# Psychotherapy for Military-Related PTSD A Review of Randomized Clinical Trials

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Review

# Psychotherapy for Military-Related PTSD
## A Review of Randomized Clinical Trials

Maria M. Steenkamp, PhD; Brett T. Litz, PhD; Charles W. Hoge, MD; Charles R. Marmar, MD

**IMPORTANCE** Posttraumatic stress disorder (PTSD) is a disabling psychiatric disorder common among military personnel and veterans. First-line psychotherapies most often recommended for PTSD consist mainly of "trauma-focused" psychotherapies that involve focusing on details of the trauma or associated cognitive and emotional effects.

**OBJECTIVE** To examine the effectiveness of psychotherapies for PTSD in military and veteran populations.

**EVIDENCE REVIEW** PubMed, PsycINFO, and PILOTS were searched for randomized clinical trials (RCTs) of individual and group psychotherapies for PTSD in military personnel and veterans, published from January 1980 to March 1, 2015. We also searched reference lists of articles, selected reviews, and meta-analyses. Of 891 publications initially identified, 36 were included.

**FINDINGS** Two trauma-focused therapies, cognitive processing therapy (CPT) and prolonged exposure, have been the most frequently studied psychotherapies for military-related PTSD. Five RCTs of CPT (that included 481 patients) and 4 RCTs of prolonged exposure (that included 402 patients) met inclusion criteria. Focusing on intent-to-treat outcomes, within-group posttreatment effect sizes for CPT and prolonged exposure were large (Cohen *d* range, 0.78-1.10). CPT and prolonged exposure also outperformed waitlist and treatment-as-usual control conditions. Forty-nine percent to 70% of participants receiving CPT and prolonged exposure attained clinically meaningful symptom improvement (defined as a 10- to 12-point decrease in interviewer-assessed or self-reported symptoms). However, mean posttreatment scores for CPT and prolonged exposure remained at or above clinical criteria for PTSD, and approximately two-thirds of patients receiving CPT or prolonged exposure retained their PTSD diagnosis after treatment (range, 60%-72%). CPT and prolonged exposure were marginally superior compared with non–trauma-focused psychotherapy comparison conditions.

**CONCLUSIONS AND RELEVANCE** In military and veteran populations, trials of the first-line trauma-focused interventions CPT and prolonged exposure have shown clinically meaningful improvements for many patients with PTSD. However, nonresponse rates have been high, many patients continue to have symptoms, and trauma-focused interventions show marginally superior results compared with active control conditions. There is a need for improvement in existing PTSD treatments and for development and testing of novel evidence-based treatments, both trauma-focused and non–trauma-focused.

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Posttraumatic stress disorder (PTSD) is a disabling psychiatric condition common among military personnel and veterans, and consequently, a significant public health challenge. Approximately 13% of Iraq or Afghanistan veterans[1] and 10% of Gulf War veterans who experienced combat have PTSD,[2] and 11% of Vietnam veterans continue to report PTSD symptoms that impair functioning 40 years after the war.[3] Military-related PTSD is often accompanied by a variety of mental and physical health conditions, particularly depression, anxiety, and substance misuse.[4,5] War veterans with PTSD also have extensive functional impairments such as unemployment and income disparities,[6] family and relationship difficulties,[7] aggressive behavior,[8] and poor quality of life.[9] Twenty-three percent of Vietnam veterans with PTSD (compared with 4% among those without PTSD) reported being unemployed when assessed 15 or more years after service, 33% (compared with 16%) reported perpetrating serious interpersonal violence in the past year, and 40% (compared with 10%) reported low well-being.[10] Risk factors for PTSD in military populations include war zone exposure, being wounded, younger age when deployed, less education, greater exposure to childhood trauma, and less social support during and after deployment.[11] If left untreated, military-related PTSD often follows a chronic course, resulting in lifelong dysfunction.[12]

Over the past 10 years, an increasing number of randomized clinical trials (RCTs) of PTSD treatments in military personnel and veterans have emerged, coinciding with a major policy shift in the Departments of Defense (DoD) and Veterans Affairs (VA) toward therapies considered evidence-based.[13] Psychotherapy is more consistently recommended as first-line treatment for PTSD than medications across clinical practice guidelines and in DoD and VA practice settings. In this review, we focus on RCTs of individual and group psychotherapies for PTSD in military and veteran populations to examine the degree of symptom improvement and efficacy relative to control conditions.

## Methods

We searched PubMed, PsycINFO, and PILOTS for RCTs of psychotherapy for PTSD among military personnel or veterans, published from January 1980 (the year the PTSD diagnosis was first introduced) to March 1, 2015. PTSD was defined according to the diagnostic criteria accepted at the time of the RCTs, which most often followed the *Diagnostic and Statistical Manual for Mental Disorders* (Fourth Edition, Text Revision).[14] This definition included 3 clusters of symptoms following trauma, present for at least 1 month, including reexperiencing the trauma (eg, intrusive thoughts or nightmares), avoiding reminders of the trauma, and hyperarousal (eg, hypervigilance, irritability, difficulty concentrating). We also manually searched reference lists of articles, selected reviews, and meta-analyses.

We selected only English-language RCTs that (1) were conducted with service members, veterans, or both; (2) reported PTSD as an inclusion criterion; (3) reported at least pretreatment and posttreatment total scores on standardized PTSD clinical measures; (4) used either individual or group psychotherapy; and (5) did not solely involve pharmacotherapies, pharmacologically augmented psychotherapy, or other biological treatments. We did not include trials of collaborative care models, dosing studies, trials targeting specific symptoms (eg, insomnia, anger) rather than the full syndrome, or trials targeting substance use disorders comorbid with PTSD. We focused on intent-to-treat outcomes, when available.

## Results

Of 891 publications initially identified, 36 were included (**Table 1**[15-27,29,58] and **Table 2**[30-50]; eFigure in the Supplement). We grouped trials of the most commonly studied first-line trauma-focused therapies (ie, therapies given the highest evidence recommendations in clinical guidelines) (Table 1), followed by second-line interventions (ie, therapies for which there is less evidence supporting effectiveness) (Table 2). The principal efficacy criteria, reported variably in published trials, included degree of clinically significant PTSD symptom improvement (typically defined as a 10- or 12-point decline in self-reported or interviewer-assessed PTSD symptoms),[23] mean PTSD symptom level at posttreatment and follow-up, loss of PTSD diagnosis, degree of symptom remission, and effect sizes (most commonly Cohen *d*, calculated as the difference between 2 mean PTSD severity scores divided by the pooled SD [a *d* of 0.20 indicates a small effect size; a *d* of 0.50, a medium effect size; and a *d* of 0.80, a large effect size]).

### First-Line Psychotherapies

The diverse range of PTSD psychotherapies are broadly grouped into "trauma-focused" and non–trauma-focused. Trauma-focused therapies are cognitive-behavioral treatments that involve a range of techniques that attend to the details of the trauma or associated emotions or cognitive processes (beliefs, assumptions). The 3 most widely studied trauma-focused therapies, which are considered leading evidence-based psychotherapies by all major clinical guidelines,[51] are cognitive processing therapy (CPT), prolonged exposure therapy, and eye movement desensitization and reprocessing (EMDR) therapy (**Box**). All are manualized (ie, protocolized in a session-by-session manner), delivered principally in specialty care settings, use different techniques and theoretical rationales, require sustained engagement (typically 12 sessions), and can be emotionally demanding for patients. Prolonged exposure includes asking patients to repeatedly recount the trauma to extinguish fear responses associated with the memory (a technique known as imaginal exposure) and to practice facing trauma reminders and triggers in the real world (known as in vivo exposure). CPT involves changing maladaptive beliefs related to the trauma (known as cognitive restructuring), with the option of writing an account of the trauma. EMDR also comprises exposure and cognitive restructuring elements but asks patients to maintain dual focus on an external stimulus (eg, eye-movement tracking of therapist hand movements) while thinking about the trauma.

Meta-analyses of mostly civilian studies show large pre-post treatment effects (within-group) and between-group effects compared with control conditions for these treatments, with generally comparable outcomes for CPT, prolonged exposure, EMDR, and other trauma-focused modalities.[52] In contrast, non–trauma-focused therapies attend principally to current life stressors, reactions, goals, or relationships. The only non–trauma-focused therapy that has received high-level evidence statements in PTSD clinical

Table 1. Summary of Outcomes From RCTs of First-Line Interventions for Military-Related PTSD

| Source | Participants (No.) | Conditions | Longest Follow-up, mo | No. (%) | | Mean Posttreatment Total PTSD Score | Pre-Post Decrease in PTSD Symptoms | No. (%) | | Between-Group ES (95% CI) From Pretreatment to Posttreatment |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Drop Out | Remission at Post-Treatment | | | % Attaining Clinically Meaningful Change at Posttreatment | % Retaining PTSD Diagnosis at Posttreatment | |
| **CPT** | | | | | | | | | | |
| Monson et al,[15] 2006 | Veterans (30) | CPT | 1 | 6 (20) | NR | 52.14 (CAPS ITT) | 24.59 (CAPS ITT) | 15 (50) (CAPS ITT) | 18 (60) (CAPS ITT) | *g* = 1.12 (−0.58 to 1.67) (CAPS ITT) |
| | Veterans (30) | Waitlist | 1 | 4 (13) | NR | 76.03 (CAPS ITT) | 3.07 (CAPS ITT) | 3 (10) (CAPS ITT) | 29 (97) (CAPS ITT) | |
| Forbes et al,[16] 2012 | Australian veterans (30) | CPT | 3 | 9 (30) | 6 (27) (CAPS ITT) | 48.03 (CAPS ITT) | 27.5 (CAPS ITT) | 16 (67) (CAPS ITT) | 15 (63) (CAPS completer) | *d* = 0.97 (0.43 to 1.51) |
| | Australian veterans (29) | TAU | 3 | 9 (31) | 1 (3)CAPSITT | 57.73 (CAPS ITT) | 6.82 (CAPS ITT) | 8 (35) (CAPS ITT) | 20 (87) (CAPS completer) | |
| Surís et al,[17] 2013 | Veterans with military sexual trauma (72) | CPT | 6 | 18 (35) | NR | 64.97 (CAPS ITT) | 20.1 (CAPS ITT) | 66% (CAPS ITT) | 72% (CAPS ITT) | *d* = 0.49 (0.22 to −0.76) (CAPS ITT) |
| | Veterans with military sexual trauma (57) | PCT | 6 | 6 (18) | NR | 68.64 (CAPS ITT) | 15.17 (CAPS ITT) | 48% (CAPS ITT) | 74% (CAPS ITT) | |
| Morland et al,[18] 2014 | Veterans (61) | Group CPT-C via telemedicine | 6 | 10 (16) | NR | 58.7 (CAPS ITT) | 10.2 (CAPS ITT) | 71 (57) overall (CAPS ITT) | 89 (71) overall (CAPS ITT) | *d* = 0.27 (CAPS ITT) |
| | Veterans (64) | Group CPT-C in person | 6 | 8 (13) | NR | 55.6 (CAPS ITT) | 16.4 (CAPS ITT) | 71 (57) overall (CAPS ITT) | 89 (71) overall (CAPS ITT) | |
| Resick et al,[19] 2015 | Active duty soldiers (56) | Group CPT-C | 12 | 15 (27) | NR | 23.0 (PSSI) | 4.7 (PSSI) | 15 (49) (PCL) | NR | *d* = 0.21 (PSSI) |
| | Active duty soldiers (52) | Group PCT | 12 | 7 (13) | NR | 23.9 (PSSI) | 3.2 (PSSI) | 14 (34) (PCL) | NR | |
| **Prolonged Exposure, Imaginal Exposure, and Group Exposure** | | | | | | | | | | |
| Cooper & Klum,[20] 1989 | Veterans (8) | TAU + implosive therapy/flooding | 3 | 6 (27) overall | NR | NR | NR | NR | NR | NR |
| | Veterans (8) | TAU | 3 | 6 (27) overall | NR | NR | NR | NR | NR | |
| Keane et al,[21] 1989 | Vietnam veterans (11) | Implosive therapy | 6 | NR | NR | NR | NR | NR | NR | NR |
| | Vietnam veterans (13) | Waitlist | 6 | NR | NR | NR | NR | NR | NR | |
| Boudewyns & Hyer,[22] 1990 | Inpatient veterans (19) | Exposure | 3 | 13 (25) overall | NR | NR | NR | NR | NR | NR |
| | Inpatient veterans (19) | TAU | 3 | 13 (25) overall | NR | NR | NR | NR | NR | |
| Schnurr et al,[23] 2003 | Veterans (180) | Group exposure | 12 | 41 (23) | NR | 74.00 (CAPS ITT) | 6.41 (CAPS ITT) | 39% (CAPS ITT) | NR | NR |
| | Veterans (180) | Group PCT | 12 | 16 (9) | NR | 76.03 (CAPS ITT) | 5.98 (CAPS ITT) | 38% (CAPS ITT) | NR | |

(continued)

Table 1. Summary of Outcomes From RCTs of First-Line Interventions for Military-Related PTSD (continued)

| Source | Participants (No.) | Conditions | Longest Follow-up, mo | No. (%) | | Mean Posttreatment Total PTSD Score | Pre-Post Decrease in PTSD Symptoms | No. (%) | | Between-Group ES (95% CI) From Pretreatment to Posttreatment |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Drop Out | Remission at Post-Treatment | | | % Attaining Clinically Meaningful Change at Posttreatment | % Retaining PTSD Diagnosis at Posttreatment | |
| Schnurr et al,[24] 2007 | Female veterans primarily with sexual trauma (141) | PE | 6 | 53 (38) | 24 (17) | 52.9 (47.7 to 58.0) (CAPS ITT) | 24.7 (CAPS ITT) | 99 (70) (CAPS ITT) | 86 (61) (CAPS ITT) | *d* = 0.27 CAPS ITT |
| | Female veterans primarily with sexual trauma (143) | PCT | 6 | 30 (21) | 10 (7) | 60.1 (55.3 to 64.8) (CAPS ITT) | 17.8 (CAPS ITT) | 84 (59) (CAPS ITT) | 114 (80) (CAPS ITT) | |
| Nacasch et al,[25] 2011 | Israeli survivors of combat or terrorism (15) | PE | 12 | 2 (13) | NR | 18.9 (PSSI ITT) | 18.2 (PSSI ITT) | NR | NR | *d* = 1.80 PSSI ITT |
| | Israeli survivors of combat or terrorism (15) | TAU | 12 | 2 (13) | NR | 35.0 (PSSI ITT) | 1.8 (PSSI ITT) | NR | NR | |
| Yehuda et al,[26] 2014 | Veterans (37) | PE | 3 | 12 (31) | NR | NR | 23 (CAPS) | NR | 14 (56) (CAPS completer) | NR |
| | Veterans (15) | Minimal attention | 3 | 3 (21) | NR | NR | 14 (CAPS) | NR | 10 (83) (CAPS completer) | |
| Rauch et al,[27] 2015 | Veterans (18) | PE | None | 7 (39) | NR | 30.0 (CAPS completer) | 49.2 (CAPS completer) | 10 (91) (CAPS completer) | NR | *d* = 0.98 CAPS completer |
| | Veterans (18) | PCT | None | 3 (17) | NR | 53.6 (CAPS completer) | 23.8 (CAPS completer) | 9 (60) (CAPS completer) | NR | |
| **EMDR** | | | | | | | | | | |
| Boudewyns & Hyer,[58] 1996 | Veterans (21) | EMDR | None | NR | NR | 50.09 (CAPS) | 25.14 (CAPS) | NR | NR | NR |
| | Veterans (18) | EMDR without eye movement | None | NR | NR | 67.50 (CAPS) | 18.1 (CAPS) | NR | NR | |
| | Veterans (22) | TAU | None | NR | NR | 67.18 (CAPS) | 14.05 (CAPS) | NR | NR | |
| Carlson et al,[29] 1998 | Veterans (10) | EMDR | 3 | 0 | NR | NR | NR | NR | 2 (22) | |
| | Veterans (13) | Biofeedback relaxation | 3 | 1 (3) | NR | NR | NR | NR | 7 (78) | |
| | Veterans (12) | Routine care | 3 | 0<br>12 (26) overall prior to group assignment | NR | NR | NR | NR | NR | NR |

Abbreviations: CAPS, Clinician Administered PTSD Scale; completer, treatment completer sample only; CPT, cognitive processing therapy; CPT-C, CPT cognitive-only version; EMDR, eye movement desensitization and reprocessing; ES, effect size; ITT, intent-to-treat; NR, not reported; PCL, PTSD Checklist; PCT, present-centered therapy; PSSI, PTSD Symptom Scale Interview; PTSD, posttraumatic stress disorder; RCT, randomized clinical trial; TAU, treatment as usual.

practice guidelines is stress inoculation training, which involves stress management skills (eg, breathing, muscle relaxation) and applying these skills to day-to-day stressors and reminders of the trauma.

In 2008, CPT and prolonged exposure were selected by the VA for nationwide dissemination in an attempt to better standardize care for veterans, and 98% of VA centers now offer both.[53,54] Initially, neither intervention was validated sufficiently in active duty military or veteran populations; they were originally tested largely in civilian female survivors of sexual assault. EMDR has not been disseminated within the VA and DoD, and EMDR research has received comparatively little VA or DoD funding but has strong evidence in civilian studies and high-level endorsement from many guidelines internationally. RCTs of stress inoculation training are lacking in veterans, and it is infrequently used in the VA and DoD.

### Efficacy of CPT

Five trials of CPT (that included 481 patients) met inclusion criteria; 4 enrolled veterans[15-18] and 1 enrolled active-duty soldiers.[19] The first included a waitlist comparison,[15] and subsequent studies used either a treatment-as-usual comparison or an active comparison condition known as present-centered therapy, a non–trauma-focused treatment protocol focused largely on current life problems. One noninferiority trial compared group CPT delivered in person vs via telemedicine.[18] Treatment dropout rates ranged from 16% to 35%.

Within-group intent-to-treat effect sizes for CPT were reported in 3 trials and were large ($d$ = 0.78,[18] $d$ = 1.10,[19] and $d$ = 1.02[17]). All trials reported the percentage of patients attaining meaningful symptom change (49%-67%), and the mean posttreatment PTSD scores, which remained at or above clinical cutoffs (eg, 50 on the Clinician Administered PTSD Scale [CAPS] and 20 on the PTSD Scale-Interview [PSSI]), with a range of 48.03 to 64.97 for CAPS and 23.00 for PSSI. Four trials reported posttreatment PTSD diagnosis,[15-18] with approximately two-thirds of patients retaining their diagnosis (60%-72%). Only 1 trial reported symptom remission (CAPS score <20) of 27%.[16]

Concerning comparisons to control conditions, CPT outperformed waitlist approaches for mean PTSD symptom reduction ($g$ = 1.12), loss of diagnosis, and meaningful symptom change, although the latter was no longer statistically significant by 1 month posttreatment.[15] CPT produced significantly greater symptom remission and clinically meaningful symptom improvement than treatment as usual in a study of Australian veterans ($d$ = 0.97). Group differences in loss of diagnosis and meaningful symptom improvement were nonsignificant at 3-month follow-up but remained significant for symptom remission.[16] In a trial comparing CPT and present-centered therapy for military sexual trauma, CPT resulted in significantly greater reduction in self-reported PTSD symptoms at posttreatment ($d$ = 0.85), although group differences were no longer significant by 2-, 4-, or 6-month follow-up.[17] There were no significant group differences in interviewer-assessed PTSD symptoms. A trial comparing group CPT with group present-centered therapy in active-duty soldiers also found that self-reported PTSD symptoms improved in both groups but statistically significantly more so in the CPT group ($d$ = 0.40).[19] Between-group differences were small and not significant for interviewer-assessed PTSD symptoms at posttreatment ($d$ = 0.21), 6-month ($d$ = 0.22), and 12-month ($d$ = 0.21) follow-up. There were no significant differences between groups in the percentage of patients attaining clinically significant change in self-reported symptoms at posttreatment, 6-month, or 12-month follow-up.

In sum, trials of CPT for military-related PTSD have included both veterans and active-duty personnel with combat or military sexual trauma, have shown high methodological rigor (although fidelity problems were present in 1 trial),[17] and have had large effect sizes when compared with no treatment (waitlist) or treatment as usual. However, CPT was marginally superior to active, non–trauma-focused control comparisons.

### Efficacy of Prolonged Exposure

Four RCTs of prolonged exposure (that included 402 patients) met inclusion criteria.[24-27] Earlier trials examined similar exposure-based mechanisms but not the full prolonged exposure protocol[20-22] and included a large trial of an exposure-based group therapy that did not lead to meaningful PTSD symptom reduction or outperform a present-centered control.[23] The most robust trial of prolonged exposure compared prolonged exposure with present-centered therapy in female veterans with sexual trauma,[24] while 3 small studies of combat veterans used minimal attention,[26] treatment as usual,[25] or present-centered therapy[27] control conditions. Two of these trials[26,27] focused primarily on glucocorticoid-related biomarker responses associated with clinical improvement. Treatment dropout rates ranged from 13% to 39%.

Within-group intent-to-treat effect size for prolonged exposure was reported in 1 trial and was large ($d$ = 0.80).[24] One trial reported on clinically meaningful PTSD symptom reduction in the intent-to-treat sample, which occurred in 70% of patients.[24] Mean posttreatment intent-to-treat symptom scores were reported in 2 trials and remained at or above clinical cutoffs for PTSD (52.9 [CAPS][24] and 18.9 [PSSI][25]). One trial reported loss of diagnosis in the intent-to-treat sample and found that 61% retained their diagnosis after treatment.[24] The only trial to report remission (≤20 CAPS) found remission in 17% of the intent-to-treat sample.[24]

When compared with control conditions, both prolonged exposure and present-centered therapy improved symptoms in female veterans with predominantly sexual assault trauma, with a small intent-to-treat effect size favoring prolonged exposure ($d$ = 0.27); there were no significant group differences for clinically meaningful improvement at any point and no significant group differences for loss of diagnosis or symptom remission at either the 3- or 6-month follow-up.[24] In a small sample of Israeli veterans, prolonged exposure resulted in greater symptom reduction than psychodynamic therapy ($d$ = 1.80), and outcomes were maintained through 12-month follow-up.[25] Prolonged exposure failed to outperform a minimal-attention control that consisted of 30-minute weekly symptom monitoring phone calls; both groups significantly improved, with no significant group differences.[26] Last, a small RCT examining cortisol response following prolonged exposure found no significant differences between prolonged exposure and present-centered therapy on interviewer-assessed PTSD outcomes in the intent-to-treat sample, although significant differences favoring prolonged exposure were found in completers ($d$ = 3.16 for prolonged exposure vs $d$ = 1.08 for present-centered therapy).[27]

In sum, fewer methodologically robust trials for military-related PTSD are available for prolonged exposure than for CPT. With

Table 2. Summary of Outcomes From RCTs of Second-Line Interventions for Military-Related PTSD

| Source | Participants (No.) | Conditions | Longest Follow-up, mo | No. (%) | | Mean Post-Treatment Total PTSD Score | Pre-Post Drop in PTSD Symptoms | No. (%) | | Between-Group ES From Pretreatment to Posttreatment |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Drop Out | Remission at Post-Treatment | | | % Attaining Clinically Meaningful Change At Posttreatment | % Retaining PTSD Diagnosis at Posttreatment | |
| Watson et al,[30] 1997 | Vietnam veterans (30) | Relaxation | None | NR | NR | 95.0 (PTSD-I completer) | 0.4 (PTSD-I completer) | NR | NR | NR |
| | Vietnam veterans (30) | Relaxation + deep breathing | None | NR | NR | 97.8 (PTSD-I completer) | 0.3 (PTSD-I completer) | NR | NR | |
| | Vietnam veterans (30) | Relaxation + deep breathing + biofeedback | None | NR | NR | 89.4 (PTSD-I completer) | 1.1 (PTSD-I completer) | NR | NR | |
| Dunn et al,[31] 2007 | Veterans (55) | Self-management therapy | 12 | 17 (33) | NR | 73.93 (CAPS completer) | 2.01 (CAPS completer) | NR | NR | *d* = 0.23 |
| | Veterans (56) | Psychoeducation group therapy | 12 | 6 (12) | NR | 77.10 (CAPS completer) | +1.05 (CAPS completer) | NR | NR | |
| Frueh et al,[32] 2007 | Veterans (21) | In-person group CBT | 3 | 9 (43) | NR | 56.58 (PCL completer) | 5.8 (PCL completer) | NR | NR | NR |
| | Veterans (17) | Telepsychiatry group CBT | 3 | 8 (47) | NR | 68.11 (PCL completer) | +1.11 (PCL completer) | NR | NR | |
| Litz et al,[33] 2007 | Active duty personnel (24) | Internet CBT | 6 | 12 (27) overall | 7 (42.9) (PSS-I<6) | 14.86 (PSS-I completer) | 9.16 (PSS completer) | NR | NR | *d* = 0.41 |
| | Active duty personnel (21) | Internet supportive counseling | 6 | 12 (27) overall | 1 (6.3) (PSS-I<6) | 20.00 (PSS-I completer) | 11.85 (PSS-I completer) | NR | NR | |
| Bormann et al,[34] 2008 | Veterans (14) | Mantram repetition | None | 4 (12) overall | NR | NR | 4.79 (CAPS ITT) | NR | NR | *d* = 0.33 |
| | Veterans (15) | Waitlist | None | | NR | NR | 2.64 (CAPS ITT) | NR | NR | |
| Lande et al,[35] 2010 | Active duty soldiers (22) | Biofeedback + TAU | None | NR | NR | NR | NR | NR | NR | NR |
| | Active duty soldiers (17) | TAU | None | NR | NR | NR | NR | NR | NR | |
| Ready et al,[36] 2010 | Vietnam veterans (6) | Virtual reality exposure | 6 | 1 (17) | NR | 59.20 (CAPS completer) | 31.8 (CAPS completer) | NR | NR | *d* = 0.28 |
| | Vietnam veterans (5) | PCT | 6 | 1 (20) | NR | 75.50 (CAPS completer) | 23.0 (CAPS completer) | NR | NR | |
| Beidel et al,[37] 2011 | Vietnam veterans (14) | Trauma management therapy | None | 5 (14) overall | NR | 69.0 (CAPS completer) | 15.9 (CAPS completer) | NR | NR | NR |
| | Vietnam veterans (16) | Exposure therapy | None | | NR | 65.5 (CAPS completer) | 25.1 (CAPS completer) | NR | NR | |
| Kent et al,[38] 2011 | Veterans (20) | Resilience-oriented group therapy | None | 1 (5) | NR | 23.00 (PDS ITT) | 12.90 (PDS ITT) | NR | NR | *d* = 1.40 |
| | Veterans (19) | Waitlist | None | 2 (11) | | 36.90 (PDS ITT) | 0.63 (PDS ITT) | NR | NR | |

(continued)

Table 2. Summary of Outcomes From RCTs of Second-Line Interventions for Military-Related PTSD (continued)

| Source | Participants (No.) | Conditions | Longest Follow-up, mo | No. (%) | | Mean Post-Treatment Total PTSD Score | Pre-Post Drop in PTSD Symptoms | No. (%) | | Between-Group ES From Pretreatment to Posttreatment |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Drop Out | Remission at Post-Treatment | | | % Attaining Clinically Meaningful Change At Posttreatment | % Retaining PTSD Diagnosis at Posttreatment | |
| McLay et al,[39] 2011 | Active duty service members (10) | Virtual reality graded exposure therapy | None | 0 | NR | 48.1 (CAPS ITT) | 35.4 (CAPS) | 7 (70) showed improvement of >30% | NR | NR |
| | Active duty service members (10) | TAU | None | 1 (10) | NR | 72.3 (CAPS ITT) | 9.4 (CAPS) | 1 (11%) | NR | |
| Possemato et al,[40] 2011 | OEF/OIF veterans (15) | Written emotional disclosure | 3 | 0 | NR | NR | NR | NR | NR | $\eta^2_p$ = .03 |
| | OEF/OIF veterans (16) | Writing control | 3 | 5 (31) | NR | NR | NR | NR | NR | |
| Jain et al,[41] 2013 | Active duty Marines (68) | HT + GI + TAU | None | 6 (9) | NR | 40.7 (37.0-44.2) (PCL ITT) | 13.3 (PCL ITT) | NR | NR | *d* = 0.85 (PCL ITT) |
| | Active duty Marines (55) | TAU | None | 15 (27) | NR | 52.0 (48.0-56.0) (PCL ITT) | 3.6 (PCL ITT) | NR | NR | |
| Kearney et al,[42] 2012 | Veterans (22) | MBSR + TAU | 4 | 2 (8) | NR | 52.45 (PCL ITT) | 7.43 (PCL ITT) | 8 (36) | NR | *d* = 0.51 (0.11-1.12) |
| | Veterans (25) | TAU | 4 | 1 (5) | NR | 58.5 (PCL ITT) | 4.41 (PCL ITT) | 5 (25) | NR | |
| Niles et al,[43] 2012 | Veterans (17) | Mindfulness | 6 wk | 4 (24) | NR | 47.46 (CAPS completer) | 13.46 (CAPS completer) | 5 (38.5) (20 points on CAPS) | NR | NR |
| | Veterans (16) | Psychoeducation | 6 wk | 2 (13) | NR | 74.00 (CAPS completer) | +1.5 (CAPS completer) | 1 (7.1) (20 points on CAPS) | | |
| Strachan et al,[44] 2012 | OEF/OIF veterans and active duty service members (20) | BA-TE in person | None | 5 (25) | NR | 47.9 (PCL completer) | 11.1 (PCL completer) | NR | NR | *d* = 0.33 |
| | OEF/OIF veterans and active duty service members (20) | BA-TE telehealth | None | 4 (20) | NR | 41.4 (PCL completer) | 15.8 (PCL completer) | NR | NR | |
| Bormann et al,[45] 2013 | Veterans (71) | Mantram repetition + TAU | 6 wk | 5 (7) | $\eta^2_p$ = .03 | 66.16 (CAPS ITT) | 16.92 (CAPS ITT) | 18 (24) | NR | NR |
| | Veterans (75) | TAU | 6 wk | 5 (7) | | 72.59 (CAPS ITT) | 10.24 (CAPS ITT) | 9 (12) | NR | |
| Church et al,[46] 2013 | Veterans (30) | EFT + TAU | 6 | 1 (3) | 39 (80) overall (including the waitlist that received EFT) | 39.41 (PCL completer) | 22.6 (PCL completer) | NR | 3 (10) | NR |
| | Veterans (29) | TAU/waitlist | 6 | 4 (14) | 39 (80) overall (including the waitlist that received EFT) | 63.23 (PCL completer) | + 0.52 (PCL completer) | NR | 28 (96) | |

*(continued)*

Table 2. Summary of Outcomes From RCTs of Second-Line Interventions for Military-Related PTSD (continued)

| Source | Participants (No.) | Conditions | Longest Follow-up, mo | No. (%) | | Mean Post-Treatment Total PTSD Score | Pre-Post Drop in PTSD Symptoms | No. (%) | | Between-Group ES From Pretreatment to Posttreatment |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Drop Out | Remission at Post-Treatment | | | % Attaining Clinically Meaningful Change At Posttreatment | % Retaining PTSD Diagnosis at Posttreatment | |
| Kip et al,[47] 2013 | Service members and veterans (29) | ART | 3 | 3 (10) | NR | 42.00 (PCL ITT) | 15.4 (PCL ITT) | 17 (65) (PCL completer) | NR | *d*= 1.25 |
| | Service members and veterans (28) | Attention control | 3 | NR | NR | 54.3 (PCL ITT) | 2.1 (PCL ITT) | 3 (13) (PCL completer) | NR | |
| Engel et al,[48] 2014 | Active duty soldiers (28) | Acupuncture + TAU | 12 wk | 1 (4) | NR | 38.8 (PCL ITT) | 19.3 (PCL ITT) | NR | NR | NR |
| | Active duty soldiers (27) | TAU | 12 wk | 0 | NR | 51.5 (PCL ITT) | 3.9 (PCL ITT) | NR | NR | |
| Kuckertz et al,[49] 2014 | Inpatient active duty personnel (20) | Attention bias modification | None | 8 (40) | NR | 42.83 (PCL completer) | 20.25 (PCL completer) | NR | NR | NR |
| | Inpatient active duty personnel (17) | Attention control condition | None | 0 | NR | 51.65 (PCL completer) | 10.06 (PCL completer) | NR | NR | |
| Moradi et al,[50] 2014 | Iranian veterans (12) | MEST | 3 | 0 | NR | 50.17 (IES-R ITT) | 30.91 (IES-R ITT) | NR | NR | *d* = 4.79 |
| | Iranian veterans (12) | Waitlist | 3 | 0 | NR | 75.34 (IES-R ITT) | + 0.01 (IES-R ITT) | NR | NR | |

Abbreviations: ART, accelerated resolution therapy; BA-TE, behavioral activation and therapeutic exposure; CAPS, Clinician Administered PTSD Scale; CBT, cognitive behavioral therapy; completer, treatment completer sample only; EFT, emotional freedom techniques; ES, effect size; HT + GI, healing touch with guided imagery; IES-R, Impact of Event Scale–Revised; ITT, intent-to-treat; MBSR, mindfulness-based stress reduction; MEST, memory specificity training; $\eta^2_p$, partial eta-squared; NR, not reported; PCL, PTSD Checklist; PCT, present-centered therapy; PSSI, PTSD Symptom Scale Interview; PTSD, posttraumatic stress disorder; TAU, treatment as usual.

1 notable exception,[24] sample sizes have tended to be smaller, and no large methodologically robust trials of prolonged exposure have been published in US male veterans with combat trauma. The only available data on prolonged exposure in US combat-exposed male veterans come from 2 small trials that studied biomarkers associated with clinical outcomes.[26,27]

### Efficacy of EMDR

RCTs of EMDR for military-related PTSD (all conducted prior to the wars in Iraq and Afghanistan) involved small samples, tested only brief interventions (1-3 sessions),[28,55,56] or involved dismantling comparisons (eliminating eye movements).[57] They also generally did not use methodology consistent with modern trials. In the 2 trials testing adequate doses of EMDR there were large symptom reductions,[58] and 78% of completers no longer met criteria for PTSD.[29] EMDR performed comparably to variants in which the eye tracking was removed or when compared with an active non–trauma-focused therapy.[58] EMDR outperformed waitlisting (ie, no treatment) and biofeedback-assisted relaxation, with results maintained at 9-month follow-up.[29] In sum, the efficacy of EMDR remains largely based on civilian studies[59]; additional studies in military populations are needed.

## Second-Line Interventions

Given high dropout and nonresponse rates from first-line therapies, an increasing number of trials have examined an array of alternatives, including variations of cognitive-behavioral therapy[38,44] or novel delivery modalities, such as virtual reality[36,39] or web-based content.[33] A variant of EMDR, accelerated resolution therapy, demonstrated large effects (*d* = 1.25) compared with an educational control condition similar to waitlisting in a preliminary RCT of veterans with PTSD.[47]

Other trials have tested complementary and alternative therapies that are theoretically and mechanistically distinct. Acupuncture combined with usual care outperformed usual care alone (*d* = 1.7)[48]; small trials have shown some evidence of efficacy for mindfulness-based interventions,[43] mantram repetition (ie, silent repetition of a word or phrase with spiritual significance),[34,45] attention bias modification,[49] and memory specificity training.[50] Healing touch therapy, involving tapping body points while engaging in non–exposure-based guided imagery, also demonstrated efficacy over treatment as usual (*d* = 0.85).[41] These findings suggest that a variety of disparate treatment mechanisms are associated with reduced PTSD symptoms.

In contrast, treatments that have failed to demonstrate efficacy among veterans include relaxation, deep breathing, biofeedback, and mindfulness-based stress reduction.[30,35,42] A brief 3-session intervention consisting of writing about combat traumas produced little meaningful PTSD improvement and did not outperform writing about one's use of time.[40] Cognitive-behavioral group therapy aimed at comorbid PTSD and depression,[31] and

comorbid PTSD and substance dependence, did not substantially improve symptoms and was equivalent to controls.

## Discussion

The past 10 years has seen unprecedented interest in identifying effective PTSD treatments for service members and veterans. Findings from RCTs indicate a significant need for further treatment development and improvement. CPT and prolonged exposure, the 2 most widely used first-line (ie, recommended) therapies, show large within-group (pretreatment to posttreatment) effect sizes. However, effect sizes, which are more commonly used in psychology literature than in medical literature, reflect mean outcomes and do not adequately capture heterogeneity in patient outcomes; between one-third and one-half of patients receiving CPT or prolonged exposure did not demonstrate clinically meaningful symptom change (when this outcome was reported). Approximately two-thirds of patients receiving CPT or prolonged exposure retained their diagnosis posttreatment. Mean PTSD scores have tended to remain at or above diagnostic thresholds after treatment, and the 2 studies reporting remission rates suggest that symptom remission is relatively uncommon. Most importantly, many trials of CPT and prolonged exposure have compared patients receiving the intervention with patients not receiving any standardized intervention (waitlist) or with patients receiving treatment as usual. When CPT and prolonged exposure were compared with non–trauma-focused psychotherapies, such as present-centered therapy, similar levels of symptom improvement were often observed, particularly at follow-up intervals.

Approximately one-fourth of patients enrolled in clinical trials and receiving CPT and prolonged exposure dropped out during treatment. These proportions are broadly comparable to the proportions of dropouts in studies of trauma-focused therapies in civilians[60] and trials of depression in veterans.[61] Treatment nonretention has been a significant problem in military-related PTSD care more generally; several large observational studies in both the VA and DoD found that only a small proportion of individuals receive a minimally adequate number of mental health encounters after PTSD diagnosis.[62] Reasons for not seeking treatment and dropout are complex and include stigma, confidentiality concerns, time demands, perceived treatment inefficacy, and discomfort with the therapist.[62]

Current VA policies emphasize CPT and prolonged exposure as treatments of choice. Clinical practice guidelines (including the VA/DoD guideline[52]), based largely on studies in civilians, also include CPT and prolonged exposure as first-line recommendations for adults with PTSD, although EMDR and other trauma-focused therapies are given at least equal standing (separate recommendations for service members and veterans are not made). Some evidence suggests that outcomes for PTSD treatment tend to be better among civilians than among veterans,[63,64] although this has not been consistent and remains an empirical question. Potential reasons why treatment outcomes may be worse among military and veteran populations include the extended, repeated, and intense nature of deployment trauma[65] and the fact that service members are exposed not only to life threats but to traumatic losses and morally compromising experiences that may require different treatment approaches.[66-68] A recent meta-analysis comparing trauma-focused and non–trauma-focused therapies (both civilian and military trauma) found that, in populations with more complex trauma, such as veterans and refugees, there was little difference in efficacy; moderate differences favoring trauma-focused therapies were only present for less complex traumas.[69] Additional likely reasons for worse outcomes in veterans include comorbidities (eg, 87% of veterans with PTSD presenting to VA primary care clinics have at least 1 psychiatric comorbidity, with the mode being 3-4 disorders[70]) and disability compensation incentives. To contextualize these findings, a recent narrative review of cognitive-behavioral therapy for depression in veterans similarly showed that relatively few trials are available, cognitive-behavioral therapy often does not outperform controls, and results compare unfavorably with civilian outcomes.[61]

One unresolved issue is whether focusing on the trauma, either through exposure or cognitive reframing, is necessary for recovery. The findings that interventions such as present-centered therapy and, in civilians, interpersonal psychotherapy[71] are associated with efficacy similar to that of trauma-focused therapy needs to be reconciled with the common assumption in the field that fidelity to a trauma-focused approach is essential for symptom improvement. VA/DoD treatment guidelines, and other guidelines, specify that patient preference should be a guiding factor in treatment selection. Yet little research has been conducted on patient preferences or on other behavioral and biological predictors of dropping out of care, clearly the strongest influence on treatment effectiveness.[62]

Several large-scale military-related PTSD trials are currently ongoing, including trials with active-duty service members, a population rarely studied but an important target for early interventions.

**Box. Descriptions of First-Line Interventions**

**Cognitive therapy.** Focuses on modifying dysfunctional thoughts, beliefs, and expectations by identifying, challenging, and replacing maladaptive cognitions. Cognitive processing therapy (CPT) is the most widely used example of cognitive therapy in the Departments of Defense and Veterans Affairs.

**Exposure therapy**. Comprises psychoeducation, imaginal or narrative exposure (targeting trauma memories), in vivo exposure (targeting external stimuli or situations that the patient avoids because of the trauma), and processing of thoughts and emotions, with the aim of confronting, rather than avoiding, feared memories and stimuli. Prolonged exposure therapy (PE) is the most widely used example of exposure therapy in the Departments of Defense and Veterans Affairs.

**Eye movement desensitization and reprocessing (EMDR).** Asks patients to attend to emotionally disturbing material in brief sequential doses while focusing on an external stimulus, typically therapist-directed lateral eye movements. Additionally, treatment involves identifying bodily sensations associated with the image, identifying an aversive cognition associated with the trauma, and identifying an alternative positive cognition to replace the aversive cognition.

**Stress inoculation training (SIT)**. Teaches anxiety-management skills including relaxation training, breathing retraining, positive thinking and self-talk, assertiveness training, and thought stopping. It may also include cognitive restructuring and exposure, although these are optional elements.

A large (N = 900) multisite trial is directly comparing CPT and prolonged exposure in veterans,[72] although it remains to be seen to what extent continued focus on efficacy comparisons will improve care, particularly since equivalency between leading interventions has consistently been demonstrated in civilians.[59,73] Ongoing trials focus almost exclusively on 2 trauma-focused interventions, despite these therapies being rarely used in actual VA and DoD clinical practice (less than 10% of the time, in one estimate of New England region VA centers[74]). The effectiveness of psychotherapies for PTSD as actually delivered in the VA and DoD has received little empirical attention.[75]

Limitations of this descriptive review (which did not use formal meta-analytic techniques or access all international databases) include the relatively small number of studies and sample sizes, limiting generalizability. Studies often did not report key outcomes, such as symptom remission, loss of diagnosis, or clinically important subthreshold PTSD[76,77] (which would include individuals who met previous diagnostic criteria but no longer meet the latest criteria).[78] It is also noteworthy that the metrics of meaningful symptom improvement (typically a 10- or 12-point decrease in PTSD scores) are researcher-defined, not patient-defined; patient perspectives and preferences have not been a primary focus of research. Likewise, most trials have reported only total PTSD symptom scores, and the potential for differential treatment effects across symptom clusters remains unexamined. Trials also have not reported the need for continued care following CPT or prolonged exposure; for many patients, 12 sessions of manualized trauma- or non–trauma-focused treatment is insufficient. Definitions of treatment dropout also differ between studies, and studies often fail to delineate why patients dropped out. Moreover, military personnel and veterans participating in PTSD trials are often taking psychotropic medications concurrently (approximately three-fourths of participants in CPT and prolonged exposure trials), creating potential confounding. Data are lacking on the relative efficacy of psychotherapy compared with medication or the synergistic effects of combined treatments.[79] Last, although we considered group and individual therapy together, these 2 modalities are practically and mechanistically distinct. A recent meta-analysis of civilian and veteran group therapies found smaller effect sizes in combat samples; although group therapy outperformed waitlist controls, it did not outperform active-comparison conditions.[80]

## Conclusions

PTSD in military and veteran populations is a complex and difficult-to-treat disorder for which first-line trauma-focused psychotherapy approaches are not optimal. Although efficacious for some patients, first-line treatments have high nonresponse and dropout rates, and patients often remain symptomatic. Two principal clinical conclusions can be drawn from this review. First, the available evidence supports the use of either trauma-focused or structured non–trauma-focused therapies, depending on patient preferences or other factors that might promote treatment retention. Second, there is a need for improvement in existing PTSD treatments as well as the development and testing of novel evidence-based treatment strategies, whether trauma-focused or non–trauma-focused. An increasing number of novel therapeutic approaches have been shown efficacious to varying degrees, but progress in the field is unlikely without better understanding of treatment mechanisms, patient preferences, factors influencing treatment engagement and retention, and behavioral and biomarker prediction of differential treatment responses.

### Clinical Bottom Line

- Posttraumatic stress disorder (PTSD) is a disabling psychiatric condition common among military personnel and veterans
- A range of psychotherapies are available, but military-PTSD is complex and difficult to treat
- The available evidence supports the use of structured trauma-focused or non–trauma-focused approaches
- Although trauma-focused and non–trauma-focused interventions often improve symptoms, many patients continue to meet criteria for PTSD after treatment
- There is an urgent need for innovative treatment strategies, whether trauma-focused or non–trauma-focused


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*Study concept and design:* Steenkamp, Litz.
*Acquisition, analysis, or interpretation of data:* Steenkamp, Litz, Hoge, Marmar.
*Drafting of the manuscript:* Steenkamp, Litz, Marmar.
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