Treating Posttraumatic Stress Disorder in Military Populations:

A Meta-Analysis

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Abstract

Background: Military and Veteran populations experience higher rates of posttraumatic stress disorder (PTSD) compared to civilians. While trauma-focused psychotherapies are generally recommended as first-line treatments, the effectiveness of various treatments in military populations requires further investigation.

Objective: This meta-analysis aims to synthesize the current literature regarding effectiveness of psychotherapies, pharmacotherapies, and combination treatments for PTSD in military populations.

Data Sources: This preregistered review (PROSPERO: CRD42021245754) was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Cochrane guidelines. A search was conducted using PsycINFO, MEDLINE, Embase, CINAHL, and ProQuest Dissertations and Theses.

Study Selection: The final sample included data from 414 studies.

Data Extraction: Full study methodologies can be found in the published protocol (Liu et al, 2021).

Results: The pooled random-effects model found effect size across all PTSD treatments ($k = 712$) was $g = 0.96$, compared to $g = 0.45$ for control conditions ($k = 122$). Clinician-administered measures indicated larger treatment effects ($g = 1.02$) than self-reported measures ($g = 0.82$). Combination therapies yielded the largest effects ($g = 2.17$), outperforming both psychotherapies and pharmacotherapies alone. No significant differences were found across control conditions.

Conclusion: Findings suggest that integrating psychotherapies and pharmacotherapies may address multiple dimensions of PTSD more effectively than monotherapies. However, these results contrast with the prioritization of trauma-informed psychotherapies over pharmacotherapies, as recommended by the 2023 US Department of Veterans Affairs/Department of Defense guidelines. Future research should focus on subclass analyses and long-term outcomes to refine treatment strategies for PTSD in military populations. Tailoring treatment plans to individual needs remains crucial for optimizing recovery and long-term symptom management.

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Posttraumatic stress disorder (PTSD) presents with a complexity of symptoms and challenges for the individual. The primary symptom clusters for diagnosis include re-experiencing the traumatic event, avoidance of internal or external triggers, and stimuli that may remind the individual of the trauma, emotional and cognitive distress, and hyperarousal.[1,2] Military and Veteran populations experience comparably higher rates of PTSD relative to civilians.[3] Furthermore, substantive literature highlights distinctions in PTSD risk factors, etiology, prognosis, and recovery in military populations due to the nature and extent of military-related trauma exposures.[4] Altogether, these nuances add a layer of complexity to an already difficult mental illness to treat. Meanwhile, meta-analytic evidence and treatment guidelines for PTSD have often focused on findings from civilians and general populations,[5–7] with restrictive criteria of inclusion that often limits evidence to randomized control trials. Together, they reduce the applicability of evidence to real-life contexts that are often marked by issues of comorbidities and treatment of chronic conditions with multiple interventions.

Editor's Note

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Clinical Points

- This meta-analysis revealed that pharmacotherapy and psychotherapy are equally effective for treating military-related PTSD.
- Combining pharmacotherapy and psychotherapy produced the most significant effects, outperforming either approach used alone.
- Treatment planning for military and Veteran populations should prioritize patient-centered approaches, incorporating combination therapies to address complex symptom profiles where appropriate.

Treating PTSD

In practice, treating PTSD often begins with either trauma-focused psychotherapy or psychotropic medication. Past meta-analyses have generally found trauma-focused psychotherapies to be of greater effect compared to psychotropic medications (eg, effect size [95% CI] of −2.74 [−2.97 to −2.50] vs −1.50 [−1.56 to −1.43]).[7] Indeed, trauma-focused psychotherapies are recommended as first-line treatment, and "gold standard" interventions include cognitive processing therapy, eye movement desensitization and reprocessing, and prolonged exposure.[8,9]

Medication treatments are also frequently prescribed for PTSD. Pharmacotherapy focuses on managing psychiatric symptoms by modulating neurotransmitters in the brain. First-line pharmacologic treatments include the use of selective serotonin reuptake inhibitors (SSRIs: eg, citalopram, paroxetine, sertraline, fluoxetine) and selective serotonin and norepinephrine reuptake inhibitors (SNRI: eg, venlafaxine, duloxetine).[8] The SSRIs primarily enhance serotonergic signaling to regulate hyperactivity in the amygdala, improve connectivity with the prefrontal cortex for emotional regulation, and normalize hippocampal activity, while SNRIs additionally increase norepinephrine levels, addressing adrenergic dysregulation to reduce hyperarousal and improve prefrontal control over limbic activity. Together, these modulations establish balance in neural circuits responsible for fear response, emotional regulation, and memory processing.[10] Outside of commonly used antidepressants, other agents may be used, including sympatholytic (eg, clonidine; modulate the adrenergic system to reduce hyperarousal),[11] anxiolytics (eg, benzodiazepines; enhance GABAergic activity to exert calming effects on the limbic system), antipsychotics and anticonvulsants (eg, quetiapine, lamotrigine; modulate dopaminergic or glutamatergic pathways, respectively, impacting neural circuits involved in emotional regulation and hyperexcitability, such as the striatum and hippocampus).[12–14]

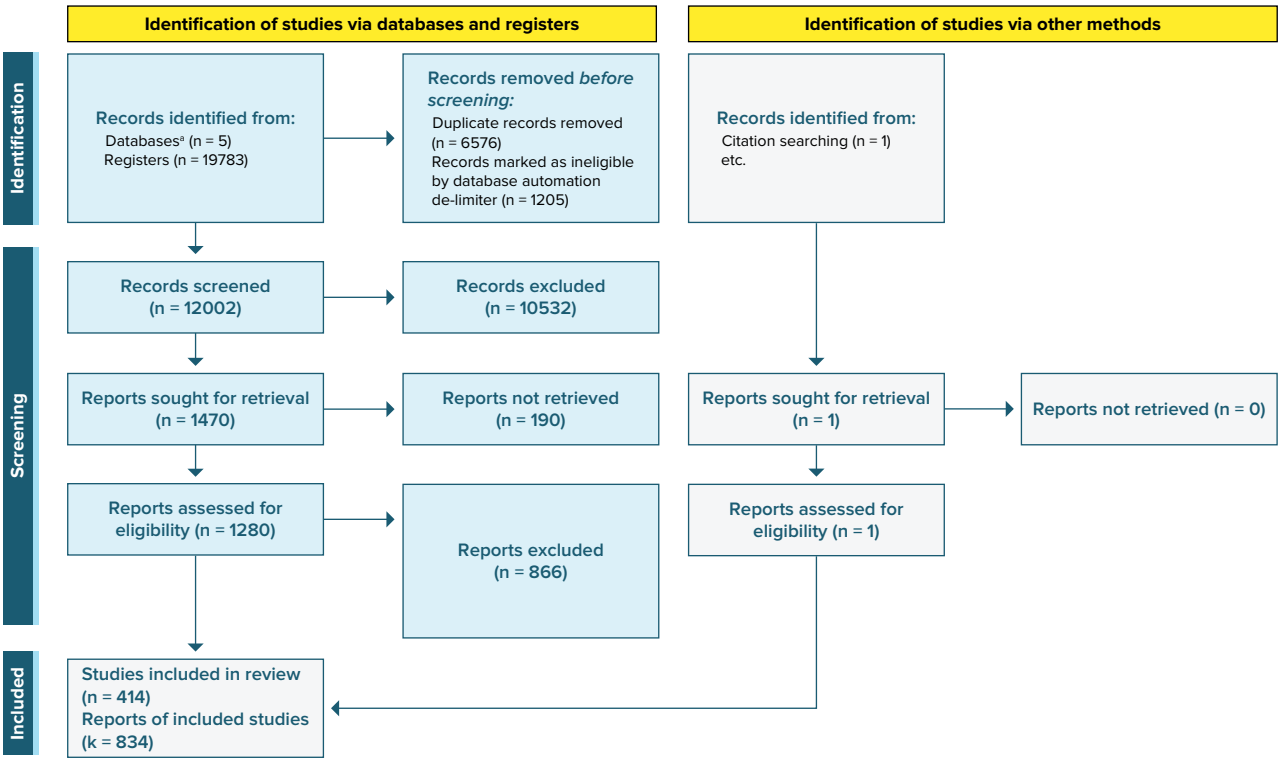
Beyond standard psychotherapies and pharmacotherapies, there has been an increased focus on the exploration of alternative and emerging treatments for PTSD. For example, psychedelics or alternative treatments such as psilocybin,[15] 3,4-methylenedioxymethamphetamine (MDMA),[16] and ketamine[17] are being explored in clinical trials for their potential to enhance psychotherapy in treatment-resistant cases. Animal-assisted therapy, often conducted with canines and horses, has been found to be effective in reducing depression, PTSD, and anxiety symptoms.[18] Mindfulness-based interventions, which focus on cultivating presence and awareness, are also adopted for their day-to-day benefits in stress management.[19] Altogether, these treatments represent a shift towards more diverse and holistic approaches to PTSD intervention and care.

The use and effectiveness of various treatments for PTSD in military populations may be influenced in different ways. First, military personnel adhere to strict regimens and participate in structured mental health training and routines as part of initiatives such as the Comprehensive Soldier and Family Fitness Program.[20] Relatedly, military culture and core values such as duty, honor, and resilience can influence treatment outcomes serving as both protective and risk factors.[21] These cultural factors can encourage treatment adherence but may also contribute to internalized stigma about seeking help. High rates of avoidance have been observed in military populations with PTSD, which may hinder session attendance, negatively impacting compliance with between session work, and ultimately result in high dropout rates for psychotherapies.[22] In addition, there may be a more pronounced degree of distrust for professionals observed in military populations, which may influence therapeutic alliance.[23–25] This distrust may be further exacerbated by real (eg, air crews) or misperceived potential career consequences associated with seeking psychiatric treatment, which may contribute to hesitancy among active-duty military personnel.[26] Finally, treatment outcomes may also depend on availability of health care coverage, clinician familiarity and previous success in using similar treatments, avoidance of specific side effects, and patient preference.[27,28] Altogether, obtaining a satisfactory treatment response may necessitate successive trials of several treatment modalities.

Review Aims

In 2023, the US Department of Veterans Affairs/Department of Defense PTSD Clinical Practice Guidelines reduced the number of recommended treatments and prioritized trauma-focused psychotherapy over pharmacotherapies as initial interventions. As of 2023, evidence reviewing the relative effectiveness of psychotherapies and pharmacotherapies for PTSD in military populations has been mixed, with a dearth of reviews synthesizing relevant literature in military populations.[5–7] While most reviews found the effects of psychotherapies to be greater than those of pharmacotherapies,[29] a few studies have indicated that pharmacotherapies may be superior.[30] However, it should be noted that most reviews are not

Figure 1.
Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) Flow Diagram



[a]PsycINFO-OVID (n = 5050); MEDLINE-OVID (n = 3978); EMBASE-OVID (n = 5631); CINAHL (n = 5033); ProQuest Dissertation & Theses (n = 91).

focused on military populations and thus may overlook the nuances in which PTSD treatment may be distinct within these populations.

This study aims to address the lack of tailored meta-analytic evidence for PTSD treatments in military populations by synthesizing the effectiveness of psychotherapies, pharmacotherapies, and combination treatments specific to this group. While current treatment guidelines often prioritize trauma-focused psychotherapies, this analysis evaluates whether such prioritization is fully supported by evidence in military contexts. In this review, we will focus on overall differences between treatment groups and compare their effects against each other and to controls.

METHODS

The current meta-analysis is registered via PROSPERO (CRD42021245754)[31] and performed following PRISMA reporting guidelines. A search was conducted across the following databases: PsycINFO, MEDLINE, Embase, CINAHL, and ProQuest Dissertation and Theses. The search strategy used the following keywords: *treatment*, *trial*, *intervention*, *military*, *combat*, *soldiers*, *veterans*, *PTSD*, and *posttraumatic stress disorder*. The final sample included data from 414 studies published between 1980 and 2021 (Figure 1; for full list of included articles, see: https://osf.io/rt6zu/). Studies were included if they met the following criteria: (1) adult participants, (2) military population, (3) PTSD diagnosis attributed to military service, (4) incorporated some form of treatment, and (5) PTSD symptom change were measured using validated PTSD tools. Exclusion criteria included (1) reviews, (2) studies with fewer than 5 participants, (3) studies without a primary or secondary focus on PTSD in military populations, and (4) studies without quantitative data (eg, protocols).

Studies included treatment groups assessing psychotherapies ($k = 387$; interventions grounded in mental health care through psychotherapy delivered by registered mental health professionals), pharmacotherapies ($k = 86$; treatments that involve using medications as the primary method of therapy), combination therapies ($k = 55$; eg, combined treatments of psychotherapy and pharmacotherapy, multiple psychotherapies, and/or psychotherapy with experimental approaches), alternative therapies ($k = 184$; nonconventional and/or emerging approaches [eg, animal-assisted therapy or ketamine]), and 122 controls (waitlist control, active control/placebo, and treatment-as-usual). For combination therapies, we additionally distinguished between psychotherapy and

pharmacotherapy combinations, and other combinations in subgroup analyses. Of note, multiple samples may be extracted from the same study, and each study may contain more than one experimental condition (eg, psychotherapy vs pharmacotherapy vs control). In addition to study characteristics, sample characteristics, and moderator information, data extraction included pre-post changes on continuous measures of PTSD symptoms via validated self-report and clinician-administered measures of PTSD. Full study methodologies can be found in the published protocol via Liu et al.[31]

Data Integration and Analysis

Comprehensive Meta-Analysis[32] software and R[33] were used for all analyses. The inter-rater reliability for study inclusion following 2 rounds of screening by independent screeners was determined at $\kappa = 0.88$, indicating a high level of agreement. Studies were grouped based on treatment type and participant characteristics. Hedges g effect size was computed using the mean difference of pre- and postintervention values to determine treatment efficacy. A pre-post correlation of $r = 0.77$ was determined using mean correlation values of previous published meta-analysis.[34] While the meta-analytic database included data for all treatment conditions for both self-reported and clinician-administered data, the current paper will focus on examinations of psychotherapies, pharmacotherapies, and combination therapies relative to controls.[35]

RESULTS

Characteristics of the Included Studies

A total of 834 samples from the included studies contained data from 37,808 participants. Sample sizes ranged from 5 through 522, with significant variations across studies. Studies were conducted predominantly in the United States, followed by other allied nations, including Canada, the United Kingdom, and Australia. Of the samples included, 62 (–7%) were mixed military samples, 60 were active duty (–7%), and the remaining 712 were Veterans (–85%). Effect sizes reported in the current meta-analysis ranged from $g = -0.66$ to 17.25, $Q_{833} = 17{,}098.90$, $I^2 = 95.12$, $P < .001$. The Q and I^2 statistic indicate significant heterogeneity among the effect sizes, meaning variability is unlikely due to random chance alone. The mean effect size reported across all samples was a point estimate of 0.89, SE = 0.02, CI = 0.85–0.93.

Overall Effects of PTSD Treatments

To evaluate the overall effects of PTSD treatments, we pooled samples that contained psychotherapies, pharmacotherapies, combination therapies, and alternative or emerging forms of treatments. The overall mixed-model random effects model determined the effect size across all

Table 1.
Test Statistics for Comparison Analyses

				95% CI			
	k	*g*	SE	Lower	Upper	I^2	*Q*
Psychotherapy	*139*	*1.06*	*0.06*	*0.95*	*1.17*	96.56	–
Pharmacotherapies	–	–	–	–	–	96.02	0.47
Alternative	–	–	–	–	–	96.03	2.87
Combination	–	–	–	–	–	96.73	17.35***
Control	–	–	–	–	–	95.96	31.20***
Pharmacotherapy	*62*	*1.13*	*0.08*	*0.97*	*1.29*	93.88	–
Alternative	–	–	–	–	–	93.39	4.21*
Combination	–	–	–	–	–	95.37	14.59***
Control	–	–	–	–	–	93.36	28.20***
Alternative	*44*	*0.90*	*0.08*	*0.75*	*1.05*	92.53	–
Combination	–	–	–	–	–	95.46	21.96***
Control	–	–	–	–	–	91.93	10.97**
Combination	*18*	*2.17*	*0.26*	*1.66*	*2.68*	95.89	–
Control	–	–	–	–		95.19	35.72***
Controls	*47*	*0.56*	*0.07*	*0.43*	*0.70*	90.93	*4.54*
Active control/placebo	19	0.74	0.14	0.47	1.02	94.81	–
TAU	16	0.52	0.10	0.31	0.72	88.63	–
No treatment	12	0.41	0.07	0.28	0.54	55.23	–

Italicized values in Table 1 represent the reference subgroup's sample size (k), effect size (g), standard error (SE), and 95% confidence interval.
*$p < .05$; ** $p < .01$; *** $p < .001$.
Abbreviations: CI = confidence interval, g = Hedges g, k = number of samples, Q = Q-statistics (Cochran's observed dispersion), SE = standard error, TAU = treatment as usual.

treatment samples ($k = 712$) to be $g = 0.96$, SE = 0.02, CI = 0.92–1.01, compared to $g = 0.45$, SE = 0.04, CI = 0.37–0.52 for control conditions ($k = 122$). Of these reported effects, some were assessed using self-report measures, while others relied on clinician-administered interviews. We thus evaluated whether the mean estimate would vary as a result of measurement using Q-statistics.[36] Indeed, there was a significant difference between clinician-administered ($k = 263$) and self-reported ($k = 449$) values, $Q = 19.72$, $P < .001$. Across samples, clinician-administered measures of PTSD detected larger treatment effects ($g = 1.11$, SE = 0.04, CI = 1.01–1.19) compared to self-reported ($g = 0.89$, SE = 0.02, CI = 0.91–0.99). Given the observed differences in effect sizes, subsequent analyses were conducted with clinician-administered measures of PTSD.

Subgroup Analyses

To assess the effects of the treatment groups on clinician-administered PTSD symptom measures, a total of 263 samples were entered into a mixed, random effect model. The results indicated a significant difference across treatment groups; $Q_3 = 23.37$, $P < .001$. The pooled effect size showed a positive effect for all treatment groups ranging from $g = -0.90$ to 2.17. All treatments were significantly more effective compared to controls, while the evaluation of effect sizes between control groups did not detect differences across types of controls ($P = .1$). Effect sizes also did not significantly differ between psychotherapies and pharmacotherapies

Figure 2.
Funnel Plots of Standard Error by Hedges *g*[a]

[a]Funnel plot depicting the relationship between the standard error and Hedges *g* for the studies included in the meta-analysis. Blue circles represent actual studies, and red circles represent imputed studies identified through Duval and Tweedie's trim and fill method to adjust for potential publication bias. Studies above 0 on the x-axis represent positive effect sizes, whereas those below 0 indicate negative effect sizes. The symmetrical spread of circles around the mean effect size suggests lower risk of publication bias, while asymmetry indicates potential bias, with missing studies imputed to balance the distribution.

(*P* = .49), though pharmacotherapies were found to be more robust compared to alternative therapies (*P* = .04). Notably, combination therapies yielded significantly larger effects compared to monotherapies (psychotherapies, pharmacotherapies, and alternative therapies alone) (Table 1). While the unit of analyses were too small to compare combination treatments that included alternative therapies (eg, rTMS), we compared those that combined multiple psychotherapies ($g = 1.23$, SE = 0.21, CI = 0.81–1.65), with interventions combining psychotherapies with pharmacotherapies, $g = 2.48$, SE = 0.41, CI = 1.68–3.29. Between-groups analysis revealed a significant difference, $Q_1 = 7.32$, $P = .007$, suggesting that the robustness of combination therapies lies in psycho-pharmacologic interventions. Table 1 demonstrates the effects of various treatment and control groups in comparison analyses.

Publication Bias

Publication bias was assessed through several proxy measures, including visual evaluation of funnel plot, classic fail-safe N, and Duval and Tweedie's trim and fill. These variable indexes offer evaluations of entire biases that may be observed in study effects, as well as nuanced assessment of the degree of influence biases may have in the current sample.

Funnel plot. Visual inspection of the funnel plot of SE by Hedges *g* observes higher concentration of studies on the right side of the mean, relative to the left (Figure 2). Indeed, imputed SE values (in red) denote the number of missing studies. These observed values reflect that smaller studies with larger than average effects are likely published, potentially contributing to biases in effects represented in publications.

Classic fail-safe N. This meta-analysis incorporates data from 834 samples, which yield a z-value of 161.90289 and corresponding 2-tailed *P*-value of .00000. The fail-safe N is 5,690,042. This means that we would need to locate and include 5,690,042 "null" samples in order for the combined 2-tailed *P*-value to exceed .050. In other words, 6,822.6 missing studies would be needed to nullify the effects of the observed studies.

Duval and Tweedie's trim and fill. Under the random effects model, the point estimate and 95% CI for the combined studies are 0.89 (0.85–0.93). Using trim and fill, the imputed point estimate is 0.63 (0.58–0.67).

DISCUSSION

This meta-analysis summarizes outcomes for PTSD treatments in military populations. Our findings revealed that clinician-administered measures of PTSD indicated larger treatment effects compared to self-reported measures, likely due to clinicians' ability to detect subtle symptom changes and avoid biases inherent in self-reporting. In contrast to prior reviews,[37,38] the pooled estimates did not vary widely between individual psychotherapies, pharmacotherapies, and alternative treatments. Instead, we found the most robust evidence in support of combining therapies, and in particular, the combination of psycho-pharmacologic interventions relative to monotherapies alone.

These results align with growing evidence supporting the effectiveness of combination therapies, as highlighted by recent reviews, such as that by Guidi and Fava,[38] that suggest the sequential administration of psychotherapy

following pharmacotherapy may reduce the risk of relapse, further supporting the efficacy of combination therapies. Similarly, Stewart and Wrobel[30] emphasized that pharmacologic interventions might be particularly effective as initial treatments when symptom severity hinders psychotherapeutic engagement. Combination treatments may be more efficacious than monotherapies for several reasons. First, pharmacotherapy may provide rapid symptom relief, setting the stage for more effective psychotherapeutic interventions.[39] Further, the use of combination therapies is complementary to structured approaches to treatments as well as target-based approaches that use a combination of psychoeducation, psychotherapy, and pharmacotherapy to manage specific symptoms and outcomes.

Our findings suggest that prioritization of trauma-focused psychotherapy over medications is not fully supported by evidence.[40] This paper was intended to provide a high-level overview of treatment effects while contributing additional information to debates on the effectiveness between psychotherapy and pharmacotherapy in military populations. Despite the robust findings in support of combination therapies, the choice between treatment modalities should ultimately be tailored to individual patient needs by incorporating clinician recommendations, patient preferences, symptom profiles, and logistical considerations such as access to care and support systems. Study findings complement the need for client-centered and open-minded treatment planning when treating PTSD in military populations.

Limitations

While this paper conducts broad comparative analyses, they are not intended to be a substitute for specific assessments of each treatment type. Further research is necessary to investigate distinctions among groups and therapy categories, including different categories of psychotherapies, classes of pharmacotherapies, emerging and alternative interventions, treatment modalities, and study and population characteristics. In addition, our efforts to be inclusive in our inclusion criteria may increase the heterogeneity of study samples and designs that contribute to underlying variabilities in methodologies, therapeutic interventions, and outcome measures, contributing to potential biases. Notably, the studies included in this meta-analysis spanned from 1980 to 2021, a period marked by significant changes in PTSD diagnostic criteria and treatments. These changes are represented via the heterogeneity in our sampled data, as evidenced in the I^2 and Q statistics presented. However, while the data are heterogeneous, they are uniformly heterogeneous across subgroups, thus suggesting results are unlikely due to chance. Future analyses may look at the impact of publication year and changes in diagnostic criteria on study effects. In our paper, we also focus exclusively on clinician-administered PTSD measure, which could underrepresent patient-reported experiences on treatment effectiveness. Finally, while the current review highlights differences in psychotherapies and pharmacotherapies, our review limits the comparison to other types of interventions. Future analyses will delve deeper into subclass analyses as well as explore networks of symptoms and comorbidities within the included sampled studies. The chronicity of symptoms also remains a concern, with long-term follow-up required to assess the sustainability of treatment effects.

CONCLUSION

In conclusion, this study highlights the importance of tailoring PTSD treatment plans to the unique needs of military populations. While trauma-focused psychotherapies remain an essential part of care, our findings suggest that pharmacotherapies and combination treatments should not be overlooked as viable and effective alternatives. Rigid prioritization of one treatment modality over others, particularly in the absence of strong supporting evidence, risks limiting the scope of care and may reduce the likelihood of optimal outcomes. Clinicians should adopt a flexible, evidence-based, and patient-centered approach to treatment planning, integrating both psychotherapy and pharmacotherapy where appropriate. Ultimately, this work underscores the need for expanded, nuanced strategies to better support recovery and resilience in military populations with PTSD.

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References

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5, Text Revision*. 5th ed. Text Rev. American Psychiatric Publishing; 2022.
2. World Health Organization (WHO). *International Classification of Diseases: 11th Revision (ICD-11)*. World Health Organization; 2022. Accessed April 14, 2021. https://icd.who.int/en.
3. Wisco BE, Marx BP, Wolf EJ, et al. Posttraumatic stress disorder in the US veteran population: results from the National Health and Resilience in Veterans Study. *J Clin Psychiatry*. 2014;75(12):1338–1346.
4. Leon MR, Osburn HK, Bellairs T. Processing war: similarities and differences in PTSD antecedents and outcomes between military and civilian war survivors. In: Harms PD, Perrewé PL, eds. *Occupational Stress and Well-being in Military Contexts*. 16. Emerald Publishing Limited; 2018:1–22.
5. Bisson JI, Ehlers A, Matthews R, et al. Psychological treatments for chronic post-traumatic stress disorder: systematic review and meta-analysis. *Br J Psychiatry*. 2007;190(2):97–104.
6. Bradley R, Greene J, Russ E, et al. A multidimensional meta-analysis of psychotherapy for PTSD. *Am J Psychiatry*. 2005;162(2):214–227.
7. Lee DJ, Schnitzlein CW, Wolf JP, et al. Psychotherapy versus pharmacotherapy for posttraumatic stress disorder: systematic review and meta-analyses to determine first-line treatments. *Depress Anxiety*. 2016;33(9):792–806.
8. VA/DoD Clinical Practice Guideline for Management of Posttraumatic Stress Disorder and Acute Stress Disorder. *VA/DoD Clinical Practice Guideline for Management of Posttraumatic Stress Disorder and Acute Stress Disorder*. U.S. Government Printing Office; 2023.
9. American Psychological Association. *Clinical Practice Guideline for the Treatment of Posttraumatic Stress Disorder (PTSD) in Adults*. American Psychological Association; 2017.
10. Huang ZD, Zhao YF, Li S, et al. Comparative efficacy and acceptability of pharmaceutical management for adults with post-traumatic stress disorder: a systematic review and meta-analysis. *Front Pharmacol*. 2020;11:559.
11. Arnsten AFT. Stress signalling pathways that impair prefrontal cortex structure and function. *Nat Rev Neurosci*. 2009;10(6):410–422.
12. McEwen BS, Nasca C, Gray JD. Stress effects on neuronal structure: hippocampus, amygdala and prefrontal cortex. *Neuropsychopharmacology*. 2016; 41(1):3–23. [Internet].
13. Howes O, McCutcheon R, Stone J. Glutamate and dopamine in schizophrenia: an update for the 21st century. *J Psychopharmacol*. 2015;29(2):97–115.
14. Khouzam HR. Pharmacological and psychoactive agents for treatment resistant posttraumatic stress disorder. *Adv Neurol Neurosci*. 2021;4(1):83–89.
15. Davis AK, Levin AW, Nagib PB, et al. Study protocol of an open-label proof-of-concept trial examining the safety and clinical efficacy of psilocybin-assisted therapy for veterans with PTSD. *BMJ Open*. 2023;13(5):e068884.
16. Mitchell JM, Bogenschutz M, Lilienstein A, et al. MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study. *Focus*. 2023;21(3):315–328.
17. Feder A, Parides MK, Murrough JW, et al. Efficacy of intravenous ketamine for treatment of chronic posttraumatic stress disorder: a randomized clinical trial. *JAMA Psychiatry*. 2014;71(6):681–688.
18. O'Haire ME, Guérin NA, Kirkham AC. Animal-assisted intervention for trauma: a systematic literature review. *Front Psychol*. 2015;6:1121.
19. Stephenson KR, Simpson TL, Martinez ME, et al. Changes in mindfulness and posttraumatic stress disorder symptoms among veterans enrolled in mindfulness based stress reduction. *J Clin Psychol*. 2017;73(3):201–217.
20. Office of the Deputy Chief of Staff. A leader's guide to soldier health and fitness headquarters. Department of the Army [Report]. 2016. Accessed April 14, 2021. https://media.defense.gov/2023/Jul/26/2003268435/-1/-1/1/LEADERS-GUIDE-TO-SOLDIER-HEALTH-AND-FITNESS.PDF
21. Hall-Clark BN, Wright EC, Fina BA, et al. Military culture considerations in prolonged exposure therapy with active-duty military service members. *Cognitive Behav Pract*. 2019;26(2):335–350.
22. Blais RK, Hoerster KD, Malte C, et al. Unique PTSD clusters predict intention to seek mental health care and subsequent utilization in US veterans with PTSD symptoms. *J Trauma Stress*. 2014;27(2):168–174.
23. Hartman A, Schuermann H, Kenney J. US Army soldiers' trust and confidence in mental health professionals. *Prof Couns*. 2018;8(3):213–225.
24. Hoge CW, Grossman SH, Auchterlonie JL, et al. PTSD treatment for soldiers after combat deployment: low utilization of mental health care and reasons for dropout. *Psychiatr Serv*. 2014;65(8):997–1004.
25. Kim PY, Britt TW, Klocko RP, et al. Stigma, negative attitudes about treatment, and utilization of mental health care among soldiers. *Mil Psychol*. 2011;23(1):65–81.
26. Heyman RE, Slep AMS, Parsons AM, et al. Systematic review of the military career impact of mental health evaluation and treatment. *Mil Med*. 2022;187(5–6):e598–e618.
27. Carvajal C. Poor response to treatment: beyond medication. *Dialogues Clin Neurosci*. 2022;6(1):93–103.
28. Mulvale G, Hurley J. Insurance coverage and the treatment of mental illness: effect on medication and provider use. *J Ment Health Pol Econ*. 2008;11(4):177–199.
29. VA/DoD Evidence-Based Practice Working Group. *VA/DoD Clinical Practice Guidelines*. U.S. Department of Veterans Affairs and Department of Defense; 2017.
30. Stewart CL, Wrobel TA. Evaluation of the efficacy of pharmacotherapy and psychotherapy in treatment of combat-related post-traumatic stress disorder: a meta-analytic review of outcome studies. *Mil Med*. 2009;174(5):460–469.
31. Liu JW, Nazarov A, Easterbrook B, et al. Four decades of military posttraumatic stress: protocol for a meta-analysis and systematic review of treatment approaches and efficacy. *JMIR Res Protoc*. 2021;10(10):e33151.
32. Borenstein M. Comprehensive meta analysis software. In: Egger M, Higgins JPT, Smith GD, eds. *Systematic Reviews in Health Research: Meta Analysis in Context*. Wiley; 2022:535–548.
33. RStudio Team. *RStudio: Integrated Development for R. RStudio*. PBC; 2020. Accessed April 14, 2021. https://www.rstudio.com/.
34. Liu JW, Ein N, Gervasio J, et al. Comprehensive meta-analysis of resilience interventions. *Clin Psychol Rev*. 2020;82:101919.
35. Liu JW, Nazarov A, Easterbrook B, et al. *The Effectiveness of Pharmacotherapy Versus Psychotherapy for Treating Post-Traumatic Stress Disorder in Military Populations: A Meta-Analysis*. PROSPERO; 2021. Accessed April 14, 2021. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021245754.
36. Tipton E, Pustejovsky JE, Ahmadi H. A history of meta-regression: technical, conceptual, and practical developments between 1974 and 2018. *Res Synth Methods*. 2019;10(2):161–179.
37. Coventry PA, Meader N, Melton H, et al. Psychological and pharmacological interventions for posttraumatic stress disorder and comorbid mental health problems following complex traumatic events: systematic review and component network meta-analysis. *PLoS Med*. 2020;17(8):e1003262.
38. Guidi J, Fava GA. Conceptual and clinical innovations of well-being therapy. *Int J Cogn Ther*. 2021;14(1):196–208.
39. Puetz TW, Youngstedt SD, Herring MP. Effects of pharmacotherapy on symptoms of post-traumatic stress disorder: a meta-analysis. *J Clin Psychiatry*. 2015;76(9):1234–1242.
40. Sonis J, Cook JM. Medication versus trauma-focused psychotherapy for adults with posttraumatic stress disorder: a systematic review and meta-analysis. *Psychiatry Res*. 2019;282:112637.