Prescribing Trends in US Active Duty Service Members With Posttraumatic Stress Disorder:

A Population-Based Study From 2007–2013

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ABSTRACT

Objective: The US Veterans Affairs (VA)/Department of Defense (DoD) Posttraumatic Stress Disorder (PTSD) Clinical Practice Guidelines provide evidence-based pharmacologic treatment recommendations. Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are considered first-line medications. Benzodiazepines are relatively contraindicated with a warning that they may cause harm. This population-based study is the first to describe prescribing patterns for active duty service members (ADSMs) diagnosed with PTSD.

Methods: Health-care–related administrative DoD data from federal fiscal years 2007 through 2013 identified ADSMs with PTSD using *ICD-9* codes. Prescription frequencies for antidepressants, benzodiazepines, antipsychotics, anticonvulsants, and other psychotropic medications were calculated for each year.

Results: Between 2007 and 2013, ADSMs with a PTSD diagnosis increased from 16,931 to 70,942. SSRI or SNRI prescribing decreased from 55.4% in 2007 to 41.8% in 2010 before increasing to 54.9% in 2013. Benzodiazepine prescribing was stable between 20.9% and 22.3% through 2010 before increasing to 24.7% by 2013. Antipsychotic prescribing declined from 22.6% in 2007 to 14.6% in 2013, driven by a decrease in low-dose quetiapine (≤ 300 mg/d) prescribing, which declined from 19.1% in 2007 to 8.2% in 2013.

Conclusions: The increase in SSRI or SNRI prescribing after 2010 and the overall increase in prazosin and decrease in low-dose quetiapine prescribing all suggest increased concordance with the VA/DoD PTSD Clinical Practice Guidelines. The decline in SSRI prescribing up to 2010 is not concordant. The increase in benzodiazepine prescribing, a trend opposite that observed in the VA, is concerning.

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Posttraumatic stress disorder (PTSD) is a common clinical presentation for US active duty service members (ADSMs) with a reported risk of 1.11% in 2011.[1] Between 2001 and 2014, 2.6 million US military personnel deployed in support of Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF). Among ADSMs deployed for OEF or OIF, PTSD prevalence rates range from 4% to 20%.[2]

To assist the clinical management of patients with PTSD, the US Department of Veterans Affairs (VA) and the US Department of Defense (DoD) initially published and revised Clinical Practice Guidelines (CPGs) in 2004 and 2010, respectively, providing evidence-based psychotherapy and pharmacotherapy treatment recommendations.[3,4] Per the CPGs, selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are the only medication classes considered Level A, indicating strong evidence supporting their use. Benzodiazepines are Level D (ie, the assigned designation when the harm outweighs benefits) with a recommendation against their use and with their being considered relatively contraindicated. Atypical antipsychotics are considered Level I, indicating insufficient evidence to recommend for or against routine use. Risperidone is the exception, receiving a Level D recommendation following a large multicenter VA study[5] that showed no improvement in symptoms, but more adverse events compared to placebo. A 2012 DoD memorandum[6] cautioned against the use of atypical antipsychotics for treating PTSD or sleep disturbance, citing great concern for their overprescription. Additionally, a US Army memorandum issued in 2012 argued that the Level D recommendation be extended to other atypical antipsychotics, specifically quetiapine, as they "carry similar clinical concerns," though having "not undergone the same level of rigorous testing."[7(p9)]

There are several studies[8–17] in the scientific literature on the prescribing patterns for veterans with PTSD in the VA. However, we could not identify any published studies pertaining to ADSMs with PTSD and found only 2 published white papers.[2,18]

The objective of this retrospective, population-based study was to characterize psychotropic prescribing frequencies relative to the VA/DoD PTSD CPGs among ADSMs with PTSD over a 7-year period and to assess whether the 2010 CPG revision correlated with any changes. Our methods purposefully drew from a prior study[11] of prescribing trends of veterans with PTSD to provide comparable data in ADSMs.

Clinical Points

- Guidelines provide recommendations for treating posttraumatic stress disorder (PTSD), but how closely they align with actual clinical practice in the Department of Defense (DoD) is unknown.
- From the perspective of the Veterans Affairs/DoD PTSD Clinical Practice Guidelines, psychotropic medication prescribing in the DoD was a mixed picture, with the increase in prescribing of benzodiazepine being of particular concern, if not alarm.

METHODS

Data Source

Data were obtained through the Military Health System Data Repository/Management Analysis and Reporting Tool.[19] This system is the most comprehensive source of health-care information for both US military and TRICARE commercial/private providers for over 9.5 million US Uniformed Services beneficiaries. Data were obtained for US federal government fiscal years (FY) 2007 through 2013, from October 1, 2006, through September 30, 2013. The study was approved by the Naval Medical Center San Diego Institutional Review Board.

Patients

The study population comprised all TRICARE-eligible beneficiaries with at least 1 outpatient encounter/visit or inpatient discharge claim for PTSD based on the *International Classification of Diseases, Ninth Revision* (*ICD-9*) code of 309.81 as the primary or secondary diagnosis received while in active duty status during a given FY. TRICARE-eligible beneficiaries included those receiving care at a US military treatment facility (direct care) or at a civilian facility (purchased care) in the United States, including Alaska and Hawaii, as well as those receiving care outside the United States. ADSMs were excluded if they were never enrolled to a military treatment facility or a civilian facility provider in the United States, nor lived in the United States, when diagnosed with PTSD during the study period. National Guard or Reserve members were omitted from the analysis as these persons often have primary health care outside of TRICARE.

Medication Use

Prescription records were examined for all ADSMs with a PTSD diagnosis for each FY from 2007 through 2013. Medication use for each patient was based on having at least 1 prescription fill of any quantity, days' supply, or dosage for the selected therapeutic class or drug. Therapeutic classes were based on the categorization used by Bernardy and colleagues,[11] which was created in accordance with the 2010 VA/DoD PTSD CPGs (Table 1).

Analysis

Annual frequencies of drug dispensed by specific drug class of interest were calculated for each FY. Frequencies were estimated as the ratio of total number of ADSMs having received at least 1 prescription for the drug in the class of interest over the total number of unique ADSMs with a diagnosis of PTSD during the same FY. The overall change and change from 2010 were calculated as absolute percent change, where negative values reflect decreased frequency of usage during the respective time period.

Table 1. Summary of VA/DoD PTSD Clinical Practice Guidelines for Medication Recommendations[a]

	Recommended Level of Evidence[b]	
Medication Class	2004 Guideline	2010 Guideline
Antidepressants		
SSRI	A	A
SNRI	C	A
TCA	B	B
MAOI	B	B (phenelzine) [caution]
Mirtazapine	C	B
Nefazodone	C	B [caution]
Bupropion	C	I
Trazodone	C	I (adjunctive)
Antipsychotics		
Conventional	D	I
Atypical	I	I (as monotherapy) I (except risperidone, as adjunct) D (risperidone)
Benzodiazepines	D	D [harm]
Nonbenzodiazepine hypnotics (including ramelteon)	I	I
Buspirone	I	I
Prazosin	C	B (adjunctive for sleep/nightmares) C (for global PTSD) I (for monotherapy)
Anticonvulsants	I	D (as monotherapy) tiagabine, valproate, topiramate I (as monotherapy) gabapentin, lamotrigine I (as adjunctive)
Central α-agonists	C	I (clonidine) D (guanfacine)
Propranolol	C	I

[a]Based on the 2004[3] and 2010[4] Clinical Practice Guidelines for Management of Post-Traumatic Stress. Adapted with permission from Bernardy et al, 2012.[11]

[b]Level of Evidence codes:
A: A strong recommendation that clinicians provide the intervention to eligible patients.
B: A recommendation that clinicians provide the intervention to eligible patients.
C: No recommendation for or against the routine provision of the intervention is made. Intervention may be considered.
I: Insufficient evidence to recommend for or against routinely providing the intervention.
D: A recommendation against routinely providing the intervention.

Abbreviations: DoD = US Department of Defense, MAOI = monoamine oxidase inhibitor, PTSD = posttraumatic stress disorder, SNRI = serotonin-norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant, VA = US Department of Veterans Affairs.

RESULTS

Among 125,719 unique ADSMs with at least 1 PTSD diagnosis from FY 2007 through 2013, the majority were men (84%) on active duty in the US Army (66.2%), Marines

(14.2%), Navy (9.6%), Air Force (8.7%), Coast Guard (0.8%), and other/unknown (0.4%). The proportion of ADSMs with a PTSD diagnosis increased over 4-fold, from 16,931 in 2007 to 70,942 in 2013, and 85.4% had deployed to OEF/OIF (107,339 ADSMs) (Table 2). The proportion receiving at least 1 prescription for a psychotropic medication of interest decreased from 78.3% in 2007 to a low of 71.8% in 2009 and then increased to 93.0% in 2013.

Table 2. PTSD Diagnosis and Medication Prescription Among ADSMs by Fiscal Year

	Fiscal Year						
ADSMs	2007	2008	2009	2010	2011	2012	2013
With PTSD, n	16,931	30,900	42,917	53,268	63,178	71,124	70,942
With at least 1 prescription for medications of focus							
n	13,264	23,370	30,825	38,983	50,384	59,750	66,000
%	78.3	75.6	71.8	73.2	79.7	84.0	93.0

Abbreviations: ADSMs = active duty service members, PTSD = posttraumatic stress disorder.

Antidepressants

In 2007, 63.4% of ADSMs diagnosed with PTSD received a prescription for an antidepressant (Table 3). This decreased to 50.8% in 2010 and then increased steadily to 67.4% in 2013.

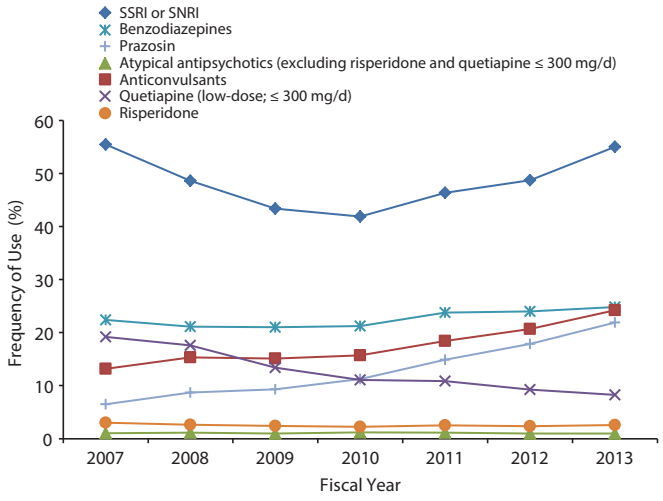
SSRIs or SNRIs were prescribed to 55.4% of ADSMs with PTSD in 2007, decreasing to 41.8% in 2010 before increasing to 54.9% in 2013 (Figure 1). Prescriptions for SNRIs were relatively stable between 2007 and 2010 and then gradually increased through 2013. This same trend was observed when examining venlafaxine and duloxetine individually. However, prescriptions for SSRIs were largest in 2007, where half (50.9%) of ADSMs diagnosed with PTSD received an SSRI. This decreased to 1

Table 3. Frequency of Medication Use Among ADSMs With PTSD by Fiscal Year

	Frequency (%) of Medication Use by FY							Absolute Change (%)		
Drug class or specific drug	2007	2008	2009	2010	2011	2012	2013	FY 2007–2010	FY 2007–2013	FY 2010–2013
Antidepressants	63.4	56.8	51.6	50.8	56.4	59.9	67.4	−12.6	4.1	16.7
SSRI[a] or SNRI[b]	55.4	48.5	43.3	41.8	46.2	48.6	54.9	−13.6	−0.4	13.2
SSRI[a]	50.9	43.4	37.7	36.1	39.8	41.3	45.9	−14.8	−5.0	9.9
SNRI	8.1	9.3	9.3	9.3	10.2	11.7	14.0	1.2	5.9	4.7
Venlafaxine	7.0	7.9	7.6	7.5	8.1	9.1	11.0	0.6	4.0	3.5
Duloxetine	1.4	1.7	1.8	1.9	2.3	2.9	3.5	0.5	2.0	1.5
TCAs[c]	5.5	6.7	6.1	6.8	7.4	8.1	9.1	1.3	3.6	2.3
Amitriptyline	3.6	4.6	4.4	4.6	4.9	5.3	5.7	1.0	2.1	1.1
Doxepin	0.4	0.4	0.5	0.5	0.9	1.1	1.5	0.1	1.1	1.0
TCAs (excluding amitriptyline or doxepin)	1.7	1.9	1.5	2.0	2.0	2.1	2.3	0.2	0.6	0.3
MAOI[d]	0.0	0.0	0.2	0.1	0.1	0.0	0.0	0.1	0.0	−0.1
Mirtazapine	4.4	4.4	4.4	4.3	5.3	6.4	7.2	−0.1	2.9	2.9
Nefazodone	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.0	0.0	0.0
Bupropion	9.7	8.9	8.9	9.1	10.9	12.0	14.3	−0.6	4.6	5.1
Other [amoxapine, maprotiline, standard-dose trazodone (≥ 300 mg/d)]	0.4	0.3	0.3	0.6	0.8	0.8	0.9	0.3	0.6	0.3
Trazodone (low-dose; < 300 mg/d)	15.8	15.8	14.5	13.9	15.9	17.5	19.8	−1.9	4.0	5.8
Anticonvulsants[e]	13.1	15.2	15.0	15.6	18.3	20.6	24.1	2.6	11.1	8.5
Antipsychotics	22.6	21.1	17.4	15.5	16.2	14.9	14.6	−7.1	−8.1	−0.9
Typical[f]	0.3	0.3	0.3	0.2	0.3	0.4	0.5	0.0	0.2	0.2
Atypical[g] (excluding risperidone and quetiapine ≤ 300 mg/d)	1.0	1.0	0.9	1.1	1.1	0.9	0.9	0.1	−0.1	−0.2
Risperidone	2.9	2.5	2.3	2.1	2.4	2.2	2.5	−0.8	−0.4	0.3
Quetiapine (low-dose; ≤ 300 mg/d)	19.1	17.5	13.3	11.0	10.8	9.2	8.2	−8.1	−10.9	−2.8
Benzodiazepines[h]	22.3	21.0	20.9	21.1	23.7	23.9	24.7	−1.2	2.4	3.6
Nonbenzodiazepine hypnotics[i]	27.3	25.1	23.5	22.8	25.4	26.1	26.7	−4.5	−0.6	3.9
Buspirone	1.9	2.2	2.2	2.6	3.3	4.0	5.4	0.6	3.4	2.8
Central α-agonists[j]	1.6	2.0	1.9	1.8	2.0	2.3	2.5	0.2	0.9	0.6
Prazosin	6.4	8.6	9.2	11.2	14.8	17.7	21.8	4.8	15.4	10.6
Propranolol	2.8	3.2	3.4	3.6	4.4	4.8	5.9	0.8	3.1	2.3
Ramelteon	0.9	0.4	0.7	0.6	0.5	0.5	0.5	−0.3	−0.4	−0.1

[a]SSRIs include citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline.
[b]SNRIs include desvenlafaxine, duloxetine, milnacipran, venlafaxine.
[c]TCAs include amoxapine, clomipramine, desipramine, imipramine, maprotiline, nortriptyline, protriptyline.
[d]MAOIs include isocarboxazid, phenelzine, tranylcypromine.
[e]Anticonvulsants include gabapentin, lamotrigine, pregabalin, tiagabine, topiramate, valproate.
[f]Typical antipsychotics include chlorpromazine, fluphenazine, haloperidol, loxapine, mesoridazine, molindone, perphenazine, pimozide, promazine, thioridazine, thiothixene, trifluoperazine.
[g]Atypical antipsychotics (excluding risperidone and quetiapine ≤ 300 mg/d) include aripiprazole, asenapine, clozapine, iloperidone, lurasidone, olanzapine, paliperidone, quetiapine (> 300 mg/d), ziprasidone.
[h]Benzodiazepines include alprazolam, chlordiazepoxide, clobazam, clonazepam, clorazepate, diazepam, estazolam, flurazepam, halazepam, lorazepam, midazolam, oxazepam, prazepam, quazepam, strazepam, temazepam, triazolam.
[i]Nonbenzodiazepine hypnotics include eszopiclone, zaleplon, zolpidem.
[j]Central α-agonists include clonidine, guanfacine.
Abbreviations: ADSMs = active duty service members, DoD = US Department of Defense, FY = fiscal year, MAOI = monoamine oxidase inhibitor, PTSD = posttraumatic stress disorder, SNRI = serotonin-norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant.

Figure 1. Frequency of Medication Use Among ADSMs With PTSD by Drug or Drug Class and Fiscal Year



Abbreviations: ADSMs = active duty service members, PTSD = posttraumatic stress disorder, SNRI = serotonin-norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor.

in 3 (36.1%) in 2010 before increasing to almost 1 in 2 (45.9%) in 2013.

Tricyclic antidepressant (TCA) prescribing remained relatively stable between 2007 and 2010 and then gradually increased through 2013. Amitriptyline was the most commonly prescribed TCA; however, rates were relatively constant over this interval, increasing slightly in 2012 and 2013. Doxepin, initially prescribed to 0.4% of ADSMs with PTSD in 2007, increased between 2011 and 2013 to 1.5%, representing a greater than 3-fold increase. TCAs other than amitriptyline and doxepin remained stable over the interval.

Mirtazapine prescribing frequencies remained relatively constant around 4% until 2011 when they increased from 5.3% to 7.2% in 2013. Bupropion prescriptions demonstrated a similar pattern, remaining around 9%, and then increased from 10.9% in 2011 to 14.3% in 2013. Monoamine oxidase inhibitor and nefazodone prescribing rates were negligible, as were antidepressants grouped as "other."

Low-dose trazodone, defined as less than 300 mg daily, was separated from standard-dose trazodone due to its common use as a sedative hypnotic.[20] Prescription frequencies of low-dose trazodone decreased from 15.8% in 2007 to a low of 13.9% in 2010 before progressively increasing to 19.8% in 2013.

Antipsychotics

Typical antipsychotic prescribing was consistently at or below 0.5% through the study period. Low-dose prescribing of the atypical antipsychotic quetiapine, defined as less than or equal to 300 mg per day, was separated from other atypical antipsychotics due to its common use as a sedative hypnotic.[11] In 2007, almost 1 in 5 (19.1%) ADSMs with PTSD were prescribed low-dose quetiapine, progressively decreasing to 8.2% in 2013. Risperidone prescriptions remained stable at around 2.5%. Prescribing of all other atypical antipsychotics, including quetiapine at doses greater than 300 mg, remained around 1%.

Benzodiazepines, Nonbenzodiazepine Hypnotics, and Ramelteon

Benzodiazepine prescribing decreased from 22.3% in 2007 to 20.9% in 2009 before steadily increasing to 24.7% in 2013. Prescriptions of nonbenzodiazepine hypnotics, including eszopiclone, zaleplon, and zolpidem, decreased from 27.3% in 2007 to 22.8% in 2010 before increasing to 26.7% in 2013. Ramelteon, a melatonin-receptor agonist, was consistently prescribed to less than 1% of ADSMs diagnosed with PTSD.

Other Medications

Prescriptions of anticonvulsants steadily increased from 13.1% in 2007 to 24.1% in 2013. Buspirone prescribing was approximately 2% through 2009 before progressively increasing to 5.4% by 2013. Propranolol prescribing gradually increased from 2.8% in 2007 to 5.9% in 2013.

Central α-agonist prescribing remained approximately stable at 2% throughout the study period. Prazosin prescribing steadily increased over 3-fold from 6.4% in 2007 to 21.8% in 2013.

DISCUSSION

The study objective was to characterize psychotropic prescribing for US ADSMs with PTSD relative to the VA/DoD PTSD CPGs for FY 2007 through 2013 and to compare these frequencies to those reported among veterans with PTSD. Over this interval, the prevalence of PTSD diagnosed among ADSMs increased over 4-fold.[2]

The proportion of ADSMs receiving at least 1 prescription for a psychotropic medication of interest decreased from almost 8 in 10 (78.3%) in 2007 to a low of just over 7 in 10 (71.8%) in 2009. This decline was due to a decrease in medications considered Level A (SSRIs) and Level I (antipsychotics, principally quetiapine, and nonbenzodiazepine hypnotics), after which was seen a steady increase to over 9 in 10 ADSMs receiving at least 1 prescription for a psychotropic medication of interest in 2013 (93.0%), reflecting increases for both Level A and Level B medications (SSRIs and SNRIs, and prazosin as an adjunctive) and Level D and Level I medications (benzodiazepines, bupropion, anticonvulsants, and nonbenzodiazepine hypnotics). While the increase was largest for Level A and Level B recommended medications, the concurrent increase in recommended Level I and Level D medications argues against the assumption that the prescribing trends were simply aligning with the release of the 2010 revision of VA/DoD PTSD CPGs. In contrast, between 1999 and 2009, psychotropic prescription rates remained relatively constant between 81% and 84% in the VA.[11] We were unable to identify VA data after 2009.

SSRIs and SNRIs were the most frequently prescribed medication classes, consistent with the Level A recommendation. However, the decline in SSRI prescribing between 2007 and 2010 possibly associated with perceived limited effectiveness, particularly for treating combat-related PTSD, was unexpected. For example, a randomized, double-blind, multicenter VA study comparing sertraline to placebo found no difference in veterans with chronic PTSD.[21] Alternatively, this decrease may reflect lack of awareness of the CPGs or perceived lack of their relevance due to their release in 2004.[22] The subsequent increase in SSRI prescribing after 2010 is noteworthy for coinciding with release of the updated CPGs, as is the increase in SNRI prescribing, which changed from Level C (ie, no recommendation for or against) in 2004 to Level A in 2010.

A 2016 RAND study[18] of ADSMs diagnosed with PTSD in the first half of 2012 described a greater proportion receiving an antidepressant (77.8%) than that observed in the commensurate fiscal years (2011 and 2012) described earlier. We suspect this difference may exist for 2 reasons. First, we excluded low-dose trazodone from the antidepressant category due to its sedative hypnotic use. Second, inclusion criteria of the RAND report were more restrictive, requiring observation for 12 continuous months on active duty status. The resulting cohort of 14,576 ADSMs was about a fifth of the 2011 cohort in our study, though enrollment occurred for half of the year.

In the VA, SSRI and SNRI prescribing frequency for 2003 through 2009 was consistently between 58.7% and 59.8%, and 55.7% in 2012.[11] No data for 2010 or 2011 were available. The relative stability of SSRI and SNRI prescribing in the VA over an interval including both the 2004 and 2010 versions of the CPGs stands in contrast to the DoD.

Although bupropion was Level C in 2004 and Level I in 2010, between 8.9% and 14.3% of ADSMs received a prescription, which may have been to address side effects of SSRIs, including sexual dysfunction. In our experience, sexual dysfunction is one of the primary reasons for SSRI nonadherence. Bupropion may also have been prescribed to assist with smoking cessation or as a nonstimulant treatment for ADHD. Alternatively, some prescribers may be targeting core PTSD symptoms with bupropion in spite of the guideline recommendations, particularly if first-line agents are not helpful.

TCAs, which are Level B medications, are prescribed much less frequently than SSRIs and SNRIs, which may be due to concerns for toxicity in overdose relative to SSRIs and SNRIs; to side-effect profile, including drowsiness and an increased anticholinergic burden; or to prescribers' lack of familiarity with this class. However, in particular for the TCAs that are more sedating, they may be worth considering prior to a trial with a benzodiazepine.

The VA/DoD PTSD CPGs recommend against the use of benzodiazepines (Level D), considering them relatively contraindicated and indicating they may cause harm. Nevertheless, in this study, no fewer than 1 in 5 ADSMs were prescribed a benzodiazepine in a given FY, with frequency increasing to almost 1 in 4 by 2013 (24.7%). Similarly, the 2016 RAND report[18] described a high frequency of benzodiazepine prescribing (34.5%). The more restrictive inclusion criteria of the RAND study allows us to infer that ADSMs with PTSD who stay on active duty status are more likely to be prescribed benzodiazepines.

Between 1999 and 2009, the VA observed a steady decline in benzodiazepine prescribing from 36.7% to 30.6%, continuing to 27.5% in 2012.[10,11] This trend, while consistent with the VA/DoD PTSD CPG recommendations, contrasts with our findings. This difference is particularly important as, by definition, ADSMs are earlier in their PTSD treatment than are veterans. Limiting benzodiazepine prescribing for individuals early in the care continuum is important due to problems with dependence and discontinuation, comorbid substance use, and safety concerns.[9,15]

The increase in benzodiazepine prescribing frequency in our study occurred alongside an increase in the absolute number of ADSMs diagnosed with PTSD. The 3.6% increase in benzodiazepine prescribing between 2010 and 2013 represents an increase of over 6,000 ADSMs, which calls into question the relevance of the CPGs to the actual provision of care in the DoD, particularly as this increase coincides with the release of the 2010 version.

The concerning trend in benzodiazepine prescribing may suggest a few issues. It may point to perceived limitations of the effectiveness of SSRIs and SNRIs in this population, either for global PTSD symptoms or for specifically sleep-related problems.[21] In the VA, benzodiazepine prescribing tends to occur after a patient fails first-line medication options.[16] Perhaps benzodiazepines are being prescribed for comorbid diagnoses, such as anxiety disorders, which our study did not collect. However, VA studies[14,16,17] have consistently found that most veterans diagnosed with PTSD who receive a benzodiazepine lack a comorbid anxiety diagnosis. Further, studies of veterans with PTSD[15,16,23] found that approximately two-thirds of benzodiazepine prescriptions were long-term, defined as greater than 90 continuous days. Comparable data describing long-term benzodiazepine prescribing in the DoD are needed, as are data on the frequency of pairing benzodiazepines with other sedatives due to the known increased risks for adverse clinical outcomes, the most common pairing in the VA being with opioids.[12,24] Alternatively, prescribing for PTSD treatment in the DoD may simply occur independent of consideration for the VA/DoD CPGs. What barriers are responsible for this trend, and what can be done to address them are important unanswered questions.[25]

From FY 2007 through 2013, the frequency of antipsychotic prescriptions for ADSMs declined by 8%, which was driven by a decline in low-dose quetiapine prescribing. Frequently used as a sedative hypnotic, low-dose quetiapine prescribing declined nearly 11% between 2007 and 2013.[10,11,14] Most of the decline occurred before 2010 (8.1%), prior to the release of the revised guidelines and the 2012 DoD or Department of Army memoranda. It is possible that the decrease in low-dose quetiapine was driven

by prescribers switching to prazosin. Prazosin prescribing did increase more than 15% during this interval, a trend closely mirrored in the VA.[8,11] However, most of this increase (10.6%) occurred between 2010 and 2013, later than the corresponding decline in low-dose quetiapine. Examination of geographic diffusion of prazosin prescribing in the VA suggests that geographic proximity, possibly mediated by "socio-professional contagion," accounts for adoption.[13] Even if prazosin prescribing accounts for displacement of low-dose quetiapine prescribing, it may not be the result of CPG adherence.

The frequency of risperidone prescribing was constant between 2% and 3% over the study period in spite of risperidone's change from Level C (no recommendation for or against) to Level D (recommendation against) in the 2010 CPG revision, a high-profile VA study's finding risperidone did not reduce PTSD symptoms compared to placebo, and warnings about antipsychotic prescribing issued by the DoD and Army.[5–7] Atypical antipsychotic prescribing, excluding risperidone and low-dose quetiapine, was negligible, at around 1%. Typical antipsychotic prescribing was negligible (0.2%–0.5%) and consistent with reported trends in the VA.[11] The extent to which antipsychotic prescribing was in the context of comorbid schizophrenia or bipolar spectrum diagnoses is unknown, although VA data[14,17] suggest that most is not.

The progressive increase in anticonvulsant prescribing is noteworthy, with almost 1 in 4 ADSMs receiving a prescription in 2013. This occurred in spite of the 2010 CPG recommendation changing from Level I (insufficient evidence) to Level D (recommendation against) the anticonvulsants tiagabine, valproate, and topiramate monotherapy. The extent of prescribing for comorbid indications is unknown. In a study of veterans with PTSD,[14] of 22% receiving anticonvulsants (including lithium), only 4% had a co-occurring seizure or bipolar disorder. A possible explanation is that anticonvulsants are being prescribed for traumatic brain injury–related symptoms. Should that be the case, it suggests the importance of addressing common comorbidities in future versions of the CPGs.

This study has a number of limitations. We did not account for comorbid diagnoses nor could we know if prescribing was intended for PTSD or other indications, though we did ensure that each prescription was coincident with a PTSD diagnosis. Also, this study does not address treatment duration or dosage or sequence of prescribing. Further, since the active duty status was confirmed only at the time of each PTSD diagnosis, medication dispensed at other times may have occurred outside of active status. This study has several strengths. To our knowledge, it is the first to report overall prescribing trends in the ADSM population with a PTSD diagnosis over an extended period. In addition, this study relied on data extracted from robust systems, which capture all health care delivered to ADSMs, allowing for conclusions at the population level.

In conclusion, on the basis of the VA/DoD PTSD CPGs, psychotropic medication prescribing for PTSD in the DoD was a mixed picture. The increase in SSRI and SNRI prescribing after 2010 and the overall increase in prazosin prescribing and decrease in low-dose quetiapine prescribing all suggest increased guideline concordance. The decline in SSRI prescribing up to 2010 and the overall steady increase in anticonvulsant prescribing are not reflective of the guidelines. However, the increase in benzodiazepine prescribing, a trend opposite that observed in the VA, warrants serious attention and even alarm. Lastly, the absence of change in risperidone prescribing rates, in spite of risperidone's change from Level C to Level D with the 2010 CPG revision and the 2012 DoD and US Army memoranda is concerning and warrants further research as to why these recommendations have not changed prescribing patterns. Risperidone has numerous serious side effects, and understanding the reasons why prescribers continue to use this medication despite lack of evidence for use is important. Additionally, further investigation into CPGs and prescribing concordance in the DoD are warranted. For example, to what extent are prescribers familiar with the CPGs? And, for those who are familiar, how do they factor CPGs into clinical decision making? For the DoD clinical population, what is the clinical ineffectiveness of first- and second-line agents?

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