Symptom Presentation and Prescription of Sleep Medications for Veterans With Posttraumatic Stress Disorder

Mark A. Greenbaum, MS, MA, Thomas C. Neylan, MD,†‡ and Craig S. Rosen, PhD*§‖*

Abstract: This study tested whether sleep medications prescribed to veterans diagnosed with posttraumatic stress disorder (PTSD) are being targeted to patients who report more severe insomnia or nightmares. Secondary analysis of survey and pharmacy data was conducted in samples of veterans from two periods: from 2006 to 2008 and from 2009 to 2013. Logistic regression tested associations between self-reported insomnia and nightmare severity, and being prescribed trazodone, prazosin, zolpidem, and benzodiazepines, controlling for PTSD severity and other covariates. In both samples, insomnia severity independently predicted trazodone receipt, and nightmare severity independently predicted prazosin receipt. In the later study, insomnia severity predicted receipt of zolpidem. Veterans in the later sample were more likely to receive trazodone, prazosin, and non-benzodiazepine hypnotics, and less likely to receive benzodiazepines than those in the earlier sample. Further research is needed to evaluate and optimize pharmacological and psychosocial treatments for sleep problems among veterans with PTSD.

Key Words: Sleep disorders, posttraumatic stress disorder, psychopharmacology, veterans, practice guidelines

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Sleep disturbance is a prominent and common feature of posttraumatic stress disorder (PTSD), associated with increased psychiatric and physical comorbidity and worsened role functioning (Brownlow et al., 2015; McLay et al., 2010). We focus here on the pharmacological treatment of insomnia (trouble falling asleep, staying asleep, or both) and nightmares (recurring, distressing dreams). These two sleep problems are especially widespread in US veterans diagnosed with PTSD: prevalence estimates for insomnia range from 44% to 91%, and nightmare prevalence may be as high as 90% (Hasler and Germain, 2009; Maher et al., 2006). Recent models emphasize that sleep problems are an independent but related feature of PTSD (Babson and Feldner, 2010; Spoormaker and Montgomery, 2008), often benefitting from sleep-specific treatment (Nappi et al., 2012; Schoenfeld et al., 2012).

Management of PTSD is complex. Patients may present with a diverse range of complaints (Rosen et al., 2013), and polypharmacy and off-label prescribing are frequent. Within this context, sleep disturbance could be overlooked and undertreated (Mohamed and Rosenheck, 2008). Alternatively, some clinicians may prescribe sleep-related medications to nearly all their PTSD-diagnosed patients, potentially exposing them unnecessarily to risk of medication adverse effects. Although PTSD-related sleep problems are among patients' foremost concerns, there has been little examination of how clinicians respond to these problems in actual practice (Mohamed and Rosenheck, 2008). Ideally, clinicians would selectively target sleep medications to patients who most need them (Sutton, 2014).

As the largest health care system in the country and one with unique concerns about PTSD, the Veterans Health Administration (VHA) plays a leading role in PTSD care. The VHA was an early adopter of routine PTSD screening, use of prazosin for nightmares, and evidence-based psychotherapies such as prolonged exposure. Moreover, VHA has partnered with other health agencies and the private sector to improve treatment services for veterans and civilians diagnosed with PTSD (*e.g.*, Tanielian et al., 2014).

The 2010 Department of Veterans Affairs/Department of Defense clinical practice guidelines (CPGs) for PTSD (Department of Veterans Affairs, Department of Defense [DVA/DoD], 2010) recommend cognitive-behavioral therapy for insomnia (CBT-I) and sleep hygiene as first-line treatments for sleep problems. However, the CPGs also endorse trazodone and prazosin as second-line treatments for insomnia and nightmares if behavioral approaches are unavailable or inadequate. In reality, access to behavioral treatments is limited (Karlin et al., 2013), so medications are often the primary interventions used for insomnia and nightmares. The CPGs state that if treatment with hypnotics is indicated, non-benzodiazepine hypnotics may be preferable to benzodiazepines because of their safety advantages, but for short-term use only. Benzodiazepines were regarded as relatively contraindicated, with limited support for their efficacy and concerns about dependence (DVA/DoD, 2010). Before examining prescribing practices, we briefly review evidence behind the practice guideline recommendations, as well as results from more recent well-designed studies.

Trazodone

Trazodone is an antidepressant used frequently for PTSD-associated insomnia at doses less than 200 mg, despite limited research evidence regarding efficacy (Bossini et al., 2015; Mendelson, 2005). The DVA/DoD CPGs state that trazodone may help insomnia, but cite just two open-label, uncontrolled studies. The few randomized controlled trials (RCTs) reporting improved sleep with trazodone did not focus specifically on participants with PTSD (*e.g.*, Roth et al., 2011).

Prazosin

The DVA/DoD CPGs recommend prazosin as a moderately effective treatment for nightmares and insomnia. Supporting evidence was limited but positive: in RCTs with PTSD-diagnosed veterans and civilians, prazosin reduced sleep disturbance and combat-related dream

*Department of Veterans Affairs (DVA), PTSD Methods and Evaluation Core, VISN 21 Sierra Pacific MIRECC; National Center for PTSD, DVA Palo Alto Healthcare System, Menlo Park Division; †DVA, PTSD Research Core, VISN 21 Sierra Pacific MIRECC; DVA San Francisco Healthcare System; ‡University of California at San Francisco Medical School; §DVA Affairs Palo Alto Healthcare System and HSR&D Center for Implementation to Innovation, Menlo Park; and ‖Stanford University Department of Psychology and Behavioral Sciences, CA.

Send reprint requests to Mark A. Greenbaum, MS, MA, National Center for PTSD (NCPTSD-324), VA Palo Alto Medical Center, 495 Willow Road, Menlo Park, CA 94025. E-mail: Mark.Greenbaum@va.gov.

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content (Raskind et al., 2003, 2007; Taylor et al., 2006). In a recent study of active-duty veterans with PTSD, prazosin reduced nightmares and improved sleep quality, daytime functioning, and global PTSD (Raskind et al., 2013). This broad range of positive outcomes was confirmed in a recent meta-analysis by Seda et al. (2015).

Hypnotics

Although benzodiazepines are widely prescribed for PTSD-related insomnia (DVA/DoD, 2010), the CPGs advised against their use because of inefficacy, adverse effects, and the potential for dependence and abuse (Cates et al., 2004; Krystal, 2009). The non-benzodiazepine hypnotics, including zolpidem, eszopiclone, zaleplon (the "Z-drugs"), and ramelteon present many of the same risks as do benzodiazepines, and zolpidem has been associated with rare but dangerous sleep behaviors (DVA/DoD, 2010; Gunja, 2013). If hypnotic pharmacotherapy is indicated, the CPGs state that non-benzodiazepines may be preferable to benzodiazepines because of "their shorter half-life and lower risk of dependency," but for short-term use only (DVA/DoD, 2010, p. I-185; see also MacFarlane et al., 2014). To our knowledge, there has been only one RCT examining non-benzodiazepine hypnotic treatment of sleep problems among patients with PTSD (Pollack et al., 2011): individuals randomly assigned to eszopiclone, compared with those receiving placebo, improved significantly on measures of sleep quality and PTSD.

Practice Patterns

The VHA prescribing practices for sleep problems are changing, with use of non-benzodiazepine hypnotics and prazosin increasing rapidly between fiscal year (FY) 1999 and FY 2009 (Bernardy et al., 2012). Our analysis of national VHA outpatient administrative records between FY 2006 and FY 2013 shows that the percentage of PTSD-diagnosed veterans who received one or more prescriptions for trazodone decreased slightly, from 26% to 23%, whereas receipt of prazosin rose from 5% to 16%. Rates for receipt of non-benzodiazepine hypnotics increased from 4% to 13%. In contrast, receipt of benzodiazepines decreased from 23% to 18% over this interval.

However, these overall prescribing trends do not indicate whether these medications are being targeted to the patients who need them most. The VA administrative databases contain little information on patient symptoms other than diagnoses. Clinicians often make symptom-guided prescribing choices, especially when patient problems do not reach diagnostic thresholds or are not otherwise given a diagnosis. This is particularly likely for sleep problems, which are often underdiagnosed or regarded as secondary to more severe psychiatric disorders (Hermes and Rosenheck, 2014). Results of several studies suggest that prescriptions without an associated diagnosis are likely given for sleep problems (*e.g.*, Bernardy et al., 2013; Jain et al., 2012; Mohamed and Rosenheck, 2008). However, we are unaware of any studies that have directly tested this proposition.

High rates of diagnosed comorbid depressive, substance use, and anxiety or panic disorders among PTSD-diagnosed patients (Kessler et al., 1995) may obscure prescription practices targeting PTSD-related sleep problems as well. These conditions may maintain or exacerbate sleep disturbance (*e.g.*, Fairholme et al., 2013; Lauterbach et al., 2011; Vandrey et al., 2014; but see Germain et al., 2004) and are associated with increased polypharmacy (Bernardy et al., 2014; Hermes and Rosenheck, 2014).

Clinicians' prescribing practices for PTSD-related insomnia and nightmares vary widely, in part due to a limited and sometimes contradictory evidence base (DVA/DoD, 2010; Lund et al., 2013a; Krystal, 2009; Hermes and Rosenheck, 2014), and may be influenced by other several factors, including local prescribing practices and the presence of comorbidities (Bernardy et al., 2012; Harpaz-Rotem and Rosenheck, 2009; Lund et al., 2013a). Thus, questions about the targeting of sleep medications in patients diagnosed with PTSD cannot be addressed using administrative data alone; they require examination of primary data on patient-reported sleep problems and comorbidities and the pharmacological treatment these patients receive in actual practice.

To help clarify pharmacological practices targeting sleep complaints, this study addresses the following research question: after controlling for PTSD severity, psychiatric comorbidities, and other key covariates, are patients in VHA with more severe insomnia or nightmare symptoms more likely to receive guideline-recommended trazodone and prazosin, as well as non-benzodiazepine hypnotics and benzodiazepines? To address this question, we combined administrative prescription and diagnostic records with self-report measures of sleep problems and PTSD severity. To increase generalizability and to facilitate comparison with national time-trend data, we conducted parallel analyses in two samples of VHA patients diagnosed with PTSD from two periods (from 2006 to 2008 and from 2009 to 2013).

METHODS

This secondary analysis used data from two studies of VHA patients diagnosed with PTSD. Procedures for the original studies were overseen by the Stanford University Institutional Review Board, and written informed consent was obtained from all participants. Use of sleep medications was not an inclusion or exclusion criterion in either study.

Participants

PTSD-Diagnosed Sample: Longitudinal Veterans Health Survey

This study examined treatment utilization and outcomes among a national sample of 482 veterans newly diagnosed with PTSD who had VHA outpatient visits between May 31, 2006, and December 7, 2007. Baseline surveys were completed between August 11, 2006, and April 6, 2008. Participants were randomly drawn from four sampling strata: male (n = 134, 28%) or female (n = 109, 23%) Iraq/Afghanistan veterans, and male (n = 121, 25%) or female (n = 118, 25%) veterans from earlier service periods. The mean age was 41.3 years (Table 1). Additional sample details were published previously (Rosen et al., 2011).

PTSD Outpatient Sample: Homecoming Line

This RCT compared usual PTSD care to usual care augmented by telephone case management. Prescription practices did not vary by condition, so study arms were combined for this analysis. Participants were 358 veterans beginning a new phase of PTSD outpatient treatment at one of three VA facilities. Surveys were completed between April 14, 2009, and April 22, 2013. The mean age was 48.4 years (Table 1).

Measures

Medical Record Data

Diagnostic and pharmacological data were obtained from VA administrative databases. Posttraumatic stress disorder and comorbid disorders were recorded if at least one corresponding *ICD-9* diagnosis was found in the primary or secondary diagnostic fields of the outpatient National Patient Care Dataset in the year before the survey date. We used the Decision Support System National Data Extract database to identify sleep medicines and other psychotropics commonly prescribed for PTSD ordered during the period beginning 60 days before the survey date (if the supply lasted at least through the survey date) and 6 months later. Patients were said to have received a medication if the database reported at least one prescription during this period. Thus, Longitudinal Veterans Health Survey (LVHS) prescriptions were ordered between August 11, 2006, and October 5, 2009 (the first week

TABLE 1. Sample Characteristics

	PTSD-Diagnosed Sample (LVHS, n = 482)		PTSD Outpatient Treatment Sample (HCL, n = 358)	
Characteristic				
Baseline period	11/2006–4/2008		4/2009–4/2013	
	N	%	n	%
Male	255	53%	305	85%
Any insomnia problem[a]	430	89%	337	94%
Restless sleep	384	80%	326	91%
Falling or staying asleep[b]	398	83%	324	91%
Nightmares	325	67%	298	83%
Anxiety or panic disorder diagnosis	109	23%	92	26%
Insomnia diagnosis	40	8%	39	11%
PTSD symptoms (mean ± SD)	49.9 ± 19.6[c]		64.0 ± 13.2[d]	
Depression, CESD (mean ± SD)[e]	31.7 ± 12.3		36.5 ± 10.7	
ASI, drug problems (mean ± SD)[f]	0.04 ± 0.1		0.02 ± 0.1	
ASI, alcohol problems (mean ± SD)[f]	0.1 ± 0.2		0.1 ± 0.2	
Age (mean ± SD)	41.3 ± 13.4		48.4 ± 14.2	

[a]Endorsed at least one of the following items: trouble "falling asleep," "staying asleep" (LVHS) or "staying or falling asleep" (HCL), and restless sleep.

[b]Endorsed trouble "falling asleep," and/or "staying asleep" (LVHS) or "staying or falling asleep" (HCL).

[c]Posttraumatic stress disorder symptom severity measured with the IES-R. Possible scores range from 0 to 88, with higher scores indicating more severe symptoms.

[d]Posttraumatic stress disorder symptom severity measured with the PCL. Possible scores range from 17 to 85, with higher scores indicating more severe symptoms.

[e]Depression symptom severity measured with the CESD. Possible scores range from 0 to 60, with higher scores indicating more severe symptoms.

[f]Addiction Severity Index drug problems and ASI alcohol problems measured with the ASI. Possible scores for each scale range from 0 to 1, with higher scores indicating more severe symptoms.

of FY 2009), and Homecoming Line (HCL) prescriptions between April 14, 2009, and October 21, 2013 (the third week of FY 2014). Prescriptions obtained only during inpatient or residential stays were not used, as patients' sleep patterns often change when away from home, and prescription practice may differ in these settings. Polypharmacy was calculated by summing the number of VA medication classes prescribed (exclusive of medications used as dependent variables), including selective serotonin and selective norepinephrine reuptake inhibitors, other antidepressants, antipsychotics, adrenergics, mood stabilizers, and antihistamines.

Self-Report Measures

Age and sex (female = 1, male = 0) were determined by self-report. In the LVHS study, prior week PTSD severity was assessed with the Impact of Events Scale–Revised (IES-R; Weiss and Marmar, 1997); in the HCL study, past month PTSD severity was assessed with a variant of the civilian version of the PTSD Checklist (PCL-C; Blanchard et al., 1996). Internal consistency was high for both measures (IES-R, α = .95; PCL, α = .93). Depression severity was measured with the Center for Epidemiological Study of Depression (CESD; Radloff, 1977) scale (LVHS, α = .92; HCL, α = .90). Alcohol and drug problem severity were measured with Addiction Severity Index (ASI) subscales (McLellan et al., 1980).

We assessed insomnia and nightmares with items from the PCL, IES-R, and CESD previously used to measure sleep disturbance (*e.g.*, Gellis et al., 2010; Kutner et al., 2001; McLay et al., 2010; Neylan et al., 2001). In the LVHS sample, insomnia was assessed with three items: CESD item K, which asks participants how much they have been affected by restless sleep, scored from 0 ("rarely or none of the time") to 3 ("most or all of the time"), and IES-R items B and O, which ask participants how much they were distressed or bothered by "trouble staying asleep" and "trouble falling asleep," scored from 0 ("not at all") to 4 ("extremely"). LVHS nightmare severity was rated with IES-R item T, which asks participants how much they were distressed by dreams about a stressful event. In the HCL sample, insomnia was assessed with the CESD restless sleep item and PCL item K, which asks participants how much they were bothered by "trouble falling or staying asleep," scored from 1 ("not at all") to 5 ("extremely"). Nightmares were assessed with PCL item B, asking participants how much they were bothered by "recurring, distressful dreams." To describe sample characteristics, we dichotomized sleep problems as present (versus absent) if a participant rating was above the lowest two categories on the response scale (*i.e.*, rated the problem a "2" or above on a 0–3 scale, or a "3" or above on a 1–5 scale).

In regression analysis, all continuous independent variables were standardized. We computed a composite insomnia severity score by averaging the CESD restless sleep item with either two IES-R items (LVHS) or one PCL item (HCL) related to difficulty sleeping (LVHS sample, α = .86; HCL sample, α = .83). Nightmare severity was measured using the distressing dream item from the IES-R or PCL. To control for overall PTSD symptom severity independent of insomnia and nightmares, we measured "nonsleep PTSD severity" by averaging z-scores on the IES-R and on the PCL, excluding items related to sleep problems (α = .94 and .92, respectively). Similarly, we measured "nonsleep depression severity" with the CESD, excluding restless sleep (LVHS, α = .92; HCL, α = .90).

Analytic Plan

Descriptive statistics were used to profile sample characteristics and prescribing patterns. Logistic regression models tested whether patients who reported more severe insomnia, nightmares, or both were more likely than those with less severe sleep problems to receive trazodone, zolpidem, non-benzodiazepine hypnotics, and benzodiazepines. Prescription of non-benzodiazepine hypnotics other than zolpidem was rare, so regression analysis for this class was limited to zolpidem. Each of the eight multivariate models (two samples by four medications) regressed receipt of a sleep medicine on continuous measures of insomnia symptom severity, nightmare severity, and nonsleep PTSD

severity. Within each sample, additional covariates were added to each multivariate sleep medication receipt model if their bivariate Pearson's correlation with that medicine was at the $p < 0.05$ level. Potential covariates included nonsleep depression severity, diagnosis of panic or anxiety disorders, alcohol problem severity and drug problem severity, polypharmacy, age, and sex. We included study entry date to control for changes in national prescription rate changes during the study period (Bernardy et al., 2012; Harpaz-Rotem and Rosenheck, 2009). We examined correlations between independent variables for evidence of multicollinearity. Analyses were conducted with SPSS 18.0.

RESULTS

Longitudinal Veterans Health Survey Sample (2006 to 2008)

In the LVHS sample, 89% of participants reported insomnia problems and 67% reported problems with nightmares (Table 1). Insomnia severity and nightmare severity were each significantly associated with severity of nonsleep-related PTSD symptoms ($r = 0.64$ and $r = 0.70$, $p < 0.001$) and with each other ($r = 0.54$, $p < 0.001$).

As shown in Table 2, 42% ($n = 204$) of sample participants were prescribed one or more of the four medication types. These included trazodone (received by 22% of the sample), prazosin (4%), nonbenzodiazepine hypnotics (4%; zolpidem, eszopiclone, or zaleplon), and benzodiazepines (23%). Table 3 shows the results of multivariate logistic regressions of receipt of trazodone and benzodiazepines on insomnia severity, nightmare severity, nonsleep PTSD severity, and other covariates. Receiving trazodone was predicted by insomnia severity (odds ratio [OR], 1.46; confidence interval [CI], 1.00–2.12; $p < 0.05$) and polypharmacy (OR, 1.47; CI, 1.17–1.86; $p < 0.001$). Multivariate analysis showed significant associations between benzodiazepine receipt and having an insomnia diagnosis, depression severity, having a panic or anxiety disorder diagnosis, ASI drug problems composite score, polypharmacy, and older age ($\chi^2 = 81.23$, $df = 9$, $p < 0.001$). Because too few patients received prazosin and zolpidem for us to run full models, these medications were not included in Table 3. Instead, each medication was regressed on insomnia severity and on nightmare severity, controlling for nonsleep PTSD severity only. In these analyses, the only significant finding was that patients who received prazosin were more likely to report greater nightmare severity (OR, 2.10; CI, 1.07–4.13; $p < 0.05$).

Homecoming Line Sample (2007–2013)

In this treatment-seeking sample, 94% of sample participants reported insomnia problems; 83% reported nightmare problems (Table 1). Insomnia severity and nightmare severity were again significantly associated with severity of nonsleep-related PTSD symptoms ($r = 0.53$ and $r = 0.65$, $p < 0.001$) and with each other ($r = 0.46$, $p < 0.001$).

Over half of the sample (54%) received one or more of the four medication types, including trazodone (25%), prazosin (22%), nonbenzodiazepine hypnotics (15%), and benzodiazepines (14%; Table 2). In multivariate analyses (Table 4), trazodone receipt was predicted by insomnia severity (OR, 1.51; CI, 1.02–2.23; $p < 0.05$). Prazosin receipt was predicted by nightmare severity (OR, 2.99; CI, 1.87–4.77; $p < 0.001$), polypharmacy (OR, 1.39; CI, 1.06–1.82; $p < 0.05$), and year (OR, 1.43; CI, 1.09–1.87; $p < 0.01$). Zolpidem receipt was predicted by insomnia severity (OR, 2.00; CI, 1.12–3.59; $p < 0.05$) and by year (OR, 1.49; CI, 1.09–2.03; $p < 0.01$). Benzodiazepine receipt was predicted by a diagnosis of a panic or anxiety disorder and by polypharmacy ($\chi^2 = 21.35$, $df = 6$, $p < 0.01$).

DISCUSSION

It seems that clinicians are appropriately targeting guideline-recommended trazodone and prazosin to PTSD-diagnosed patients with the most severe insomnia and nightmares. In both the LVHS and HCL studies, trazodone prescription was associated with greater insomnia severity, and prazosin prescription was predicted by greater nightmare severity. Receipt of these medications was not related to PTSD or depression severity, only to sleep-related complaints.

These findings suggest that VHA clinicians' prescribing practices for PTSD-related insomnia and nightmares are responsive specifically to patients' sleep problems and not more generally directed at other PTSD and depressive symptoms. This is consistent with research showing that sleep and nonsleep PTSD symptoms may follow independent courses and require different treatments. In addition, receipt of trazodone and prazosin was not associated with the relatively infrequent diagnosis of insomnia. Given concerns that those without an insomnia diagnosis may be undertreated (Hermes and Rosenheck, 2014), this may represent a positive, patient-centered outcome.

Study differences in prescription rates were generally consistent with FY 2006 to FY 2009 VHA prescription rates (Bernardy et al., 2012) and with our analysis of FY 2006 to FY 2013 VHA prescription rates. The HCL study participants were more likely to receive guideline-concordant trazodone and prazosin than were participants in

TABLE 2. Prescriptions Received

Sample	PTSD-Diagnosed Sample LVHS ($n = 482$)		PTSD Outpatient Treatment Sample HCL ($n = 358$)	
Medication	*n*	%	*n*	%
Trazodone, prazosin, hypnotics[a]	204	42%	193	54%
Trazodone	106	22%	88	25%
Prazosin	21	4%	78	22%
Hypnotics[b]	127	26%	91	25%
Zolpidem	17	3%	52	15%
Eszopiclone or zaleplon	2	0.4%	0	0%
Benzodiazepines	113	23%	50	14%
Sum of other VA medication classes[c]	1.1 ± 1.1		1.4 ± 1.1	

[a]Includes trazodone, prazosin, non-benzodiazepine hypnotics (zolpidem, eszopiclone, and zaleplon), and benzodiazepines.

[b]Includes zolpidem, eszopiclone, zaleplon, and benzodiazepines.

[c]Includes VA medication classes: selective serotonin reuptake inhibitors and selective norepinephrine reuptake inhibitors, other antidepressants, antipsychotics, adrenergics, mood stabilizers, and antihistamines; excludes trazodone, prazosin, non-benzodiazepines, and benzodiazepines.

TABLE 3. Adjusted Odds of Receiving Sleep Medications in the LVHS Sample

	Trazodone		Benzodiazepines	
n processed for adjusted models	470		467	
Predictors	OR	CI	OR	CI
Insomnia severity	1.46*	1.00–2.12	1.26	0.85–1.88
Nightmare severity	0.92	0.67–1.26	1.23	0.87–1.73
Nonsleep PTSD severity	0.98	0.67–1.44	0.72	0.48–1.08
Nonsleep depression severity	1.17	0.87–1.57	1.67**	1.21–2.29
Panic/anxiety disorder diagnosis	–	–	1.89*	1.10–3.23
Insomnia diagnosis	–	–	3.39**	1.55–7.40
ASI, drug problems	–	–	1.24*	1.01–1.52
Sum of other VA drug classes	1.47***	1.17–1.86	1.66***	1.30–2.11
Age	–	–	1.29*	1.00–1.68
Sex	1.45	0.91–2.32	–	–
Model fit	$\chi^2_6 = 31.85$, $p < 0.001$		$\chi^2_9 = 81.23$, $p < 0.001$	

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

the earlier LVHS study (40% *vs.* 25%, respectively), due largely to the substantial increase in receipt of prazosin.

About one in four patients in both samples received hypnotics, with higher rates among patients with insomnia. In the LVHS sample, 23% of all patients and 45% of those diagnosed with insomnia received benzodiazepines. In the later HCL study, 25% of the sample received hypnotics, with prescriptions fairly evenly split between benzodiazepines and zolpidem. However, insomnia severity was associated only with prescriptions for zolpidem, not benzodiazepines.

Although the CPGs favor short-term prescription of non-benzodiazepine hypnotics over benzodiazepines because of safety advantages, they also caution that hypnotics are recommended only for short-term use. We are unable to determine the extent to which use of hypnotic medications was short term or long term. This analysis was beyond the scope of this article and would have required access to more complete pharmacy records, as well as clinical consensus on how to operationalize "short-term" use. A study by Hawkins et al. (2012), examining FY03 and FY10 prescription records at VA facilities in the Pacific Northwest, found that about 61% of PTSD-diagnosed veterans prescribed benzodiazepines received greater than 90 days of supply. A similar investigation of non-benzodiazepine hypnotic treatment duration would help evaluate the extent to which they are being prescribed for nonrecommended long-term use.

The CPGs also caution about the potential for abuse of benzodiazepines in a population with high rates of comorbid substance abuse disorders. It is concerning that receipt of benzodiazepines was positively associated with higher ASI drug problem scores in the LVHS study. Other studies with PTSD-diagnosed veterans have also found that veterans with drug use problems, especially opioid abuse, are equally or more likely to receive benzodiazepine prescriptions than are veterans without substance use disorders (Bernardy et al., 2014; Bowe and Rosenheck, 2015; Hawkins et al., 2012; but see Kosten et al., 2000). Better screening of substance abuse problems (Hawkins et al., 2012) and improved coordination among prescribers (Bernardy et al., 2014) could reduce the risk of harm from benzodiazepines.

This observational study has several limitations. These samples may not be fully representative of all VHA patients with PTSD-related sleep problems during the study periods. Both studies were conducted at five or fewer VHA sites, including a site that was an early adopter of prazosin, and included only patients who agreed to participate in research. However, the very high rates of insomnia and

TABLE 4. Adjusted Odds of Receiving Sleep Medications in the HCL Sample

Adjusted Models	Trazodone		Prazosin		Zolpidem		Benzodiazepines	
n processed for adjusted models	355		357		357		346	
Predictors	OR	CI	OR	CI	OR	CI	OR	CI
Insomnia severity	1.51*	1.02–2.23	0.68	0.45–1.02	2.00*	1.12–3.59	1.09	0.68–1.75
Nightmare severity	1.06	0.75–1.48	2.99***	1.87–4.77	1.29	0.85–1.97	1.09	0.70–1.71
Nonsleep PTSD severity	0.79	0.49–1.27	0.84	0.56–1.25	0.73	0.47–1.13	1.20	0.75–1.93
Nonsleep depression severity	1.33	0.86–2.06	–	–	–	–	–	–
Panic/anxiety disorder diagnosis	–	–	0.60	0.31–1.19	–	–	2.75**	1.42–5.34
ASI, drug problems	–	–	–	–	–	–	1.21	0.93–1.58
Sum of other VA drug classes	1.24	0.97–1.59	1.39*	1.06–1.82	1.28	0.95–1.71	1.44*	1.05–1.97
Year	–	–	1.43**	1.09–1.87	1.49**	1.09–2.03	–	–
Model fit	$\chi^2_5 = 13.38$, $p < 0.05$		$\chi^2_6 = 49.81$, $p < 0.001$		$\chi^2_5 = 20.75$, $p < 0.001$		$\chi^2_6 = 21.35$, $p < 0.01$	

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

nightmare problems are comparable to those reported by other studies, and the prescription rates during the two sampling periods (roughly FY06 to FY08 and FY09 to FY13) are similar to national prescription trends during those years.

These samples enabled us to examine associations between symptoms and prescribing, but we could not confirm whether sleep medications were prescribed specifically in response to patient-reported insomnia and nightmares. Research into prescribers' pharmacological decision making for sleep disorders, perhaps through qualitative interviews (Bernardy et al., 2012), may help elucidate provider, patient, and setting factors that affect the selection, sequencing, and dosing of medications for sleep problems (Alexander et al., 2015; Lund et al., 2013a, 2013b).

We do not have information on prescription duration. We also did not have measures developed specifically for sleep quality, but rather relied on items embedded in other scales. Given that more items on a scale reduces measurement error, it is all the more remarkable that prescription of CPG-endorsed medication was consistently associated with severity of insomnia or nightmares (each measured with only one to three items) and not with severity of other PTSD symptoms (measured with psychometrically strong scales).

Importantly, our study was limited to pharmacotherapy. We were unable to examine the use of psychosocial treatments, including sleep hygiene, CBT-I, and imagery rehearsal therapy. The CPGs rate these nonpharmacological approaches as superior or equal to stand-alone or combined pharmacotherapy, especially for long-term treatment (but see Perlis et al., 2015; Roth et al., 2005). We were also unable to examine whether patients were assessed or treated for problems such as sleep-disordered breathing or movement disorders, although these are often comorbid with PTSD and are associated with nightmares and insomnia (Maher et al., 2006).

More research is needed on identifying appropriate pharmacological and nonpharmacological sleep therapies for short-term and maintenance treatment (Augedal et al., 2013; Morin et al., 2009). Future studies may wish to examine the extent to which clinicians holistically assess sleep problems and to target interventions to address the sleep problem heterogeneity associated with PTSD (Krystal, 2015; Wallace et al., 2015). Establishing treatment approaches that incorporate provider expertise and patient preferences may improve outcomes among patients experiencing PTSD-related sleep problems (Watts et al., 2015).

CONCLUSIONS

Data from two samples in different periods suggest that a substantial proportion of veterans diagnosed with PTSD report sleep problems. By linking administrative records with patient self-report, we found that veterans who reported more severe PTSD-related insomnia and nightmare symptoms were more likely to receive DVA/DoD guideline–concordant trazodone and prazosin, even after controlling for other psychiatric and demographic variables. Further study of the duration of hypnotic treatment would help evaluate concordance with practice guidelines. Additional research is needed to identify and optimize clinicians' use of pharmacological, psychosocial, and combined therapies to treat the sleep problems of patients diagnosed with PTSD.

DISCLOSURE

The authors declare no conflict of interest.

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