Predictors of Long-Term Treatment Outcome in Combat and Peacekeeping Veterans With Military-Related PTSD

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ABSTRACT

Objective: Posttraumatic stress disorder (PTSD) is a significant psychiatric condition that may result from exposure to combat; it has been associated with severe psychosocial dysfunction. This study examined the predictors of long-term treatment outcomes in a group of veterans with military-related PTSD.

Method: The study consisted of a retrospective chart review of 151 consecutive veterans treated at an outpatient clinic for veterans with psychiatric disorders resulting from their military operations between January 2002 and May 2012. The diagnosis of PTSD was made using the Clinician-Administered PTSD Scale. As part of treatment as usual, all patients completed the PTSD Checklist-Military version and Beck Depression Inventory (BDI-II) at intake and at each follow-up appointment, the Short-Form Health Survey (SF-36) at intake, and either the SF-36 or the 12-item Short-Form Health Survey at follow-up. All patients received psychoeducation about PTSD and combined pharmacotherapy and psychotherapy.

Results: Analyses demonstrated a significant and progressive improvement in PTSD severity over the 2-year period ([n = 117] Yuan-Bentler $\chi^2_{40} = 221.25$, $P < .001$). We found that comorbid depressive symptom severity acted as a significant predictor of PTSD symptom decline ($\beta = -.44$, SE = .15, $P = .004$). However, neither alcohol misuse severity nor the number of years with PTSD symptoms (chronicity) was a significant predictor of treatment response.

Conclusions: This study highlights the importance of treating comorbid symptoms of depression aggressively in veterans with military-related PTSD. It also demonstrates that significant symptom reduction, including loss of probable PTSD diagnosis, is possible in an outpatient setting for veterans with chronic military-related PTSD.

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Veterans with combat or peacekeeping experience are at increased risk of posttraumatic stress disorder (PTSD)[1–5]; and lifetime prevalence estimates of PTSD among military samples range from 9%–30%.[6–9] The lifetime prevalence rate of PTSD in the Canadian Forces is estimated to be approximately 7%,[10] and the past 1-month prevalence rate among Canadian Forces veterans with pensionable medical conditions is 10.3%.[11] Military-related PTSD contributes to impaired psychosocial functioning[12,13] and can be chronic and treatment refractory.[14–16] Posttraumatic stress disorder often presents with psychiatric comorbidities, such as major depressive disorder and alcohol use disorder,[17,18] and rates of comorbidities are elevated among military PTSD samples.[19,20]

Treatment guidelines for PTSD include both psychotherapeutic and pharmacologic interventions.[21–26] Trauma-focused psychotherapy, such as prolonged exposure,[21,27,28] cognitive processing therapy,[29,30] and eye movement desensitization and reprocessing therapy,[31,32] is among the most promising psychotherapeutic interventions available[33,34]; but, while effect sizes are generally greater for psychotherapy than pharmacotherapy,[35] a meta-analysis by Stewart and Wrobel[36] demonstrated a greater reduction in both PTSD and depressive symptoms for pharmacotherapy compared to psychotherapy in military-related PTSD.

The pharmacologic treatment of military-related PTSD may also be challenging.[14,37,38] In a recent meta-analysis of all placebo-controlled studies from 1982 to 2012, Watts and colleagues[35] demonstrated efficacy for the selective serotonin reuptake inhibitors (SSRIs) paroxetine, sertraline, and fluoxetine; and the serotonin-norepinephrine reuptake inhibitor (SNRI) venlafaxine. This is in contrast to a previously published Cochrane review,[39] which demonstrated efficacy only for SSRIs. In both meta-analyses, pharmacotherapy appeared to be less effective for military-related PTSD.[35,39]

Atypical antipsychotics and anticonvulsants are commonly used in combination with an antidepressant to treat PTSD. The efficacy of atypical antipsychotics such as risperidone, olanzapine, and aripiprazole in combination with an antidepressant has been mixed. While several randomized controlled trials[40–42] have reported positive results for atypical antipsychotics, Watts and colleagues[35] demonstrated efficacy only for risperidone, in contrast to Krystal and colleagues,[43] who failed to show efficacy for risperidone for military-related PTSD. Nonetheless, these agents may be particularly beneficial in managing hyperarousal and severe dissociative symptoms[14] and for treatment-resistant depression,[44] which may present as a complicating factor in PTSD. Anticonvulsants such as carbamazepine, valproate, topiramate, and lamotrigine are also increasingly used in combination with antidepressants to treat symptoms of depression, mood instability, and impulsivity observed in PTSD.[45–50] With the exception of topiramate, which has demonstrated efficacy for PTSD as a monotherapy,[35] these agents are generally reserved as third-line agents and used in combination with first- or second-line agents.

Historically, treatment programs for military-related PTSD were less successful in achieving long-term symptom reduction and recovery.[12,51,52]

Clinical Points

- In this real-world study of veterans with military-related posttraumatic stress disorder (PTSD), comorbid depressive symptom severity acted as a significant predictor of PTSD symptom response.
- A critical need exists to assess and aggressively treat comorbid depressive symptom severity in veterans with military-related PTSD.
- Encouraging patients to remain in long-term treatment is important, as progressive improvement in PTSD severity can be achieved over a 2-year period.

Recent advances in the delivery of mental health care, such as stepped-care models, should allow for improved treatment outcomes.[53–56] However, the likelihood of experiencing psychosocial impairment consequent to military-related PTSD[13,57] suggests the importance of studying treatment outcomes for military-related PTSD in real-world clinical practices.

Factors associated with poor treatment response for military-related PTSD include chronicity and presence of comorbid psychiatric conditions,[18,37,38] a history of psychiatric illness,[58] and military-specific factors (ie, deployment experiences).[59–61] However, a number of weaknesses have also been identified in these studies. Many veterans included in Veterans Affairs–based studies have chronic PTSD and histories of poor treatment response.[62] Veterans may overendorse symptom severity and underreport symptom improvement to protect their disability benefits.[63,64] Finally, few studies have made use of growth modeling, relying instead on a single crude comparison of the entire sample's mean value over time.[65,66]

Therefore, the objective of the current study is to identify predictors of long-term treatment outcomes among a sample of treatment-seeking Canadian Forces veterans and members by using growth modeling. We hypothesize that comorbid psychiatric conditions and chronicity of PTSD symptoms will have a negative effect on long-term treatment outcomes.

METHOD

Participants and Procedure

The study consisted of a retrospective chart review of 151 veterans referred for outpatient treatment between January 2002 and May 2012 at the Parkwood Operational Stress Injury Clinic in London, Ontario, Canada. Individuals referred for psychiatric follow-up only, who no longer met *DSM-IV* criteria for PTSD, were excluded from the study. Approval was received from the Office of Research Ethics of the University of Western Ontario.

The Operational Stress Injury Clinic follows a standardized assessment protocol.[67] Participants completed the PTSD Checklist-Military version (PCL-M)[68] and Beck Depression Inventory-II (BDI-II)[69] at intake and at each follow-up appointment, the 36-Item Short-Form Health Survey (SF-36) at intake, and either the SF-36 or the 12-Item Short-Form Health Survey (SF-12) at follow-up.[70,71] All subjects received a comprehensive psychiatric evaluation and relevant laboratory tests.

Intervention

Upon intake, patients received psychoeducation about PTSD, the phases of treatment, and symptom management to set appropriate expectations for treatment.[23,59,72–74] Psychiatric care, focusing on symptom management, treatment of comorbid conditions, and management of functional impairment,[23,24,75] was provided every 2–4 weeks until symptom stabilization was achieved. Once patients were stable, psychiatric care was provided every 1–3 months. In addition to psychiatric care, patients were offered individual psychotherapy provided weekly or once every 2 weeks by a master's-level social worker or PhD-level psychologist. Over a 2-year period, treatment was tailored to meet the unique needs of each patient; participants were treated with varying pharmacologic agents and an array of evidence-based psychotherapeutic modalities. All patients were initially prescribed a first-line antidepressant such as an SSRI or an SNRI such as venlafaxine.[26] Treatment response was assessed by using psychiatric rating scales and was recorded at each follow-up appointment. Partial response to or intolerance of first-line treatment was addressed by changing antidepressant classes; combining 2 antidepressants of a different class, eg, adding mirtazapine or bupropion to an SSRI or augmenting venlafaxine with second- or third-line agents; or adding atypical antipsychotics or anticonvulsants.[41,45–50] Once symptom stabilization was achieved, patients remained on their medication combination for at least 2 years or until they had completed trauma-focused psychotherapy.

Instruments

The Clinician-Administered PTSD Scale (CAPS)[76] is a structured clinical interview that assesses frequency and intensity of PTSD symptoms. It has excellent interrater reliability, convergent and discriminant validity, and diagnostic utility.[77] The diagnosis of PTSD was made using the CAPS FI/I2/TSEV65 rule (ie, item frequency ≥ 1 and intensity ≥ 2 for at least 1 PTSD criterion B symptom, 3 criterion C symptoms, and 2 criterion D symptoms, and total severity > 65).[78] The Life Events Checklist[79] was used to establish the criterion A event before administering the CAPS.

The PCL-M was used to assess change in PTSD symptoms over time. The PCL-M is a 17-item, *DSM-IV*-based tool that uses a 5-point Likert-type scale (1 = "not at all" to 5 = "extremely") to assess military-related PTSD symptoms experienced over the previous month. Consistent with previous research studies and recommendations,[68] a cutoff score of 50 was used to establish the presence of "probable" PTSD.

To assess depressive symptom severity, the 21-item self-report BDI-II[69,80,81] was administered. It is a widely used depression scale demonstrating good reliability, yielding mean internal consistency estimates of 0.86 across studies.

The BDI-II has been well validated, with concurrent validity ranging from 0.55 to 0.96.

The 10-item Alcohol Use Disorders Identification Test (AUDIT)[82,83] was administered to assess the quantity and frequency of alcohol consumption and the presence of harmful and hazardous drinking. To identify cases of problematic alcohol use, we utilized the recommended cut off score of 8.[84]

Health-related quality of life (HRQoL) was assessed by the Physical Component Summary (PCS) score and the Mental Component Summary (MCS) score, reflecting physical and mental HRQoL, respectively.[85,86] The validity and reliability of the SF-36 and SF-12 have been well established in large samples, including veterans and patients with medical and mental health disorders.[87–92]

Exclusions and Treatment of Missing Data

As we were specifically interested in examining predictors of long-term treatment outcome, participants who did not complete 1 year of treatment (n = 17) or who were currently in treatment for less than 1 year (n = 17) were excluded from the analyses. The majority (n = 30, 88.2%) of the excluded individuals were missing over 70% of their treatment outcome data and had an unacceptable level of missing values to estimate the remainder of their missing values. Further, there were no significant differences in the demographic variables between patients who were included and excluded in the analysis. Results of independent sample *t* tests indicated no differences in age ($t_{149} = -1.56$, $P = .12$), baseline depression scores ($t_{147} = -1.02$, $P = .31$), and baseline PTSD scores ($t_{147} = 0.31$, $P = .76$). Results of χ^2 analyses indicated no differences in sex ($\chi^2_1 = 1.54$, $P = .66$), household income ($\chi^2_6 = 4.17$, $P = .65$), marital status ($\chi^2_2 = 3.39$, $P = .18$), and educational status ($\chi^2_5 = 1.84$, $P = .87$) between the 2 groups. For the remaining subjects with missing data, variables were estimated using maximum likelihood procedures with robust standard errors (SEs) for the growth modeling and multiple imputations for all other analyses.

Effective Sample Characteristics

Participants had a mean age of 40.18 years (SD = 8.10), and the majority were men (n = 112, 95.7%). Participants served a mean of 15.81 years in the military (SD = 8.52); and most were Canadian Forces veterans (n = 82, 70.1%), while 29.9% (n = 35) were still serving in the Canadian Forces. Additional relevant demographic data can be found in Table 1. A subset of the sample (n = 67) completed a questionnaire about exposure to potentially traumatic deployment experiences. Most who completed the questionnaire reported seeing dead bodies or human remains (85.1%, n = 57), knew someone seriously injured or killed (76.1%, n = 51), or received small arms fire (68.7%, n = 46).

Prevalence of PTSD per the CAPS diagnostic algorithm was 100%, with the mean CAPS score being 86.91 (SD = 17.2). Most participants were prescribed a combination of 2 or more antidepressants (n = 81, 69.2%) or a combination of antidepressants and antipsychotics (n = 62, 53.0%; see Table 1).

Table 1. Demographics for Treatment-Seeking Veterans

Variable	n (%)
Relationship status	
Common law/marriage	84 (71.8)
Divorced/separated	24 (20.5)
Never married	9 (7.7)
Work status	
Working/attending school or retraining	57 (48.8)
Unemployed	49 (41.9)
Sick leave	11 (9.4)
Education	
Completed secondary	49 (41.9)
Some postsecondary	17 (14.5)
Completed postsecondary	15 (12.8)
Deployment	
Balkan states (former Yugoslavia/Kosovo)	49 (41.9)
Africa (Somalia, Rwanda, Eritrea, and Sierra Leone)	17 (14.5)
Afghanistan	31 (26.5)
Traumatic event exposure	
Combat/war zone	103 (88.0)
Assault with weapon	92 (79.3)
Physical assault	83 (73.5)
Transportation accident	68 (59.1)
Captivity	21 (17.9)
Pharmacologic agents prescribed	
Antidepressant	111 (94.9)
Anticonvulsant	34 (29.1)
Antipsychotic	63 (53.8)
Stimulant	13 (11.1)
Benzodiazepine	6 (5.1)
Combination treatment	
≥ 2 Antidepressants	81 (69.2)
Antidepressants and antipsychotics	62 (53)
	Mean (SD)
Age, y	40.18 (8.10)
CAPS total baseline score	86.57 (17.30)
PCL-M total baseline score	64.30 (10.68)
BDI-II total baseline score	33.15 (10.45)
AUDIT total baseline score	8.47 (8.89)

Abbreviations: AUDIT = Alcohol Use Disorders Identification Test, BDI-II = Beck Depression Inventory-II, CAPS = Clinician-Administered PTSD Scale, PCL-M = PTSD Checklist-Military version, PTSD = posttraumatic stress disorder.

Baseline mean AUDIT score was 8.47 (SD = 8.89), and mean number of years with PTSD symptoms (chronicity) was 10.41 (SD = 6.97). Baseline mean BDI-II score was 33.15 (SD = 10.45), indicating depressive symptoms in the severe range, compared with 19.45 (SD = 10.48) after 2 years. Baseline mean PCL-M score was 64.30 (SD = 10.68) compared to 43.26 (SD = 13.06) after 2 years of treatment. By using a cutoff score of fifty, 65.8% (n = 77) of participants no longer met the probable PTSD diagnosis after 2 years of treatment.

Baseline mean MCS score was 18.37 (SD = 9.64) compared to 33.19 (SD = 10.73) after 2 years of treatment. Baseline mean PCS score was 36.54 (SD = 15.39) at baseline compared to 35.70 (SD = 11.63) after 2 years.

Statistical Analysis

Latent curve growth modeling[93] was conducted using Mplus 6.[94] Symptom trajectories for PCL-M and BDI-II scores were analyzed longitudinally over 9 time points (at 3-month intervals beginning at baseline and ending at 2 years

of treatment). For both PCL-M and BDI-II scores, we used an unconditional model centered at baseline (trajectory from baseline until 2 years of treatment). The growth factors of intercept (baseline scores) and slope (change in PCL-M/BDI-II scores) were modeled as latent variables. Random effects modeling allowed growth factors to vary across individuals. Lastly, residual covariances were fixed to 0, and maximum likelihood procedures with robust SEs was used as the estimation method.[95]

For the unconditional models, which did not have covariates, we assessed the interaction between the slope and intercept for the PCL-M scores and then BDI-II scores to evaluate whether baseline scores influenced participants' PTSD or depressive symptom severity change over time.

For the PTSD conditional model, we added 3 covariates: baseline depressive symptom severity (BDI-II) scores, chronicity of symptoms (years with PTSD symptoms), and baseline alcohol use scores (AUDIT). For the depressive symptom severity conditional model, we added the same covariates, substituting baseline PCL-M scores for baseline BDI-II scores. In both models, covariates were regressed on both the intercept and slope of the PTSD or depressive symptom latent trajectory, respectively.

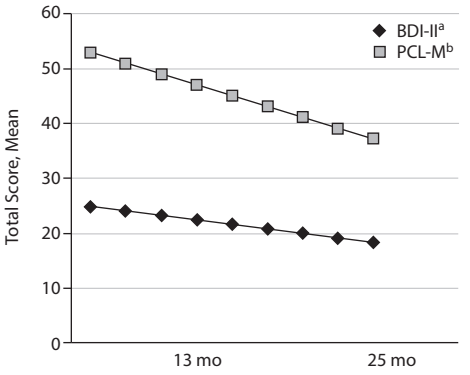
RESULTS

Unconditional Models

PTSD symptom severity. The PCL-M's unconditional growth model centered at baseline was significant ([n = 117] Yuan-Bentler $\chi^2_{40} = 221.25$, $P < .001$), indicating a significant decrease in PTSD severity over the 2-year follow-up period. The lack of a significant interaction between the slope and intercept (β = –.24, SE = .19, $P = .193$) suggests that baseline PCL-M scores were not related to changes in PCL-M scores over the 2-year period. The mean level of improvement in PTSD severity per time point was −1.97 units (β = –.96, SE = .24, $P < .001$). Significant variation across participants in terms of their baseline PTSD severity scores ($B = 168.84$, SE = 44.43, $P < .001$) and in their rate of improvement over time ($B = 4.19$, SE = 1.61, $P = .009$) supported the use of random rather than fixed-effects modeling.

Depressive symptom severity. The BDI-II's unconditional growth model centered at baseline was significant ([n = 117] Yuan-Bentler $\chi^2_{40} = 162.23$, $P < .001$), indicating a significant decrease in depressive symptom severity over the 2-year follow-up period. The significant interaction between the slope and intercept (β = –.344, SE = .147, $P = .019$) suggests a relationship between participants' baseline BDI-II scores and change in BDI-II scores over the 2-year period. The mean level of improvement in depressive symptom severity per time point was −0.83 units (β = –.62, SE = .215, $P = .004$). Significant variation across participants in terms of baseline BDI-II scores ($B = 120.558$, SE = 25.117, $P < .001$) and rates of improvement over time ($B = 1.778$, SE = .779, $P = .023$) supported the use of random rather than fixed-effects modeling.

Figure 1. Growth Model Estimated BDI-II and PCL-M Severity Scores (25-mo follow-up)



[a](n = 117) Yuan-Bentler $\chi^2_{40} = 162.23$, $P < .001$.
[b](n = 117) Yuan-Bentler $\chi^2_{40} = 221.25$, $P < .001$.
Abbreviations: BDI = Beck Depression Inventory-II, PCL-M = PTSD Checklist-Military version, PTSD = posttraumatic stress disorder.

Latent trajectories for both unconditional models are plotted in Figure 1.

Conditional Models

PTSD symptom severity. Depressive symptom severity had a significant effect on the intercept (β = .67, SE = .20, P = .001), indicating that baseline BDI-II scores were positively related to PTSD severity. Baseline BDI-II score was the only covariate that had a significant effect on the change in PTSD severity over a 2-year period (β = –.44, SE = .15, P = .004). Lastly, the lack of a significant interaction between the slope and intercept (β = .19, SE = .38, P = .627) indicates baseline PCL-M was not related to change in PTSD severity scores over a 2-year period as influenced by the covariates.

Depressive symptom severity. Baseline PCL-M scores (β = .47, SE = .09, P < .000) had a significant effect on the intercept, meaning baseline PCL-M scores were positively related to BDI-II scores. However, none of the covariates had a significant effect on change in BDI-II severity over a 2-year treatment period. The significant interaction between the slope and intercept (β = .47, SE = .13, P < .001) indicates a relationship between baseline BDI-II scores and change in BDI-II scores over the 2-year period as influenced by the covariates.

DISCUSSION

This study suggests that treatment gains, in terms of symptom reduction and loss of probable PTSD diagnosis, are possible with sustained treatment over a 2-year period. We found that depressive symptom severity was a significant predictor of PTSD treatment trajectory; however, unlike other studies,[62,96,97] we did not find evidence for chronicity and harmful alcohol use as predictors of PTSD treatment trajectory. Our response rate was also better than the 33%–50% reported in other outcome studies involving combat veterans.[96] The low response rate reported in previous studies may be due to the inclusion of veterans with previous treatment failures,[62] unlike our study in which many veterans

were seeking treatment for the first time. The flexibility in the treatment protocol of this real-world clinical study may have maximized potential treatment outcomes.

Participants in this study demonstrated significant reductions in PTSD and depressive symptom severity. Consistent with a previous study[98] and in contrast to others,[18,62] we did not find that greater PTSD symptom severity at intake was associated with greater symptom reduction. This finding was unexpected, as higher initial scores should have allowed for greater symptom improvement. This may be a result of overendorsement of self-reported symptoms at intake.[18]

After 2 years of treatment, 65.8% no longer met PCL-M criteria for probable PTSD, and there was observable improvement in MCS scores. However, even after 2 years of treatment, the observed mean MCS score of 33.19 suggests persistent impairment in mental health domains, stressing the importance of including functional impairment in treatment outcome monitoring.

Patients in this study saw a mean improvement in their PCL-M score of 1.97 units every 3 months. This finding is consistent with those of Davidson,[99] which demonstrated that patients treated for 6 months or more show a greater improvement in symptoms. The finding that patients continue to improve beyond 1 year stresses the importance of encouraging patients to persist with treatment. However, further studies would be needed to demonstrate whether participants who no longer met criteria for probable PTSD maintain their treatment gains following termination.

An important limitation of this study was the absence of a control group. As such, we cannot confidently conclude that the changes observed over time were due to the treatment provided. Although spontaneous recovery has been reported in more than 60% of patients with PTSD 1 to 6 years following a trauma,[100] patients in this study had, on average, experienced symptoms of PTSD for more than 10 years, making it less likely that they would experience a spontaneous recovery. Additionally, the current study used the PCL-M rather than the CAPS to measure PTSD severity over time. Readministering the CAPS may have led to a different conclusion. This study examined treatment response among treatment-seeking veterans at a specialized tertiary care clinic, which might constitute a distinctive subgroup of veterans. It is possible that intervening variables may have moderated treatment effects—for example, merely participating in treatment decreases social isolation, which may contribute to a positive outcome. The data also did not permit examination of the unique contributions of medication and psychotherapy on treatment outcome. As such, the results from this study should be viewed as an examination of clinical practice in a specialized outpatient clinic to provide a starting point for improving treatment programs for military-related PTSD. Furthermore, it could be argued that we should have implemented an intention-to-treat analysis in response to missing data. We chose, however, to exclude drop-outs (see Method section), as most of these individuals were missing over 70% of the time points. Those missing fewer data were retained and accounted for within the analyses. Finally, it is unclear to what extent disability compensation might have influenced the results. Unlike the United States, however, Canada has moved to a 1-time disability award, which might have mitigated the compensation-seeking effects reported in other studies.

CONCLUSIONS

Military-related PTSD is a common and disabling condition requiring prompt and evidence-informed treatment. Our results demonstrate that significant symptom reduction, including loss of probable PTSD diagnosis, is possible in an outpatient setting, and they emphasize the importance of encouraging patients to persist with treatment and evidence-based interventions focusing on comorbidity, especially symptoms of depression, to maximize treatment outcomes.

Drug names: aripiprazole (Abilify), bupropion (Wellbutrin, Aplenzin, and others), carbamazepine (Carbabtrol, Equetro, and others), fluoxetine (Prozac and others), lamotrigine (Lamictal and others), mirtazapine (Remeron and others), olanzapine (Zyprexa and others), paroxetine (Paxil, Pexeva, and others), risperidone (Risperdal and others), sertraline (Zoloft and others), topiramate (Topamax and others), venlafaxine (Effexor and others).

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