

**“Gender Differences in Prescribing among
Veterans Diagnosed with Posttraumatic
Stress Disorder”**

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Acknowledge

- My mentor and collaborator, Dr. Matthew J. Friedman, past Executive Director and now consultant, NCPTSD
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Objectives

- Briefly review first line recommended treatments for PTSD, particularly guidance regarding benzodiazepines and our work examining prescribing practices in PTSD
- Discuss gender-specific findings and possible explanations
- Share new work focused on polysedatives and implications for the way forward

Poll Question #1

- What is your primary role in VA?
 - student, trainee, or fellow
 - mental health clinician
 - primary care clinician
 - researcher
 - administrative, manager or policy-maker
 - other

Pharmacotherapy for PTSD: Summary

	Balance = Benefit - Harm			
SR	SUBSTANTIAL	SOMEWHAT	UNKNOWN	NONE or HARM
A	SSRIs, SNRIs			
B		Mirtazapine, TCAs, MAOIs (phenelzine), Prazosin (nightmares), Nefazodone (caution)	<p><i>SR = Strength of recommendation</i> (Full Guideline, p. 149)</p>	
C				
D	http://www.healthquality.va.gov/guidelines/MH/ptsd/			Guanfacine, Topiramate, Valproate, Tiagabine Benzodiazepines (harm) Risperidone (adjunct)
I			Buspirone, Bupropion, Non-benzodiazepine Hypnotics, Lamotrigine, Gabapentin, Clonidine, Trazodone (adjunct), Atypical antipsychotics (mono), Atypical antipsychotics (besides Risperidone) (adjunct) Conventional antipsychotics, Propranolol	

Problem with this Guidance

- Role of benzodiazepines in PTSD management remains contentious
- What small clinical trials have been done showed no benefit in alleviating or preventing PTSD symptoms
- Evidence-based literature regarding the significant risks of chronic benzodiazepines is large and very, very clear and is growing rapidly
- Lack of evidence of efficacy plus clearly evidenced high risk profile support the PTSD Clinical Practice Guideline recommendation

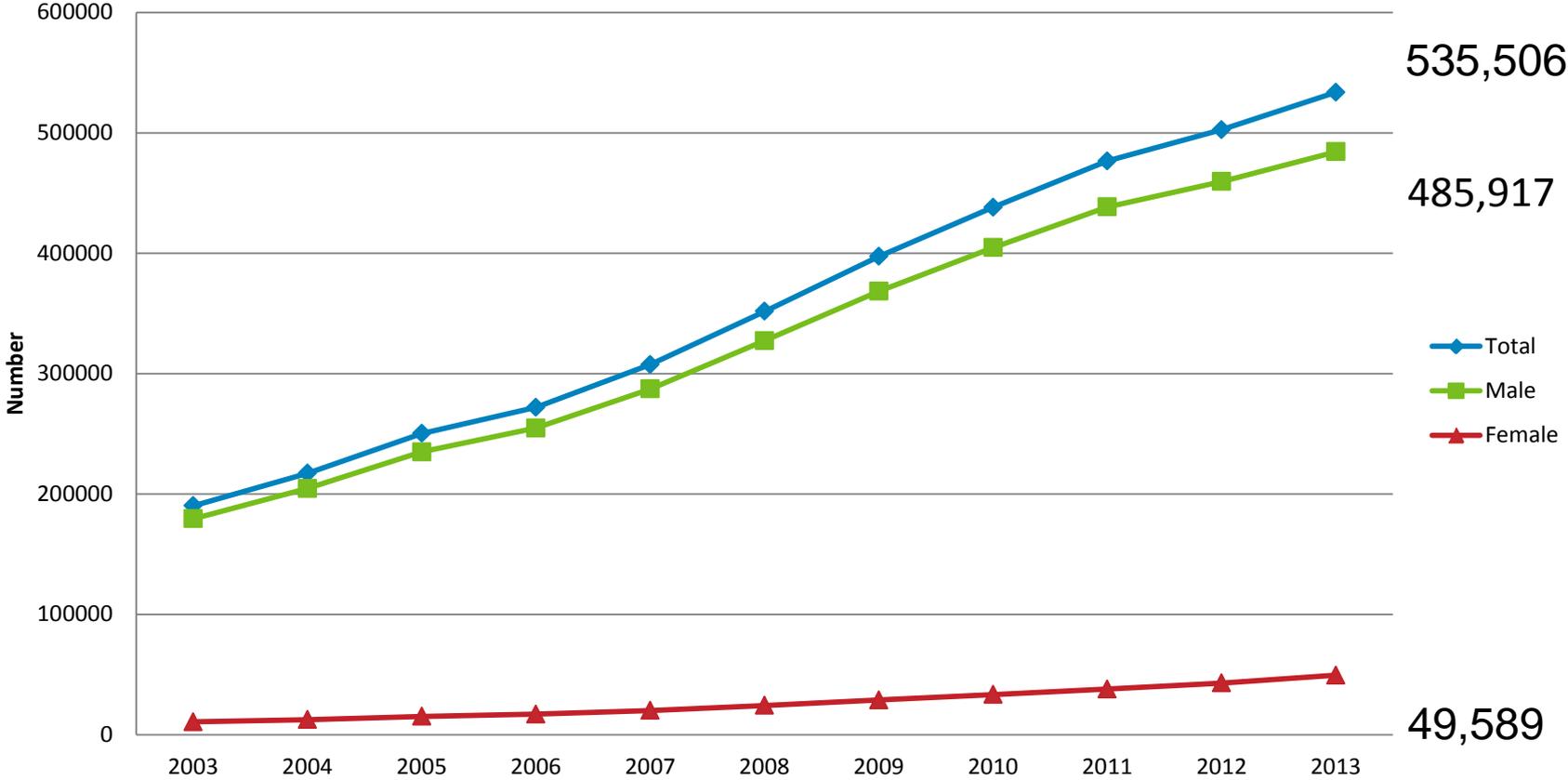
Benzodiazepines in PTSD

- Commonly prescribed to manage insomnia and anxiety but there are now better treatment options – both medications and psychotherapy
- Two common comorbidities, mTBI and SUD, are contraindications to benzodiazepine use
- Some clinical evidence that benzodiazepines can reduce the effectiveness of evidence-based cognitive behavioral treatments (CBT) in real world patients
- Tolerance, dependence, withdrawal symptoms and dramatic rebound are concerns but most adverse effect may be cognitive “fogginess”
- New evidence suggests increased risk of dementia (de Gage et al., 2012), increased detrimental effects on immune system (Huang et al., 2014), and significantly higher ratios for mortality associated with long term use of benzodiazepines prescribed for sleep (Weich et al., 2014)

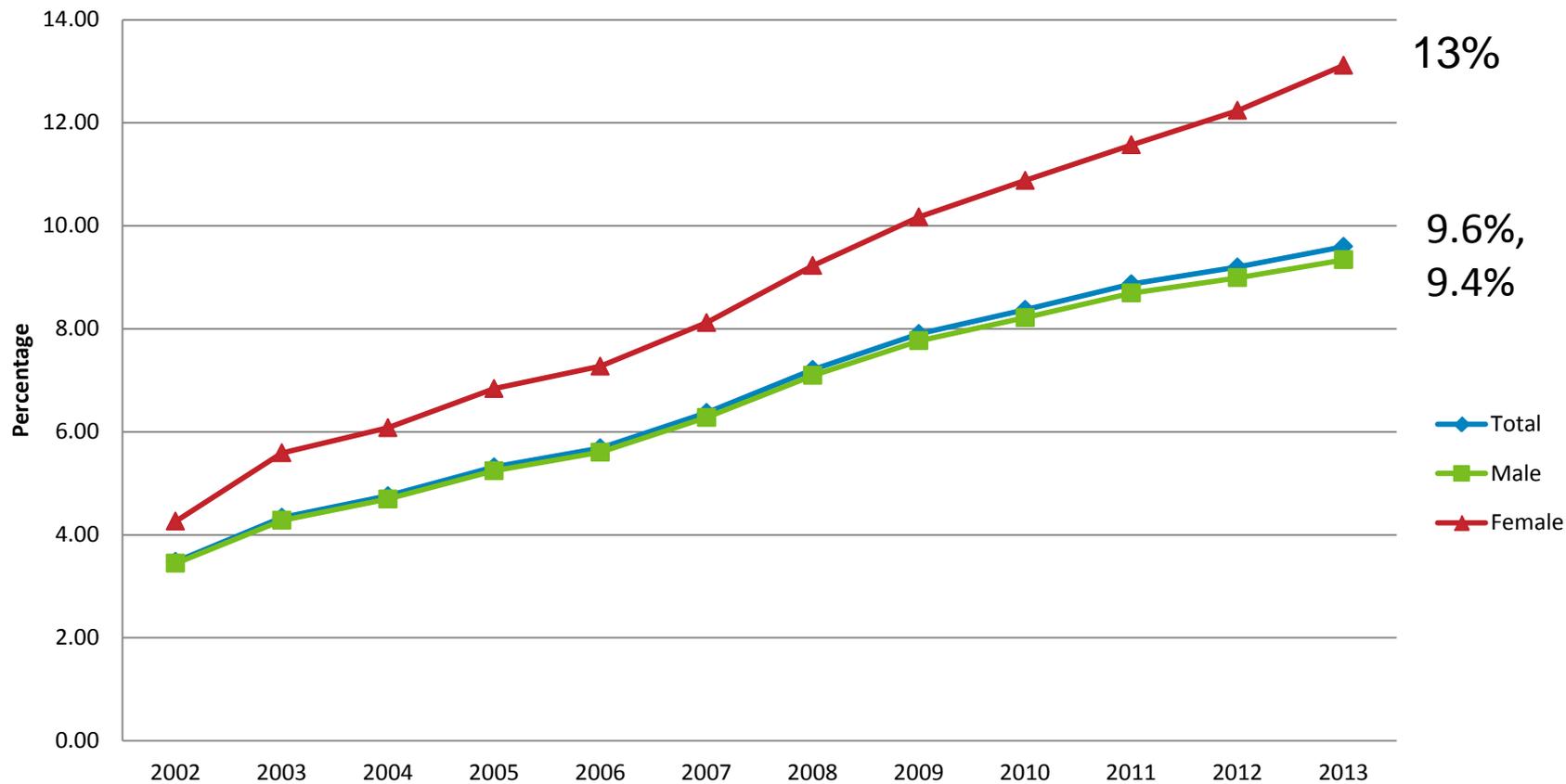
VA's Commitment to Women's Health Needs

- Women are now the fastest growing cohort within the Veteran community
- Represent approximately 16% of OEF/OIF/OND
- Virtually no work conducted to examine the role of pharmacotherapy in management of PTSD in women Veterans

Total number of Veterans in VHA with a diagnosis of PTSD, by year



Percentage of Veterans in VHA with a diagnosis of PTSD, by year



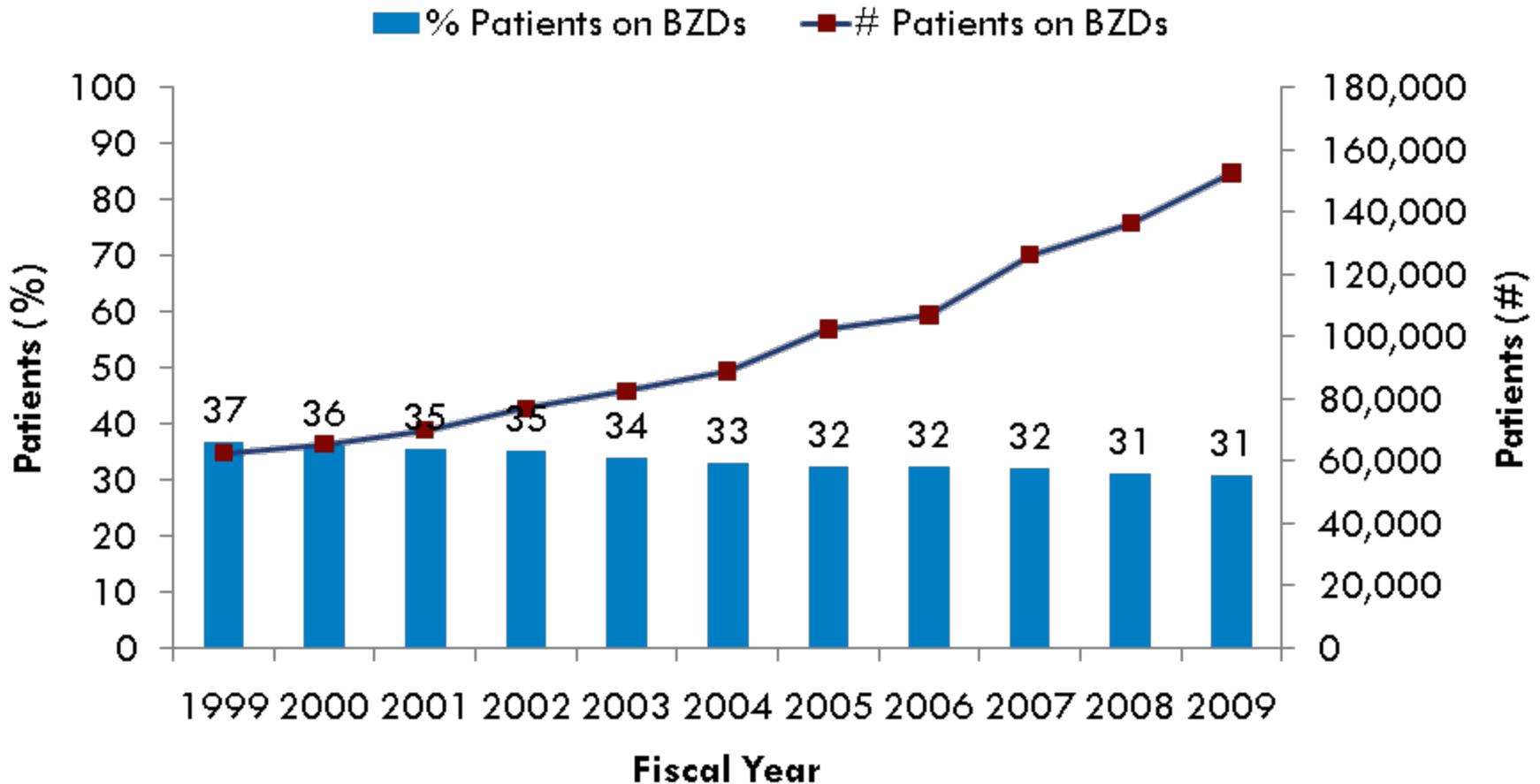
POLL Question 1

What method do you prefer for learning new clinical information?

- A. Webinar such as this
- B. Written materials, study books or journal articles
- C. Mobile Applications on Smart Phone or iPad-like device
- D. Live Lecture Grand Rounds with case presentations
- E. Face-to-face discussion such as that with a pharmaceutical company representative or staff member

Declining Benzodiazepine Use in Veterans with PTSD

Is Benzodiazepine Use Increasing or Decreasing?



(Lund et al., 2012)

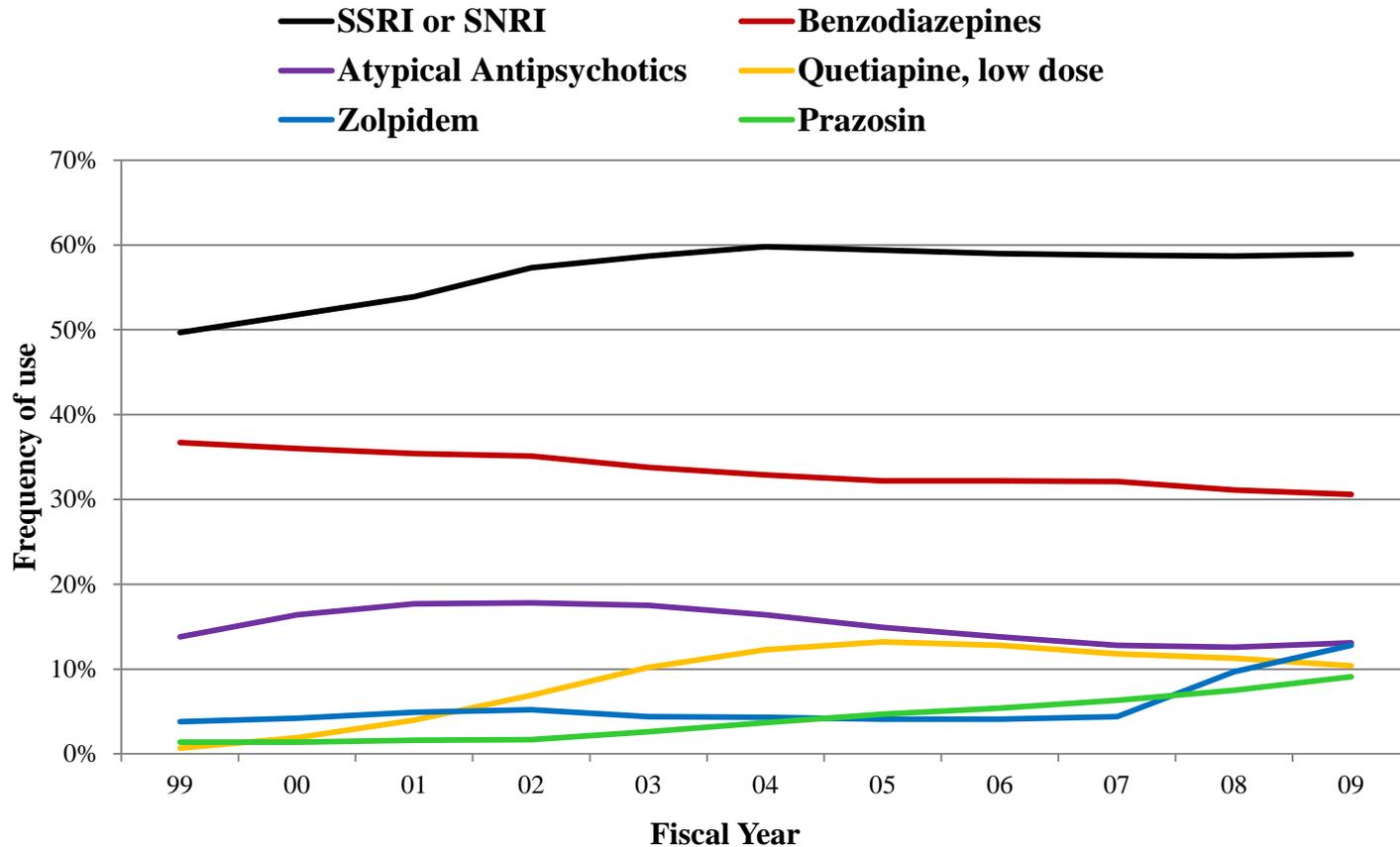
Prescribing Trends in Veterans with PTSD

Results – a Good News Story?

- Proportion receiving either SSRI and SNRI, top 2 recommended pharmacotherapy treatments for PTSD increased from 49.7% in 1999 to 58.9% in 2009 – this increase represents more than 46,000 Veterans receiving these meds
- In addition to reduced BZ prescribing, overall frequency of antipsychotic use declined 6.1% from 20% in 1999 to 13.9% in 2009
- Nonbenzodiazepine hypnotic prescribing tripled when zolpidem (Ambien) was added to formulary in 2008.

General Prescribing Trends in PTSD

Frequency of Medication Use by Drug Class and Fiscal Year



Where the Medications were Prescribed

1. 70% of prescribing of SSRI/SNRIs to Veterans with PTSD (65.7%) was attributable to mental health care providers
2. 80% of prescribing of atypical antipsychotics to these Veterans (25.6%) was from mental health care providers
3. Benzodiazepines were prescribed for 37.0% of the sample and 69% of the prescribing was again from mental health prescribers
4. Confirmed that Veterans with PTSD are frequently prescribed medications not supported by the guidelines and most of the prescriptions are written by mental health care providers

Identify Predictors Associated with Benzodiazepine Prescribing

Patient Level Correlates of Benzodiazepine Use: Univariate Comparisons (FY09)

Patient Characteristic	Characteristic Frequency	Benzodiazepine Frequency	OR (95% CI)
Women	7.5%	38.3%	1.47 (1.43, 1.50)
Age \geq 30 years	89.0%	31.6%	Reference
Rural	26.9%	33.2%	Reference
Service connection \geq 50%	55.0%	35.5%	1.72 (1.70, 1.75)
Vietnam era	56.2%	32.3%	Reference
\geq 3 year duration	54.7%	36.0%	Reference

Gender Differences Background

- Women disproportionately receive prescriptions for psychotropic medications (1 in 4 American women compared to 15% of men)
- Particularly true of anti-anxiety drugs where approx. 11% of women (ages 45-64) received benzodiazepines in 2010 compared to a rate half that seen in men (5.7%)
- Women suffer more frequently from psychiatric disorders than men
- Greater diagnostic frequency, gender differences in acceptance/receipt of mental health treatment, or gender-based inequity?

General Methodology

- Time period
 - Fiscal years (FY) 1999 through 2009
- Patients
 - Veterans with ≥ 1 encounter coded for PTSD ICD-9 code (309.81) from inpatient discharges and outpatient encounters
- Medication use based on at least one outpatient prescription record of any days supply and included SSRIs, SNRIs, atypical antipsychotics, benzodiazepines, non-benzodiazepine hypnotics and prazosin

Demographic characteristics

Variable	Mean, % in women	Mean, % in men
Age	43.3 +/- 11.9*	54.7 +/- 14.5
Urban residence	79.6%*	72.6%
Post Vietnam era	86.4%	33.3%
Service connection >50%	46.5%	55.6%*
PTSD diagnosis duration*		
New diagnosis	26.2%	21.7%
1-2 years	25.2%	23.1%
3+ years	48.6%	55.2%

*<0.0001

Comorbidity characteristics

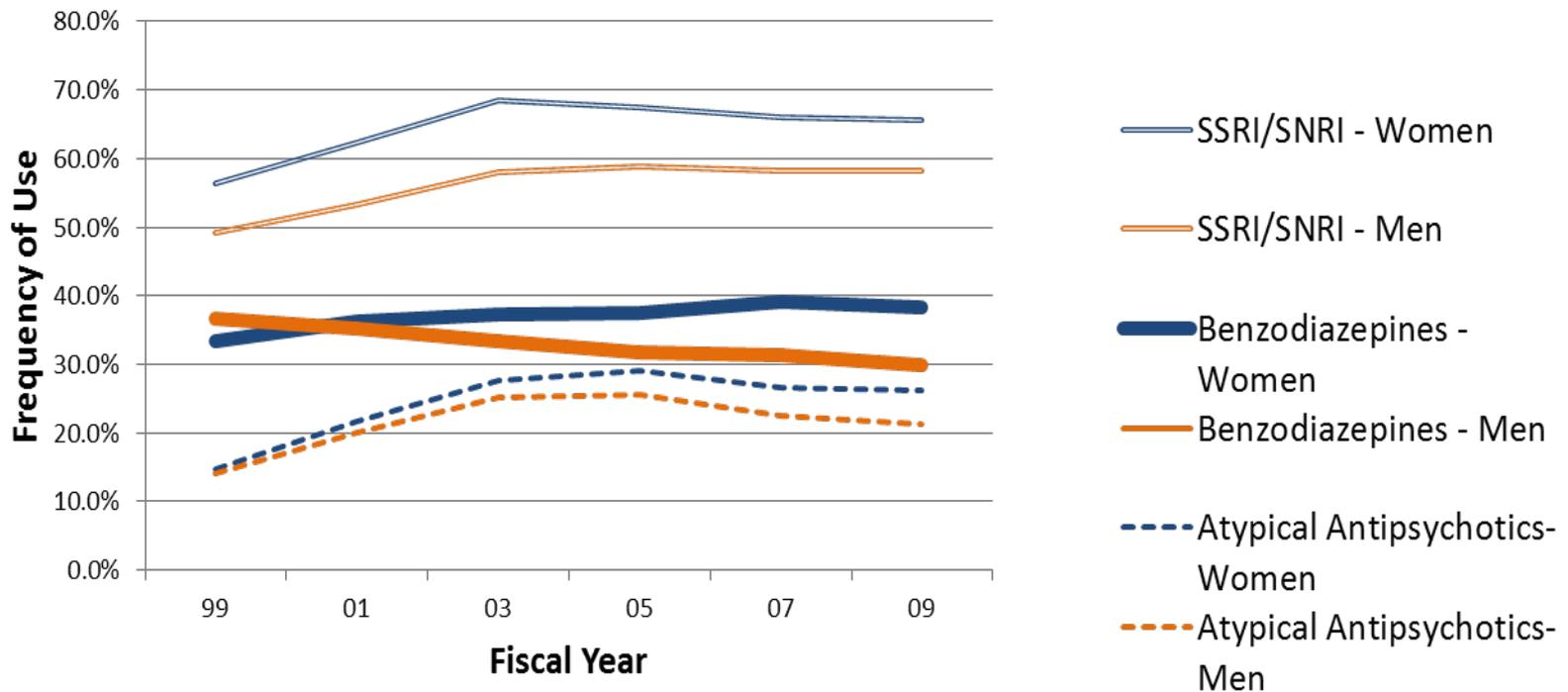
Variable	Mean, % in women	Mean, % in men
Depressive disorder	65.6%*	47.3%
Anxiety disorder, any	14.8%*	7.5%
Panic disorder	8.2%*	3.5%
GAD	6.2%*	3.8%
OCD	1.8%*	0.7%
Social phobia	0.4%*	0.3%
Substance use disorder	17.8%	22.8%*
Traumatic brain injury	3.4%	4.5%*

*<0.0001

Gender Differences in Prescribing Trends

	FY99	FY03	FY07	FY09
SSRI/SNRI				
Women	56.4%	68.4%	66.1%	65.7%
Men	49.2%	58.0%	58.2%	58.3%
OR (95% CI)	1.34 (1.28, 1.39)	1.57 (1.51, 1.62)	1.40 (1.36, 1.44)	1.37 (1.34, 1.40)
Benzodiazepines				
Women	33.4%	37.3%	39.1%	38.3%
Men	36.7%	33.4%	31.3%	29.8%
OR (95% CI)	0.86 (0.83, 0.90)	1.18 (1.14, 1.23)	1.41 (1.38, 1.45)	1.47 (1.43, 1.50)
Atypical antipsychotics				
Women	14.6%	27.6%	26.6%	26.3%
Men	14.1%	25.1%	22.5%	21.3%
OR (95% CI)	1.05 (0.99, 1.11)	1.14 (1.10, 1.18)	1.25 (1.22, 1.29)	1.31 (1.28, 1.35)
Zolpidem				
Women	3.8%	5.6%	6.1%	16.9%
Men	3.8%	4.3%	4.2%	12.4%
OR (95% CI)	1.02 (0.92, 1.13)	1.33 (1.24, 1.43)	1.48 (1.40, 1.56)	1.43 (1.39, 1.48)
Prazosin				
Women	0.2%	1.9%	5.0%	7.1%
Men	1.5%	2.6%	6.4%	9.3%
OR (95% CI)	0.14 (0.09, 0.21)	0.73 (0.64, 0.82)	0.76 (0.72, 0.80)	0.75 (0.72, 0.78)

Gender Differences in Temporal Prescribing Trends



Independent Predictors of Gender Differences in Prescribing

- Demographic characteristics and psychiatric comorbidities were examined for SSRIs, benzodiazepines and atypical antipsychotics
- Age had substantial impact on BZs and AAs – younger reproductive-age women had lower rates of receipt of both, increased with age for BZs
- AAs showed an inverted U pattern where lower rates were seen in younger, increased in middle age and decreased in older for both men and women
- An increased percentage of VA service-connected disability (>50%) contributed to an increase in prescribing of all medications for both men and women

Independent Predictors of Prescribing

- Psychiatric comorbidity has significant impact
- Likelihood of SSRI/SNRI use was 3-fold higher in patients with co-occurring depressive disorder
- BZ use was more common for all anxiety disorder comorbidities, particularly with panic disorder
- Elevated prescribing of AAs was observed in both men and women with co-occurring SUD
- TBI was associated with increased prescribing across all classes except for SSRI use in women
- Benzodiazepine use was actually higher for women with co-occurring SUD whereas the opposite was true for men

Gender differences in prescribing among Veterans diagnosed with PTSD

Model	SSRI/SNRI		Benzodiazepines		Atypical Antipsychotics	
	OR (95% CI) *	c statistic	OR (95% CI)	c statistic	OR (95% CI)	c statistic
Unadjusted	1.37 (1.34, 1.40)	0.511	1.47 (1.43, 1.50)	0.514	1.31 (1.28, 1.35)	0.510
Demographics only	1.34 (1.31, 1.37)	0.567	1.63 (1.60, 1.67)	0.608	1.08 (1.05, 1.10)	0.605
Comorbidity only	1.13 (1.10, 1.15)	0.630	1.27 (1.24, 1.30)	0.590	1.25 (1.22, 1.28)	0.607
Demographics and comorbidity	1.15 (1.12, 1.18)	0.658	1.47 (1.44, 1.51)	0.653	1.08 (1.05, 1.11)	0.652

* Odds-ratio and 95% confidence interval for the likelihood of receiving medication in women compared to men

Gender Differences in Prescribing SSRIs/SNRIs

- Women Veterans were more likely to receive psychotropic medications across all classes except prazosin which was more likely in men
- Substantial increases in SSRI/SNRIs reflect a positive shift to evidence-based care – additional 18,388 women receiving first-line recommended medications
- When adjusted for comorbidities, still higher frequencies of SSRIs/SNRIs in women

Prescribing of Atypical Antipsychotics

- Observed comparable guideline-concordance prescription patterns with atypical antipsychotics with similar gender frequencies until a shift occurred in 2003 that saw an increase for women that stayed elevated compared to men
- When adjusted for demographic characteristics, still elevations in frequency for women not accounted for by more severe service-connected disability
- May target insomnia symptoms in women as there is evidence of gender differences in arousal symptoms
- Atypical antipsychotics were recommended adjunctively to SSRIs in CPG before modified in 2012 but concerns about side effects should be considered

Prescribing of Benzodiazepines

- Significant exception
- Decreased prescribing in men, steady increases for women despite CPG recommendations of harm
- Not only did we observe increased rates of prescribing in women but in women with co-occurring SUD and TBI where contraindicated, elevations were seen
- Age appeared to also be a related factor: reduced prescribing in reproductive-age group encouraging but being older and having a greater service connection contributed to elevated prescribing

Possible Reasons for this Discrepancy (Disparity?)

- Women may exhibit higher rates of distress (King et al., 2013); Men report more nightmares, numbing and hypervigilance
- Clinicians may also prescribe benzodiazepines for symptoms that are not an indication for their use such as headache, fatigue, chest pain and vertigo
- Sleep symptom management is clearly playing a role
 - Extraordinary 10% increase in zolpidem use in women from 2007 to 2009 confirms how much sleep difficulties are part of the clinical presentation of PTSD and this may not be a good substitute
 - Not clear why prazosin use would be the exception and more widely used in men

Possible Reasons for this Discrepancy

- Gender-specific mechanisms have been suggested to underlie relationship between sleep impairment and development of PTSD (Kobayashi, 2013)
- Research suggests discrepant findings but overall, appears to suggest that males with PTSD report more PTSD-related sleep disturbances
- In other words, PTSD may not be driving the discrepancy in women but it may be age and gender factors contributing to this – again, are women more willing to take medications for sleep?

Limitations

- Use of administrative data allows us to examine these trends but not to fully determine justification for use
- Were able to capture important comorbidities but not insomnia symptoms associated with PTSD
- Other co-occurring disorders may be relevant that were not captured
- Nor can we confirm the timing (current active or history) or severity of the co-

Conclusions

- Important to explore reasons for increased prescribing of benzodiazepines for women with PTSD
- Complexity of patients may cause clinicians to respond to treatment failures by indiscriminately trying different, non-recommended medications
- Important to look at gender differences in response to cognitive-behavioral therapy for insomnia (CBT-I)
- Provider education is sorely needed for this reproductive-aged cohort to inform clinicians about gender differences in side effects, dosing and sex differences in pharmacokinetics of psychotropic medications to ensure quality PTSD care for our Veteran women

POLL Question 3

Provider Prescribing Report Cards Used as Audit and Feedback in PTSD Care

Do you think these tools would be:

- A. Helpful for showing providers they are outliers in their prescribing
- B. Not used because the data is too difficult to acquire in our healthcare practice
- C. A bad idea, as they just cause providers to get upset when they see someone is looking at their prescribing.

Polysedative Prescribing

- PTSD treatment is often complicated by co-occurring conditions including pain, insomnia, brain injury and other MH disorders
- Pharmacologic approaches to these conditions can produce an accumulation of sedating medications with potential for safety concerns

Background

- Unfortunately the evidence base concerning coordinated treatment recommendations for these co-occurring conditions is limited.
 - Seal (2012) noted among OEF/OIF Veterans with chronic pain, the presence of PTSD was associated with increased likelihood of opioid prescribing, as well as high risk behaviors and adverse outcomes.
 - This study also showed that those with PTSD were more likely to receive 2 or more opioids concurrently, as well as sedative hypnotics and opioids concurrently.
 - A small cross-sectional study found that 47% of Veterans with PTSD taking benzodiazepines were concurrently prescribed opioids (Hawkins, 2012).
 - Recent work by Dr. Park and others in the VA noted considerable regional variability of overlap of benzodiazepines and opioid agonist therapies (2014)

Demographic Subgroups

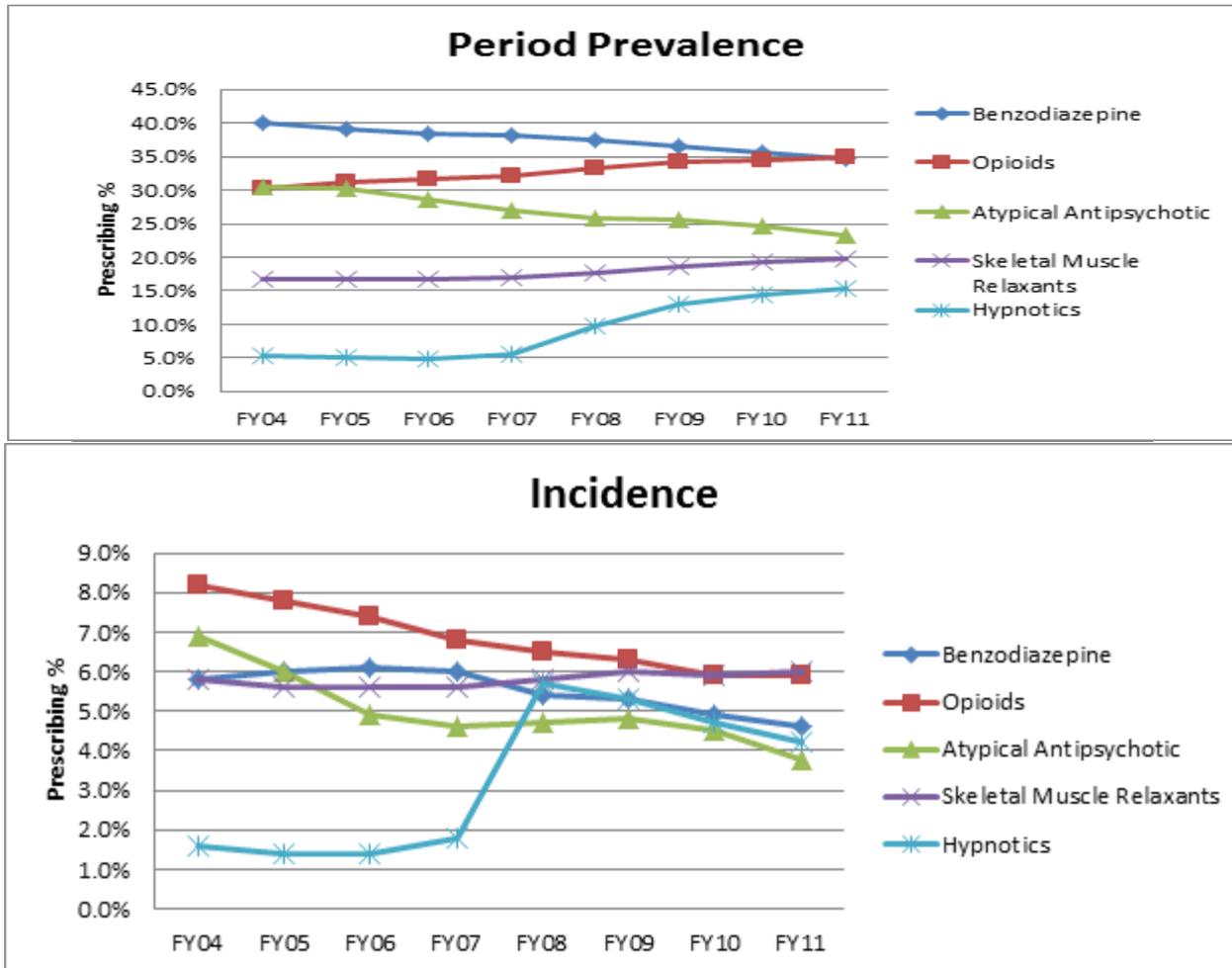
Demographic Characteristic	Benzodiazepines		Opioids	
	Prevalence	Incidence	Prevalence	Incidence
Sex				
Men (n=332,957)	33.8%	4.5%	34.7%	5.8%
Women (n=26,034)	44.4%	6.5%	38.1%	6.2%
Age group				
Adults, <65 yrs (n=283,757)	35.5%	4.8%	36.7%	5.9%
Older adults (n=75,234)	31.2%	3.9%	28.2%	5.8%
Residence				
Urban (n=251,380)	33.6%	4.6%	33.6%	5.7%
Rural (n=102,494)	36.2%	4.7%	38.6%	6.2%
Race/ethnicity				
White (n=231,699)	38.4%	4.7%	36.8%	5.9%
Black (n=62,498)	21.9%	4.5%	32.1%	6.0%
Hispanic (n=23,289)	36.6%	4.7%	30.3%	5.6%
Asian (n=5,707)	31.9%	4.9%	31.2%	6.2%
Native American (n=3,690)	33.0%	4.3%	44.0%	6.9%
Unknown (n=32,108)	31.1%	3.9%	30.0%	5.4%

Period Prevalence of any Concurrent Polysedative Use

Number of concurrent sedative classes	2004, N=165,391 n (%)	2011, N=358,992 n (%)
None	41 837 (25.3%)	91 709 (25.6%)
1	66 988 (40.5%)	136 067 (37.9%)
2	40 440 (24.5%)	87 842 (24.5%)
3	13 607 (8.2%)	34 620 (9.6%)
4	2 422 (1.5%)	7 997 (2.2%)
5	97 (0.1%)	757 (0.2%)
≥ 1	123 554 (74.7%)	267 283 (74.4%)
≥ 2	56 566 (34.2%)	131 216 (36.6%)
≥ 3	16 126 (9.8%)	43 374 (12.1%)

Trends in Sedative Use

Figure. Period prevalence and incidence in sedative prescribing



Frequency of Concurrent Polysedative Use Stratified by Demographic Subgroup

Demographic Characteristic	2004		2011	
	2 or more	3 or more	2 or more	3 or more
Sex				
Men	33.6%	9.4%	35.5%	11.4%
Women	46.7%	15.7%	49.7%	20.8%
Age group				
Adults, <65 yrs	37.2%	11.1%	39.6%	13.6%
Older adults, >= 65 yrs	20.4%	3.6%	25.2%	6.3%
Residence				
Urban	33.4%	9.5%	35.7%	11.6%
Rural	35.9%	10.4%	38.3%	13.1%
Race				
Native American	39.4%	12.4%	41.0%	14.3%
White	37.2%	11.2%	39.0%	13.4%
Hispanic	34.6%	8.5%	36.2%	11.7%
Asian	29.7%	7.5%	32.5%	10.7%
Black	29.6%	7.4%	31.5%	9.2%
Unknown	25.5%	6.2%	29.5%	8.6%
All patients	34.2%	9.8%	36.6%	12.1%

Period Prevalence of any Concurrent Use of Polysedative Combinations in 2011

	Observed Prevalence (Expected Prevalence*)			
	Hypnotics	Atypical antipsychotics	Opioids	Skeletal muscle relaxants
Benzodiazepines	5.2% (5.3%)	9.5% (8.1%)	15.9% (12.1%)	7.1% (6.8%)
Hypnotics		3.3% (3.6%)	6.1% (5.3%)	3.0% (3.0%)
Atypical antipsychotics			8.9% (8.1%)	4.7% (4.6%)
Opioids				10.8% (6.9%)

The Impact of Musculoskeletal Pain

- Women are more likely to have musculoskeletal disorders – 4.6% vs. 4.1%
- For women and men Veterans who use VA, the prevalence of painful musculoskeletal conditions including back, joint and musculoskeletal problems increases every year after deployment...
- But, it increases more for women than men, so by 7 years post-deployment:
 - 20% of women and 17% of men have back problems
 - 12% of women and 10% of men have musculoskeletal conditions
 - 19% of women and 17% of men have joint problems

Pain burden among Veterans entering PTSD treatment

	N, severe pain	%, severe pain	N, non-severe pain	%, non-severe pain
Men	4642	39.15%	7215	60.85%
Women	662	42.46%	897	57.54%

Unpublished data, Hoff et al., 2014

Conclusions

- There is a significant pain burden associated with PTSD that may make treatment engagement more difficult
- We need to know more about concurrent pain management with PTSD treatment and guidance for PTSD and other mental health clinicians as to how best to address pain in treatment
- It is possible that an improvement in PTSD symptoms with treatment may increase perceptions and recognition of pain
- Area where there is a great need for more research – particularly in our women Veterans

What have we learned?

- Location of provider matters; Mental Health is doing the bulk of prescribing of benzodiazepines and atypical antipsychotics; Primary Care is bearing the burden of dealing with pain – Coordination of care is critically important
- Prescribing variability and patterns for women may reflect a difficult, complex patient mix or a failure to effectively disseminate the CPG recommendations
- Women and comorbidities present a dilemma
- Attempts to address PTSD-related sleep problems
- Opportunities for educational products and training

Future Steps

- OMHO Psychopharmacology initiative and use of the academic detailing model are encouraging to improve practices
- Development of shared decision making tools that inform Veterans and their family members about the risks of some medications and safer options
- Determine if it is feasible to use a CBT protocol to taper Veterans from some of these medications, broader dissemination

Encouraging New Research

- Recent research has suggested that interventions to taper patients from benzodiazepines can be effective
 - A Spanish group found two structured interventions in primary care led to significant reductions in long-term benzodiazepine use in patients without severe comorbidity (not PTSD patients) – written individualized stepped-dose reduction (Vicens, et al, 2014)
 - In Canada direct patient education was used to discontinue benzodiazepines in community-dwelling older adults and was found to be effective. (Tannenbaum, et al., 2014)
 - A Dutch group found letters sent to long-term benzodiazepine users effectively reduced use. (Gorgels, et al., 2005)
 - Patient materials were more effective at creating change than those that were aimed at physicians (Pimlott, et al., 2003)

Effective Treatments for PTSD: Helping Patients Taper from Benzodiazepines



Quick Facts

- Taper anyone taking benzodiazepines for 2 weeks or longer.
- Withdrawal symptoms may occur after only 2-4 weeks of treatment
- Risks of recurrence or rebound symptoms may occur as early as a few days to 1 week.
- Concurrent use of other sedatives may alter withdrawals

Benzodiazepines Overview

Continuing to renew benzodiazepine (BZ) prescriptions to certain subgroups of your patients with PTSD may be a high risk practice. These medications may no longer be of benefit to your patients and carry significant risks associated with chronic use. Due to the lack of evidence for their effectiveness in the treatment of PTSD, it is worthwhile for you to implement strategies for assessing patients who are taking them to determine if a taper is appropriate. It is also important to consider alternate treatment options and to minimize new benzodiazepine prescriptions whenever possible in the veteran PTSD population.

This brochure offers you valuable resources to help you taper your patients from benzodiazepines and information on alternatives.

Despite the involved challenges, strategies to taper existing benzodiazepine prescriptions are effective.

Before You Begin:

- A team-based approach will be most effective in efforts to taper a patient from benzodiazepines
- Build a stable relationship with your patient
- Evaluate and treat any co-occurring conditions
- Obtain complete drug and alcohol history and random drug screen
- Review recent medical notes (ER visits) and coordinate care with other providers
- If available, query prescription drug monitoring database

Priorities:

Tapering Existing Prescriptions

- Anyone on multiple BZDs or BZDs combined with prescribed amphetamines, and/or opiates
- Anyone with an active (or history of) substance abuse or dependence
- Anyone with a cognitive disorder or history of TBI
- Older veterans (risk of injury, cognitive effects)
- Younger veterans (better outcomes long term with SSRIs and evidence-based psychotherapies)





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Upcoming Topics in Our Monthly Lecture Series

Third Wednesday of the Month – 2-3PM (ET)

June 18

PTSD and Sleep Problems: An Update on Medical Management

Bruce Capehart, MD

July 16

Pain and PTSD: Behavioral Mechanisms and Interventions

Niloo Afari, PhD and Matthew Jakupcak, PhD

Questions/Comments?

Use the Q&A box located on the right-hand side of your screen.

For more information
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Gender Differences in Prescribing Among Veterans Diagnosed with Posttraumatic Stress Disorder

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OBJECTIVE: The Department of Veterans Affairs (VA) and Department of Defense (DoD) issued a revised posttraumatic stress disorder (PTSD) Clinical Practice Guideline (CPG) in 2010 with specific pharmacotherapy recommendations for evidence-based quality care. The authors examined prescribing frequencies over an 11-year period prior to the release of the new guideline to determine gender differences in pharmacotherapy treatment in veterans with PTSD.

METHOD: National administrative VA data from 1999 to 2009 were used to identify veterans with PTSD using ICD-9 codes extracted from inpatient discharges and outpatient clinic visits. Prescribing of antidepressants, antipsychotics and hypnotics was determined for each year using prescription drug files.

RESULTS: Women were more likely than men to receive medication across all classes except prazosin where men had higher prescribing frequency. The proportion of women receiving either of the first-line pharmacotherapy treatments for PTSD, selective serotonin reuptake inhibitors (SSRI) and serotonin-norepinephrine reuptake inhibitors (SNRI), increased from 56.4 % in 1999 to 65.7 % in 2009, higher rates than seen in men (49.2 % to 58.3 %). Atypical antipsychotic prescriptions increased from 14.6 % to 26.3 % and nonbenzodiazepine hypnotics increased from 3.8 % to 16.9 % for women, higher frequencies than seen in men for both medications (OR = 1.31, 1.43 respectively). The most notable gender discrepancy was observed for benzodiazepines where prescriptions decreased for men (36.7 % in 1999 to 29.8 % in 2009) but steadily increased for women from 33.4 % to 38.3 %.

CONCLUSION: A consistent pattern of increased prescribing of psychotropic medications among women with PTSD was seen compared to men. Prescribing frequency for benzodiazepines showed a marked gender difference with a steady increase for women despite guideline recommendations against use and a decrease for men. Common co-occurring disorders and sleep symptom management are important factors of PTSD pharmacotherapy and may contribute to gender differences seen in prescribing benzodiazepines in women but do not fully explain the apparent disparity.

KEY WORDS: gender; posttraumatic stress disorder; pharmacology.

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INTRODUCTION

American women represent a disproportionate number of adults who receive prescriptions for psychotropic medications, with one in four women receiving such medications compared to 15 % of men.¹ This is particularly true of anti-anxiety drugs where approximately 11 % of middle-aged American women (ages 45–64) were receiving benzodiazepines in 2010 compared to a rate that was half that seen in comparable-aged men (5.7 %).¹ One possible contributor to the higher prescribing rates is the fact that over their lifetimes women suffer more frequently from psychiatric disorders than men.² Another factor may be that women are also more likely to seek and receive mental health treatment compared to men.³ It is not clear if elevated psychiatric medication prescribing among women is solely attributable to greater diagnostic frequency or whether other reasons such as gender differences in acceptance and receipt of mental health treatment may contribute to a significant degree.

VA is committed to identifying and focusing on women veterans' unique health care needs. Women are now the fastest growing cohort within the veteran community and represent approximately 16 % of military personnel who have served in Afghanistan and Iraq.⁴ The rapid growth of women veterans makes it particularly important to examine gender differences in one of the most common diagnoses among veterans seeking care, PTSD. Unfortunately, there are virtually no data concerning prescribing differences across genders in VA, despite the prominent role that pharmacotherapy plays in the management of PTSD. Approximately 60 % of privately insured patients with PTSD receive pharmacotherapy for the disorder,⁵ while close to 80 % of veterans receiving care for PTSD in VA are treated with psychiatric medications.⁶ In the privately insured patients, women were 1½ times more likely to

receive psychotropic medications given a PTSD diagnosis than men, but we do not know if this is the case for women veterans treated in the VA.⁵

Given the prominent role that pharmacotherapy has in the management of PTSD, we sought to characterize gender differences in demographic characteristics and psychiatric comorbidity among veterans with PTSD to examine differences in prescribing trends among men and women veterans over an 11-year period (1999–2009) prior to the release of the new VA guideline and to determine the extent to which gender-based differences in prescribing frequencies were explained by demographic and comorbidity variables.

METHODS

Data Source

National administrative VA data were obtained for fiscal years 1999 through 2009, including outpatient visit data and inpatient discharge data from the VA Austin Information Technology Center (Austin, TX) and pharmacy data from the VA Pharmacy Benefits Management Services (Hines, IL). Patient-level data were linked between these sources using a scrambled patient identification number. This study was approved by the University of Iowa Institutional Review Board and the Iowa City Veterans Administration Research and Development Committee.

Patients

Veterans with PTSD were identified using diagnostic codes extracted from inpatient and outpatient clinic visit data. Patients were considered to have PTSD during a given year if they had at least one visit coded for PTSD as either primary or secondary diagnosis. PTSD was identified using the International Classification of Diseases, Ninth Revision (ICD-9) code of 309.81. This case definition has been used in prior work examining medication use in veterans with PTSD.^{6–9} The estimated rate of false-positive cases due to administrative miscoding is infrequent (<4 %) using this case definition.^{10,11}

Medication Use

Medication use for each patient was based on having at least one outpatient prescription fill of any quantity, days' supply or dosage from within selected therapeutic classes. Medications were selected based on their classification in the VA/DOD CPG for PTSD and prior studies of prescribing practices among veterans with PTSD.^{6,9,12} These classes included selective serotonin reuptake inhib-

itors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), atypical antipsychotics, benzodiazepines, non-benzodiazepine hypnotics (included zolpidem, eszopiclone, zaleplon and ramelteon) and prazosin. Prazosin was included in the analysis based on its recommendation in the CPG for targeting symptoms of sleep disturbances and nightmares.

Demographic Characteristics and Psychiatric Comorbidity

Demographic and psychiatric comorbidity variables were determined during 2009. Demographic variables included gender, age and urban residence. Urban residence was determined according to Rural–urban Commuting Areas.¹³ Military service variables included level of VA service-connected disability rating (monetary benefit paid for injury or illness incurred during active military service) and service era, categorized as prior to, during, and post Vietnam era. Time since first PTSD diagnosis was categorized as new, 1–2 year history or ≥ 3 year history of PTSD in VA. Psychiatric comorbidities were identified by ICD-9 codes using the same case definition as for PTSD, which required at least one clinic visit coded as either primary or secondary diagnosis. The psychiatric comorbidities included in the analysis were depressive disorders, substance use disorders, traumatic brain injury, panic disorder, generalized anxiety disorder, obsessive-compulsive disorder and social phobia.

Statistical Analysis

Demographic characteristics and psychiatric comorbidity frequencies were compared between men and women using a *t* test for continuous variables and chi-squared test for categorical variables. Medication prescribing frequencies were reported separately for men and women spanning the study time period of 1999–2009. Temporal changes in gender-based differences in prescribing frequencies were expressed using odds ratios, where values greater than one indicated a higher prescribing frequency for women compared to men.

The influence of demographic characteristics and psychiatric comorbidity on the likelihood of prescribing was examined using multiple logistic regression, with separate analyses conducted for three medication classes commonly prescribed to veterans with PTSD: SSRI/SNRIs, atypical antipsychotics and benzodiazepines. The first step was to report individual multivariable models for men and women to examine the independent influence of demographic and comorbidity variables on prescribing and contrast effects across gender. Comorbidities were selected for analysis from among DSM-IV Axis I disorders that are

commonly co-occurring with PTSD or disorders that are valid indications or relative contraindications to benzodiazepine use. The second step was to create four logistic regression models predicting the likelihood of prescribing: (1) gender effect only, (2) gender effect adjusted for demographic variables, (3) gender effect adjusted for comorbidity variables and (4) gender effect adjusted for both demographic and comorbidity variables. Changes in odds ratio for the gender effect across these four models characterized the extent to which gender-based differences in prescribing frequencies were explained by demographic and comorbidity variables. All statistical analyses were conducted using SAS version 9.3 (Cary, NC).

RESULTS

The number of female veterans being treated for PTSD in the VA health care system tripled during our time frame, from 10,484 in 1999 or 6.2 % of the population to 36,978 in 2009, which represents 7.5 % of the treated population. Compared to men, women were younger, more likely to have an urban residence, less likely to have a service-connected disability greater than 50 % and primarily from the post-Vietnam era (Table 1). Women had higher rates of all comorbidities examined except for substance use disorder and traumatic brain injury.

Gender Differences in Prescribing

Women with PTSD were more likely to receive medication across all classes except prazosin (Table 2). Prescribing frequency of SSRIs and SNRIs increased for both men and women. Among women, SSRI/SNRI use increased from 56.4 % in 1999 to 65.7 % in 2009. As prescribing also increased in men, the gender ratio for SSRI/SNRIs remained relatively consistent across the 11-year study period, ranging from 1.34 to 1.57. Gender-based differences, however, were substantial for benzodiazepines. Prescriptions for men decreased over time, consistent with treatment guidelines, but conversely increased over time among women, from 33.4 % in 1999 to 38.3 % in 2009. Although benzodiazepine prescriptions were less common initially among women than men (OR = 0.86), this pattern reversed such that women were much more likely to receive a benzodiazepine by 2009 (OR = 1.47). At the beginning of the study period, atypical antipsychotic prescriptions were similar between men and women (OR = 1.05). Rates peaked for both genders in 2005 and decreased thereafter, with higher use ultimately seen among women in 2009 (OR = 1.31). Low-dose quetiapine was examined separately and showed an initial tendency for higher use among women (OR = 1.88), but by 2009 there was no longer any meaningful gender gap in its prescribing (OR = 1.04). Non-benzodiazepine hypnotic prescriptions remained stable in both men and women until zolpidem was placed on the national formulary in 2007, resulting in a tripling of its

Table 1. Gender Differences in Patient Characteristics, FY09

Characteristic	All N=495,309	Women N=36,978	Men N=458,331	Statistics χ^2 or t; DF; p
Demographics				
Age in years, mean (SD)	53.8 (14.6)	43.3 (11.9)	54.7 (14.5)	174; 46,321; <0.0001
Age group, years				29,233; 1; <0.0001
<30	54,343 (11.0 %)	6,535 (17.7 %)	47,808 (10.4 %)	
30–39	41,453 (8.4 %)	7,221 (19.5 %)	34,232 (7.5 %)	
40–49	52,472 (10.6 %)	10,896 (29.5 %)	41,576 (9.1 %)	
50–64	282,451 (57.0 %)	11,409 (30.9 %)	271,042 (59.1 %)	
≥65	64,590 (13.0 %)	917 (2.5 %)	63,673 (13.9 %)	
Urban residence	359,120 (73.1 %)	29,191 (79.6 %)	329,929 (72.6 %)	862; 1; <0.0001
Service connection >50 %	272,189 (55.0 %)	17,798 (46.5 %)	254,991 (55.6 %)	1,151; 1; <0.0001
Service era				41,275; 1; <0.0001
Pre-Vietnam	32,477 (6.6 %)	408 (1.1 %)	32,069 (7.0 %)	
Vietnam	278,299 (56.2 %)	4,625 (12.5 %)	273,674 (59.7 %)	
Post-Vietnam	184,533 (37.3 %)	31,945 (86.4 %)	152,588 (33.3 %)	
PTSD dx duration in VA				644; 1; <0.0001
New diagnosis	109,159 (22.0 %)	9,674 (26.2 %)	99,485 (21.7 %)	
1–2 years	115,282 (23.3 %)	9,331 (25.2 %)	105,951 (23.1 %)	
3+ years	270,868 (54.7 %)	17,973 (48.6 %)	252,895 (55.2 %)	
Comorbidity				
Depressive disorder	240,920 (48.6 %)	24,257 (65.6 %)	216,663 (47.3 %)	4 600; 1; <0.0001
Anxiety disorder, any	39,710 (8.0 %)	5,458 (14.8 %)	34,252 (7.5 %)	2,464; 1; <0.0001
Panic disorder	19,084 (3.9 %)	3,027 (8.2 %)	16,057 (3.5 %)	2025; 1; <0.0001
GAD	19,719 (4.0 %)	2,303 (6.2 %)	17,416 (3.8 %)	528; 1; <0.0001
OCD	3,809 (0.8 %)	676 (1.8 %)	3,133 (0.7 %)	587; 1; <0.0001
Social phobia	1,388 (0.3 %)	161 (0.4 %)	1,227 (0.3 %)	34; 1; <0.0001
Substance use disorder	111,010 (22.4 %)	6,594 (17.8 %)	104,416 (22.8 %)	482; 1; <0.0001
Traumatic brain injury	21,652 (4.4 %)	1,249 (3.4 %)	20,403 (4.5 %)	94; 11; <0.0001

prescribing rate within 2 years. Again, women were consistently receiving significantly more of these prescriptions than men in 2009 (OR = 1.43). Prazosin prescribing was distinct in that prescriptions were consistently lower for women than men, though prazosin use increased in both genders. Notably, the gender gap in prazosin use decreased markedly from an odds ratio of 0.14 in 1999 to 0.75 in 2009.

Independent Predictors of Prescribing

Demographic characteristics and psychiatric comorbidities were then examined as independent predictors of prescribing for SSRI/SNRIs, benzodiazepines and atypical antipsychotics (Table 3). Age had minimal impact on prescribing for SSRI/SNRIs in either gender but had substantial effect on prescribing of benzodiazepines and atypical antipsychotics. Younger reproductive-age women had lower rates of receipt of both medications. The atypical antipsychotics showed an inverted U-shaped pattern of prescribing where lower rates were seen in younger veterans, increased in middle age and then showed large decreases in the oldest age group in both men and women. An increased percentage of VA service-connected disability (>50 %) contributed to an increase in prescribing of all medications for both men and women.

Psychiatric comorbidity had significant impact on prescribing. The likelihood of SSRI/SNRI use was nearly three-fold higher among patients with co-occurring depressive disorder. Benzodiazepine use was more common for all anxiety disorder comorbidities, though most dramatically with panic disorder. Elevated prescribing of atypical antipsychotics was observed in both men and women with co-occurring substance use disorder. Traumatic brain injury was associated with increased prescribing across all medication classes, except for SSRI/SNRI use in women. The impact of comorbidity on prescribing was generally consistent across genders. However, a notable exception was benzodiazepine use among veterans with comorbid substance use, which is considered a contraindication according to guideline recommendations. Among women veterans, benzodiazepine use was actually higher for women with co-occurring substance use disorder, whereas the opposite was true for men.

Gender Effects of Demographic Characteristics and Comorbidities

The impact of demographic characteristics and psychiatric comorbidities on gender-based differences in prescribing is examined in Table 4. Differences in SSRI/SNRI prescribing were largely attributable to differences in comorbidity frequency between genders, as shown by the shift in the

gender effect toward a value of one, from an unadjusted odds ratio of 1.37 to 1.13 after adjustment for psychiatric comorbidity. In contrast, adjustment for demographic variables had no effect on the ratio of SSRI/SNRI prescribing across genders. Competing effects were seen for benzodiazepine use, where adjustment for demographic characteristics increased impact of gender, whereas adjustment for comorbidity decreased impact. The net result of simultaneous adjustment for these effects was a persistence in gender-based discrepancy in benzodiazepine prescribing (OR = 1.47) that could not be explained by underlying difference between genders in demographics or psychiatric comorbidities. Finally, gender-based differences in atypical antipsychotic prescribing were primarily attributable to differences in demographic characteristics, reflected by an unadjusted odds ratio of 1.31 to 1.08 after the adjustment for demographics.

DISCUSSION

The primary objective of this work was to examine gender differences in psychopharmacological prescribing among veterans with PTSD and determine the extent to which these differences may be explained by underlying variation in the frequency of demographic characteristics and comorbid diagnoses. Women veterans with PTSD are more likely to have been recently diagnosed, are younger than men by a decade, have less VA service-connected disability and are primarily post-Vietnam era. Women were more likely to have co-occurring depressive and anxiety disorders, whereas men experienced elevated rates of substance use disorder and traumatic brain injury.

Women veterans were more likely to receive psychotropic medications across all classes except prazosin, which was more likely in men. The substantial increases in prescribing of SSRI/SNRIs in women reflect a positive shift toward evidence-based pharmacological care. This translates to an additional 18,388 women receiving first-line recommended medications for the management of PTSD. When adjusted for psychiatric comorbidities, there are still higher frequencies of SSRI/SNRIs in women. It is possible that there are comorbid disorders not accounted for in our analyses unique to women that contribute to this gender difference such as premenstrual dysphoric disorder. It is also possible known sexual side effects cause men to decline SSRI/SNRIs, and they may represent an undertreated group. In any case, the increased frequency of SSRI/SNRIs for women with PTSD should be viewed as a positive outcome.

We observed comparable guideline-concordant prescription patterns with atypical antipsychotics with similar gender frequencies until a shift occurred in 2003 that saw an increase for women that stayed elevated compared to

Table 2. Gender Differences in Temporal Prescribing Trends

	FY99	FY01	FY03	FY05	FY07	FY09
SSRI/SNRI						
Women	56.4 %	62.3 %	68.4 %	67.5 %	66.1 %	65.7 %
Men	49.2 %	53.3 %	58.0 %	58.9 %	58.2 %	58.3 %
OR (95 % CI)	1.34 (1.28, 1.39)	1.45 (1.40, 1.51)	1.57 (1.51, 1.62)	1.45 (1.41, 1.49)	1.40 (1.36, 1.44)	1.37 (1.34, 1.40)
Benzodiazepines						
Women	33.4 %	36.3 %	37.3 %	37.5 %	39.1 %	38.3 %
Men	36.7 %	35.2 %	33.4 %	31.7 %	31.3 %	29.8 %
OR (95 % CI)	0.86 (0.83, 0.90)	1.05 (1.01, 1.09)	1.18 (1.14, 1.23)	1.30 (1.26, 1.33)	1.41 (1.38, 1.45)	1.47 (1.43, 1.50)
Atypical antipsychotics						
Women	14.6 %	21.6 %	27.6 %	29.0 %	26.6 %	26.3 %
Men	14.1 %	20.1 %	25.1 %	25.6 %	22.5 %	21.3 %
OR (95 % CI)	1.05 (0.99, 1.11)	1.09 (1.05, 1.15)	1.14 (1.10, 1.18)	1.19 (1.15, 1.22)	1.25 (1.22, 1.29)	1.31 (1.28, 1.35)
Zolpidem						
Women	3.8 %	5.7 %	5.6 %	5.5 %	6.1 %	16.9 %
Men	3.8 %	4.9 %	4.3 %	3.9 %	4.2 %	12.4 %
OR (95 % CI)	1.02 (0.92, 1.13)	1.18 (1.09, 1.28)	1.33 (1.24, 1.43)	1.44 (1.35, 1.53)	1.48 (1.40, 1.56)	1.43 (1.39, 1.48)
Prazosin						
Women	0.2 %	0.7 %	1.9 %	3.5 %	5.0 %	7.1 %
Men	1.5 %	1.6 %	2.6 %	4.8 %	6.4 %	9.3 %
OR (95 % CI)	0.14 (0.09, 0.21)	0.41 (0.32, 0.51)	0.73 (0.64, 0.82)	0.73 (0.67, 0.79)	0.76 (0.72, 0.80)	0.75 (0.72, 0.78)

those for men. When adjusted for demographic characteristics, there were still elevations in frequency in women that were not accounted for by different prescribing patterns in different age groups and for more severe service-connected disability. It is possible that atypical antipsychotics may be targeted at insomnia symptoms in women as there is evidence of gender differences in arousal symptoms.¹⁴ However, when we examined low-dose quetiapine separately, no gender differences in prescribing were seen. It is important to note that during this time there were a number of studies suggesting that atypical antipsychotics were effective adjunctive treatments for PTSD, and it is possible again that men were actually undertreated rather than overuse seen in women.

Prescribing frequencies for benzodiazepines were the significant exception. As opposed to decreased prescribing for men, which is guideline-concordance practice, prescriptions steadily increased for women despite recommendations in the CPG against their use in PTSD because of safety and efficacy concerns. Chronic use of benzodiazepines can cause cognitive problems, increase the risk of falls and accidents and have possible detrimental effects on the recommended psychotherapies for PTSD. With their abuse and dependence properties, benzodiazepines are contraindicated in those with comorbid substance use disorder in patients with PTSD¹⁵ as well as contraindicated in those with TBI.¹² Not only did we find increased rates of prescribing in women, but in women with co-occurring substance use disorder, rates of benzodiazepine prescriptions were elevated compared to men, a practice discouraged in the CPG and one previously noted in a smaller sample.¹⁷ Similarly, elevated benzodiazepine prescriptions were seen in both men and women with TBI, again a contraindicated

practice. The impact of adjustment for demographic characteristics and psychiatric comorbidities on benzodiazepines was not straightforward. Some increased frequency of prescriptions for benzodiazepines in women is clearly accounted for by comorbidities and again may be related to co-occurring disorders that were not controlled for in our analyses. However, demographic differences also are influential, and age is one such factor. Reduced prescribing of benzodiazepines in the youngest reproductive-age group of women when contrasted to their male counterparts is encouraging. Being older and having a greater service-connected disability contributed to elevated benzodiazepine prescribing. It is possible high rates of distress seen in newly returning veterans from the wars in Iraq and Afghanistan may be a reason for an increase in benzodiazepine prescribing.^{16,17} It is also possible that clinicians prescribe benzodiazepines to women for symptoms that are not an indication for their use, including headache, fatigue, chest pain and vertigo.¹⁸

Sleep symptom management clearly plays a prominent role in PTSD pharmacotherapy. It is possible that increased prescribing of atypical antipsychotics and benzodiazepines in women is an attempt to address insomnia symptoms. We are unable to capture insomnia symptoms associated with PTSD using administrative data but think that it is important that this be examined in future work. The extraordinary 10 % increase in zolpidem use in women from 2007 to 2009 after the drug became available on formulary confirms how much sleep difficulties are part of the clinical presentation of PTSD. It is not clear why this medication increased so much in women compared to men nor why prazosin would be the exception and more widely used in men. The increased use of nonbenzodiazepine hypnotics does not necessarily reflect a considerably safer

Table 3. Demographic Characteristics and Psychiatric Comorbidity as Independent Predictors of Prescribing, Multivariable Logistic Regression, FY09

Diagnosis	SSRI/SNRI		Benzodiazepine		Atypical antipsychotics	
	Women	Men	Women	Men	Women	Men
	OR (95 % CI)	OR (95 % CI)				
Demographics						
Age group, years						
<30	0.80 (0.75, 0.86)	0.85 (0.82, 0.87)	0.59 (0.55, 0.64)	0.78 (0.75, 0.80)	0.58 (0.54, 0.63)	0.66 (0.64, 0.69)
30–39	0.96 (0.89, 1.02)	1.01 (0.98, 1.04)	0.78 (0.73, 0.83)	0.93 (0.90, 0.96)	0.81 (0.75, 0.87)	0.89 (0.86, 0.92)
40–49	Reference	Reference	Reference	Reference	Reference	Reference
50–64	1.02 (0.96, 1.09)	0.96 (0.93, 0.99)	1.01 (0.95, 1.07)	1.00 (0.96, 1.03)	0.85 (0.79, 0.90)	0.87 (0.84, 0.90)
≥65	0.88 (0.72, 1.06)	0.85 (0.81, 0.88)	0.84 (0.70, 1.01)	0.86 (0.83, 0.90)	0.36 (0.28, 0.47)	0.59 (0.57, 0.62)
Urban residence	0.90 (0.85, 0.95)	0.88 (0.86, 0.89)	0.90 (0.85, 0.95)	0.86 (0.84, 0.87)	0.94 (0.88, 0.99)	0.95 (0.94, 0.97)
Service connection >50 %	1.26 (1.20, 1.32)	1.29 (1.27, 1.31)	1.47 (1.40, 1.54)	1.46 (1.43, 1.48)	1.28 (1.22, 1.35)	1.19 (1.17, 1.21)
Service era						
Pre-Vietnam	0.70 (0.54, 0.92)	0.80 (0.77, 0.82)	0.92 (0.71, 1.20)	1.07 (1.03, 1.11)	0.98 (0.68, 1.42)	0.80 (0.77, 0.84)
Vietnam	Reference	Reference	Reference	Reference	Reference	Reference
Post-Vietnam	0.89 (0.82, 0.97)	1.00 (0.98, 1.03)	0.82 (0.76, 0.89)	0.92 (0.90, 0.95)	0.96 (0.88, 1.04)	1.32 (1.28, 1.36)
PTSD dx duration in VA						
New diagnosis	0.76 (0.71, 0.80)	0.69 (0.68, 0.70)	0.63 (0.59, 0.67)	0.53 (0.52, 0.54)	0.58 (0.54, 0.62)	0.47 (0.46, 0.48)
1–2 years	1.06 (1.00, 1.13)	0.98 (0.96, 0.99)	0.80 (0.76, 0.85)	0.73 (0.72, 0.74)	0.84 (0.79, 0.89)	0.70 (0.69, 0.72)
3+ years	Reference	Reference	Reference	Reference	Reference	Reference
Comorbidity						
Depressive disorder	2.88 (2.75, 3.01)	2.61 (2.58, 2.64)	1.36 (1.30, 1.42)	1.41 (1.39, 1.43)	1.04 (0.99, 1.10)	1.43 (1.41, 1.45)
Panic disorder	1.72 (1.57, 1.89)	1.71 (1.65, 1.77)	3.48 (3.21, 3.78)	4.51 (4.36, 4.67)	1.31 (1.21, 1.42)	1.55 (1.50, 1.61)
GAD	1.31 (1.19, 1.45)	1.41 (1.36, 1.46)	1.92 (1.75, 2.10)	2.46 (2.38, 2.54)	1.12 (1.02, 1.24)	1.30 (1.26, 1.35)
OCD	1.65 (1.37, 1.99)	1.88 (1.72, 2.05)	1.53 (1.30, 1.80)	1.62 (1.50, 1.74)	2.14 (1.82, 2.51)	2.29 (2.12, 2.46)
Social phobia	1.44 (0.97, 2.13)	1.61 (1.40, 1.84)	1.30 (0.93, 1.81)	1.58 (1.40, 1.78)	1.20 (0.85, 1.70)	1.34 (1.19, 1.52)
Substance use disorder	1.29 (1.22, 1.37)	1.10 (1.08, 1.11)	1.11 (1.05, 1.18)	0.92 (0.90, 0.93)	2.71 (2.56, 2.87)	1.92 (1.89, 1.95)
Traumatic brain injury	1.00 (0.88, 1.13)	1.16 (1.12, 1.20)	1.23 (1.09, 1.39)	1.32 (1.27, 1.36)	1.14 (1.00, 1.30)	1.21 (1.17, 1.25)

Each column is a separate multiple logistic regression model

alternative to benzodiazepines. Safety concerns in non-benzodiazepine hypnotics have been noted with elevated hazards of dying compared to those prescribed no hypnotics.¹⁹ It is imperative that if these patterns reflect an

attempt to assist with sleep symptom management that different treatment approaches be considered that include cognitive behavioral therapy for insomnia (CBT-I) and safer medication options.

Table 4. Impact of Adjustment for Demographic Characteristics and Psychiatric Comorbidity on Gender-Based Differences in Prescribing, Multivariable Logistic Regression, FY09

Model	SSRI/SNRI		Benzodiazepine		Atypical antipsychotics	
	OR (95 % CI)*	c statistic	OR (95 % CI)	c statistic	OR (95 % CI)	c statistic
Unadjusted	1.37 (1.34, 1.40)	0.511	1.47 (1.43, 1.50)	0.514	1.31 (1.28, 1.35)	0.510
Demographics only	1.34 (1.31, 1.37)	0.567	1.63 (1.60, 1.67)	0.608	1.08 (1.05, 1.10)	0.605
Comorbidity only	1.13 (1.10, 1.15)	0.630	1.27 (1.24, 1.30)	0.590	1.25 (1.22, 1.28)	0.607
Demographics and comorbidity	1.15 (1.12, 1.18)	0.658	1.47 (1.44, 1.51)	0.653	1.08 (1.05, 1.11)	0.652

*Odds ratio and 95 % confidence interval for the likelihood of receiving medication in women compared to men

This study has several limitations. The use of administrative data allows us to describe prescribing trends among veterans with PTSD and to determine predictors of prescribing but does not allow us to fully determine the justifications for the prescribed medications. While we were able to determine rates of comorbid disorders using administrative data, it is difficult to confirm their accuracy, and there are other co-occurring disorders that may be relevant that were not captured. Nor can we confirm the timing (e.g., current active problem as in the case of a co-occurring SUD or distant history) or severity of the co-occurring disorders examined. It is also possible that there may be gender-specific coding biases.

This work highlights important findings regarding gender and PTSD that speak to the need for additional work in several areas. We found differences between men and women that are not explained by comorbidities, especially in the area of prescribing of benzodiazepines. It is encouraging to see prescriptions written for first-line pharmacotherapy treatments for women with PTSD. Reduced benzodiazepine findings in men are also encouraging, but we are left with more questions than we have answers regarding the increased prescribing frequency of benzodiazepines in women. It is still possible that the observed gender differences in prescribing are for what might be considered “appropriate reasons” that take into account other co-occurring disorders or that they reflect a greater willingness among women toward taking medications for mental health problems rather than decision making among prescribers. It is also possible the complexity of these patients may cause clinicians to respond to treatment failures by indiscriminately trying different medications. VA has an opportunity to develop policies and interventions that will improve the care that women veterans returning from war receive for PTSD and decrease the heavy burden of greater comorbid mental health disorders, particularly in the treatment of SUD and TBI. Provider education is sorely needed for this primarily reproductive-aged cohort to inform clinicians about gender differences in side effects, medication dosing and particularly about sex differences in pharmacokinetics of psychotropic medications in order to provide access to quality PTSD care for our veteran women.

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