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ORIGINAL PAPER

Multimorbidity among Veterans Diagnosed with PTSD in the Veterans Health Administration Nationally

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Abstract

Over 30% of veterans treated for psychiatric disorders in the Veterans Health Administration (VHA) are diagnosed with Post-Traumatic Stress Disorder (PTSD), with most receiving treatment for war-zone stress they experienced decades previously. We examined psychiatric multimorbidity among these patients and consider its implications for treatment and research. Using national VHA data from Fiscal Year 2012 on all veterans diagnosed with PTSD, we compared those with PTSD only to those with one, two, and three or more concurrent (non-substance use) psychiatric disorders. Comparisons of these four groups on sociodemographic characteristics, medical and substance use co-morbidities, health service use, and psychotropic prescription fills were conducted using bi-variate and ordinal logistic regression methods. Of 638,451 veterans diagnosed with PTSD in FY2012, only 29.8% had PTSD alone; 36.7% had one concurrent psychiatric diagnosis, 21.3% had two, and 12.2% had three or more. Anxiety disorder and major depressive disorder were the most common concurrent diagnoses. Veterans with higher levels of multimorbidity were younger, had greater likelihood of recent homelessness, substance use disorder, and diverse medical diagnoses, along with increased mental health and medical service use and greater psychotropic medication use. Psychiatric multimorbidity is highly prevalent among VHA patients diagnosed with PTSD, and may represent an underappreciated and poorly understood clinical complication that poses unique challenges to effective treatment. Clinical attention and both epidemiological and interventional research on multimorbidity in PTSD patients are needed in order to better understand and treat this common but understudied phenomenon.

Keywords Veterans · PTSD · Multimorbidity · Comorbidity · War zone trauma

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Introduction

With a lifetime prevalence of 8% in the general adult population [1], post-traumatic stress disorder (PTSD) carries a substantial morbidity burden for both affected individuals and for the larger society [2], yet relatively few studies have considered correlates of its potentially decades-long course. A recent systematic review of naturalistic long-term studies suggested that between 18% and 50% of individuals experienced stable recovery from PTSD within three to seven years of baseline assessment [3], while an international study of 1575 people diagnosed with lifetime PTSD suggested 77% recovered within 10 years [4]. While many individuals with PTSD appear to experience a relatively brief trajectory, a sizable subset does not recover within one or more decades.

Veterans exposed to high levels of war-zone stress are among those at greatest risk for PTSD [5]. The National Vietnam Veterans Readjustment Study (NVVRS) reported a lifetime PTSD rate among male theater veterans of 31% [6], while fewer than 5% met diagnostic criteria for current PTSD when assessed four decades after their return from the combat zone [7]. A recent review of studies assessing health and mental health among those who served in the Vietnam war suggests that a substantial minority continue to suffer from mental and physical health problems including greater mortality, reduced functioning and well-being 40 years after the war [8].

PTSD is the most rapidly increasing diagnosis among veterans receiving mental health services from the Veterans Health Administration (VHA) and one of the most prevalent, affecting over 600,000 veterans per year, or 30% of all VHA patients diagnosed with a psychiatric disorder [9]. The treated prevalence of PTSD in VHA has continued to increase, both among younger veterans of recent Middle East conflicts, as well as among Vietnam Era veterans (virtually all of whom are over 60 years old) [9]. The magnitude and continuing increase in clinical prevalence of PTSD in VHA, especially among Vietnam Era veterans [10] is noteworthy, particularly in light of epidemiological evidence of extensive PTSD recovery within only a decade of trauma exposure [4]. However, combat experiences and witnessing atrocities was observed to be associated with reduced odds of early PTSD recovery [4]. The potential chronicity of PTSD has been previously noted among Vietnam era veterans [11], but combat-related PTSD outcome studies spanning decades are costly and remain scarce, and thus several observed inconsistencies within the longitudinal literature remain poorly understood.

War-zone stressors including combat and perceived threats are known to contribute to high rates of PTSD in veterans [12]. Since approximately 90% of VHA patients diagnosed with PTSD served during wartime eras [10], a reasonable assumption is that the vast majority of these individuals' PTSD symptoms relate, at least in part, to war-zone trauma. With 70% of military service members enlisting by age 21 [13] and approximately 80% serving 10 years or less [14], the majority of war zone trauma experienced by Vietnam era veterans occurred decades ago, during their 20s. Consideration of the distinctive clinical status of war-zone veterans many years after their traumatic experience is needed, given that as of 2018, virtually all Vietnam veterans are more than four decades past their war zone trauma (while most veterans of The Gulf War era and ongoing Middle Eastern conflicts have now surpassed the decade mark). Thus, the present study was motivated by an interest in identifying factors that may contribute to the sizable portion of veterans continuing to suffer from PTSD decades following their war-zone trauma [8].

A potentially illuminating perspective on the course PTSD over the very long term may lie in the emergent field of multimorbidity [15–17] as applied to military-related PTSD. It is

widely recognized that PTSD frequently presents with co-occurring conditions such as depression, anxiety, and substance use disorders [18]. For example, the National Vietnam Veterans Longitudinal Study (NVVLS) found comorbid major depression in 37% of Vietnam veterans with current war-zone-related PTSD four decades after their war zone service [7]. As many as 83% of civilians with PTSD meet diagnostic criteria for other psychiatric or substance use disorders (SUDs) [19], while 46% of a national sample of US veterans meeting lifetime criteria for PTSD also met lifetime criteria for SUD [20] and 22% of Veterans treated for PTSD in VHA nationally also had a current SUD [21]. While co-occurrence of PTSD and substance use has received considerable attention [22], and research increasingly examines the comorbidity of PTSD and medical conditions such as pain [23, 24], cardiometabolic disease [25, 26] and and traumatic brain injury (TBI) [27, 28], examination of multimorbidity among veterans with PTSD, more broadly conceived to include all concurrent psychiatric disorders, has yet to be undertaken.

Multimorbidity is defined as the occurrence of two or more chronic mental and/or medical conditions affecting the same individual at the same time [15–17], highlightingthe clinical reality that most patients do not present with a single "primary" diagnosis but rather with a tapestry of several diagnoses. Multimorbidity has been identified as "the most common condition" among older adults, and is thought to have adverse effects on overall health, functioning, perceived stress and quality of life because concurrent disorders tend to exacerbate each other, impairing psychosocial functioning as reflected in vocational disability, homelessness, and criminal justice involvement [15–17, 29, 30]. Greater medical multimorbidity has been consistently reported among VHA patients as compared to the general population [31, 32]. Multimorbidity has been examined within older [33] and younger veterans, with recent studies of both older [34] and younger veterans returning from recent conflicts [35–38] observing high rates of multimorbidity. Accordingly, this heightened multimorbidity has been found to be associated with increased service use, healthcare costs, and overall clinical complexity [32, 39–41]. In particular, a recent study found that 18% of the highest cost VHA patients have a PTSD diagnosis, and high cost PTSD patients had, on average, four or more additional medical diagnoses [39].

A key observation of the growing multimorbidity literature is that most randomized control trials (RCTs) exclude patients with comorbidities, potentially limiting generalizability of their findings to a minority of real-world patients [15, 40]. A recent review of the PTSD trial literature showed the vast majority (72%) of RCTs for PTSD treatments excluded individuals with comorbid substance use disorders [42] and a comparable proportion (75%) also excluded certain psychiatric disorders. In addition, a recent study examining generalizability of findings from studies of pharmacologic and psychotherapeutic treatments for PTSD found that 60–70% of individuals with PTSD would have been excluded from these trials [43]. Accordingly, the reduced or null efficacy of antidepressant treatment for PTSD observed among veterans [44–46] may relate, at least in part, to complexities associated with multimorbidity. The fact that multimorbidity excludes the majority of individuals with PTSD from participating in RCTs suggests that greater attention to this phenomenon is needed.

Steinert and colleagues [3] suggest that social factors and comorbid physical or mental health conditions may adversely affect the long-term course of PTSD and the few available longitudinal studies suggest that recovery from PTSD can be impeded by co-occurring psychiatric conditions and co-existing social dysfunction [5]. Older Vietnam veterans with PTSD have been found to have poorer self-rated health, greater risk of cancer, and higher reported treatment for stroke, high blood pressure, lung conditions, and hearing loss [47].

Moreover, recent research from the NVVLS suggest that 16% of all Veterans who were alive in the 1980s are now deceased, largely (79%) due to chronic diseases [48]. As those with PTSD were more than twice as likely to have died than those without [48], such findings further underscore the complicating and potentially lethal correlates of multimorbidity.

To better understand the clinical epidemiology of multimorbidity associated with PTSD in VHA, we examined all veterans diagnosed with PTSD in Fiscal Year (FY) 2012, and determined the proportions with PTSD as their only psychiatric diagnosis (PTSD+0); PTSD plus one other psychiatric diagnosis (PTSD+1), two other psychiatric diagnoses (PTSD+2), and three or more additional diagnoses (PTSD+≥3). In addition, we compared these four multimorbidity groups on sociodemographic variables; comorbid medical, substance use and psychiatric diagnoses; and health service and psychotropic prescription use. We hypothesized that psychiatric multimorbidity would be common in veterans with PTSD in VHA and would be associated with other health problems, indicators of social dysfunction, and high levels of service use.

Method

Sample and Source of Data

Using national VHA administrative data from FY2012 (October 1, 2011 – September 30, 2012), we identified all patients with at least one clinic visit or hospitalization associated with a PTSD diagnosis (ICD-9 code 309.81). These veterans were then classified into four groups based on psychiatric multimorbidity: those with PTSD alone (PTSD+0); PTSD and one other psychiatric disorder (major depressive disorder, anxiety disorder, bipolar disorder, schizophrenia, personality disorder, adjustment disorder, or other psychiatric disorder; PTSD+1); PTSD and two other psychiatric disorders (PTSD+2); and PTSD with three or more other psychiatric disorders (PTSD+≥3). Substance use disorders were not included as psychiatric disorders in this classification as our focus was specifically on psychiatric multimorbidity, but they were examined as potential concomitant disorders. Data on sociodemographic characteristics, clinical diagnoses, outpatient and inpatient service use and psychotropic prescription fills used to compare these groups were obtained from VHA administrative files.

Measures

Sociodemographic characteristics included age, race, sex, receipt of VA compensation or pension benefits and homelessness assessed by receipt of specialized homeless services or a V60 ICD-9 code during FY2012.

Clinical diagnoses including medical, psychiatric and substance use disorders were identified by ICD-9 codes. Medical diagnoses were identified through codes representing common serious chronic medical problems making up the Charlson Comorbidity Index [49]: i.e., conditions such as hypertension, diabetes mellitus, and chronic obstructive airway disease that together predict 10-year mortality. General medical risk factors including pain diagnoses, Body Mass Index, tobacco use disorder, and insomnia were also examined [50].

The number of outpatient primary care, specialty medical-surgical, general psychiatric, substance use, inpatient/residential, psychosocial rehabilitation, and emergency department visits were recorded using relevant clinic codes [51]. Psychotropic medications were classified

into five groups, including antidepressants, antipsychotics, anxiolytics/sedative/hypnotics, stimulants, and mood stabilizers. Prescriptions filled for prazosin, lithium and opioid pain medication were also examined.

Data Analysis

First, we classified the population of veterans diagnosed with PTSD into the four multimorbidity groups. Bivariate analysis was used to identify characteristics associated with multimorbidity, i.e., characteristics that had substantially greater prevalence among those with one or more additional psychiatric diagnoses as compared to those with PTSD alone.

Due to the large study sample, representing all VHA patients diagnosed with PTSD, we elected to use effect sizes as the criteria for substantial differences rather than *p*-values, consistent with past methodological approaches used in analyzing data from large medical data sets including some from VHA [52]. Use of effect sizes rather than p-values has been recommended to address the limitations of p-values including the sensitivity of p-values to sample size and their failure to determine the practical significance of statistically significant relationships [53]. For example, in a very large sample such as that of the present study, every variable is likely to have a "significant effect even if too small to be of importance. Moreover, in medical research, it is critical to determine the magnitude of the effect of a factor of interest [52]. Thus, Cohen's *d* was calculated for continuous variables (difference in means divided by the pooled standard deviations), and risk ratios were calculated for categorical variables to reflect the magnitude of the association of each patient characteristic and each of the groups as compared to the PTSD+0 group. Dichotomous variables with risk ratios greater than 1.5 or less than 0.67 [53], and continuous variables with Cohen's $d \geq 0.2$ or < -0.2 [54] were considered to be substantially different from the PTSD+0 group.

Because we developed four multimorbidity groups, representing an ordered dependent variable, we elected to use ordinal logistic regression [55] to identify independent predictors of increasing levels of multimorbidity (i.e., from PTSD+0 increasing to PTSD+ ≥ 3) with the PTSD+0 group as the reference group. Variables identified as substantial predictors of increasing multimorbidity in bivariate analyses were included in the ordinal logistic regression model. Because some variables were dichotomous and others were continuous, standardized regression coefficients were used as measures of effect to allow comparison of the association of categorical and continuous independent variables with increasing levels of psychiatric multimorbidity. Odds ratios are also presented showing the association of a one unit change in each independent variable to one-level increase in multimorbidity level e.g. age (per 10 years), receipt of a VA pension, homelessness, insomnia, TBI, hepatic disease, any pain diagnosis, alcohol use disorder, substance use disorder (any other substance combined), tobacco use disorder, mental health inpatient treatment, psychosocial rehabilitation, psychiatric or substance use outpatient visits (per 10 visits), emergency department visits, psychotropic medication use, and opioid pain medication use. A variable representing the date of the first VA outpatient visit during the fiscal year was used to control for potential differences in exposure to VA services during FY12 and, presumably, likelihood of diagnosis of additional conditions.

All analyses were conducted using SAS statistical software (version 9.2; SAS Institute, Inc., Cary, NC, USA). The study was approved by the institutional review board (IRB) of the VA Connecticut Healthcare System and was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki. A waiver of informed consent was granted for the study by

Table 1 Psychiatric comorbidities by multimorbidity group

	PTSD +1 Disorder $N = 234,126$ (36.7%)	PTSD +2 Disorders $N = 136,013$ (21.3%)	PTSD + >3 Disorders $N = 77,878$ (12.2%)	Effect Size PTSD+2 vs PTSD+1	Effect Size PTSD+ > 3 vs. PTSD+1
Psychiatric comorbidities				Risk Ratio	Risk Ratio
Major depression	41,257 (17.6)	47,029 (34.6)	44,910 (57.7)	1.96*	3.27*
Anxiety disorder	28,580 (12.2)	58,089 (42.7)	53,054 (68.1)	3.50*	5.58*
Adjustment disorder	10,878 (4.6)	14,353 (10.6)	19,452 (25.0)	2.27*	5.38*
Bipolar disorder	9156 (3.9)	10,353 (7.6)	15,221 (19.5)	1.95*	5.00*
Schizophrenia	4087 (1.7)	4088 (3.0)	5941 (7.6)	1.72*	4.37*
Personality disorder	1256 (0.5)	4608 (3.4)	14,305 (18.4)	6.32*	34.24*
Other psychiatric disorder	27,641 (11.8)	36,880 (27.1)	38,137 (49.0)	2.30*	4.14*

*indicates Risk Ratio ≥ 1.5

Table 2 Demographics and medical diagnoses by multimorbidity group

	PTSD alone *N* = 190,434 (29.8%)	PTSD+1 Disorder N = 234,126 (36.7%)	PTSD+2 Disorders N = 136,013 (21.3%)	PTSD+ > 3 Disorders N = 77,878 (12.2%)	Effect Size PTSD+1 vs. Alone		Effect Size PTSD+2 vs. Alone		Effect Size PTSD+ >/=3 vs Alone	
					Cohen's *d*	Risk Ratio	Cohen's *d*	Risk Ratio	Cohen's *d*	Risk Ratio
Demographics [n (%)]										
Age (mean ± SD)	56.0 ± 15.8	54.7 ± 15.1	53.1 ± 14.9	50.7 ± 14.4	−0.08		−0.19		−0.34*	
<40 Years	39,590 (20.8)	48,632 (20.8)	30,421 (22.4)	19,642 (25.2)		1.00		1.08		1.21
40–49 Years	17,583 (9.2)	28,410 (12.1)	20,125 (14.8)	14,240 (18.3)		1.31		1.60*		1.98*
50–64 Years	84,767 (44.5)	107,892 (46.1)	61,856 (45.5)	34,147 (43.8)		1.04		1.02		0.98
65+ Years	48,181 (25.3)	48,881 (20.9)	23,426 (17.2)	9768 (25.2)		0.83		0.68		0.50*
Male	182,892 (96.0)	216,008 (92.3)	120,591 (88.7)	65,589 (84.2)		0.96		0.92		0.87
Service Connected <50%	34,447 (18.1)	41,865 (17.9)	24,938 (18.3)	14,547 (18.7)		0.99		1.01		1.03
Service Connected >50%	121,308 (63.7)	138,500 (59.2)	72,074 (53.0)	35,353 (45.4)		0.93		0.83		0.71
Income (mean ± SD)	$26,007.07 ± $34,193.97	$25,086.27 ± $32,269.27	$24,082.90 ± $31,356.74	$22,127.35 ± $27,857.40	−0.03		−0.06		−0.12	
Body Mass Index (mean ± SD)	30.3 ± 22.2	30.5 ± 19.6	30.3 ± 12.6	30.2 ± 22.8	0.00		−0.01		−0.01	
OIF/OEF Era Veterans	47,837 (25.1)	56,561 (24.2)	33,018 (24.3)	18,215 (23.4)		0.96		0.97		0.93
VA Pension	1501 (0.8)	3597 (1.5)	2909 (2.1)	2542 (3.3)		1.95*		2.71*		4.14*
Homeless during the year	5138 (2.7)	11,783 (5.0)	11,810 (8.7)	14,623 (18.8)		1.87*		3.22*		6.96*
Medical Diagnosis – General [n (%)]										
Seizures	956 (0.5)	1872 (0.8)	1709 (1.3)	1640 (2.1)		1.60		2.50*		4.19*
Insomnia	10,564 (5.5)	19,320 (8.3)	14,990 (11.0)	11,089 (14.2)		1.49		1.99		2.57*
Traumatic Brain Injury (TBI)	6195 (3.3)	10,129 (4.3)	8172 (6.0)	6594 (8.5)		1.33		1.85		2.60*
Hepatic Disease	5790 (3.0)	8303 (3.5)	5533 (4.1)	4157 (5.3)		1.17		1.34		1.76*
Diabetes Mellitus	45,978 (24.1)	57,350 (24.5)	31,470 (23.1)	16,542 (21.2)		1.02		0.96		0.88
Cancer	14,173 (7.4)	16,642 (7.1)	9145 (6.7)	4720 (6.1)		0.96		0.90		0.81
HIV	496 (0.3)	825 (0.4)	642 (0.5)	555 (0.7)		1.35		1.81*		2.74*
Congestive Heart Failure	92,361 (49.5)	120,768 (51.6)	74,073 (54.5)	46,120 (59.2)		1.06		1.12		1.22
Myocardial Infarction	2257 (1.2)	2833 (1.2)	1704 (1.3)	1064 (1.4)		1.02		1.06		1.15
Total Medical Diagnoses (mean ± SD)	1.7 ± 1.5	1.9 ± 1.5	2.0 ± 1.5	2.3 ± 1.6	0.12		0.23*		0.39*	
Charlson Medical Severity Diagnosis Index (mean ± SD)	1.4 ± 1.7	1.5 ± 1.7	1.5 ± 1.7	1.6 ± 1.8	0.04		0.06		0.09	

Table 2 (continued)

	PTSD alone *N* = 190,434 (29.8%)	PTSD+1 Disorder N = 234,126 (36.7%)	PTSD+2 Disorders N = 136,013 (21.3%)	PTSD+ > 3 Disorders N = 77,878 (12.2%)	Effect Size PTSD+1 vs. Alone		Effect Size PTSD+2 vs. Alone		Effect Size PTSD+ >/=3 vs Alone	
					Cohen's *d*	Risk Ratio	Cohen's *d*	Risk Ratio	Cohen's *d*	Risk Ratio
Pain Diagnosis [n (%)]										
Headache	14,989 (7.9)	25,170 (10.8)	19,430 (14.3)	14,970 (19.2)		1.37		1.81*		2.44*
Diabetic Pain	8387 (4.4)	11,499 (4.9)	6802 (5.0)	3597 (4.6)		1.12		1.12		1.05
Musculoskeletal Pain	51,061 (26.8)	73,784 (31.5)	49,971 (36.7)	34,110 (43.8)		1.18		1.37		1.63*
Fibromyalgia	3441 (1.8)	6577 (2.8)	5525 (4.1)	4560 (5.9)		1.56*		2.25*		3.24*
Musculospasm Pain	3303 (1.7)	5584 (2.4)	4479 (3.3)	3458 (4.4)		1.38		1.90*		2.63*
Herpetic Pain	1312 (0.7)	2140 (0.9)	1595 (1.2)	1179 (1.5)		1.33		1.70*		2.20*
Somatic Pain Diagnosis	901 (0.5)	1615 (0.7)	1397 (1.0)	1364 (1.8)		1.46		2.17*		3.70*
Any Pain Condition	100,783 (52.9)	140,540 (60.0)	91,320 (67.1)	58,384 (75.0)		1.13		1.27		1.42
Substance Use Disorder Diagnosis [n (%)]										
Alcohol Use Disorder	18,431 (9.7)	39,490 (16.9)	31,576 (23.2)	27,166 (34.9)		1.74*		2.40*		3.60*
Cannabis Use Disorder	3833 (2.0)	8935 (3.8)	8338 (6.1)	9087 (11.7)		1.89*		3.05*		5.79*
Cocaine Use Disorder	2570 (1.3)	6459 (2.8)	6323 (4.6)	7604 (9.8)		2.04*		3.44*		7.43*
Opioid Use Disorder	3821 (2.0)	8705 (3.7)	8711 (6.4)	11,302 (14.5)		1.85*		3.19*		7.23*
Any Drug Use Disorder	9968 (5.2)	22,468 (9.6)	20,698 (15.2)	22,249 (28.6)		1.83*		2.91*		5.46*
Any Substance Use Disorder (Alcohol or Other Drug)	23,864 (12.5)	46,693 (19.9)	36,851 (27.1)	32,323 (41.5)		1.59*		2.16*		3.31*
Tobacco Use Disorder	34,590 (18.2)	51,235 (21.9)	34,227 (25.2)	24,938 (32.0)		1.21		1.39		1.76*

*indicates Risk Ratio ≥ 1.5 or Cohen's $d \geq 0.2$

Table 3 Service use and psychotropic medication use by multimorbidity group

	PTSD Alone N = 190,434 (29.8%)	PTSD+1 Disorder N = 234,126 (36.7%)	PTSD+2 Disorders N = 136,013 (21.3%)	PTSD+ >3 Disorders N = 77,878 (12.2%)	Effect Size PTSD+1 vs. Alone		Effect Size PTSD+2 vs. Alone		Effect Size PTSD+ >/= 3 vs Alone	
					Cohen's *d*	Risk Ratio	Cohen's *d*	Risk Ratio	Cohen's *d*	Risk Ratio
Service Use										
Any mental health service use [n(%)]	128,901 (67.7)	204,849 (87.5)	129,684 (95.3)	76,831 (98.7)		1.29		1.41		1.46
All outpatient visits (mean ± SD)	12.9 ± 16.1	18.1 ± 22.2	25.0 ± 30.0	41.6 ± 48.8	0.19		0.44*		1.05*	
Medical or surgical visits (mean ± SD)	7.9 ± 9.4	9.4 ± 10.5	10.9 ± 11.6	13.4 ± 13.5	0.13		0.28*		0.50*	
General psychiatric outpatient visits (mean ± SD)	4.5 ± 9.9	7.5 ± 14.2	11.7 ± 20.2	21.9 ± 34.5	0.17		0.39*		0.96*	
Psychiatric or substance abuse outpatient visits (mean ± SD)	5.0 ± 12.2	8.7 ± 18.4	14.0 ± 26.3	28.2 ± 45.1	0.16		0.38*		0.98*	
Emergency room visits (mean ± SD)	0.4 ± 1.1	0.5 ± 1.3	0.8 ± 1.8	1.6 ± 3.1	0.08		0.24*		0.71*	
Any mental health inpatient treatment [n (%)]	476 (0.2)	3411 (1.5)	6992 (5.1)	15,923 (20.4)		5.83*		20.57*		81.80*
Any residential treatment [n (%)]	854 (0.4)	2681 (1.1)	3673 (2.7)	6302 (8.1)		2.55*		6.02*		18.04*
Intensive substance use treatment	847 (0.4)	2300 (1.0)	2756 (2.0)	4248 (5.5)		2.21*		4.56*		12.26*
Intensive mental health services [n (%)]	165 (0.1)	807 (0.3)	981 (0.7)	1702 (2.2)		3.98*		8.32*		25.22*
Any community-based psychosocial rehabilitation services [n (%)]	8939 (4.7)	19,406 (8.3)	19,273 (14.2)	22,404 (28.8)		1.76*		3.01*		6.13*
Vocational rehabilitation [n(%)]	1480 (0.8)	4306 (1.8)	5173 (3.8)	7216 (9.3)		2.37*		4.89*		11.92*
Legal services [n(%)]	1699 (0.9)	3196 (1.4)	3006 (2.2)	3613 (4.6)		1.53*		2.48*		5.20*
Psychosocial residential rehabilitation services [n(%)]	385 (0.2)	1399 (0.6)	1806 (1.3)	3105 (4.0)		2.96*		6.57*		19.72*
Psychotropic medications [n (%)]										
Antidepressant	105,511 (55.4)	175,530 (75.0)	112,568 (82.8)	68,458 (87.9)		1.35		1.49		1.59*
Antipsychotics	16,405 (8.6)	40,449 (17.3)	33,536 (24.7)	31,274 (40.2)		2.00*		2.86*		4.66*
Anticonvulsant/mood stabilizer	29,787 (15.6)	54,305 (23.2)	39,612 (29.1)	31,474 (40.4)		1.48		1.86*		2.58*
Anxiolytic/sedative/hypnotic	54,984 (28.9)	90,858 (38.8)	64,657 (47.5)	43,589 (56.0)		1.34		1.64*		1.94*
Stimulants	2104 (1.1)	4238 (1.8)	3374 (2.5)	2716 (3.5)		1.64*		2.25*		3.16*
Prazosin	18,826 (9.9)	34,072 (14.6)	23,577 (17.3)	16,186 (20.8)		1.47		1.75*		2.10*
Lithium	283 (0.1)	2630 (1.1)	2564 (1.9)	3269 (4.2)		7.55*		12.68*		28.24*
Any psychotropic medication	126,143 (66.2)	197,473 (84.3)	123,784 (91.0)	74,397 (95.5)		1.22		1.29		1.34
Opioid pain medications [n (%)]										
Opioids	52,970 (27.8)	77,693 (33.2)	50,718 (37.3)	33,572 (43.1)		1.19		1.34		1.55*

*indicates risk ratio ≥ 1.5 or Cohen's $d \geq 0.2$

Table 4 Logistic regression model of ptsd multimorbidity, ranked by standardized estimate in regression model

	Estimate	Standard error	Standardized estimate	*OR*	95% CI
Any psychotropic medication (Yes/No)*	1.13	0.01	0.22	**3.11**	[3.07, 3.15]
Psychiatric/substance use outpatient visits (Per 10 visits)*	0.15	0.00	0.21	1.16	[1.16, 1.17]
Any mental health inpatient treatment (Yes/No)*	1.65	0.01	0.19	**5.20**	[5.06, 5.35]
Age (Per 10 years)*	−0.11	0.00	−0.09	0.90	[0.89, 0.90]
Medical or surgical visits*	0.01	0.00	0.08	1.01	[1.01, 1.01]
Insomnia (Yes/No)*	0.41	0.01	0.07	**1.51**	[1.48, 1.53]
Emergency department visits*	0.07	0.00	0.06	1.07	[1.06, 1.07]
Alcohol use disorder (Yes/No)*	0.26	0.01	0.05	1.30	[1.28, 1.32]
Any pain diagnosis (Yes/No)*	0.20	0.01	0.05	1.23	[1.21, 1.24]
Any substance use disorder (Yes/No)*	0.26	0.01	0.05	1.30	[1.28, 1.32]
Homelessness (Yes/No)*	0.30	0.01	0.04	1.35	[1.32, 1.38]
TBI diagnosis (Yes/No)*	0.31	0.01	0.04	1.36	[1.33, 1.39]
Any residential treatment (Yes/No)*	−0.41	0.01	−0.03	0.66	[0.65, 0.68]
VA pension (Yes/No)*	0.44	0.02	0.03	**1.56**	[1.50, 1.62]
Tobacco use disorder (Yes/No)*	0.07	0.01	0.02	1.07	[1.06, 1.08]
Hepatic disease (Yes/No)*	−0.07	0.01	−0.01	0.94	[0.91, 0.96]
Opioid pain medication use (Yes/No)*	0.00	0.01	0.00	1.00	[0.99, 1.01]

Bold indicates variable is a substantial predictor of multimorbidity based on effect size (Odds Ratio > |1.5|)

*Note: all *p*s < .0001 except for opiates, which is $p = .8774$.

the VA Connecticut IRB, as the data was administrative VHA data and does not include patient identifiers.

Results

The sample included 638,451 VHA patients with a current PTSD diagnosis in FY2012. Less than one-third (29.8%) had PTSD alone, i.e., with no co-occurring psychiatric disorder. Slightly over one-third (36.7%) had PTSD plus one other psychiatric disorder, while 21.3% had PTSD plus two other psychiatric disorders, and an additional 12.2% had PTSD plus three or more other psychiatric conditions.

Depression and anxiety disorders had the highest prevalence within each of the groups (Table 1) and ranged from 17.6% to 57.7% for depression and from 12.2% to 68.1% for anxiety disorders across multimorbidity groups. Personality disorders also appear highly associated with multimorbidity, as those in the highest multimorbidity group showed a 4.9 times higher proportion of veterans this disorder than the group with PTSD+1 disorder.

Sociodemographic, medical, and substance use diagnostic data are described in Table 2 by PTSD multimorbidity group. The group with the greatest multimorbidity was younger than groups with less morbidity, reflecting a monotonic trend. Multimorbidity was also associated with homelessness and receipt of a VA pension (marked in bold and with an asterisk in Table 2). In addition and of note, levels of service connected disability did not increase with multimorbidity. In fact, the proportion of veterans with service connected disability ratings grater than 50% declined as multimorbidity increased, albeit not to a substantial degree as defined here.

Medical diagnoses associated with multimorbidity included seizures, insomnia, TBI, hepatic disease and HIV as well as the total number of medical diagnoses. Each type of pain diagnosis, with the exception of diabetic pain, was also associated with progressively higher levels of multimorbidity. In addition, each substance use diagnosis as well as tobacco use disorder showed a substantial relationship to PTSD multimorbidity, with monotonic increases in diagnosed prevalence.

Almost every indicator of service use (medical and/or surgical visits, psychiatric and/or substance use outpatient visits, inpatient and/or residential treatment, intensive mental health or substance use treatment, community-based psychosocial rehabilitation, etc.) showed substantial, bi-variate associations with PTSD multimorbidity (Table 3). Each class of psychotropic medications also showed substantially increased use at higher levels of multimorbidity.

Ordinal logistic regression results indicated that each variable included in the model, with the exception of opioid pain medication use, was statistically significantly associated with higher levels of multimorbidity (all ps < .0001), and are ranked by the size of the standardized regression estimates (Table 4).

Examination of standardized regression coefficients showed the strongest independent correlates of higher levels of multimorbidity were use of psychotropic medication, numbers of psychiatric or substance use outpatient visits, and mental health inpatient treatment. These were followed in magnitude by younger age, use of medical or surgical visits, insomnia, emergency department visits, alcohol and substance use disorders, and pain diagnoses.

Discussion

We observed that a minority of the growing number of VHA patients diagnosed with PTSD had PTSD alone (30%) – the vast majority (70%) being diagnosed with at least one additional non-substance use psychiatric diagnosis, most often major depressive disorder and anxiety disorders. The frequent co-occurrence of these disorders with PTSD has been noted previously in a representative epidemiological sample [1, 56]; however, to our knowledge, this has not been documented in clinical samples and within a multimorbidity framework, in which all concurrent diagnoses are considered together. In particular, increased multimorbidity was associated with a substantial increase in personality disorders, with 18.4% of those in the highest multimorbidity group being diagnosed with personality disorders (vs. 10% in the general population) [57].

Bivariate analyses identified correlates of PTSD multimorbidity including homelessness, receipt of VA pension, substance use disorders, pain, health service use, and psychotropic and opioid pain medication use, all increasing monotonically in parallel with multimorbidity. Several behaviorally salient non-mental health diagnoses also had substantial associations with multimorbidity; namely hepatic disease, TBI, seizures, and insomnia.

Ordinal logistic regression identified independent correlates of PTSD multimorbidity and found the most robust associations with service use measures, especially psychotropic medication use, psychiatric or substance use outpatient visits, and mental health inpatient treatment. Other independent correlates included younger age, medical or surgical visits, insomnia, emergency department visits, alcohol and substance use disorders, and pain diagnoses. It appears that increased distress and dysfunction associated with multimorbidity may relate to these robustly increased levels of mental health service use. The strong association of psychiatric multimorbidity with high levels of mental health service use may represent a

common underlying vulnerability that increases with multimorbidity (beyond any unitary diagnosis) in leading to increased help-seeking behavior. The basis for such an underlying vulnerability, however, cannot be identified through administrative data, and requires further study through primary data collection.

Although our cross-sectional data showing that veterans seeking help for PTSD from VHA are many decades past their war zone service, these data cannot be compared directly to longitudinal epidemiological research suggesting that most PTSD remits within 10 years or less [3, 4]. Nevertheless, these data highlight the distinct multimorbid clinical status of these veterans, virtually all of whom are decades past the time of their war-zone trauma. Previous research suggesting that concurrent anxiety and/or depression are associated with persistence of PTSD psychopathology [20, 58, 59] underlines the importance of the high prevalence of these co-occurring conditions in the generally older population of VHA patients with PTSD, likely contributing to their ongoing morbidity and extensive service use.

Although previous studies have addressed specific concomitant diagnoses associated with PTSD, especially substance use, anxiety disorders, and depression, no studies to our knowledge have examined at overall patterns of multimorbidity associated with PTSD in a clinical setting such as VHA. This study identified a distinctive pattern in which greater levels of psychiatric multimorbidity were associated with increased odds of having a host of other conditions as well as higher levels of health service and psychotropic medication use. Given that depression and anxiety disorders were the most common concomitant conditions, the multimorbidity perspective suggests that PTSD may not be specifically associated with depression or anxiety per se, but rather that these concomitant diagnoses may reflect an underlying vulnerability that increases risk for both PTSD and other psychiatric conditions. If true, this vulnerability may involve through heightened sensitivity to dysphoric affect and/or vulnerability to psychosocial dysfunction. Although VHA administrative data do not include direct measures of quality of life, functional capability, or psychological distress, the extensive use of psychosocial rehabilitation services including legal and vocational services, along with high rates of homelessness among those with increased multimorbidity, suggest a broad array of psychosocial problems beyond the clinical diagnosis of PTSD.

Consistent with the present findings of high levels of service use in association with multimorbidity, previous research has reported that patients with medical multimorbidity account for a disproportionate share (90%) of VHA healthcare expenditures [60], with the most costly 5% of multimorbid medical patients accounting for approximately half of all VHA health care costs [41]. As a result, medical multimorbidity is increasingly recognized as a challenge for VHA [32, 60] and other healthcare systems. Analysis of the total number of outpatient mental health outpatient visits among veterans with PTSD multimorbidity (N = 6,138,987 visits) divided by the total number of outpatient mental health outpatient visits among all veterans with PTSD (N = 7,084,784) indicates that 87% of all mental health contacts with veterans diagnosed with PTSD involve veterans with some degree of multimorbidit (e.g., PTSD plus one or more additional psychiatric diagnosis).

While the specific implications of multimorbidity for policy or practice are not yet clear, it will be important to attend to multimorbidity in clinical practice, recognizing that the ostensible 'primary' diagnosis of PTSD may represent only part of a more extensive clinical pattern. War-zone-related PTSD has received a great deal of clinical, educational and research emphasis in VHA in the years since it was formally defined in 1980, and this organizational focus may have led to a singular emphasis on PTSD as the primary problem in many instances. In fact, psychosocial functioning issues may be the most treatable components of multimorbidity,

and balanced efforts to address the diverse diagnostic and functional facets of multimorbid PTSD may be the optimal approach [15]. The importance of such a broad perspective is underscored by findings that chronicity and severity of PTSD is consistently associated with psychosocial dysfunction in both clinical and epidemiological studies [1, 3, 5, 61].

It is further noteworthy that most clinical practice guidelines, including those for PTSD are disorder-specific, and tend to ignore or minimize concomitant diagnoses or dysfunction, in large part because the RCTs on which guidelines are based typically exclude comorbidities [42, 43], and even major psychosocial factors like unstable housing [15]. Although it would not be feasible to examine every possible mix of multimorbid conditions, research studies could focus on identification and evaluation of representative mixes of diagnoses [62], as those currently participating in clinical trials currently represent a relatively small fraction of veterans receiving clinical services for PTSD since only 30% are diagnosed with PTSD alone.

Our findings of high psychiatric and other types of multimorbidity among VHA patients diagnosed with PTSD could potentially inform reported findings regarding poorer efficacy of antidepressants among veterans [44–46]. However, future RCTs examining psychopharmacologic treatments addressing multimorbidity are needed to clarify this relationship, as the present study does not assess drug efficacy. One method to address multimorbidity in future research may involve identification of common multimorbidity groups (e.g., a Mixed Depression/Anxiety/PTSD Cluster or a Dual Diagnosis cluster) and developing interventions tailored to each combination of disorders, and test them with clinical trials of veterans within these distinct clusters of diagnoses [62], or otherwise stratifying patients by co-morbid diagnoses [39].

A more ambitious goal would be to identify underlying vulnerability factors that contribute to extensive multimorbidity in veterans of war zone trauma. For example, TBI alone and in the presence of PTSD has been associated with multimorbidity [27]. As suggested by previous literature, alternative methods of providing support and care for chronic illnesses are likely needed for these more complex patients [63], such as co-locating psychiatric staff in clinics where conditions highly multimorbid with PTSD are treated (e.g., TBI [27], pain [38]), formally assigning responsibilities for patient care coordination, and other approaches to integrating complex treatments [39]). Indeed, the VHA has instituted several initiatives to address integrated treatment for mental health conditions like PTSD, such as primary care mental health integration [64, 65] and HUD-VASH for homelessness [66], which offer the potential to address multimorbidity via integrated services. These developments represent positive steps to incorporating multimorbidity considerations into PTSD treatment, as the present findings suggest it may be myopic to apply evidence-based treatments for PTSD alone for these psychiatrically and medically complex patients with the expectation this will adequately address their myriad needs. Instead, providers must attend to the fact that patients' trauma history interacts with a complex system of biopsychosocial issues, including other psychiatric and medical illnesses that have emerged since the time of the trauma.

Limitations

An important limitation of the present study is that diagnostic data are based entirely on administrative records for which validity is untested, but which have the advantage of reflecting the assessments of treating clinicians in real-world practice. It is not possible to determine conclusively whether high levels of service use are a response to multimorbidity, or

whether the observed multiplicity of diagnoses may instead reflect extensive service use motivated by other factors, leading secondarily to receipt of multiple diagnoses. For example, one might imagine that interest in obtaining or maintaining service connected disability would contribute to increased service use regardless of clinical severity. However, our data suggests multimorbidity is not associated with service connected disability and ratings of over 50% service connected disability in fact decline in frequency with higher levels of multimorbidity. Moreover, it has been suggested that under-diagnosis of comorbidities is likely amongst patients with severe and/or chronic conditions [41]. We believe the limited data available suggest that high levels of service use likely results from greater levels of multimorbidity, rather than the reverse.

As noted earlier, our data are cross-sectional therefore cannot speak directly to the longitudinal course of PTSD in clinical settings. In addition, these administrative data are from 2012 and therefore it is possible they may not completely reflect the clinical reality of 2018, which is characterized by increasing numbers of younger veterans of recent conflicts presenting to VHA clinics. However, the findings of this study identify a clinical presentation, multimorbidity, which contributes to the high proportion of all VHA patients with PTSD continuing to receive treatment for PTSD decades after their traumatic war-zone exposure. Moreover, our findings suggest that if anything, younger veterans with PTSD display increased multimorbidity, indicating that multimorbidity may prove to be an ongoing clinical phenomenon in VHA. However, only time will tell whether younger veterans of recent conflicts will experience similarly chronic PTSD trajectories which are characterized by multimorbidity.

Conclusion

Psychiatric multimorbidity may be one explanation for, or at least an important concomitant feature of, chronic PTSD in VHA. We propose that this multimorbidity, and more specifically, some as yet undiscovered underlying vulnerability, may be responsible for high numbers of older veterans continuing to suffer from, and receive services related to, PTSD in VHA as observed in present study. Correspondingly, there is a clear need for systematic attention to the psychiatric multimorbidity associated with PTSD in clinical care, education and representative research to develop improved evidence-based treatments.

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Compliance with Ethical Standards

Ethical Approval All procedures performed in the present study were in accordance with the ethical standards of the VA Connecticut IRB and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of Interest The authors declare that they have no conflicts of interest.

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