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CME Objective

After studying this article, you should be able to:

- Talk with patients who have PTSD about their medication preferences and receiving concurrent evidence-based psychotherapy

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A Retrospective Comparative Effectiveness Study of Medications for Posttraumatic Stress Disorder in Routine Practice

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ABSTRACT

Objective: Fluoxetine, paroxetine, sertraline, topiramate, and venlafaxine have consistently shown efficacy for posttraumatic stress disorder (PTSD) in meta-analyses of randomized controlled trials. However, no study has compared the effectiveness of these agents in routine clinical practice. We conducted a retrospective comparative effectiveness study of these 5 medications using electronic medical record data.

Methods: We identified 2,931 Department of Veterans Affairs outpatients initiating treatment for PTSD between fiscal years 2004 and 2013 who received 1 of the 5 medications at an adequate dose and duration, combined with baseline and endpoint PTSD Checklist (PCL) measurements. Patients were identified based on clinical diagnoses of PTSD (*DSM-IV* criteria). We weighted participants in order to balance pretreatment characteristics. We compared continuous changes on total PCL score, symptom cluster scores, and sleep items, as well as categorical changes including reliable improvement and loss of PTSD diagnosis, using weighted regression analyses. We conducted exploratory analysis to determine whether any patient characteristics or service use variables predicted loss of PTSD diagnosis.

Results: Patients improved by a mean of 5–6 points on the PCL over approximately 6 months of treatment. While half of patients had a reliable improvement of 5 points or more on the PCL, less than a fifth achieved loss of PTSD diagnosis. There were no differences between medications. The only significant ($P < .001$) predictor of loss of PTSD diagnosis was concurrent treatment with evidence-based psychotherapy.

Conclusions: Available evidence-based medications for PTSD are equally effective in clinical practice. Although effective, our data suggest that patients choosing medication treatment for PTSD should consider concurrent treatment with evidence-based psychotherapy in order to maximize their chances of meaningful improvement.

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Clinical Points

- Five medications for PTSD with consistent efficacy in meta-analyses of randomized controlled trials—including fluoxetine, paroxetine, sertraline, topiramate, and venlafaxine—are also effective in routine clinical practice.
- It does not appear that any one of these agents is more effective than the others for PTSD, so patient preference should weigh heavily when choosing among these medications.
- Patients who elect to take one of these medications for PTSD should consider undergoing concurrent treatment with evidence-based psychotherapy delivered in an individual format, such as prolonged exposure or cognitive processing therapy.

Posttraumatic stress disorder (PTSD) is a serious condition that can follow exposure to a traumatic event, characterized by intrusive reexperiencing of the trauma in the form of flashbacks and nightmares, avoidance of trauma reminders, negative alterations in cognitions and mood, and increased arousal and reactivity.[1] PTSD has a lifetime prevalence of almost 8% in the United States.[2] Over 10% of veterans receiving care in the Department of Veterans Affairs (VA) health care system have PTSD, and the VA has a caseload of almost 600,000 veterans receiving PTSD treatment.[3]

Randomized controlled trials (RCTs) show that effective treatments for PTSD include both pharmacologic and psychotherapeutic approaches.[4,5] There have been multiple meta-analyses examining the effectiveness of medications to treat PTSD, which have differed in their methods and conclusions. Watts and colleagues' meta-analyses of all RCTs of PTSD treatment conducted through 2012 showed results consistently favoring 4 antidepressants (fluoxetine, paroxetine, sertraline, and venlafaxine), 1 anticonvulsant (topiramate), and 1 antipsychotic (risperidone) when compared directly to placebo.[5] A similar review by Hoskins et al[6] favored fluoxetine, paroxetine, and venlafaxine, but not sertraline, topiramate, or risperidone. A meta-analysis by Lee et al[7] that included RCTs of medications for PTSD published through 2015 suggested superior efficacy for sertraline, venlafaxine, and nefazodone compared to other medications. Two studies used network meta-analysis to make indirect comparisons between medications.[8] First, a 2013 Agency for Healthcare Research and Quality (AHRQ) network meta-analysis of published RCTs concluded that paroxetine and topiramate were most effective, but that fluoxetine, sertraline, and venlafaxine were also effective.[4] Second, Cipriani et al[9] concluded that phenelzine was superior to other medications for PTSD when considering both efficacy and dropouts. Data supporting the phenelzine finding came from 1 small RCT,[10] and Cipriani et al called for further study rather than prioritization of phenelzine in clinical practice.[9] Given available data, the preponderance of meta-analyses suggest fluoxetine, sertraline, paroxetine, topiramate, and venlafaxine as treatments for PTSD.

While several medications have demonstrated efficacy for PTSD in clinical trials, there have been few head-to-head comparisons and no large trials. Furthermore, while multiple medications for PTSD have shown superiority to placebo in RCTs, little is known about their effectiveness in routine clinical practice. There are several reasons to question whether medications found efficacious in highly controlled clinical studies are beneficial in typical clinical practice. First, patients with comorbidities such as substance abuse are common in the population,[11] yet are routinely excluded from efficacy trials of PTSD treatments.[12] Second, RCTs of psychotropic medications for PTSD typically prohibit patients from undergoing concurrent psychotherapy,[5] whereas these interventions are often delivered together in practice.[13] Given advancements in data, including increasing availability of patient reported outcome data in the electronic medical record (EMR)[14] and the need for large numbers to support research on more personalized medicine,[15] observational studies are a logical extension of comparative effectiveness research on psychotropic medications for PTSD.

We conducted a retrospective comparative effectiveness study of medications for PTSD using VA EMR data. We examined medications already determined as effective for PTSD in multiple meta-analyses, including fluoxetine, paroxetine, sertraline, topiramate, and venlafaxine. On the basis of the AHRQ network meta-analytic results, we expected that participants receiving paroxetine and topiramate might have superior symptomatic outcomes. However, given limitations about both the applicability of RCT results to the clinical population and the relatively limited evidence for topiramate, it was not possible to make a formal prediction. We elected not to examine medications whose efficacy was supported in a single meta-analysis or single study since, in most cases, these medications have been used too infrequently in VA practice to yield reliable results.[16] Lastly, we examined predictors of response to medication treatment generally as well as to each of the agents individually.

METHODS

Data Sources

We used the VA Corporate Data Warehouse (CDW) to identify VA users with new PTSD treatment episodes from fiscal years 2004 through 2013 and obtain information on services use, clinical diagnoses, pharmacy data, and standardized measures of PTSD symptoms. This study was approved by the Veterans Institutional Review Board (IRB) of Northern New England, which is the IRB of record for the White River Junction VAMC.

Participants

Participants were drawn from a large retrospective cohort of VA users with new PTSD treatment episodes between fiscal years 2004 and 2013 that has been described elsewhere.[11,17] This parent cohort included VA users who received a primary diagnosis of PTSD at 2 or more outpatient encounters, at

least 1 of which occurred in a mental health setting, over the course of 90 days.[18,19] Participants meeting this criterion during the prior 2 years were excluded. We examined 1 year of treatment receipt following the first encounter with a qualifying diagnosis of PTSD. The study sample was further restricted to those who had an adequate medication trial (AMT, defined below), received baseline PTSD symptom measurement at the start of treatment (up to 2 months prior and 2 weeks after the start of an AMT), and received follow-up PTSD symptom measurement (greater than 8 weeks and less than 6 months after initiating an AMT). To minimize heterogeneity and confounding, participants who received 2 or more AMTs concurrently were excluded. When patients had 2 or more AMTs sequentially, we examined only the first. Due to increasing use of standardized measurement of PTSD symptoms in clinical practice in more recent years,[20,21] participants in this analysis were treated in fiscal year 2008 and later.

PTSD Symptoms

We measured PTSD symptoms using the PTSD Checklist (PCL), which is administered in clinical practice and recorded in the VA EMR. During the time period we examined, the VA used the version of the PCL corresponding to PTSD diagnostic criteria in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV*).[22,23] The PCL is a 17-item measure with each item rated on a 5-point Likert-type scale and with total scores ranging from 17 through 85. Minimal symptomatic criteria for PTSD using the PCL include 1 reexperiencing symptom, 3 avoidance and numbing symptoms, and 2 hyperarousal symptoms, all rated "moderately" or higher. Participants are asked to rate symptoms over the last month. Previous research in veterans shows that a change of 5 points cannot be attributed to measurement error,[24] so we used a 5-point drop as our threshold for reliable improvement. The combination of a meaningful change in PTSD symptoms and no longer meeting diagnostic criteria for PTSD has been shown to be an important marker of improved quality of life.[25] Therefore, we also employed no longer meeting *DSM-IV* criteria for PTSD as measured by the PCL, plus a clinically meaningful drop of 10 points,[26] as our threshold for loss of diagnosis.

In addition to examining overall change in symptoms, we evaluated change in subscores for PTSD symptoms clusters as well as sleep difficulties using the sum of 2 items: nightmares and insomnia. Diagnostic criteria for PTSD changed in May 2013 with the publication of *DSM-5*.[1] A key change in the criteria is replacement of the "avoidance and numbing cluster" with "avoidance" and "negative alterations in cognitions and mood" clusters. To approximate this distinction, we divided "avoidance" and "numbing" symptoms. Our symptom clusters consisted of 5 reexperiencing items, 2 avoidance items, 5 emotional numbing items, and 5 hyperarousal items.

Psychotropic Medication Receipt

We developed algorithms to measure whether participants received an AMT of sertraline, fluoxetine, paroxetine, venlafaxine, or topiramate, defined as 8 weeks of a daily dose at least as high as the dose used in the efficacy trials supporting the treatment recommendation.[4,5] While the length of efficacy trials of psychotropic medications for PTSD varies, the VA practice guideline in use during the time period we examined recommended medication trials of at least 8 weeks.[27] Therefore, participants receiving continuous treatment of one of the following medications daily for 8 weeks or more were considered to have received an AMT: fluoxetine 20 mg or more daily, paroxetine 20 mg or more daily, sertraline 100 mg or more daily, topiramate 100 mg or more daily, and venlafaxine 150 mg or more daily.

Independent Variables

Participant variables included demographics, military service characteristics, commonly occurring medical and mental health disorders, and baseline PCL score. Health system variables included the type of VA facility and the prescribing clinician's service section. Service use characteristics during the year following the index PTSD diagnosis included concurrent psychotropic medication, total number of psychotherapy encounters, number of psychotherapy encounters in which participants received evidence-based psychotherapy (EBP) for PTSD, defined as prolonged exposure (PE)[28] or cognitive processing therapy (CPT),[29] and counts of medication management encounters, primary care encounters, and outpatient visits. We measured PE and CPT use with a natural language processing (NLP) algorithm that classifies psychotherapy notes in individual (I) and group (G) delivery formats.[30] In our pilot NLP work, we attempted to identify other evidence based psychotherapies for PTSD including eye movement desensitization and reprocessing (EMDR) and Stress Inoculation Therapy.[31] Despite manual review of over 7,500 notes written about patients attending PTSD clinics, we were unable to detect any examples of these therapies in routine clinical practice in VA. Therefore, their use was not included in further analysis steps.

Analysis

To understand how participants selected for this analysis differed from the rest of the parent cohort during the relevant fiscal years, we compared patient characteristics using χ^2 analysis and *t* tests, as appropriate. We compared these same characteristics among participants who received each of the 5 medications within the smaller analytic cohort using pairwise testing with step-down Bonferroni-adjusted *P* values.

To account for baseline differences among participants who received each of the 5 medications, we used the RAND Toolkit for Weighting and Analysis of Nonequivalent Groups (TWANG).[32] The TWANG package supports causal modeling of observational data through the estimation and evaluation of propensity scores and associated weights. In our application, the propensity score represented the probability that a particular patient would receive each medication.[33] We estimated propensity scores with multinomial logistic regression using generalized booster effects,[34] in which the dependent variable is an indicator for

each psychotropic medication and the independent variables are an antiparsimonious specification of variables that have a plausible correlation with the outcome.[33,34] Using these propensity scores, we weighted participants in order to balance the pretreatment covariate distributions.

We compared continuous and categorical outcomes among the 5 groups with regression analyses using psychotropic medication received as the sole independent variable. In general, weighted means can have greater sampling variance than unweighted means. Therefore, we used survey commands, which account for the weights, to perform the outcomes analyses when comparing the weighted groups. For continuous outcomes, we used linear regression analysis, whereby the coefficient of the variable tests the hypothesis that each of the 5 psychotropic medications has the same mean change in PTSD symptoms. For categorical outcomes, we used logistic regression analysis, whereby the coefficient of the variable tests the hypothesis that each of the 5 psychotropic medications results in the same percentage of patients achieving reliable improvement or loss of PTSD diagnosis. Finally, we conducted exploratory univariate logistic regression analyses to determine whether any independent variables predicted achievement of our categorical response criteria of loss of PTSD diagnosis by pooling all 5 groups together and using the unweighted data. Because there were 50 independent variables (see Table 2), we used a Bonferroni-corrected value of $P < .001$ for significance in these exploratory analyses. Analyses were performed using R, Version 3.2.0 (http://CRAN.R-project.org).

RESULTS

While 29.0% (142,276) of 491,040 VA users meeting our criteria for a new episode of PTSD care between fiscal years 2008 and 2013 had a qualifying medication trial, only 0.6% (2,931) also received outcome measurement within our specified time frames. The 2,931 participants included in our analyses differed from patients with AMT who did not have PCL measurement in almost every measurable way in terms of demographics, service use, comorbidity, and concurrent medication use (Table 1). Many of these differences were statistically significant but of unclear clinical relevance. In some ways, the analytic sample differed in ways that were likely clinically meaningful. Most notably, compared to the general population with PTSD, the analytic sample contained younger participants (on average 8 years younger) more likely to be Operations Enduring Freedom/Iraqi Freedom/New Dawn (OEF/OIF/OND) veterans (69.2% vs 34.9%), with higher rates of VA disability (68.2% vs 55.6%). The analytic sample also differed in important ways regarding their mental health services use: they were more likely to receive medications from a mental health clinician (86.7% vs 38.3%), had more individual psychotherapy visits (mean of 16.2 vs 6.5), and were more likely to receive group psychotherapy (61.9% vs 34.8%).

The number of participants in the analytic cohort receiving each medication ranged from 1,376 who received sertraline to 105 who received topiramate (Table 2). The number of eligible participants grew across treatment years, with the majority of participants in the analytic sample treated in fiscal years 2012 and 2013. While there were notable differences among the medication treatment groups, our weighting procedure allowed us to balance almost all covariates (Table 3). The exception was whether baseline PCL administration occurred during the medication titration period. For medications that commonly require a lengthier titration period—sertraline, topiramate, and venlafaxine—baseline PCL score was measured during the titration period more often than for fluoxetine and paroxetine, where both treatments generally start at full dose. We did not further adjust for this difference because it is more likely related to medication characteristics than to participant characteristics. The mean AMT length was 254.1 (SD = 119.5) days when continuation of treatment beyond the index year was included. Relative to the start of the AMT, participants' baseline PCLs were administered at 9.7 (SD = 11.8) days prior to the start of the AMT and endpoint PCLs were administered at 174.7 (SD = 99.5) days after the start of the AMT. In the unweighted model, mean baseline PCL scores indicated a high burden of symptoms, ranging from 61.5 to 62.5 (Table 4).

All 5 of the medications that were studied demonstrated a significant effect on PTSD symptoms. The mean improvement in PTSD symptoms measured by the PCL scores ranged from 5.0 to 6.3 points, indicating statistically reliable but modest improvements; between 41.9% and 52.9% of participants achieved an improvement of 5 points or more. As inclusion in the cohort was based on encounter-based diagnostic information (2 PTSD diagnoses within 90 days, at least 1 of which was in a mental health clinic), 12.4% (n = 363) patients did not meet PCL-based diagnostic criteria at baseline. However, there were no overall or pairwise differences among agents at baseline. Among those who met PCL-based diagnostic criteria for PTSD at baseline, between 13.6% and 20.4% of participants achieved our threshold for loss of diagnosis, an outcome associated with substantial clinical improvement. As measured by the PCL, there was a very limited range of baseline PTSD symptom clusters and sleep item scores and changes on these scores. There were no significant differences between medications in any outcome using the unweighted model. A weighted model adjusting for differences between the medication treatment groups was very similar to the unadjusted analysis, and there continued to be no differences in outcomes (Table 5), meaning that the 5 medications performed about equally in reducing PTSD symptoms, even after adjusting for differences between treatment groups.

In our exploratory univariate logistic regression models, the only significant ($P < .001$) patient-level predictors of loss of diagnosis were related to receipt of EBP for PTSD, including PE and CPT, delivered in an individual format (EBT-I). Across all treatment groups, the number of sessions of EBT-I during the index year of treatment predicted improvement (OR = 1.07), and the effect was greater if

Table 1. VA Users With New Episodes of PTSD Care From 2008 to 2013, by Receipt of an Adequate Trial of an Effective Medication for PTSD and by Availability of Time-Constrained Outcome Measurement as Measured With the PTSD Checklist

	Overall (491,040)	Qualifying Trial 29.0% (142,276)	Plus Measurement 0.6% (2,931)
Demographic Characteristics			
Age, mean (SD), y	48.5 (16.0)	48.4 (15.1)**	40.2 (12.8) ††
Men, % (n)	90.7 (445,583)	89.5 (127,282)**	87.9 (2,577)†
Married, % (n)	52.7 (258,764)	54.2 (77,177)**	56.6 (1,660)†
White non-Hispanic, % (n)	63.5 (311,756)	65.5 (93,154)**	64.0 (1,876)†
Black non-Hispanic, % (n)	19.1 (93,666)	18.1 (25,799)**	16.7 (490)
Hispanic, % (n)	8.1 (39,827)	7.9 (11,303)*	11.1 (322)††
OEF/OIF/OND veteran, % (n)	34.9 (171,364)	33.9 (48,228)**	69.2 (2,028)††
Rural, % (n)	35.0 (171,644)	36.7 (52,202)**	35.0 (1,025)†
Homeless, % (n)	5.4 (26,574)	5.8 (8,295)**	5.0 (148)
Combat exposure, % (n)	28.6 (140,344)	27.7 (39,458)**	28.8 (845)
Sexual trauma while in military, % (n)	9.3 (45,803)	10.6 (15,091)**	12.4 (362)†
VA disability level 70 or greater, % (n)	55.6 (273,242)	60.4 (85,925)**	68.2 (1,998)††
Service Use Characteristics			
Plurality of care at a VA Medical Center, % (n)	60.4 (296,563)	60.5 (86,069)	65.4 (1,916)††
Plurality of care at a community based outreach clinic, % (n)	30.8 (151,106)	30.6 (43,585)	23.4 (686)††
Medication was from a primary care prescriber, % (n)	4.2 (20,436)	8.8 (12,671)**	7.4 (216)†
Medication was from a mental health prescriber, % (n)	38.3 (187,999)	84.6 (120,387)**	86.7 (2,541)††
Primary care visits, mean (SD)	3.3 (3.2)	3.6 (3.3) **	3.7 (3.0)
Any individual psychotherapy, % (n)	86.5 (424,983)	89.8 (127,761)**	98.5 (2,886)††
All individual psychotherapy visits, mean (SD)	6.5 (7.9)	7.6 (8.6)**	16.2 (11.6)††
Individual evidence based therapy sessions, mean (SD)	0.6 (2.3)	0.6 (2.3)	3.4 (5.0)††
Has any group psychotherapy, % (n)	34.8 (170,816)	36.9 (52,478)**	61.9 (1,815)††
All group psychotherapy visits, mean (SD)	5.2 (15.5)	6.2 (17.5)**	13.7 (26.6)††
Group cognitive processing therapy, mean (SD)	0.6 (2.6)	0.7 (2.7)**	2.4 (4.6)††
Other mental health visits, mean (SD)	8.5 (10.1)	10.6 (10.8)**	15.4 (13.8)††
Substance abuse/detox visits, mean (SD)	1.8 (11.1)	2.2 (12.1)**	3.8 (16.4)††
Comorbid Diagnoses			
Pain disorder, % (n)	64.9 (318,802)	69.4 (98,764)**	76.0 (2,228)††
Headache disorder, % (n)	25.1 (123,441)	28.8 (40,922)**	41.8 (1,224)††
Psychotic disorders, % (n)	4.2 (20,682)	4.7 (6,748)**	3.5 (102)††
Bipolar mood disorders, % (n)	6.2 (30,560)	6.5 (9,223)**	5.8 (169)
Depressive mood disorders, % (n)	60.3 (296,071)	71.4 (101,557)**	79.6 (2,332)††
Non-PTSD anxiety disorders, % (n)	28.5 (139,779)	33.0 (46,940)**	43.2 (1,267)††
Traumatic brain injury and cognitive disorders, % (n)	13.4 (65,834)	14.7 (20,882)**	27.3 (799)††
Personality disorders, % (n)	3.9 (18,959)	4.8 (6,873)**	5.0 (148)
Nicotine dependence, % (n)	39.0 (191,712)	41.9 (59,659)**	44.3 (1,299)†
Alcohol dependence, % (n)	22.6 (111,027)	24.2 (34,485)**	30.0 (880)††
Marijuana dependence, % (n)	3.2 (15,586)	3.6 (5,094)**	4.8 (141)†
Opioid dependence, % (n)	3.2 (15,903)	3.8 (5,436)**	4.4 (129)
Concurrent Medication Use			
Other antidepressant, % (n)	63.3 (310,685)	63.5 (90,308)	69.6 (2,041)††
Other anticonvulsant, % (n)	24.4 (119,808)	30.1 (42,867)**	34.0 (996)††
Lithium, % (n)	1.4 (6,848)	1.5 (2,152)**	2.1 (60)†
Antipsychotic, % (n)	20.3 (99,698)	26.8 (38,173)**	27.7 (813)
Sedative/hypnotics, % (n)	39.6 (194,681)	49.1 (69,886)**	52.8 (1,548)†
Opioids, % (n)	37.0 (181,788)	42.7 (60,687)**	41.0 (1,203)†
Prazosin, % (n)	18.6 (91,543)	25.2 (35,842)**	43.8 (1,285)††
Stimulants, % (n)	2.5 (12,521)	3.2 (4,482)**	4.4 (129)††

*$P < .05$, **$P < .001$ for overall versus those with a qualifying trial.
†$P < .05$, ††$P < .001$ for those with a qualifying trial with versus without measurement.
Abbreviations: OEF/OIF/OND = Operations Enduring Freedom/Iraqi Freedom/New Dawn, PTSD = posttraumatic stress disorder, SD = standard deviation, VA = Department of Veterans Affairs.

the sessions occurred during the AMT (OR baseline–midpoint = 1.14; OR midpoint–endpoint = 1.13). There were 4 predictors of not achieving the loss of PTSD diagnosis, including traumatic brain injury (TBI) and other cognitive disorders (OR = 0.65), male gender (OR = 0.63), OEF/OIF/OND veteran status (OR = 0.71), and non-psychotherapy mental health visits (OR = 0.98). No additional variables or patterns of variables emerged as predictors of response when we examined participants who received individual medications.

DISCUSSION

We compared the effectiveness of 5 evidence-based medications for PTSD in routine clinical practice and found that they performed similarly. During an average of 6 months of treatment, participants experienced a 5- to 6-point improvement in PCL scores. Approximately half of participants achieved a reliable improvement of 5 points or more on the PCL. Our findings are consistent with meta-analytic findings that have suggested that fluoxetine,

Table 2. Participants With an Adequate Trial of an Effective Medication for PTSD Plus Outcomes Measurement, 2008–2013 (Unweighted)

	Fluoxetine (n = 659)	Paroxetine (n = 328)	Sertraline (n = 1,376)	Topiramate (n = 105)	Venlafaxine (n = 463)	Pairwise Differences
Index Year FY 08–09, % (n)	7.1 (47)	7.6 (25)	5.2 (72)	7.6 (8)	5.4 (25)	
Index Year FY 10–11, % (n)	32.5 (214)	33.2 (109)	34.0 (468)	41.9 (44)	33.0 (153)	
Index Year FY 12–13, % (n)	60.4 (398)	59.1 (194)	60.8 (836)	50.5 (53)	61.6 (285)	
Baseline Symptoms and Alignment of Medication Initiation and Baseline Measurement						
Baseline PCL score, mean (SD)	61.8 (11.8)	62.2 (12.1)	62.0 (11.7)	61.5 (12.6)	62.5 (12.0)	No differences
Baseline PCL score before initiation, % (n)	50.7 (334)	50.0 (164)	36.9 (508)	35.2 (37)	29.6 (137)	F ≠ STV, P ≠ SV, S ≠ V
Baseline PCL score during titration, % (n)	7.1 (47)	7.9 (26)	24.6 (338)	23.8 (25)	18.4 (85)	FP ≠ STV
Baseline PCL score full dose, % (n)	42.2 (278)	42.1 (138)	38.5 (530)	41.0 (43)	52.1 (241)	FS ≠ V
Demographic Characteristics						
Age, mean (SD)	39.4 (12.4)	38.7 (13.2)	41.0 (13.2)	38.7 (10.8)	40.2 (12.1)	P ≠ S
Men, % (n)	88.0 (580)	87.2 (286)	89.8 (1,236)	71.4 (75)	86.4 (400)	FPSV ≠ T
Married, % (n)	56.3 (371)	52.7 (173)	57.1 (786)	61.9 (65)	57.2 (265)	No differences
White non-Hispanic, % (n)	63.9 (421)	66.8 (219)	60.2 (829)	62.9 (66)	73.7 (341)	FS ≠ V
Black non-Hispanic, % (n)	17.5 (115)	15.9 (52)	18.8 (258)	17.1 (18)	10.2 (47)	FS ≠ V
Hispanic, % (n)	9.1 (60)	11.9 (39)	12.1 (166)	13.3 (14)	9.3 (43)	No differences
OEF/OIF/OND veteran, % (n)	71.2 (469)	72.0 (236)	68.2 (938)	75.2 (79)	66.1 (306)	No differences
Homeless, % (n)	5.0 (33)	5.5 (18)	5.1 (70)	2.9 (3)	5.2 (24)	No differences
Combat exposure, % (n)	28.5 (188)	36.6 (120)	28.2 (388)	30.5 (32)	25.3 (117)	P ≠ SV
Sexual trauma in military, % (n)	12.0 (79)	13.4 (44)	11.0 (151)	24.8 (26)	13.4 (62)	FSV ≠ T
VA disability level ≥ 70, % (n)	66.3 (437)	67.4 (221)	67.0 (922)	74.3 (78)	73.4 (340)	No differences
Service Use Characteristics						
Plurality of care at a VAMC, % (n)	59.9 (395)	65.9 (216)	65.9 (907)	69.5 (73)	70.2 (325)	F ≠ V
AMT from a MH prescriber, % (n)	88.9 (586)	87.8 (288)	89.9 (1,237)	33.3 (35)	85.3 (395)	FPSV ≠ T
Primary care visits, mean (SD)	3.5 (2.9)	3.6 (2.8)	3.5 (3.0)	4.9 (4.1)	4.0 (2.9)	FPS ≠ T, S ≠ V
Any individual therapy, % (n)	98.5 (649)	98.5 (323)	98.3 (1,353)	98.1 (103)	98.9 (458)	No differences
Total visits, index year, mean (SD)	16.1 (11.1)	15.5 (10.5)	15.8 (11.6)	16.0 (11.6)	18.1 (12.6)	FPS ≠ V
EBP-I, index year, mean (SD)	3.4 (4.9)	3.1 (4.8)	3.6 (5.1)	3.8 (5.2)	3.2 (4.8)	No differences
EBP-I, baseline-midpoint, mean (SD)	0.9 (2.0)	0.7 (1.7)	0.8 (1.8)	1.0 (1.9)	0.7 (1.6)	No differences
EBP-I, midpoint-end, mean (SD)	1.6 (3.0)	1.4 (2.6)	1.7 (3.1)	1.8 (3.2)	1.5 (2.8)	No differences
Any group therapy, % (n)	59.9 (395)	61.6 (202)	62.8 (864)	56.2 (59)	63.7 (295)	No differences
Total visits, index year, mean (SD)	11.9 (24.4)	12.0 (22.2)	14.2 (26.2)	11.3 (24.4)	16.9 (33.0)	F ≠ V
CPT-G, index year, mean (SD)	2.1 (4.5)	2.1 (4.0)	2.5 (4.7)	2.5 (4.8)	2.8 (5.1)	No differences
CPT-G, baseline–midpoint, mean (SD)	0.5 (1.9)	0.4 (1.5)	0.6 (2.0)	0.6 (3.2)	0.5 (1.9)	No differences
CPT-G, midpoint–end, mean (SD)	1.2 (3.2)	1.2 (2.9)	1.2 (3.0)	1.1 (2.6)	1.5 (3.3)	No differences
EBP visits before AMT, mean (SD)	0.2 (0.4)	0.2 (0.4)	0.2 (0.4)	0.2 (0.4)	0.2 (0.4)	No differences
Other mental health visits, mean (SD)	14.1 (11.3)	15.3 (13.1)	15.2 (14.2)	17.0 (16.6)	17.3 (15.6)	FS ≠ V
Substance abuse visits, mean (SD)	3.5 (14.4)	3.1 (14.3)	4.1 (17.7)	1.2 (5.8)	4.4 (18.4)	No differences
Comorbid Diagnoses						
Pain disorder, % (n)	73.1 (482)	78.0 (256)	75.0 (1,032)	84.8 (89)	79.7 (369)	No differences
Headache disorder, % (n)	36.9 (243)	40.2 (132)	39.0 (537)	81.9 (86)	48.8 (226)	FS ≠ VT, P ≠ T, T ≠ V
Psychotic disorders, % (n)	3.6 (24)	4.0 (13)	3.3 (45)	7.6 (8)	2.6 (12)	No differences
Bipolar mood disorders, % (n)	5.6 (37)	5.5 (18)	5.7 (79)	8.6 (9)	5.6 (26)	No differences
Depressive mood disorders, % (n)	79.4 (523)	77.4 (254)	79.4 (1,093)	69.5 (73)	84.0 (389)	T ≠ V
Anxiety disorders, % (n)	41.3 (272)	44.2 (145)	41.1 (565)	41.0 (43)	52.3 (242)	FS ≠ V
TBI and cognitive disorders, % (n)	25.6 (169)	26.5 (87)	26.2 (361)	43.8 (46)	29.4 (136)	FPSV ≠ T
Personality disorders, % (n)	5.5 (36)	6.4 (21)	4.3 (59)	2.9 (3)	6.3 (29)	No differences
Nicotine dependence, % (n)	42.5 (280)	52.7 (173)	42.6 (586)	32.4 (34)	48.8 (226)	FST ≠ P, T ≠ V
Alcohol dependence, % (n)	33.1 (218)	33.2 (109)	29.0 (399)	18.1 (19)	29.2 (135)	FP ≠ T
Marijuana dependence, % (n)	6.2 (41)	4.9 (16)	4.1 (57)	2.9 (3)	5.2 (24)	No differences
Opioid dependence, % (n)	4.7 (31)	6.4 (21)	3.7 (51)	2.9 (3)	5.0 (23)	No differences
Concurrent medication use						
Other antidepressant, % (n)	68.4 (451)	69.8 (229)	69.1 (951)	79.0 (83)	70.6 (327)	No differences
Other anticonvulsant, % (n)	32.6 (215)	36.0 (118)	30.5 (419)	39.0 (41)	43.8 (203)	FS ≠ V
Lithium, % (n)	2.7 (18)	1.2 (4)	1.6 (22)	1.9 (2)	3.0 (14)	No differences
Antipsychotic, % (n)	25.8 (170)	28.4 (93)	25.8 (355)	30.5 (32)	35.2 (163)	FS ≠ V
Sedative/hypnotics, % (n)	52.8 (348)	57.0 (187)	49.0 (674)	61.0 (64)	59.4 (275)	S ≠ V
Opioids, % (n)	38.8 (256)	45.1 (148)	37.7 (519)	54.3 (57)	49.9 (231)	FS ≠ VT
Prazosin, % (n)	41.9 (276)	43.0 (141)	44.7 (615)	37.0 (35.2)	46.7 (216)	No differences
Stimulants, % (n)	5.8 (38)	3.0 (10)	3.3 (46)	5.7 (6)	6.3 (29)	No differences

Abbreviations: AMT = adequate medication trial, CPT-G = group cognitive processing therapy, EBP-I = individual evidence-based psychotherapy, F = fluoxetine, FY = fiscal year, MH = mental health, OEF/OIF/OND = Operations Enduring Freedom/Iraqi Freedom/New Dawn, P = paroxetine, PCL = PTSD Checklist, PTSD = posttraumatic stress disorder, SD = standard deviation, S = sertraline, T = topiramate, TBI = traumatic brain injury, V = venlafaxine, VA = Department of Veterans Affairs, VAMC = VA Medical Center.

Table 3. Participants With an Adequate Trial of an Effective Medication for PTSD Plus Outcomes Measurement, 2008–2013 (Weighted)

	Fluoxetine (n = 659)	Paroxetine (n = 328)	Sertraline (n = 1,376)	Topiramate (n = 105)	Venlafaxine (n = 463)	Pairwise Differences
Baseline Symptoms and Alignment of Medication Initiation and Baseline Measurement						
Baseline PCL score, mean (SD)	61.9 (12.0)	62.1 (12.0)	62.0 (12.0)	62.6 (16.2)	62.3 (12.4)	No differences
Baseline PCL score before initiation, % (n)	43.4 (334)	45.0 (164)	39.8 (508)	40.2 (37)	37.3 (137)	No differences
Baseline PCL score during titration, % (n)	13.6 (47)	12.8 (26)	18.7 (338)	29.3 (25)	17.5 (85)	FP≠STV
Baseline PCL score full dose, % (n)	43.0 (278)	42.2 (138)	41.5 (530)	30.5 (43)	45.2 (241)	No differences
Demographic Characteristics						
Age, mean (SD), y	39.6 (13.1)	39.9 (13.3)	40.4 (12.9)	40.6 (16.0)	39.9 (12.8)	No differences
Men, % (n)	87.9 (580)	87.0 (286)	89.1 (1,236)	83.4 (75)	88.1 (400)	No differences
Married, % (n)	57.1 (371)	53.6 (173)	57.1 (786)	64.6 (65)	60.2 (265)	No differences
White non-Hispanic, % (n)	64.5 (421)	66.2 (219)	62.4 (829)	57.9 (66)	67.1 (341)	No differences
Black non-Hispanic, % (n)	16.6 (115)	16.5 (52)	17.4 (258)	21.6 (18)	13.9 (47)	No differences
Hispanic, % (n)	9.4 (60)	12.3 (39)	11.6 (166)	9.2 (14)	11.4 (43)	No differences
OEF/OIF/OND veteran, % (n)	71.1 (469)	70.1 (236)	69.6 (938)	71.9 (79)	68.5 (306)	No differences
Homeless, % (n)	4.8 (33)	4.4 (18)	5.1 (70)	1.8 (3)	3.8 (24)	No differences
Combat exposure, % (n)	28.3 (188)	31.9 (120)	27.9 (388)	23.5 (32)	27.4 (117)	No differences
Sexual trauma in military, % (n)	12.5 (79)	14.2 (44)	11.3 (151)	16.3 (26)	11.5 (62)	No differences
VA disability level ≥ 70, % (n)	67.6 (437)	67.4 (221)	67.6 (922)	76.6 (78)	70.8 (340)	No differences
Service Use Characteristics						
Plurality of care at a VAMC, % (n)	62.7 (395)	66.5 (216)	65.7 (907)	53.5 (73)	67.4 (325)	No differences
AMT from a MH prescriber, % (n)	88.4 (586)	89.3 (288)	88.1 (1,237)	84.7 (35)	85.9 (395)	No differences
Primary care visits, mean (SD)	3.6 (3.2)	3.6 (2.8)	3.6 (3.2)	4.4 (5.5)	3.7 (2.8)	No differences
Any individual therapy, % (n)	98.6 (649)	98.8 (323)	98.5 (1,353)	99.8 (103)	98.9 (458)	No differences
Total visits, index year, mean (SD)	16.1 (12.0)	15.6 (11.1)	15.9 (11.4)	15.0 (14.4)	16.4 (11.1)	No differences
EBP-I, index year, mean (SD)	3.3 (5.1)	3.2 (5.2)	3.5 (5.1)	3.1 (6.8)	3.2 (5.1)	No differences
EBP-I, baseline–midpoint, mean (SD)	0.8 (1.8)	0.8 (1.8)	0.8 (1.8)	0.7 (2.5)	0.7 (1.8)	No differences
EBP-I, midpoint–end, mean (SD)	1.6 (3.2)	1.4 (2.8)	1.6 (3.0)	1.6 (4.3)	1.5 (2.7)	No differences
Any group therapy, % (n)	61.0 (395)	62.0 (202)	61.7 (864)	52.8 (59)	61.2 (295)	No differences
Total visits, index year, mean (SD)	11.7 (23.6)	12.2 (25.1)	13.6 (25.6)	13.4 (54.3)	13.0 (22.4)	No differences
CPT-G, index year, mean (SD)	2.1 (4.5)	2.1 (4.0)	2.5 (4.7)	2.5 (4.8)	2.8 (5.1)	No differences
CPT-G, baseline–midpoint, mean (SD)	0.4 (1.9)	0.4 (2.0)	0.6 (2.4)	0.2 (1.1)	0.5 (2.1)	No differences
CPT-G, midpoint–end, mean (SD)	1.0 (3.6)	1.1 (3.7)	1.2 (4.4)	0.8 (3.3)	1.3 (3.6)	No differences
EBP visits before AMT, mean (SD)	0.2 (0.4)	0.2 (0.4)	0.2 (0.4)	0.1 (0.5)	0.2 (0.4)	No differences
Other mental health visits, mean (SD)	14.4 (12.4)	14.6 (11.2)	15.3 (14.8)	17.6 (24.4)	15.1 (11.9)	No differences
Substance abuse visits, mean (SD)	2.9 (11.4)	2.8 (12.7)	3.7 (15.4)	1.9 (8.7)	3.4 (14.1)	No differences
Comorbid Diagnoses						
Pain disorder, % (n)	74.5 (482)	78.0 (256)	75.8 (1,032)	77.4 (89)	76.9 (369)	No differences
Headache disorder, % (n)	40.0 (243)	40.1 (132)	40.6 (537)	56.0 (86)	43.3 (226)	No differences
Psychotic disorders, % (n)	3.7 (24)	3.1 (13)	3.4 (45)	5.5 (8)	2.3 (12)	No differences
Bipolar mood disorders, % (n)	5.8 (37)	5.0 (18)	6.2 (79)	13.0 (9)	4.6 (26)	No differences
Depressive mood disorders, % (n)	78.5 (523)	78.3 (254)	79.7 (1,093)	76.7 (73)	81.3 (389)	No differences
Anxiety disorders, % (n)	41.3 (272)	44.4 (145)	42.1 (565)	41.9 (43)	45.7 (242)	No differences
TBI and cognitive disorders, % (n)	26.6 (169)	25.4 (87)	27.4 (361)	43.7 (46)	27.1 (136)	No differences
Personality disorders, % (n)	5.4 (36)	5.7 (21)	4.6 (59)	2.4 (3)	4.8 (29)	No differences
Nicotine dependence, % (n)	42.4 (280)	47.1 (173)	43.7 (586)	30.9 (34)	46.1 (226)	No differences
Alcohol dependence, % (n)	31.7 (218)	32.6 (109)	29.1 (399)	23.7 (19)	27.4 (135)	No differences
Marijuana dependence, % (n)	5.0 (41)	4.2 (16)	4.0 (57)	2.7 (3)	3.9 (24)	No differences
Opioid dependence, % (n)	4.7 (31)	5.7 (21)	3.9 (51)	3.5 (3)	3.4 (23)	No differences
Concurrent medication use						
Other antidepressant, % (n)	68.6 (451)	68.7 (229)	69.3 (951)	70.6 (83)	69.0 (327)	No differences
Other anticonvulsant, % (n)	34.0 (215)	35.5 (118)	32.4 (419)	35.9 (41)	36.3 (203)	No differences
Lithium, % (n)	2.4 (18)	0.7 (4)	1.7 (22)	4.3 (2)	2.3 (14)	No differences
Antipsychotic, % (n)	26.5 (170)	25.8 (93)	26.3 (355)	32.1 (32)	30.1 (163)	No differences
Sedative/hypnotics, % (n)	53.1 (348)	55.6 (187)	51.1 (674)	53.8 (64)	54.8 (275)	No differences
Opioids, % (n)	39.5 (256)	45.1 (148)	39.8 (519)	50.8 (57)	42.5 (231)	No differences
Prazosin, % (n)	41.3 (276)	40.9 (141)	44.8 (615)	31.2 (37)	44.9 (216)	No differences
Stimulants, % (n)	4.6 (38)	2.5 (10)	3.6 (46)	2.4 (6)	5.2 (29)	No differences

Abbreviations: AMT = adequate medication trial, CPT-G = group cognitive processing therapy, EBP-I = individual evidence-based psychotherapy, F = fluoxetine, MH = mental health, OEF/OIF/OND = Operations Enduring Freedom/Iraqi Freedom/New Dawn, P = paroxetine, PCL = PTSD Checklist, PTSD = posttraumatic stress disorder, SD = standard deviation, S = sertraline, T = topiramate, TBI = traumatic brain injury, V = venlafaxine, VA = Department of Veterans Affairs, VAMC = VA Medical Center.

Table 4. Outcomes for Participants With an Adequate Trial of an Effective Medication for PTSD Plus Outcomes Measurement (Unweighted)

	Fluoxetine (n = 659)	Paroxetine (n = 328)	Sertraline (n = 1,376)	Topiramate (n = 105)	Venlafaxine (n = 463)	Pairwise Differences
Raw Outcomes						
Baseline PCL score, mean (SD)	61.8 (11.8)	62.2 (12.1)	62.0 (11.7)	61.5 (12.6)	62.5 (12.0)	No differences
Change in PCL, mean (SD)	−6.2 (14.0)	−6.2 (15.1)	−6.1 (14.1)	−6.3 (13.8)	−5.0 (13.3)	No differences
5-point drop in PCL, % (n)	51.9 (342)	50.9 (167)	50.1 (689)	42.9 (45)	47.9 (222)	No differences
10-point drop plus loss of diagnosis, % (n)	17.6 (116)	20.4 (67)	17.2 (237)	16.2 (17)	13.6 (63)	No differences
Symptom Clusters						
Baseline reexperiencing, mean (SD)	17.7 (4.3)	17.8 (4.2)	17.8 (4.1)	17.9 (4.4)	17.9 (4.2)	No differences
Change in reexperiencing, mean (SD)	−1.7 (4.8)	−1.8 (4.8)	−1.6 (4.6)	−2.0 (5.1)	−1.2 (4.6)	No differences
Baseline avoidance, mean (SD)	7.6 (1.9)	7.8 (1.8)	7.7 (1.9)	7.4 (2.0)	7.6 (2.0)	No differences
Change in avoidance, mean (SD)	−0.7 (2.4)	−0.9 (2.5)	−0.8 (2.4)	−0.6 (2.3)	−0.6 (2.3)	No differences
Baseline numbing, mean (SD)	17.3 (4.3)	17.0 (4.3)	17.2 (4.3)	16.9 (4.6)	17.5 (4.3)	No differences
Change in numbing, mean (SD)	−1.8 (4.8)	−1.5 (5.2)	−1.8 (5.0)	−1.7 (4.9)	−1.5 (4.8)	No differences
Baseline hyperarousal, mean (SD)	19.4 (3.9)	19.5 (4.0)	19.4 (3.8)	19.5 (4.1)	19.6 (3.8)	No differences
Change in hyperarousal, mean (SD)	−2.0 (4.6)	−1.8 (4.8)	−1.9 (4.5)	−2.1 (4.5)	−1.8 (4.3)	No differences
Baseline sleep, mean (SD)	7.4 (1.9)	7.6 (1.9)	7.5 (1.9)	7.4 (2.1)	7.6 (1.9)	No differences
Change in sleep, mean (SD)	−0.8 (2.2)	−0.9 (2.1)	−0.8 (2.1)	−0.8 (2.4)	−0.6 (2.1)	No differences

Abbreviations: PCL = PTSD Checklist, PTSD = posttraumatic stress disorder, SD = standard deviation.

Table 5. Outcomes for Participants With an Adequate Trial of an Effective Medication for PTSD Plus Outcomes Measurement (Weighted)

	Fluoxetine (n = 659)	Paroxetine (n = 328)	Sertraline (n = 1,376)	Topiramate (n = 105)	Venlafaxine (n = 463)	Pairwise Differences
Raw Outcomes						
Baseline PCL, mean (SD)	61.9 (12.1)	62.0 (12.1)	62.0 (11.9)	62.7 (16.0)	62.3 (12.3)	No differences
Change in PCL, mean (SD)	−5.8 (14.4)	−5.6 (15.4)	−6.0 (14.6)	−5.0 (22.1)	−5.1 (14.4)	No differences
5-point drop in PCL, % (n)	51.1 (342)	50.2 (167)	49.7 (689)	40.4 (45)	48.3 (222)	No differences
10-point drop plus loss of diagnosis, % (n)	17.3 (116)	19.3 (67)	17.3 (237)	15.5 (17)	14.2 (63)	No differences
Symptom Clusters						
Baseline reexperiencing, mean (SD)	17.7 (4.4)	17.8 (4.2)	17.8 (4.2)	17.5 (7.0)	17.8 (4.4)	No differences
Change in reexperiencing, mean (SD)	−1.6 (4.9)	−1.6 (5.1)	−1.6 (4.9)	−1.0 (8.6)	−1.2 (5.0)	No differences
Baseline avoidance, mean (SD)	7.6 (2.0)	7.7 (1.9)	7.6 (2.0)	7.6 (2.7)	7.5 (2.1)	No differences
Change in avoidance, mean (SD)	−0.7 (2.5)	−0.8 (2.7)	−0.8 (2.6)	−0.6 (3.6)	−0.6 (2.4)	No differences
Baseline numbing, mean (SD)	17.2 (4.4)	17.0 (4.3)	17.2 (4.5)	18.0 (5.2)	17.4 (4.5)	No differences
Change in numbing, mean (SD)	−1.6 (5.0)	−1.3 (5.3)	−1.7 (5.2)	−2.0 (8.2)	−1.5 (5.3)	No differences
Baseline hyperarousal, mean (SD)	19.4 (4.1)	19.4 (4.2)	19.4 (3.8)	19.7 (5.8)	19.6 (4.1)	No differences
Change in hyperarousal, mean (SD)	−1.8 (4.8)	−1.7 (4.8)	−1.9 (4.7)	−1.7 (7.3)	−1.9 (4.9)	No differences
Baseline sleep, mean (SD)	7.4 (2.0)	7.6 (1.9)	7.5 (1.9)	7.3 (3.3)	7.5 (2.1)	No differences
Change in sleep, mean (SD)	−0.7 (2.3)	−0.7 (2.2)	−0.7 (2.3)	−0.4 (3.8)	−0.6 (2.5)	No differences

Abbreviations: PCL = PTSD Checklist, PTSD = posttraumatic stress disorder, SD = standard deviation.

paroxetine, sertraline, topiramate, and venlafaxine are effective treatments for PTSD.[4,5] However, less than a fifth of participants achieved our more stringent improvement criterion: loss of PTSD diagnosis. None of the medications led to superior outcomes in individual PTSD symptom clusters or sleep items.

The only independent variables that predicted loss of PTSD diagnosis were related to concurrent treatment with EBP-I for PTSD. Therefore, while fluoxetine, paroxetine, sertraline, topiramate, and venlafaxine appear to be equally effective in clinical practice, our findings do not support the idea that patient characteristics can guide the selection of the medication most likely to be effective.[35] Instead, it appears that there is clinical equipoise and the choice of individual agent should be up to patients who elect to take a medication for PTSD.[36] However, to maximize improvement, patients should also be encouraged to consider concurrent EBP-I. Prior analysis in the parent cohort from which this analytic sample was derived demonstrated that men and OEF/OIF/OND veterans are less likely to complete psychotherapy for PTSD.[37] While studies have clearly demonstrated that patients with TBI can tolerate and benefit from evidence-based PTSD treatment,[38–41] this evidence is largely derived from specialized residential settings and may not generalize to the outpatient care studied in this analysis. Thus, it is not particularly surprising that men, OEF/OIF/OND veterans, and those with a history of TBI or other cognitive disorders had poorer treatment outcomes given the importance of concurrent EBP-I. That more non-psychotherapy mental health visits is also a negative predictor of treatment response is not surprising, as these visits may indicate that participants had a greater variety of mental health treatment needs and comorbid mental health conditions.

There are several major limitations to our study. First, participants meeting inclusion criteria for our analytic cohort differed from the general VA PTSD treatment population in many ways. The patient sample in the analysis was younger, was more likely to be veterans of recent wars, and received

more mental health services. Because of this, it is unclear if these findings generalize to older veterans of earlier service eras receiving less mental health services. Moreover, we have no clear understanding of whether these findings would apply to non-veterans with PTSD in general. Second, we were unable to measure all related aspects of care. As an example, we could not measure medication adherence or psychotherapy protocols that are less frequently used in the VA such as EMDR. However, the mean length of treatment was 6 months, indicating that participants typically exhausted their initial fill (which can last up to 90 days) and requested refills. Lastly, we only considered PTSD outcomes. Depression and quality of life measures were not available, but they may have enriched our exclusive focus on PTSD outcomes.

While we found that all of the medication treatments for PTSD that we studied were effective in clinical practice, their effect seemed reduced compared to that seen in the clinical trials. Such comparisons are difficult to make precisely in all cases because various studies use different measures and allowed various concurrent treatments. However, as an example, Berlant and colleagues' open-label study of topiramate for PTSD found a mean change in PCL scores of 21 points (we found a 5-point change) and 34% of patients with loss of diagnosis (we found 16%).[42] The reasons for possible reduction in effectiveness are unknown. One possibility is that drug trials have more stringent criteria for inclusion, subsequently not generalizing to the typical veteran population seen in clinic (no substance use disorders, suicidality, etc). It is also possible that VA patients are more treatment-resistant than patients enrolling in RCTs. Future work using our methods should attempt to examine patients' treatment history longitudinally rather than cross-sectionally to address this concern.

We conclude that available evidence-based medications for PTSD are equally effective in clinical practice. Although effective, our data suggest that patients choosing medication treatment for PTSD should consider concurrent treatment with EBP-I for PTSD in order to maximize their chances of meaningful improvement.

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Additional information: The VA Corporate Data Warehouse (CDW) contains electronic medical record data compiled from individual VA facilities and is described at http://www.hsrd.research.va.gov/for_researchers/vinci/cdw.cfm. Researchers with VA network access can obtain descriptions of CDW data at http://vaww.virec.research.va.gov/.

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POSTTEST

To obtain credit, go to PSYCHIATRIST.COM **(Keyword: October CME) to take this Posttest and complete the Evaluation.** A nominal processing fee is required.

1. **Quasi-experimental designs such as propensity score weighting of measured pre-treatment covariates are often used to learn from clinical data using retrospective cohort designs while accounting for selection bias. What is an advantage of prospective randomized controlled trials over typical retrospective quasi-experimental designs?**
   a. The ability to maximize sample size by allowing for examination of outcomes in clinically important subgroups that may be difficult to recruit
   b. The ability to maximize internal validity of the study by distributing unmeasured confounders evenly among the experimental groups
   c. The ability to maximize external validity of the study by including a patient population that best represents typical clinical practice
   d. The ability to account for the effects of treatments that are delivered concurrently in typical practice
2. **A 67-year-old Vietnam veteran who was previously diagnosed with posttraumatic stress disorder (PTSD) presents to your clinic shortly after retiring from his position as a welder. He notes an increase in irritability, flashbacks, and nightmares pertaining to his combat experience, avoidance of traumatic reminders, loss of interest in fishing, and that he feels cut off from others. He says that he feels that the world has gotten more dangerous and no one can be trusted. He had a good response to fluoxetine for PTSD in the past and would like to restart this medication. What should you do?**
   a. Prescribe venlafaxine because you prefer to use a dual-acting agent
   b. Make a referral for group psychotherapy
   c. Prescribe the fluoxetine, but also encourage him to engage in individual prolonged exposure or cognitive processing therapy
   d. Prescribe an atypical antipsychotic to treat his paranoia
3. **Men, Iraq and Afghanistan veterans, and those with a history of traumatic brain injury had worse PTSD outcomes in this study. This finding indicates that fluoxetine, paroxetine, sertraline, topiramate, and venlafaxine should not be prescribed for PTSD in these groups.**
   a. True
   b. False