individuals who completed PCL assessment at least twice in matched comparison. Comparison group was matched Talkspace clients who did not receive intervention who were seen in a similar timeframe | Intervention<br>groups were<br>clearly defined.  | 64% of participants in CPT-Text intervention completed all 12 modules. Word count (estimate of engagement) was significantly higher for the TAU Talkspace group. Cointerventions not reported.                                       |   | Control group selected via propensity matching on baseline PTSD symptom severity and time in treatment. Matching did not take into account demographic characteristics. Demographics appear similar between groups, but race not reported for control group. Other potential confounding variables not examined. | 82% of CPT-Text participants who had completed PCL assessments at least twice were matched and included in analyses. Method of handling missing data is not described.                                    | The study was not pre-registered.   |  |



|                                  | Study Name or<br>Author Year | Bias due to confounding | Selection bias | Bias in<br>classification of<br>interventions | Bias due to<br>departures from<br>intended<br>interventions | Bias due to<br>measurement of<br>outcomes | Bias due to missing data | Bias in the selection of reported results | Overall risk of bias<br>(Low, Moderate,<br>Serious, Critical, No<br>Information) |
|----------------------------------|------------------------------|-------------------------|----------------|---|---|---|--------------------------|---|--|
| and had similar baseline scores. |                              |                         |                |   |   |   |                          |   |  |

Abbreviations. CPT=cognitive processing therapy; iCBT=internet-based cognitive behavioral therapy; PCL=PTSD Checklist; PTSD=posttraumatic stress disorder; TAU=treatment as usual.

## PRE-POST STUDIES (ROBINS-I)

| Study Name or<br>Author Year | Bias due to confounding   | Selection bias  | Bias in classification of interventions   | Bias due to<br>departures from<br>intended<br>interventions   | Bias due to measurement of outcomes   | Bias due to<br>missing data   | Bias in the selection of reported results   | Overall risk of bias<br>(Low, Moderate,<br>Serious, Critical, No<br>Information) |
|------------------------------|---|---|---|---|---|---|---|--|
| Crenshaw 2023                | High  | Low   | Low   | Unclear   | Unclear   | Unclear   | Low   | High   |
|                              | Examined differences between 2 study samples but did not account for potential confounders. | Secondary analysis of data from 2 prospective studies; included all participants from those studies (except for 1 that did not start the study and wasn't included in analyses for that study). | Baseline and<br>follow-up time<br>points aligned<br>with beginning<br>and end of<br>intervention; not<br>influenced by<br>outcome data. | 33% did not complete the program. Treatment completers completed all treatment sessions. Cointerventions not reported.                      | Assessments<br>were completed<br>online. Measures<br>were self-report<br>and participants<br>were aware of<br>receiving<br>intervention.  | Analytic sample included all participants. Model-based imputation of missing data, but level of missing data was high (37% missing posttreatment assessment).   | All outcomes<br>specified were<br>reported, except<br>for drug use, for<br>which a rationale<br>was provided. |  |
| Kuhn 2023                    | High  | Low   | Low   | Unclear   | Unclear   | Unclear   | Low   | High   |
|                              | Time trends not accounted for. No adjustment for confounders.                               | Prospective<br>study; selection<br>of participants not<br>based on<br>characteristics<br>observed after<br>the start of the<br>intervention.  | Baseline and follow-up time points aligned with beginning and end of intervention; not influenced by outcome data.                      | Intervention was not completed by 27% of participants. Treatment completers completed all treatment sessions. Cointerventions not reported. | Method of assessment not reported, but likely online consistent with other Couple HOPES study. Measures were self-report and participants were aware of receiving intervention. | ITT analyses conducted (using all available data from all randomized participants) except for tertiary outcomes (which excluded 2 couples - 13%). Missing data was handled with model-based imputation. | No indication of selective reporting.   |  |



| Study Name or<br>Author Year | Bias due to confounding                                       | Selection bias   | Bias in classification of interventions   | Bias due to<br>departures from<br>intended<br>interventions   | Bias due to<br>measurement of<br>outcomes   | Bias due to<br>missing data  | Bias in the selection of reported results | Overall risk of bias<br>(Low, Moderate,<br>Serious, Critical, No<br>Information) |
|------------------------------|---|--|---|---|---|--|---|--|
| Morland 2023                 | High  | Low  | Low   | Unclear   | Unclear   | Unclear  | Low                                       | High   |
|                              | Time trends not accounted for. No adjustment for confounders. | Prospective<br>study; selection<br>of participants not<br>based on<br>characteristics<br>observed after<br>the start of the<br>intervention. | Baseline and<br>follow-up time<br>points aligned<br>with beginning<br>and end of<br>intervention; not<br>influenced by<br>outcome data. | Intervention was<br>not completed by<br>27% of<br>participants.<br>Treatment<br>completers<br>completed all<br>treatment<br>sessions. Co-<br>interventions not<br>reported. | Method of<br>assessment not<br>reported, but<br>likely online<br>consistent with<br>other Couple<br>HOPES study.<br>Measures were<br>self-report and<br>participants were<br>aware of<br>receiving<br>intervention. | ITT analyses conducted (using all available data from all randomized participants) with the exception of tertiary outcomes (which excluded 2 couples - 13%). Missing data was handled with model-based imputation. | No indication of selective reporting.     |  |

Abbreviations. ITT=intent to treat.



## PEER REVIEW COMMENTS AND RESPONSES

| Comment #      | Reviewer #       | Comment  | Author Response   |
|----------------|------------------|--|---|
| Are the object | ctives, scope, a | and methods for this review clearly described?   |   |
| 1              | 1                | Yes  | None  |
| 2              | 2                | Yes  | None  |
| 3              | 3                | No - This report focused mainly on CBT as the internet and mobile app intervention for the treatment of PTSD. There are many other apps that are developed by the VA for the treatment of PTSD and PTSD Co-occurring conditions such as pain, depression, and suicide. Some of these apps are used as adjunctive therapies and others are used in place of CBT. Examples included, ACT, CBT-CP, Mindfulness, etc. It would be apropos to broaden the scope to include the additional apps. | Thank you for expressing your concern about the scope of the review. Studies of internet interventions and apps that aim to manage symptoms of PTSD, with or without components aimed to manage other, comorbid conditions, would have been included in this review if they had met the eligibility criteria for the review, regardless of whether the intervention was CBT-based. Often, studies were excluded because participants (at least 50%) did not meet criteria for a diagnosis of PTSD or probable PTSD or the study did not have a control group. |
| 4              | 4                | Yes  | None  |
| 5              | 5                | Yes  | None  |
| 6              | 6                | Yes  | None  |
| Is there any   | indication of bi | as in our synthesis of the evidence?   |   |
| 7              | 1                | No   | None  |
| 8              | 2                | No   | None  |
| 9              | 3                | No   | None  |
| 10             | 4                | No   | None  |
| 11             | 5                | No   | None  |
| 12             | 6                | No   | None  |
| Are there any  | y published or   | unpublished studies that we may have overlooked?   |   |
| 13             | 1                | No   | None  |
| 14             | 2                | No   | None  |
| 15             | 3                | No   | None  |
| 16             | 4                | No   | None  |
|                |                  |  |   |



| Comment #     | Reviewer #     | Comment   | Author Response  |
|---------------|----------------|---|--|
| 17            | 5              | No  | None   |
| 18            | 6              | No  | None   |
| Additional su | ggestions or c | comments can be provided below.   |  |
| 19            | 1              | Outstanding summary - thanks very much.   | Thank you  |
| 20            | 2              | For the first bullet under "future research," I think it would be helpful to add 1-2 examples of the types of populations that might be more/less receptive to digital treatments. I think when people think of the word "population," demographic groups come to mind, but I don't think that is what is meant here as that is covered by the next bullet. Judging by the evidence reviewed, it seems like these populations could be treatment-naive patients, or those with subclinical distress.                                | Based on the updated results, we have now modified some of the future research conditions. As iCBTs demonstrated limited effectiveness across the military samples, we now suggest that future treatments may want to consider targeting treatment-naïve patients in line with a promising civilian trial (Bisson et al, 2022).                      |
| 21            | 2              | This bullet in future directions seems worthy of splitting up into two. They are both important ideas that should be elaborated upon a little more: "Evaluating strategies to increase treatment adherence to online protocols and the optimal amount of guidance needed for treatments"  | We have now modified our Future Directions section in line with our updated results.   |
| 22            | 2              | I also think the report's overall conclusions and recommendations for future directions should be elaborated upon further in the executive summary, both in the initial bullets and in the narrative. I realize these are supposed to be brief summaries, but this may be all that some people read, and I think these are crucial points from the report. At present, there is one bullet that contains a lot of high-level information, and there is one concluding sentence in the narrative. I would like to see a little more. | We have elaborated on the executive summary to include a more robust summary of the conclusions and recommendations.   |
| 23            | 3              | It is not clear why this report included studies done in other countries with non-Veterans participants.  | The eligibility criteria decided on for this report, in collaboration with the Operational Partners, was not limited to US Veterans. However, we highlight studies conducted among US Veterans throughout the report as the evidence with the greatest relevance/applicability and now report results separately for this population, when possible. |
| 24            | 4              | Page vi, line 53: Says 2 studies found no difference between internet and in person. Were they non-inferior studies?  | Thank you for your question. The executive summary was edited and no longer mentions these 2 studies. However, we discuss these 2 studies in the results   |



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|           |            |   | section; 1 was a non-inferiority study and the other was not (the second was a small feasibility study).   |
| 25        | 4          | Page vii, line 43: Table subheading: PTSD appears twice. Why?   | Headings are set to repeat at the start of a new page.   |
| 26        | 4          | Page 4, line 18: I would state in PICOTS that over half of sample had to probable PTSD.   | We include a statement above the eligibility criteria explaining that we required "about half, at minimum" of the study sample to have probable PTSD. We did not use a hard cut-off of 50% (we included 1 study with 48.4% of the sample having probable PTSD).  |
| 27        | 4          | Page 5, line 21: Studies could have clinician administered or self report outcomes. could results be reported separately?   | We have added a subgroup analysis examining whether intervention effects differed based on use of a clinician-administered or self-reported outcome measure.   |
| 28        | 4          | Page 10, line 15: Is it 34 or 36 RCTs? On line 7 it is 36 and on line 15 it is 34.  | There were 36 RCTs included total, but the literature overview is then divided into 2 sections characterizing the PTSD studies and the family member/caregiver studies separately. 34 of the RCTs were on interventions for individuals with PTSD and 2 RCTs were on interventions for family members or caregivers of individuals with PTSD.  |
| 29        | 4          | Page 13, line 19: I would include % with PTSD in the table under population.  | Thank you for your suggestion. We have added % PTSD to the study characteristics table.  |
| 30        | 4          | Page 19, line 11: Could there be subgroup analyses on PTSD v subthreshold? Veteran/active duty v community?   | Thank you for your suggestions. We did not conduct subgroup analysis examining PTSD vs subthreshold PTSD due to the high degree of variation between studies in how PTSD/probable PTSD was measured and defined. We have conducted additional subgroup analysis examining Veteran/active-duty vs community samples and have added this to the results.   |
| 31        | 4          | Page 51, line 19: Bias in measurement of outcome. How was self-report rated? The way I think about it, if the assessor was not blinded, then the domain rating will be some concerns or high. It will be some concerns if either 4.4 or 4.5 are answered No (4.4: Could assessment of the outcome have been influenced by knowledge of intervention received?; 4.5: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?). The measures are not objective (like a blood test), so 4.4 is always Yes. The answer for 4.5 depends on | Thank you for your comment. We did not consider self-reported outcomes as a major concern for bias compared with clinician-reported outcomes, given that both assessment methods rely on patients' reporting of symptoms (consistent with many mental health treatment contexts). We did consider outcome assessment method to be a potential source of variability in effects across studies, however, and we have included more detailed reporting of results by |



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|           |            | the comparator condition, we have instructions that if the comparator (any arm) is inactive control then we'd rate that as Yes (there are some other circumstances where that would be rate Yes but they are less common). If 4.5 is rated yes, then the domain rating would be High (and that means the overall rating would also be High).               | assessment method. Regarding blinding, studies that did not blind patients to intervention assignment and used an active comparison condition were judged to have some concerns in this domain, while studies that did not blind patients to intervention assignment and used an inactive comparison condition were considered high risk of bias in this domain (and consequently, overall). Finally, because eligibility was limited to studies of individuals with an existing PTSD diagnosis, we did not consider use of self-reported outcome measures to be tantamount to unblinded intervention assignment. We have changed some of the ratings to be consistent with this approach. |
| 32        | 4          | Page 55, line 52: Why is unblinded CAPS rated higher than self-report?   | Studies with self-reported PTSD outcomes were only rated lower than studies with clinician-administered PTSD outcomes administered by unblinded assessors in cases where the participants were blind to group assignment or they were not blind to group assignment, but the study used an active comparison condition.  |
| 33        | 4          | Page 61, line 55: Seems like bias for measurement should be assessed separately for each outcome. There was a blinded CAPS and self-report. CAPS should be low concern.  | As mentioned above, we did not consider self-reported outcomes as a major concern for bias compared with clinician-reported outcomes, given that both assessment methods rely on patients' reporting of symptoms (consistent with many mental health treatment contexts). We did consider outcome assessment method to be a potential source of variability in effects across studies, however, and we have included more detailed reporting of results by assessment method.  |
| 34        | 4          | Page 64, line 24: Same as above. There is a blinded CAPS, therefore doesn't seem like high RoB   | Given that the CAPS relies on patients' reporting of symptoms, we were concerned with blinding of the participants as well as blinding of the outcome assessors.   |
| 35        | 5          | This is a phenomenally well-synthesized review of the extant lit on technology-based interventions for PTSD and their sequelae. Authors lay out the existing value and future potential of internet and tech-based interventions, results appear to be accurately reported, and conclusions drawn by authors are both appropriate and clinically valuable. | Thank you for this comment.  |



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| 36        | 5          | I am somewhat surprised that the title of this evidence synthesis effort refers to "clinical and at-home resources." This title is confusing and somewhat misleading, since the review seems to focus exclusively on tech-based resources. I might suggest a title revision, if possible, to reflect the subject of the review. | Thank you for this comment. We have changed the title to reflect the aims of the review more closely.   |
| 37        | 6          | The "Clinical and At-Home" part of the title is somewhat misleading.  | Thank you for this comment. We have changed the title to reflect the aims of the review more closely.   |
| 38        | 6          | On page 11, it would help to clarify who was required to have the PTSD diagnosis in the 3 studies mentioned (the patient or the family member?).  | We have edited this sentence to make it clearer that we are referring to the PTSD patient.  |
| 39        | 6          | My biggest question is which studies were testing trauma-<br>focused CBT vs. more general CBT skills? Similar to the way the<br>authors examined the inclusion of imaginal exposure as a<br>subgroup, this could be examined.   | This is a great question and prompted us to take a deeper dive into the specific treatments tested. Given the differential treatment effects for military vs civilians, and the few military studies that evaluated a TF-CBT (4) we decided not to statistically analyze this. However, we did include more details about the included military studies on whether they were CBT vs. TF-CBT, and what TF-CBT frameworks they are based on. We dedicate a paragraph to this topic in our Discussion and reference it as part of our Future Directions. |

