Post-Traumatic Stress Disorder Symptoms Contribute to Worse Pain and Health Outcomes in Veterans With PTSD Compared to Those Without: A Systematic Review With Meta-Analysis

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ABSTRACT

Introduction

Post-traumatic stress disorder (PTSD) and chronic pain are frequently co-morbid conditions in the U.S. veteran population. Although several theories about the cause of increased pain prevalence in individuals with PTSD have been presented, no synthesis of primary data informing the impact of co-morbid PTSD and pain has been completed. The purpose of this study was to systematically review the literature and quantify disability, function, and pain-related beliefs and outcomes in veterans with PTSD compared to veterans without PTSD.

Materials and Methods

A systematic search of three electronic databases was conducted. Inclusion criteria required pain-related comparison of veterans with PTSD to those without PTSD. Primary outcome measures and standardized mean differences (SMDs) were assessed for pain, function, disability, pain beliefs, and healthcare utilization using a random effects model.

Results

20 original research studies met inclusion criteria and were assessed for quality and outcomes of interest. The majority of studies were cross-sectional. Veterans with PTSD and pain demonstrated higher pain (SMD = 0.58, 95% CI 0.28–0.89), disability (SMD = 0.52, 95%CI 0.33–0.71), depression (SMD = 1.40, 95%CI 1.2–1.6), catastrophizing beliefs (SMD = 0.95, 95% CI 0.69–1.2), sleep disturbance (SMD = 0.80, 95% CI 0.57–1.02), and healthcare utilization; they had lower function (SMD = 0.41, 95% CI 0.25–0.56) and pain self-efficacy (SMD = 0.77, 95% CI 0.55–0.99) compared to veterans without PTSD.

Conclusion

In veterans with chronic pain, PTSD symptomology has a large effect for many negative health-related outcomes. This review supports the need for clinicians to screen and understand the effects of PTSD symptoms on patients with pain. Clinicians should recognize that veterans with PTSD and pain likely have elevated pain catastrophizing beliefs and decreased self-efficacy that should be targeted for intervention.

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INTRODUCTION

The "healthy warrior effect"[1] does not appear to protect service members and veterans from chronic pain. Similar to the high prevalence of pain in the U.S. population,[2] 63% of soldiers[3] and 43% of veterans[4] are diagnosed with a pain condition annually. Musculoskeletal pain is also the number one reason for a service member to be medically discharged from the military.[5] Veterans from recent conflicts are estimated to cost the U.S. between $300–$700 billion over the course of their lifetime in medical expenses and disability compensation.[6] Although the modern era service member has a greater chance of combat survival than any other period in the history of warfare because of increased body armor[7] and medical evacuation capabilities,[8] not all wounds are visible or result in a purely physical injury.[9]

One of the "wounds" that often accompanies combat trauma is post-traumatic stress disorder (PTSD), with a prevalence of ~10–17%[10] among soldiers with previous combat deployment. PTSD is diagnosed following exposure to life-threatening trauma and the presence of intrusive

symptoms, avoidance, negative cognitions, and hyperarousal. These symptoms persist for at least 1 month following trauma exposure and impair the individual's function.[11] As the Department of Defense has prioritized identifying PTSD and other neurocognitive disorders within active duty and veteran populations,[12] it is evident that PTSD is not an isolated condition.[13] Among one sample of 90 treatment seeking veterans with PTSD, 66% of them also had chronic pain.[14] The phenomenon of co-morbid pain and PTSD is not unique to the veteran population, as meta-analysis has indicated PTSD as a significant risk factor for developing chronic, widespread pain.[15] In Afari,[15] individuals with a history of combat PTSD incurred the highest odds of developing chronic, widespread pain with a pooled odds ratio of 3.06. Furthermore, increased baseline pain predicts the development of PTSD longitudinally.[16]

The bi-directional risk for pain and PTSD in the literature appears to support some of the theories offered to explain the co-morbidity of these two conditions. One theory is that individuals possess a shared vulnerability[17]; faced with a traumatic event or injury, some individuals have a higher risk for developing disability compared to a resilient individual. Another explanation involves mutual maintenance[18] in which PTSD and pain reinforce the chronicity of each other whereby hypervigilance in someone with PTSD elevates potential threats and pain serves as an on-going threat that elevates hypervigilance in a continual cycle. Finally, altered central nervous system sensitivity because of PTSD symptoms could increase nociceptive signaling and amplify the subjective pain experience.[19] While the exact mechanism for the relationship between chronic pain and PTSD may be lacking,[20] evidence certainly supports many common neurobiological processes and neuroanatomic structures between pain and PTSD.[21]

At the same time, there are several theories that postulate mechanisms for the co-occurrence of chronic pain and PTSD, and several narrative reviews have also offered potential treatment strategies for the co-morbid veteran population.[22,23] A major limitation with narrative reviews, however, is the potential for selection bias for presented articles.[24] Furthermore, despite the abundance of theory and commentary regarding PTSD and pain, controversy still exists regarding the relationship between PTSD and depression, and other overlapping symptomology[25,26] that are common in chronic pain populations.[27] Some argue that disentangling PTSD from other stress-related conditions like depression is not possible.[28] Since depression is common in individuals with pain and PTSD,[29,30] comparing those with and without PTSD might identify distinct aspects of PTSD when it comes to the pain experience.

Incomplete understanding of the unique aspects of PTSD and pain may contribute to suboptimal outcomes for individuals with co-morbid pain and PTSD. As integrated treatment programs have emerged for the veteran population with chronic pain,[31] some treatment programs specifically directed at veterans with PTSD and pain have yielded nearly 50% drop-out rates,[32,33] highlighting the need for further research. Systematically reporting the profile and characteristics of a veteran with co-morbid pain and PTSD is a first step in developing targeted interventions. The purpose of this study, therefore, was to systematically review the literature and quantify disability, function, and pain-related beliefs and outcomes in veterans with PTSD compared to veterans without PTSD.

METHODS

Article Selection

This study follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[34] The primary author performed an electronic search of CINAHL, Medline, and PsychINFO according to the strategy in Supplementary Material Table SI, resulting in 192 articles (June 1982–April 2017). During this initial stage, exact duplicates, books, dissertations, and titles that clearly did not meet inclusion criteria were removed. The authors next reviewed abstracts and full text of 163 publications.

To be included in the systematic review and meta-analysis, the following inclusion criteria were applied:

- Articles available in English.
- Participants were U.S. active duty military or veterans with at least 30% of participants reporting pain.
- The authors examined pain, disability, beliefs, or other health-related outcome.
- The authors presented group means with standard deviation, risk/odds ratio with confidence interval, or other descriptive measure between groups with and without PTSD.

Articles were excluded if they did not meet these inclusion criteria, or if the primary study population was traumatic amputee, burn injury, spinal cord injury, inpatient, sexual trauma, or headache pain. The populations in the exclusion criteria would likely add too much variability in patient characteristics and outcomes. Although this systematic review was not prospectively registered, all inclusion criteria were developed a priori except for requiring at least 30% prevalence of pain.

After applying inclusion/exclusion criteria, 18 articles were identified for systematic review and meta-analysis. The primary author also searched the reference list for all included articles for relevant publications, identifying two additional articles that met established inclusion criteria. This resulted in 20 articles that were included in the systematic review and meta-analysis (Fig. 1). Next, the primary author reviewed all articles and graded them for methodological quality and risk for bias. Since the majority of articles included in the review were observational, the primary author graded these articles with the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies[35] (NOS). The NOS is the preferred quality assessment tool for observational studies as recommended by the Cochrane group.[36] The NOS assesses potential bias

TABLE I. Methodological Quality Using the New-Castle Ottawa Quality Assessment Scale

Study	Selection (out of 4 ★s)	Comparability (out of 2 ★s)	Outcome (out of 3 ★s)	Total (out of 9)
Alschuler and Otis[53]	★★	★		**3/9**
Alschuler and Otis[54]	★★	★		**3/9**
Becker et al.[48]	★★★★	★★	★★	**8/9**
Finley[39]	★★★	★	★★	**6/9**
Helmer et al.[62]	★★	★★		**4/9**
Lew et al.[40]	★★★	★		**4/9**
Magruder et al.[49]	★★★	★★	★★★	**8/9**
Maguen et al.[41]	★★★★	★★	★★	**8/9**
McAndrew et al.[55]	★★	★	★	**4/9**
Morasco et al.[56]	★★	★★		**4/9**
Morasco et al.[42]	★★★	★	★★	**6/9**
Nunnink et al.[58]	★★	★★		**4/9**
Otis et al.[57]	★★	★★		**4/9**
Outcalt et al.[37]	★★	★		**3/9**
Outcalt et al.[43]	★★★	★★	★★	**7/9**
Outcalt et al.[38]	★★	★★		**4/9**
Rozet et al.[47]	★★★		★★	**5/9**
Seal et al.[45]	★★★	★	★★	**6/9**
Smeeding et al.[46]	★★★★	★	★	**6/9**
Taylor et al.[47]	★★★		★★	**5/9**

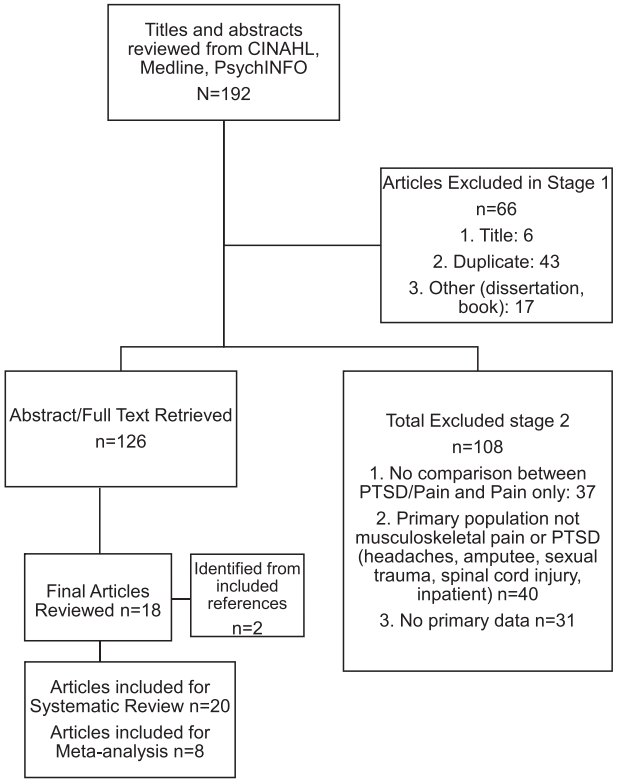


FIGURE 1. Study selection diagram.

related to selection, comparability, and outcomes (Table I). A maximum of nine stars or points is possible for each study, representing higher quality. For comparability, studies are awarded up to two stars depending on how they control for potential confounding variables. For this review, depression was selected as one covariate and a study could earn an additional star for controlling for a separate characteristic. For outcome, the follow-up period varied between 3 and 12 months, depending on the outcome assessed. Articles were reviewed and graded by the second author (PK). Discrepancies were discussed and resolved after coming to a consensus.

Data Extraction

The results of included studies reporting pain, disability, function, cognitive beliefs, and other health outcomes were summarized in tabular form for each article (Table II: population-level studies, Supplementary Material Table SII, remaining studies). When possible, the primary author extracted the group means with number of subjects per group and respective standard deviation and entered these values into Comprehensive Meta-Analysis (CMA) Software (version 2.2.064; BioStat, Englewood, NJ, USA) for meta-analysis for health outcomes in which more than one study measured a similar outcome (see Supplementary Material Table SIII). Since many of the studies utilized questionnaires and measures with different psychometric properties, the outcome measure most consistently used or most similar across studies was selected for meta-analysis and computation of the standardized mean difference (SMD). Although all these studies were within veterans and service members, the type of pain condition, population characteristics, and outcome measures varied among studies. Therefore, a random effects model was utilized in CMA except for one outcome in which two studies used identical patient populations and outcome measures.[37,38] Furthermore, as the majority of these studies were observational, bias was assessed through methodological quality assessment rather than through publication bias or funnel plot assessment.

TABLE II. Summary of Population-Level Research Studies

Study	Study type	Health outcomes	Analytic method	Results
Finley[39]	Retrospective cohort, PTSD $n = 14{,}018$, no PTSD $n = 38{,}426$	Suicide ideation, suicide attempt	Multinomial logistic regression	PTSD ↑ odds of suicide ideation, odds ratio (OR) 2.3 (2.0, 2.6) (95% confidence interval: lower limit, upper limit)
PTSD diagnosed: ICD-9	Setting: Population-level analysis of all OIF/OEF Veterans enrolled in VHA, 2009–2011			
Maguen[41]	Retrospective cohort PTSD $n = 11{,}417$, no PTSD $n = 13{,}482$	VHA MOVE! weight management program participation	Multivariate logistic regression	PTSD ↓ likelihood to achieve optimal participation (≥12 visits over 12 months) in MOVE! Program
PTSD diagnosed: ICD-9	Setting: Population-level OIF/OEF veterans with at least 1 MOVE! visit across VHA, 2008–2013			
Morasco[42]	Retrospective cohort, PTSD $n = 3593$, no PTSD $n = 19{,}053$	Risk of urine drug testing (UDT) for chronic opioid therapy (COT)	Binomial regression	PTSD ↑ risk by 19% to receive UDT
PTSD diagnosed: ICD-9	Setting: Population-level analysis of all veterans receiving chronic opioid therapy (≥90 days), 2011			Relative risk (RR) 1.19 (1.11–1.27), (95% confidence interval: lower limit, upper limit) $P < 0.0001$
Outcalt[43]	Retrospective cohort, PTSD $n = 5874$, no PTSD $n = 33{,}281$	Healthcare utilization to include primary care visits, prescriptions, specialty visits	Negative binomial	PTSD ↑ healthcare visits and medication utilization $P < 0.0001$
PTSD diagnosed: ICD-9 or PC-PTSD ≥3	Setting: All veterans enrolled in mid-west Veterans Integrated Service Network, 2002–2007			
Seal[45]	Retrospective longitudinal cohort, PTSD $n = 44{,}983$, no PTSD $n = 96{,}046$	RR of opioid prescription	Poisson regression	PTSD ↑ RR of opioid prescription by 4.32 (4.17–4.49) (95% confidence interval: lower limit, upper limit)
PTSD diagnosed: ICD-9	Setting: Population-level analysis of all OIEF/OEF veterans enrolled in VHA 2005–2008	RR of opioid-related adverse event		PTSD ↑ RR of multiple adverse events: wounds, self-inflicted injuries, overdose $P < 0.001$
Taylor[47]	Retrospective cohort, PTSD $n = 34{,}375$, no PTSD $n = 58{,}602$	Healthcare utilization, annual median cost	Descriptive, median value (interquartile range)	PTSD ↑ annual median healthcare costs
PTSD diagnosed: ICD-9	Setting: Population-level analysis of all OIEF/OEF veterans enrolled in VHA 2008–2009			$4978 ($2655–$9283), PTSD vs. $1974 ($953–$3890), without PTSD

OIF/OEF, Operation Iraqi Freedom/Operation Enduring Freedom; VHA, Veterans Health Administration.

RESULTS

PTSD Diagnosis

The most common method to assess PTSD exposure was through International Classification of Diseases (ICD-9) classification via electronic chart review.[39–48] Only one study[49] specifically referenced using the Clinician Administered PTSD Scale (CAPS)[50]—considered the gold standard in diagnosing PTSD—to generate the PTSD ICD-9 diagnosis. For chart review, two studies utilized clinical interview[40,44] while another[43] the Primary Care-PTSD Screen (PC-PTSD).[51] The next most common tool to assess PTSD symptomology was the PTSD Checklist (PCL).[52] Cut-off scores for the PCL vary between 30 and 60.[52] In this systematic review, five studies used a PCL cut-off score of $\geq$50[53–57] and two used a cut-off score of $\geq$41 in combination with the PC-PTSD.[37,38] Other studies[58,59] determined PTSD exposure included the Davidson Trauma Scale[60] $\geq$40 and the Mini-International Neuropsychiatric Interview (MINI).[61]

Quality Assessment

Quality assessment is summarized in Table I. Many of the studies were population based,[39,41–43,45,47,48] limiting selection bias. Others, however, consisted of veterans presenting for treatment at interdisciplinary pain specialty clinics.[37,38,46,53,54,57] Veterans referred to pain specialty clinics might differ in prognosis and characteristics compared to the average veteran. Adjusting for confounding factors is also important to limit potential study bias. Although most studies attempted to control for appropriate characteristics, many studies did not control for depression, which could inflate the contribution of PTSD symptoms if the PTSD group had disproportionate rates of depression. Finally, the cross-sectional design of many of the studies prevents determining the temporal relationship between PTSD symptomology and health outcomes as they were measured at the same time.

Pain and Depression

Of the seven studies that compared pain among veterans with and without PTSD symptomology, five were included in the meta-analysis.[37,38,53,56,57] Meta-analysis determined that veterans with PTSD had significantly higher self-reported pain for a pooled SMD of 0.58 (95%CI 0.28–0.89), indicating a medium effect size (Fig. 2).

Most of the studies included in the meta-analysis for pain severity did not control for major depression. One study which did adjust for major depression determined that veterans with and without PTSD did not statistically differ in the pain severity.[57] Another study, however, found significant and independent associations for pain severity between both the PTSD and depression even when adjusting for each condition.[38] For three studies,[37,38,56] it was possible to pool depressive symptoms in meta-analysis and determine that veterans with PTSD have significantly higher depressive symptoms than veterans without PTSD (SMD = 1.40, 95%CI 1.2–1.6), large effect.

Furthermore, another study determined that veterans with chronic, widespread pain (defined as pain in all four quadrants of a body pain chart) have 2.54 odds of being diagnosed with PTSD compared to those without chronic, widespread pain ($\chi^2 = 17.89$, $P < 0.001$).[62] Additionally, veterans with PTSD were less likely to achieve a clinically meaningful reduction in pain compared to individuals without PTSD in veterans receiving opioid agonist treatment.[48] This relationship persisted when adjusting for depression and other characteristics. Finally, veterans with PTSD were less likely to achieve a reduction in pain severity after completing a multidisciplinary and integrated healthcare program for pain.[46]

Disability and Function

For the studies that analyzed disability, a higher score indicates more disability. Three studies were included for meta-analysis.[37,38,57] Veterans with PTSD and pain had higher disability than veterans with pain only (SMD = 0.52, 95% CI 0.33–0.71, Fig. 2). For function, on the other hand, a higher score indicates greater participation in physical and occupational roles. Two studies[38,46] were analyzed for meta-analysis and found lower function in veterans with PTSD and pain (SMD = 0.41, 95% CI 0.25–0.56). Furthermore, one study found that veterans with PTSD and pain were much more likely to score lower than the median for physical function ($\chi^2 = 73.09$, $P < 0.001$).[62] Finally, Nunnink et al.[58] reported that veterans with PTSD scored significantly lower in physical function than veterans without PTSD; however, this relationship did not maintain significance after adjusting for other covariates.

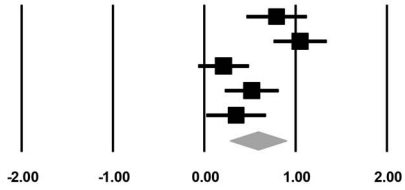
Cognitive Beliefs

Measures of pain catastrophizing and self-efficacy were included in the meta-analysis. Pain catastrophizing measures increased negative appraisals towards pain[63] and were reported by three studies in this review.[37,38,53] Compared to veterans without PTSD, veterans with PTSD report higher pain catastrophizing for a large effect size, SMD = 0.95 (95% CI 0.69–1.2). On the other hand, two studies[37,38] determined that veterans with PTSD and pain had lower self-efficacy as measured by the Arthritis Self-Efficacy Scale[64] compared to veterans with pain only. The SMD between the two groups was 0.77 (95% CI 0.55–0.99), reflecting a large effect size. These two studies indicate that veterans with PTSD and pain have decreased confidence to personally cope with their pain condition compared to veterans without PTSD.

In Outcalt et al.,[37] veterans with co-morbid PTSD and pain were more likely to rate their pain as central to their identity as measured by the Centrality of Pain Scale.[65] Another study captured a similar higher focus on physical pain despite co-morbid mental health disability; Alschuler[53] found that veterans with PTSD and pain were more likely to believe that pain

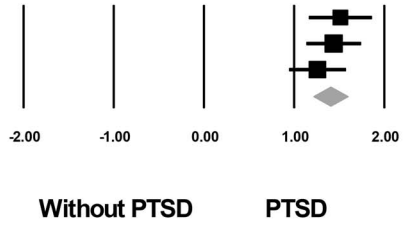
A: Pain

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Outcalt 2015, BPI*	0.792	0.171	0.029	0.456	1.128	4.624	0.000
Outcalt 2014, BPI*	1.049	0.151	0.023	0.754	1.345	6.954	0.000
Alschuler 2012, MPQ*	0.211	0.144	0.021	-0.072	0.493	1.461	0.144
Mbrasco 2013, MPI*	0.520	0.153	0.023	0.220	0.820	3.398	0.001
Otis 2010, MPQ*	0.349	0.169	0.029	0.018	0.681	2.064	0.039
	0.583	0.156	0.024	0.277	0.889	3.731	0.000



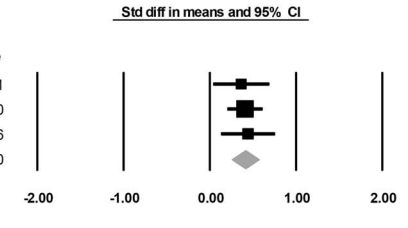
B: Depression

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Outcalt 2015, PHQ-9*	1.514	0.181	0.033	1.159	1.868	8.375	0.000
Outcalt 2014, PHQ-9*	1.439	0.157	0.025	1.130	1.747	9.141	0.000
Mbrasco 2013, BDI*	1.259	0.163	0.027	0.939	1.579	7.707	0.000
	1.398	0.096	0.009	1.210	1.586	14.556	0.000



C: Function

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Outcalt 2015, SF-36 PC*	0.364	0.168	0.028	0.034	0.694	2.162	0.031
Nunnink 2012**, SF-36 PC*	0.408	0.107	0.011	0.198	0.618	3.809	0.000
Smeeding 2010, SF-36 PF*	0.442	0.162	0.026	0.124	0.759	2.726	0.006
	0.406	0.079	0.006	0.252	0.561	5.148	0.000



D: Disability

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Outcalt 2015, Pain-specific disability days*	0.656	0.170	0.029	0.323	0.990	3.858	0.000
Outcalt 2014, RMDQ*	0.676	0.146	0.021	0.389	0.963	4.619	0.000
Alschuler 2012, SOPA-Disability	0.280	0.145	0.021	-0.003	0.564	1.939	0.053
Otis 2012, RMDQ*	0.491	0.170	0.029	0.157	0.825	2.878	0.004
	0.520	0.097	0.009	0.330	0.710	5.371	0.000

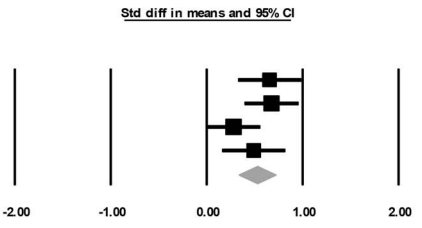


FIGURE 2. Meta-analysis of studies. ASES, arthritis self-efficacy scale; BDI, Beck depression index; BPI, brief pain inventory; CSQ, coping strategies questionnaire; MPQ, McGill pain questionnaire; MPI, multidimensional pain inventory; PC, physical component, PCS, pain catastrophizing scale; PF, physical function; PHQ, patient health questionnaire; PROMIS, patient reported outcome measurement information system; PTSD, Post-traumatic stress disorder; RMDQ, Roland Morris disability questionnaire; SOPA, Survey of Pain Attitudes.

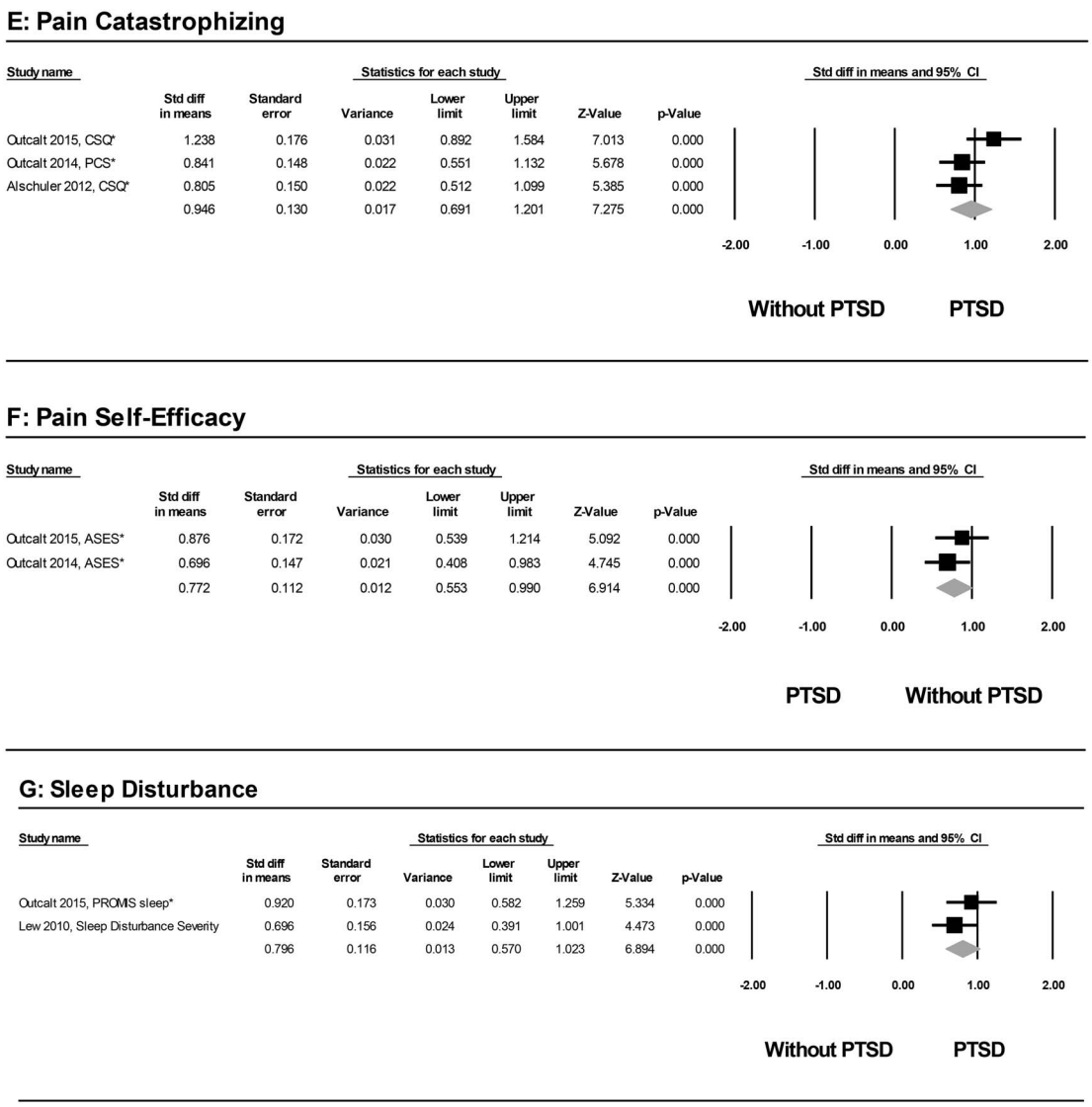


FIGURE 2. Continued.

is a sign of physical damage as measured by the Survey of Pain Attitudes (SOPA), Harm subscale[66]: 2.41(±.89) for PTSD versus 2.03(±.90) without PTSD, $P = 0.01$. The SOPA[67] is measured on a scale from 0 to 4 with 0 indicating "very untrue" and 4 "very true." This difference, however, did not remain statistically significant after Bonferroni correction.

Other maladaptive cognitions associated with PTSD symptoms include more negative affect strategies[57] and decreased mental health confidence.[59] Finally, individuals with PTSD and pain were more likely to rate the spouse's response to the veteran's pain as punishing,[54] indicating that veterans with PTSD and pain perceive their spouse responds to their pain in a negative manner.[68]

Other Health Outcomes

Two studies reported higher healthcare utilization and costs associated with PTSD and pain compared to pain only.[43,47] However, veterans with PTSD were less likely than veterans without PTSD to achieve optimal attendance of weight-management therapy sessions.[41] Additionally, veterans with PTSD and pain were more likely to be prescribed opioids for their pain.[44,45] Compared to veterans without PTSD, this resulted in a greater number of adverse events to include opioid-related overdose and accidents, and self-inflicted or violent accidents.[45] Similarly, veterans with PTSD and pain exhibited suicide-related behavior at a significantly higher rate than those with pain only.[39] In one cohort, PTSD increased the odds of suicide by 4.02 (95% CI 1.95–8.29).[49] Finally, two studies determined that veterans with PTSD had higher sleep disturbance than veterans without PTSD.[38,40] The relationship between PTSD and sleep disturbance remained significant above and beyond the pain interference.[40] These two studies were able to be included in meta-analysis and indicated a SMD of 0.80 (95% CI 0.57–1.02) for a large effect

size indicating greater sleep disturbance for veterans with PTSD.

DISCUSSION

The articles included in this systematic review and meta-analysis offer empirical support for the growing call to research and development of treatments specific to veterans with co-morbid pain and PTSD.[19,22,23,69] Previous narrative reviews have focused on clinical experiences[33] and conceptual models.[17,18,22,23] A systematic review by Fishbain et al. determined that pain and PTSD were highly associated and co-prevalent, with a particularly high co-morbidity among veterans.[70] This systematic review builds upon Fishbain et al. and identifies several additional studies in which PTSD and chronic pain are co-morbid and synthesizes the magnitude of negative health outcomes when these conditions exist together. Many veterans with pain hold maladaptive beliefs about pain regardless of PTSD diagnosis.[31] The results from this review indicate, however, that when PTSD symptomology is layered into the pain experience, veterans report significantly worse health outcomes to include higher pain intensity, pain catastrophizing, and disability. Furthermore, veterans with pain and PTSD show greater healthcare utilization, are more likely to be prescribed opioids resulting in adverse effects, and are more likely to engage in suicide-related behavior compared to veterans without PTSD. In addition, veterans with PTSD and pain have lower function and self-efficacy than veterans with pain only. These results that are notable and given their association with poor outcomes.

For example, this review revealed that veterans with PTSD had an average score of disability >15 as measured by the Roland Morris Disability Questionnaire (0–24)[71]; this score is considered at risk of poorer outcomes compared to a score of 10 or less.[72] Furthermore, a Pain Catastrophizing Scale (PCS) score of ≥ 16 has been proposed as an elevated score, increasing the risk of poor post-operative outcomes.[73] According to one study,[37] both veterans with PTSD (PCS score of 28.59 ± 12.20) and without PTSD (PCS score 18.90 ± 11.24) have elevated pain catastrophizing scores. Although such elevated pain catastrophizing should be confirmed with further studies, it appears that veterans with PTSD and pain score well above the recommended cut-off scores for pain catastrophizing. Patients with PTSD demonstrate enhanced sensitivity to threat as evidenced by increased amygdala plasticity,[74,75] which may lead to heightened attention to pain and pain catastrophizing. A recent treatment that has been proposed[76] to reduce pain catastrophizing and has been recommended for veterans with PTSD and pain is pain neuroscience education (PNE),[77] which aims to decrease the threat-value of pain.[78] When an individual is overly concerned that pain is a direct sign of tissue damage, the threat-value as well as pain itself increases according to the neuroscience of pain.[78]

In addition to pain catastrophizing, veterans with PTSD and pain demonstrated a large effect size of lower pain self-efficacy. Pain self-efficacy is the confidence to personally and actively cope with pain and is inversely related to fear of movement in patients with lower back pain.[79] According to meta-analysis, self-efficacy is a top mediator for pain and disability above and beyond pain catastrophizing.[80] Self-efficacy is one of most transcendent constructs in behavior change theories.[81] Since this characteristic is significantly lacking in veterans with PTSD and pain and plays such an important role for health outcomes, improving self-efficacy is likely an important target for treatment.

Another cognitive target for therapy is pain acceptance. Cook et al. determined that pain acceptance was negatively correlated with both disability as well as PTSD symptoms.[82] Acceptance Commitment Therapy (ACT) may be an appropriate therapy to address this finding. ACT is currently under trial in a veteran population[83] and the results from this systematic review warrant further investigation in veterans with pain and PTSD as results are promising in civilian populations for chronic pain.[84,85]

Although cognitive treatments certainly have evidence for treating the chronic pain, the risk for drop-out is high.[86,87] One review postulated that this is because patients perceive their mental health providers are not considering the biological components of their pain experience, but rather focus only on psychological contributions.[87] It may seem counter-intuitive that patients with co-morbid psychological disorders would focus more on their physical symptoms, but the evidence from this review suggests that patients with PTSD and pain consider their physical symptoms to be more concerning[53] and more central to their identity than veterans with pain only.[37] Explaining the link between post-traumatic stress and pain with PNE, therefore, may bridge the divide between cognitive and physical rehabilitation.[77] PNE may also increase patient satisfaction with biopsychosocial interventions, since patients with pain want a biological explanation for their pain[87] and frequently feel stigmatized when providers attribute mental health problems to physical pain.[88]

Limitations

There are some limitations to this review and the articles analyzed. First, the design for most of the articles precludes inferring that PTSD caused the negative health outcomes observed in these studies. Longitudinal prospective cohorts that measure PTSD symptomology as well as trauma exposure throughout the military service and before chronic pain symptoms appear that would be most ideal to ascertain the relationship of causation versus association. Second, there was a significant correlation between PTSD symptoms and depression in all studies that measured both conditions. In the studies that controlled for depression, the effects of PTSD symptoms on health outcomes were slightly

diminished,[37,38,57] but nonetheless an independent effect for PTSD could still be determined for many outcomes.[38,54] Third, there was variability among how the studies included in this review diagnosed PTSD. Only one study[49] utilized the CAPS, which is considered the gold standard for diagnosing PTSD.[50] Therefore, the most accurate description for participants included in this review is veterans with PTSD symptomology. This is not a significant limitation, however, as the diagnosis of PTSD is based on a set of symptoms following trauma exposure.[11]

Another limitation of this review is adding the requirement for articles to require at least 30% of pain prevalence among participants after initial inclusion criteria had already been developed. Since the purpose of this systematic review was to examine pain-related outcomes among veterans with and without PTSD, it was determined that some studies, which were ultimately excluded, did not adequately report on participant pain characteristics. Since population cohorts indicate pain prevalence of ~30–40%,[39,47] this study required at least 30% of participants to have pain to ensure comparability of study participants.

The diversity of symptoms captured by this systematic review is not only a strength, but also potentially a limitation. Because of the varied outcomes of the included studies, the prevalence of pain differed across studies. When pooling outcomes across these different studies, variability, and confidence intervals between subjects with and without PTSD symptomology may increase, leading to a less precise estimate of the mean differences in meta-analyses. On the other hand, including a diverse set of outcomes that are related to pain may increase the utility of this review to clinicians beyond pain specialties. Finally, many cohorts did not specify how many participants were eligible for their study but declined to participate. This could potentially introduce selection bias if for some reason veterans with more severe PTSD symptomology and health outcomes participated more in these research studies than veterans with milder PTSD symptoms.

CONCLUSION

In conclusion, this is the first systematic review with meta-analysis to capture the breadth of adverse health outcomes that are associated with PTSD and pain in veterans. This article synthesizes and quantifies significant health effects that appear to be worse in veterans with PTSD compared to those without PTSD or with pain only. As none of the pooled effect sizes crossed 0 in meta-analyses, the effects observed in the studies indicate that health outcomes are consistently worse for veterans with PTSD. Many of these effects remained even after controlling for depression. Clinicians should consider PTSD symptomology when treating veterans for pain as this review indicates a veteran with PTSD has higher pain, disability, and pain catastrophizing than veterans without PTSD. Furthermore, veterans with PTSD have lower self-efficacy and function. Research should continue to test and develop treatment strategies for veterans who have co-morbid PTSD and pain.

SUPPLEMENTARY MATERIAL

Supplementary Material is available at *MILMED* online.

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