Title

Using patient-reported outcomes to understand the effectiveness of guideline-concordant care for post-traumatic stress disorder in clinical practice.

Journal

Journal of evaluation in clinical practice, 25(4)

ISSN

1356-1294

Authors

Shiner, Brian
Gui, Jiang
Leonard Westgate, Christine
et al.

Publication Date

2019-08-01

DOI

10.1111/jep.13158

Peer reviewed

U.S. Department of Veterans Affairs
Public Access Author manuscript
J Eval Clin Pract. Author manuscript; available in PMC 2020 August 01.

Published in final edited form as:
J Eval Clin Pract. 2019 August ; 25(4): 689–699. doi:10.1111/jep.13158.

Using patient-reported outcomes to understand the effectiveness of guideline-concordant care for post-traumatic stress disorder in clinical practice

Brian Shiner, MD, MPH[1,2,3] **[Physician, Assistant Professor]**, **Jiang Gui, PhD**[2] **[Associate Professor]**, **Christine Leonard Westgate, MS**[1] **[Data Analyst]**, **Paula P Schnurr, PhD**[2,3] **[Professor, Executive Director]**, **Bradley V Watts, MD, MPH**[2,4] **[Assistant Professor, Acting Executive Director]**, **Sarah L Cornelius, BS**[1] **[Research Coordinator]**, and **Shira Maguen, PhD**[5,6] **[Psychologist, Professor]**

[1]Research Division, White River Junction VA Medical Center, White River Junction, Vermont

[2]Department of Psychiatry, Geisel School of Medicine at Dartmouth, Hanover, New Hampshire

[3]Executive Division, National Center for PTSD, Hartford, Vermont

[4]Field Office, National Center for Patient Safety, Ann Arbor, Michigan

[5]Posttraumatic Stress Disorder Clinical Team, San Francisco VA Medical Center, San Francisco, California

[6]School of Medicine, University of California San Francisco, San Francisco, California

Abstract

Rationale: Identifying predictors of improvement amongst patients receiving routine treatment for post-traumatic stress disorder (PTSD) could provide information about factors that influence the clinical effectiveness of guideline-concordant care. This study builds on prior work by accounting for delivery of specific evidence-based treatments (EBTs) for PTSD while identifying potential predictors of clinical improvement using patient-reported outcomes measurement.

Method: Our sample consisted of 2 643 US Department of Veterans Affairs (VA) outpatients who initiated treatment for PTSD between 2008 and 2013 and received at least four PTSD checklist (PCL) measurements over 12 weeks. We obtained PCL data as well as demographic, diagnostic, and health services use information from the VA corporate data warehouse. We used latent trajectory analysis to identify classes of patients based on PCL scores, then determined demographic, diagnostic, and treatment predictors of membership in each class.

Results: Patients who met our PCL-based inclusion criteria were far more likely than those who did not receive EBTs. We identified two latent trajectories of PTSD symptoms. Patients in the substantial improvement group (25.9%) had a mean decrease in PCL score of 16.24, whereas

Correspondence: Brian Shiner, VA Medical Center, 215 North Main Street, 10E2E; White River Junction, Hartford, VT 05009, brian.shiner@va.gov.

CONFLICTS OF INTEREST

Dr Shiner reports no conflict of interest (COI). Dr Gui reports no COI. Ms Westgate reports no COI. Dr Schnurr reports no COI. Dr Watts reports no COI. Ms Cornelius reports no COI. Dr Maguen reports no COI.

patients in the modest improvement group improved by a mean of 8.09 points. However, there were few differences between the groups, and our model to predict group membership was only slightly better than chance (area under the curve [AUC] = 0.55). Of the 64 covariates we tested, the only robust individual predictor of improvement was gender, with men having lower odds of being in the substantial improvement group compared with women (odds ratio [OR] 0.76; 95% confidence interval [CI] 0.58–0.96).

Conclusion: VA patients with PTSD can realize significant improvement in routine clinical practice. Although available medical records-based variables were generally insufficient to predict improvement trajectory, this study did indicate that men have lower odds of substantial improvement than women.

Keywords

delivery of health care; evidence-based medicine; mental health services; patient reported outcome measures; post-traumatic stress disorder; practice guideline

1 | INTRODUCTION

Post-traumatic stress disorder (PTSD) is a serious condition that can follow exposure to a traumatic event, characterized by intrusive re-experiencing of the trauma such as flashbacks and nightmares, avoidance of trauma reminders that are associated with or arouse intrusive symptoms, negative alterations in cognitions and mood such as inability to remember the trauma or inability to experience positive emotions, and increased arousal and reactivity such as exaggerated startle response and angry outbursts.[1] PTSD has a lifetime prevalence of 6.1% in the United States.[2] Over 10% of veterans receiving care in the Department of Veterans Affairs (VA) health-care system have PTSD, comprising an active caseload of approximately 600 000 in 2016.[3] VA patients often receive PTSD treatment for many years,[4] despite randomized controlled trials indicating that evidence-based treatments (EBTs) for PTSD are generally delivered over a 2 to 4 month time frame.[5]

To monitor progress towards recovery, VA clinicians increasingly rely on patient-reported outcome measurement using the PTSD Checklist (PCL)[6] as part of routine practice.[7] Leveraging patient-reported outcome measurement, such as longitudinal PCL data, to understand and improve the course of routine clinical treatment at the population level has been suggested as a method to expand the available evidence base in a learning health-care system.[8–10] Such work might allow health systems to learn about the factors that predict that patients do not benefit sufficiently from routine clinical care and to take steps to improve systems to improve health-care effectiveness for those patients. Consistent with this idea, Sripada et al (2017) recently performed the first national study using latent class analysis of VA PCL data to demonstrate typical symptomatic trajectories in clinical practice.[11] They identified VA patients with new PTSD diagnoses nationally in 2013, including 2237 who had four PCL scores evenly spaced over a 12-week period. They found three classes of patients including mild-improving (21.8%), moderate-improving (43.8%), and severe-stable (34.3%). Predictors of mild or moderate improvement, compared with the severe-stable class, were female gender, White race, non-Hispanic ethnicity, and a lack of comorbid depression. However, there were two important limitations to this work. First, the authors

did not apply PTSD diagnostic criteria to the baseline PCL score when defining their cohort. As such, it is possible that some patients did not have PTSD at the start of their trajectory period. Second, the authors did not account for receipt of EBTs, including medications and psychotherapy in their models predicting class membership. Thus, it was not possible to determine whether membership in improving groups was driven by receipt of guideline-concordant care.

Consistent with the results of the plurality of meta-analyses,[5,12–15] the VA/Department of Defense (DoD) clinical practice guideline (CPG) recommends four antidepressants for PTSD, including fluoxetine, sertraline, paroxetine, and venlafaxine.[16] The CPG recommends many trauma-focused psychotherapy protocols for PTSD, including prolonged exposure (PE), cognitive processing therapy (CPT), eye movement desensitization and reprocessing (EMDR), other specific cognitive behavioural therapies, brief eclectic psychotherapy, narrative exposure therapy, and written narrative exposure.[16] Below, we refer to the four medications as evidence-based antidepressants (EBAs) and the trauma-focused psychotherapies as evidence-based psychotherapies (EBPs). For most of the past decade, VA training efforts have focused on two EBPs, PE and CPT.[17]

We sought to extend the work of Sripada et al by including variables describing EBT provision as additional predictors of clinical trajectory group membership using a national sample of VA patients undergoing new episodes of PTSD care. Our goal was to identify predictors of clinical improvement while accounting for the delivery of EBTs. We hoped that contextualizing patient predictors of improvement with data about EBT receipt could provide information about which VA PTSD treatments work the best and for whom in routine clinical practice. Individual patient factors that continue to predict lack of improvement after accounting for EBT receipt would more strongly indicate that disparities in effectiveness are determined by those patient factors rather than differences in access to EBT.

2 | METHOD

2.1 | Patients and procedure

The sample was drawn from a cohort of VA patients with new PTSD treatment episodes from fiscal years 2004 through 2013, which was designed to examine patterns of care during the initial year of treatment.[18–20] We used the VA corporate data warehouse (CDW) to obtain information on services use, clinical diagnoses, prescriptions, and standardized measures of PTSD symptoms. This study was approved by the Veterans Institutional Review Board of Northern New England.

The cohort included patients who received a primary diagnosis of PTSD at two or more outpatient encounters, at least one of which occurred in a mental health setting, over the course of 90 days between fiscal years 2004 and 2013. This criterion is consistent with research that indicates requiring multiple encounter-based diagnoses, including those made by a mental health clinician, improves the validity of encounter-based diagnoses for PTSD case identification.[21–23] To focus on new episodes of PTSD care, patients who had met this criterion during the prior 2 years were excluded, requiring us to look back into fiscal years

2002 and 2003 records. For example, if a patient met our inclusion criteria on June 30, 2002, he or she would not have been eligible for cohort inclusion until July 1, 2004. Additionally, when patients met our criteria for cohort inclusion multiple times over the 10-year period, only the first episode was included. For example, a patient who entered the cohort in fiscal year 2004 and did not receive any PTSD diagnoses in fiscal years 2008 or 2009 could not have re-entered the fiscal year 2010 or later. Because of a lack of data from patient-reported outcome measurement using the PCL during the years 2004 to 2007, the sample was further restricted to those who entered the cohort in fiscal year 2008 or later, when use of the PCL began to increase.[24,25] We examined 1 year of treatment receipt following the first encounter with a qualifying diagnosis of PTSD (index diagnosis). Patients were included in our analytic sample if they met our criteria for PTSD symptoms measurement (described below) at some point during the year following their index diagnosis.

2.2 | Measures

We measured PTSD symptoms using the PCL. During the time period we examined, the VA used the version of the PCL corresponding to PTSD diagnostic criteria in the fourth version of the Diagnostic and Statistical Manual of Mental Disorders, called DSM-IV.[26,27] The PCL is a 17-item measure with each item rated on a five-point Likert-type scale with total scores ranging from 17 through 85.[6] Respondents are asked to rate how much they are bothered by each symptom over the last month. Symptom presence is determined by a response of "moderately" or greater.[6] We defined clinically meaningful improvement as a decrease of 10 points or more based on prior research in Veterans showing that 5 to 10 points is clinically meaningful.[28,29] A clinically meaningful improvement in PTSD symptoms plus no longer meeting diagnostic criteria for PTSD has been shown to be an important marker of improved quality of life.[30]

Consistent with the approach of Sripada et al to cohort inclusion, we required a minimum of four PCL scores over the course of 12 weeks, and that the timing of these PCL scores was spread across at least four of six 2-week windows (Weeks 1–2, 3–4, 5–6, 7–8, 9–10, and 11–12).[31] To ensure patients continued to experience PTSD at the start of their trajectory period, we differed from Sripada et al in requiring that patients have a score of 50 or higher,[6,32] and meet minimal symptom criteria according to DSM-IV (one re-experiencing symptom, three avoidance and numbing symptoms, and two hyperarousal symptoms) at their baseline PCL measurement.

2.3 | Independent variables

We used an extensive list of medical records-based covariates that could plausibly be associated with our outcome of PTSD symptom change.[7] Patient characteristics included demographics, military service characteristics, and commonly occurring medical and mental health disorders. We measured health-care utilization variables for all patients during their initial year of PTSD treatment. Outpatient visits included those to primary care, general mental health, specialized PTSD, and substance abuse specialty clinics. We also measured days of care in residential PTSD or substance abuse settings or in the acute inpatient psychiatry setting. EBA receipt included any filled prescription for fluoxetine, sertraline, paroxetine, or venlafaxine as well as weeks filled of each. We measured EBP receipt,

including sessions of PE and CPT, using natural language processing (NLP) algorithms to classify therapists' notes.[4] During initial development of the NLP classifiers, we attempted to identify other EBPs for PTSD such as EMDR.[33] Despite manual review of over 7500 notes written about patients attending PTSD clinics, we were unable to detect any examples of other EBPs in routine clinical practice in VA.[33] Therefore, our EBP for PTSD measure only included PE and CPT sessions. We further distinguished CPT sessions as being delivered in individual (CPT-I) or group (CPT-G) settings based on procedural billing codes. Our NLP algorithms have an overall classification accuracy of 0.99 for PE, 0.97 for CPT-I, and 0.97 for CPT-G.[4] Other mental health treatment variables included non-EBP psychotherapy provision as well as provision of non-EBA medications commonly prescribed to patients in this cohort.[34]

2.4 | Data analysis

To understand how patients selected for this analysis differed from the rest of the cohort during the relevant years, we compared patient characteristics and service use over the initial year of PTSD treatment using χ^2 analysis and *t* tests, as appropriate. We similarly compared these same characteristics based on group assignment during the 12-week trajectory period amongst patients who met our PCL-based inclusion criteria. We identified improvement groups with latent trajectory analysis using the R traj package to implement the Leffondre et al (2004) method.[35] This method was developed to identify patterns of change in large clinical databases containing repeated measures, where measurement intervals may be irregular. It has been applied broadly to detect and understand patterns of illness in general medical and mental health conditions.[36–38] In this application, we used patients' PCL scores to calculate 24 potential measures of change over time.[39] Several of the measures of change are meaningful only if there are at least four observations per patient, necessitating the requirement of at least four PCL scores for cohort inclusion.[35] After calculation of the measures, we performed factor analysis to select the subset of nonredundant measures, and cluster analysis to identify subgroups of patients with similar PTSD symptom trajectories. We determined the number of clusters based on examination of cubic clustering criterion and scree plots.

After identifying symptomatic trajectories, we performed least absolute shrinkage and selection operator (LASSO) regression to predict group membership using the R glmnet package.[40] As we had many potentially redundant covariates (variables included in Table 1 as well as baseline PCL), we selected LASSO regression because it performs feature selection. LASSO is a machine learning method that avoids the overfitting common to multivariable models and the prediction errors common to stepwise selection by setting the sum of the absolute values of the regression coefficients to be less than a fixed value. This forces the coefficient of less important features to zero, and those covariates are dropped from the model. The exact penalty parameter is selected via 10-fold cross-validation. For our application, we randomly divided data into training set (2/3 of sample) and testing test (1/3 of sample). We used a 2-step process to implement LASSO regression. First, we applied LASSO on the training set to select features and passed the coefficients to the testing set to estimate the prediction score. To evaluate the association between prediction score and clustering outcome, we plotted a receiver operating characteristic (ROC) curve and

estimated the area under the curve (AUC). Second, we evaluated the robustness of our feature selection using 100 bootstrapped samples in the training set. At the extreme ends of the distribution of bootstrapped replications, some features that are important in the full model are dropped by LASSO. This results in coefficients of zero. As the exponential function of zero is one, this results in an odds ratio (OR) of 1.00 for non-significant values.

3 | RESULTS

There were 491 040 patients who met our criteria for a new episode of PTSD care between fiscal years 2008 and 2013. Amongst these, only 0.5% (2643) met our inclusion criteria based on PCL data availability and baseline symptoms. The 2643 patients included in our analyses differed from the rest of the cohort in most covariates (Table 1). With regard to demographic characteristics, they were younger, more likely to be Black (vs White), homeless, women (vs men), and to have experienced sexual trauma while in the military. They were less likely to live in a rural area, or to have been exposed to combat. Patients in the analytic cohort had similarly high levels of comorbidity to the overall treatment population, but were more likely to have pain disorders, headache disorders, depressive disorders, and non-PTSD anxiety disorders. They were less likely to have psychotic disorders or nicotine dependence. Over the year following their index PTSD diagnosis, patients in the analytic cohort had many more psychotherapy visits, including visits where they received EBPs. For example, amongst patients who met our PCL-based inclusion criteria, 26.6% received prolonged exposure and 54.4% received cognitive processing therapy in their initial year of PTSD treatment. These rates are significantly higher than in the rest of the cohort, where 2.8% received PE and 6.6% received CPT. Receipt of EBA was similar, although patients in the analytic cohort were more likely to receive sertraline and venlafaxine.

Our latent trajectory analysis indicated a 2-cluster solution (Figure 1 and Figure A1). While there was no difference in days to initial PCL (54–55 days) and baseline PCL score (severity of 65–66), the25.9% (n = 684) of patients in the substantial improvement trajectory had a mean decrease in PCL score of 16.24 (SD = 15.42) points over 12 weeks, whereas the 74.1% (n = 1959) of patients in the modest improvement trajectory improved by a mean of 8.09 (SD = 14.40) points ($P < .001$). Similarly, 39.0% (n = 267) of patients in the substantial improvement trajectory achieved loss of PTSD diagnosis plus a 10-point improvement whereas only 16.8% (n = 329) in the modest improvement group achieved this level of improvement ($P < .001$). There were very few differences in the demographic and diagnostic characteristics or 12-week treatment receipt amongst the patients in each group (Table 2). Patients in the substantial improvement trajectory were more likely to be women, to have experienced sexual trauma while in the military, and to have comorbidities including psychotic, bipolar, personality, and alcohol use disorders. They received more outpatient mental health visits and inpatient mental health treatment. Patients in the two groups received an equal amount of EBP with the exception of group CPT, which was delivered more to patients in the modest improvement group. EBA receipt was also the same across the two groups, although patients in the substantial improvement group were slightly more likely to receive sertraline.

In the first step of our LASSO regression (model development), the ability of our model to predict group membership peaked with seven classifiers and an AUC of 0.55 (Figure 2 and Figure A2). In the second step of our LASSO regression (bootstrapping), we found that of the seven classifiers in the initial model, only gender was robust to sample selection, with an odds ratio of 0.76 men being in the substantial improvement group (95% confidence interval [CI]: 0.58–0.96). The other six classifiers were dropped by our LASSO regression model in the extreme high or low estimates, resulting in coefficients of zero and thus ORs of 1.00 (Table 3).

4 | DISCUSSION

Our results differed from those of Sripada et al[11] in that we found two rather than three PTSD symptom trajectories that both groups improved and that only the female gender predicted the level of improvement. Distinctions in our research strategies likely accounts for difference in each of these three findings. First, the difference in number of trajectories may be due to our stricter inclusion criteria for PTSD at the baseline PCL. The groups of Sripada et al had mild (mean PCL of approximately 50), moderate (approximately 60), and severe (approximately 70) PTSD symptoms at baseline. Our strategy eliminated the mild group, and our remaining groups split the difference between moderate and severe groups of Sripada et al at baseline. Second, our finding that patients in both groups improved may be related to the method used to construct our cohort. Our parent cohort was comprised of 10 yearly cross-sections of patients entering PTSD treatment between 2004 and 2013. Patients who were part of prior years' cohorts were excluded from subsequent years. Thus, in the analytic sample for this study, which included cross-sections entering PTSD treatment between 2008 and 2013, patients were either naïve to VA PTSD treatment or had not received VA PTSD treatment for many years. This is in contrast to the "180-day dormant period without a diagnosis of PTSD" of Sripada et al. Therefore, Sripada et al likely included treatment-resistant patients that would have been excluded from our sample. Finally, out of the seven predictors in our model to predict symptom trajectory, only gender was available as a covariate in the dataset of Sripada et al. Given that we used a more expanded set of patient and treatment covariates, it is not surprising that we initially found a different set of classifiers. However, in our bootstrapped analysis, only gender remained a significant predictor of symptomatic trajectory. Therefore, we are only confident in gender finding, as the other predictors may be artefacts of sampling error.

It is promising that patients in both groups experienced improvement. Even the modest improvement group was within the 5 to 10 point range of clinically meaningful improvement on the PCL.[28,29] At the same time, being in the substantial improvement group was associated with a much higher rate of loss of diagnosis plus a 10-point improvement (39.0% versus 16.8%), an outcome that is associated with increased quality of life.[30] This underscores the evidence that outcomes for patients in our two trajectory groups were appreciably different. However, with an AUC of 0.55, our model to predict membership in the substantial improvement group using available patient and treatment covariates was only slightly better than chance.

We were surprised to find that receiving EBT for PTSD was not a predictor of being in the substantial improvement group. In this dataset, having sufficient PCL measurement for trajectory analysis is essentially a proxy for receiving a high level of EBT, making it difficult to assess the effects of receiving versus not receiving guideline-concordant care on clinical trajectory. Patients in both groups who were prescribed EBAs received a mean of 9 to 10 weeks of treatment. This was in line with VA treatment guidelines at the time, which recommended that antidepressants be continued for at least 8 weeks when treating PTSD.[41] Patients in both groups received similarly high levels of individual EBPs during the 12-week trajectory period, both in terms of percent receiving PE and CPT and in terms of the mean number of sessions received. While we were unable to meaningfully predict trajectory based on available patient and treatment characteristics, unmeasured characteristics such as receipt of preferred treatment and treatment expectations could account for these differences.[42–44] Information regarding these factors is not available in the CDW.

Our findings in clinical practice regarding gender mirror the Watts et al meta-regression of published RCT data,[5] suggesting that men may not respond as well to available PTSD treatments as women. Given our approach, the finding on gender applies generally to treatments provided to men in our cohort during the trajectory period. However, a national evaluation of the VA PE implementation programme by Eftekhari et al[45] found a significantly poorer effect for men versus women (approximately 5 points on the PCL). Thus, the finding of worse outcomes in men may also apply to men receiving specific PTSD treatments in clinical practice. Research determining why men experience less benefit with treatment is warranted. This could be due to underlying gender differences in the pathology of PTSD or in the suitability of available treatments for men. Such research could lead to helpful modifications of current treatments or the design of new treatments that address issues unique to men.

There are key limitations to this work. First, sufficient PCL measurement to be included in the trajectory analysis was only available on 0.5% of our parent cohort. Therefore, our findings may not generalize to the broader VA PTSD treatment population. Use of the VA electronic medical record to administer the PCL in routine practice became more common in 2008 after implementation of an electronic decision support tool that prompted administration of the PCL to patients with PTSD diagnoses,[24] with rapid uptake of the practice between 2008 and 2013.[7] The VA's measurement-based care initiative, which encourages the use of the PCL to help guide treatment decisions, may further accelerate this process. Therefore, future studies using more recent samples are likely to be more representative of the VA PTSD treatment population. Telephone-based assessments for a representative sample of VA patients initiating care for PTSD, such as those collected through the Veterans Outcome Assessment programme,[46] may also aid in the representativeness of studies assessing the effectiveness of routine VA care. Second, we may have decreased the proportion of patients participating in PCL measurement by examining only 1 year of care. Maguen et al[4] showed that it commonly takes up to 3 years following an initial VA PTSD diagnosis to receive an EBP. This is a critical consideration for future work using clinical data, as our study indicates EBP receipt drives the use of PCL measurement. Third, it is possible that EBPs were delivered with poor fidelity or that patients who were prescribed EBAs were not actually taking them. Measures of psychotherapy treatment

fidelity and psychopharmacology treatment adherence were not widely used in clinical practice during the years we examined. Fourth, we did not account for treatment history before the index PTSD diagnosis. For example, while the cohort was designed to capture treatment during the initial year of PTSD care, it is possible that patients received multiple EBAs before their index PTSD diagnosis as these medications are frequently used for other conditions. Future work should account for longitudinal treatment history as prior treatment resistance could explain current lack of improvement.[31]

In conclusion, while we were unable to predict which VA PTSD treatments work the best and for whom in routine clinical practice, we report two highly relevant clinical findings. First, our work indicates that patients receiving a high level of PTSD care in the VA do achieve meaningful improvements in symptoms. This is important information as it indicates that routine PTSD care provided by the VA can effectively reduce PTSD symptoms. Second, we showed that men do not appear to benefit from available PTSD treatments as much as women in routine VA practice. This suggests that additional research to confirm our findings and to understand why men do not benefit as much from PTSD treatment is needed and should be a priory for the VA.

ACKNOWLEDGEMENTS

Development of the study cohort was funded by a Department of Veterans Affairs Health Services Research and Development Career Development Award (CDA11–263), VA Office of Research and Development, Washington, DC. Development of additional variables identifying the use of EBP for PTSD was funded by the Department of Defence Joint Warfighter Medical Research Program (JW140056), Congressionally Directed Medical Research Program, Fort Dietrich, MD. Development of the outcomes dataset was funded by the Department of Defence Peer Reviewed Medical Research Program (PR160203), Congressionally Directed Medical Research Program, Fort Dietrich, MD. The sponsors did not have any role in the study design, methods, analysis, and interpretation of results nor in preparation of the manuscript and the decision to submit it for publication. The views expressed in this article are those of the authors and do not necessarily represent the position or policy of the US Department of Veterans Affairs nor the US Department of Defense.

Funding information

Department of Defence Peer Reviewed Medical Research Program, Grant/Award Number: PR160203; Department of Defence Joint Warfighter Medical Research Program, Grant/Award Number: JW140056; Department of Veterans Affairs Health Services Research and Development, Grant/Award Number: CDA11-263

APPENDIX

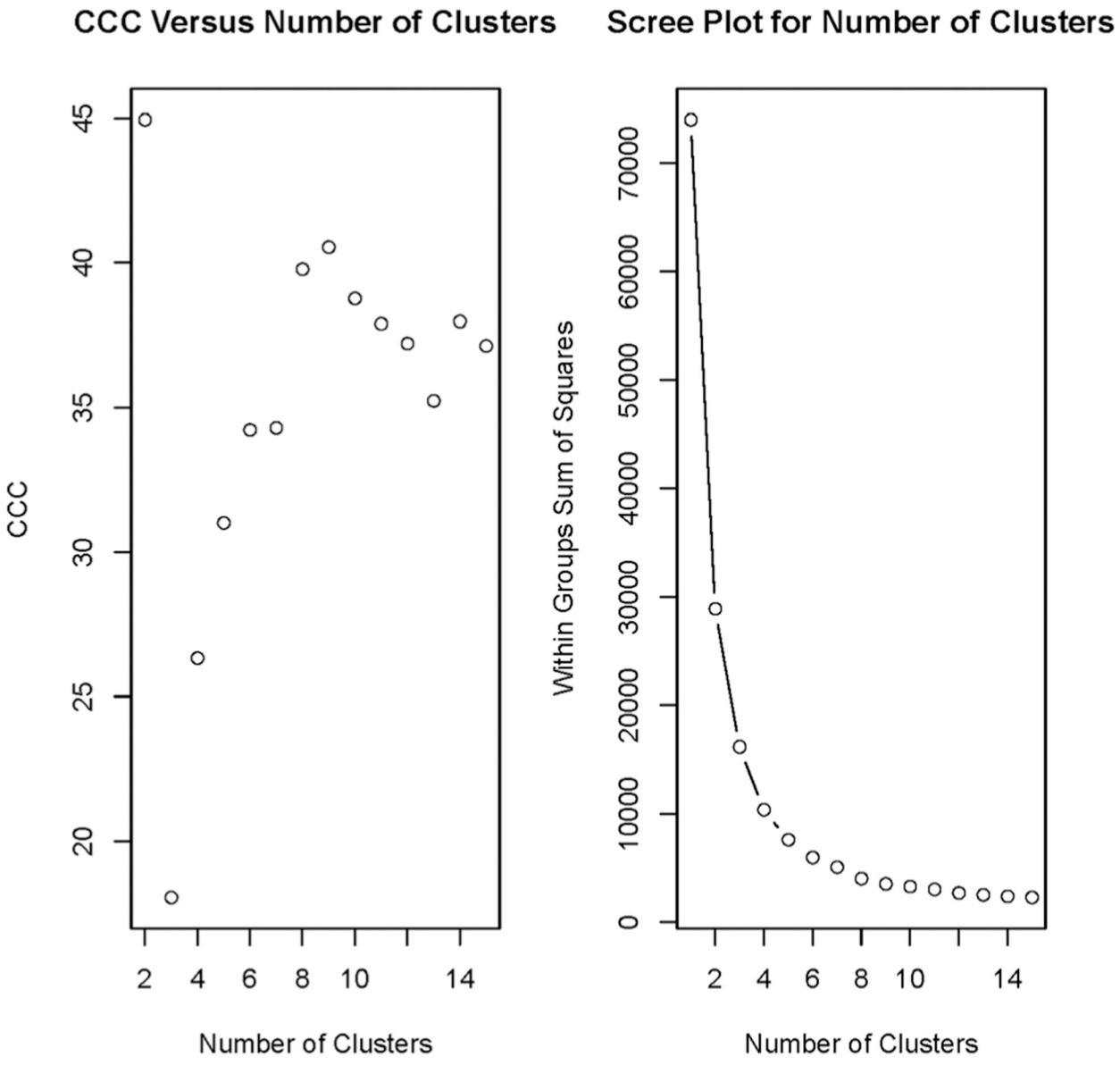

FIGURE A1.
Cluster analysis results. Please note, Cubic Clustering Criteria is represented by CCC

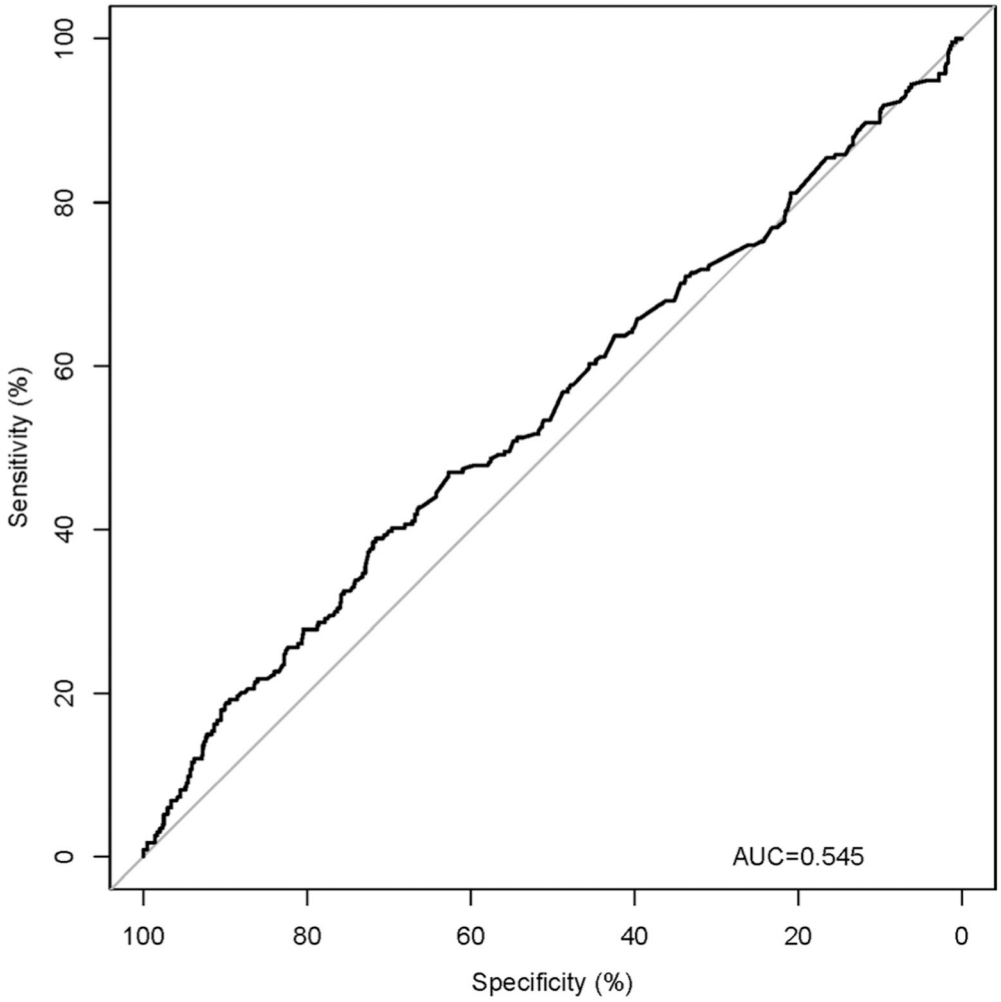

FIGURE A2.
Receiver operating characteristics. Area under the curve is represented by AUC

REFERENCES

1. Association AP. Diagnostic and statistical manual of mental disorders: DSM-5. 5th ed. Arlington, VA: American Psychiatric Association; 2013.
2. Goldstein RB, Smith SM, Chou SP, et al. The epidemiology of DSM-5 stress disorder in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions-III. Soc Psychiatry Psychiatr Epidemiol. 2016;51(8):1137–1148. [PubMed: 27106853]
3. Greenberg G, Hoff R. Veterans with PTSD Data Sheet: National, VISN, and VAMC Tables. West Haven, CT: Northeast Program Evaluation Center; 2016.
4. Maguen S, Madden E, Patterson OV, et al. Measuring use of evidence based psychotherapy for stress disorder in a large national healthcare system. Adm Policy Ment Health. 2018;45(4): 519–529. [PubMed: 29450781]
5. Watts BV, Schnurr PP, Mayo L, Young-Xu Y, Weeks WB, Friedman MJ. Meta-analysis of the efficacy of treatments for stress disorder. J Clin Psychiatry 2013;74(6):e541–e550. [PubMed: 23842024]
6. Weathers FW, Litz BT, Herman BS, Huska JA, Keane TM. The PTSD Checklist (PCL): Reliability, Validity, and Diagnostic Utility Paper presented at the Annual Convention of the International Society for Traumatic Stress Studies; 1993; San Antonio, Tx.

7. Shiner B, Westgate CL, Gui J, et al. A retrospective comparative effectiveness study of medications for stress disorder in routine practice. J Clin Psychiatry 2018;79(5):18m12145.
8. Abernethy AP, Ahmad A, Zafar SY, Wheeler JL, Reese JB, Lyerly HK. Electronic patient-reported data capture as a foundation of rapid learning cancer care. Med Care. 2010;48(6 Suppl):S32–S38. [PubMed: 20473201]
9. Etheredge LM. A rapid-learning health system. Health Aff. 2007;26(2): w107–w118.
10. Institute of Medicine. The Learning Healthcare System: Workshop Summary. Washington, DC: The National Academies Press; 2007.
11. Sripada RK, Pfeiffer PN, Rampton J, et al. Predictors of PTSD symptom change among outpatients in the US Department of Veterans Affairs Health Care System. J Trauma Stress. 2017;30(1):45–53. [PubMed: 28103415]
12. Cipriani A, Williams T, Nikolakopoulou A, et al. Comparative efficacy and acceptability of pharmacological treatments for post-traumatic stress disorder in adults: a network meta-analysis. Psychol Med. 2017;48:1–10. [PubMed: 28637524]
13. Hoskins M, Pearce J, Bethell A, et al. Pharmacotherapy for posttraumatic stress disorder: systematic review and meta-analysis. Br J Psychiatry. 2015;206(2):93–100. [PubMed: 25644881]
14. Jonas DE, Cusack K, Forneris CA, et al. Psychological and Pharmacological Treatments for Adults with Stress Disorder (PTSD) Rockville (MD): Agency for Healthcare Research and Quality; 2013.
15. Lee DJ, Schnitzlein CW, Wolf JP, Vythilingam M, Rasmusson AM, Hoge CW. Psychotherapy versus pharmacotherapy for stress disorder: systemic review and meta-analyses to determine firstline treatments. Depress Anxiety. 2016;33(9):792–806. [PubMed: 27126398]
16. The Management of Stress Disorder Work Group. VA/DoD Clinical Practice Guideline for the Management of Stress Disorder and Acute Stress Disorder. Washington, DC: United States Departments of Veterans Affairs and Defense; 2017.
17. Rosen CS, Matthieu MM, Wiltsey Stirman S, et al. A review of studies on the system-wide implementation of evidence-based psychotherapies for stress disorder in the Veterans Health Administration. Adm Policy Ment Health. 2016;43(6):957–977. [PubMed: 27474040]
18. Shiner B, Leonard Westgate C, Bernardy NC, Schnurr PP, Watts BV. Trends in opioid use disorder diagnoses and medication treatment among veterans with stress disorder. J Dual Diagn. 2017;13(3):201–212. [PubMed: 28481727]
19. Shiner B, Leonard Westgate C, Harik JM, Watts BV, Schnurr PP. Effect of patient-therapist gender match on psychotherapy retention among United States veterans with stress disorder. Adm Policy Ment Health. 2017;44(5):642–650. [PubMed: 27530121]
20. Shiner B, Westgate CL, Bernardy NC, Schnurr PP, Watts BV. Anticonvulsant medication use in veterans with stress disorder. J Clin Psychiatry. 2017;78(5):e545–e552. [PubMed: 28570793]
21. Frayne SM, Miller DR, Sharkansky EJ, et al. Using administrative data to identify mental illness: what approach is best? Am J Med Qual. 2010;25(1):42–50. [PubMed: 19855046]
22. Gravely AA, Cutting A, Nugent S, Grill J, Carlson K, Spoont M. Validity of PTSD diagnoses in VA administrative data: comparison of VA administrative PTSD diagnoses to self-reported PTSD checklist scores. J Rehabil Res Dev. 2011;48(1):21–30. [PubMed: 21328160]
23. Holowka DW, Marx BP, Gates MA, et al. PTSD diagnostic validity in veterans affairs electronic records of Iraq and Afghanistan veterans. J Consult Clin Psychol. 2014;82(4):569–579. [PubMed: 24731235]
24. Maguen S, Madden E, Neylan TC, Cohen BE, Bertenthal D, Seal KH. Timing of mental health treatment and PTSD symptom improvement among Iraq and Afghanistan veterans. Psychiatr Serv 2014;65(12): 1414–1419. [PubMed: 25082217]
25. Seal KH, Maguen S, Bertenthal D, et al. Observational evidence for Buprenorphine's impact on stress symptoms in veterans with chronic pain and opioid use disorder. J Clin Psychiatry. 2016;77(9):1182–1188. [PubMed: 27035058]
26. American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders. 4th ed., Text Revision: DSM-IV-TR Arlington, VA: American Psychiatric Association; 2000.
27. Wilkins KC, Lang AJ, Norman SB. Synthesis of the psychometric properties of the PTSD checklist (PCL) military, civilian, and specific versions. Depress Anxiety 2011;28(7):596–606. [PubMed: 21681864]

28. Monson CM, Gradus JL, Young-Xu Y, Schnurr PP, Price JL, Schumm JA. Change in stress disorder symptoms: do clinicians and patients agree? Psychol Assess. 2008;20(2):131–138. [PubMed: 18557690]
29. Shiner B, Watts BV, Pomerantz A, Young-Xu Y, Schnurr PP. Sensitivity of the SF-36 to PTSD symptom change in veterans. J Trauma Stress. 2011;24(1):111–115. [PubMed: 21351169]
30. Schnurr PP, Lunney CA. Symptom benchmarks of improved quality of life in PTSD. Depress Anxiety. 2016;33(3):247–255. [PubMed: 26882293]
31. Sippel LM, Holtzheimer PE, Friedman MJ, Schnurr PP. Defining treatment-resistant stress disorder: a framework for future research. Biol Psychiatry. 2018;84(5):e37–e41. [PubMed: 29752073]
32. Forbes D, Creamer M, Biddle D. The validity of the PTSD checklist as a measure of symptomatic change in combat-related PTSD. Behav Res Ther. 2001;39(8):977–986. [PubMed: 11480838]
33. Shiner B, D'Avolio LW, Nguyen TM, et al. Measuring use of evidence based psychotherapy for stress disorder. Adm Policy Ment Health. 2013;40(4):311–318. [PubMed: 22535469]
34. Krystal JH, Davis LL, Neylan TC, et al. It is time to address the crisis in the pharmacotherapy of stress disorder: a consensus statement of the PTSD psychopharmacology working group. Biol Psychiatry. 2017;82(7):e51–e59. [PubMed: 28454621]
35. Leffondre K, Abrahamowicz M, Regeasse A, et al. Statistical measures were proposed for identifying longitudinal patterns of change in quantitative health indicators. J Clin Epidemiol. 2004;57(10):1049–1062. [PubMed: 15528056]
36. Burti L, Mazzi M, Koeter M, et al. An empirical method to identify patterns in the course of psychotic episodes of people with schizophrenia. Int J Methods Psychiatr Res. 2009;18(4):265–278. [PubMed: 19708035]
37. Ciampi A, Bai C, Dyachenko A, McCusker J, Cole MG, Belzile E. Longitudinal patterns of delirium severity scores in long-term care settings. Int Psychogeriatr. 2017;29(1):11–17. [PubMed: 27576950]
38. Van Den Ham HA, Klungel OH, Leufkens HG, Van Staa TP. The patterns of anticoagulation control and the risk of stroke, bleeding and mortality in patients with non-valvular atrial fibrillation. J Thromb Haemost. 2013;11(1):107–115. [PubMed: 23088617]
39. Sylvestre MP, Vatnik D. Package 'traj' 2015; https://cran.r-project.org/web/packages/traj/traj.pdf. Accessed February 11, 2019.
40. Friedman J, Hastie T, Tibshirani R. Regularization paths for generalized linear models via coordinate descent. J Stat Softw 2010;33(1):1–22. [PubMed: 20808728]
41. Friedman MJ, Lowry P, Ruzek J. VA/DoD clinical practice guidelines for the management of post-traumatic stress; 2010 Available at https://www.healthquality.va.gov/guidelines/mh/ptsd/
42. Graham B, Garcia NM, Burton MS, et al. High expectancy and early response produce optimal effects in sertraline treatment for post-traumatic stress disorder. Br J Psychiatry. 2018;213(6):1–5.
43. Watts BV, Schnurr PP, Zayed M, Young-Xu Y, Stender P, Llewellyn-Thomas H. A randomized controlled clinical trial of a patient decision aid for stress disorder. Psychiatr Serv. 2015;66(2):149–154. [PubMed: 25322473]
44. Zoellner LA, Roy-Byrne PP, Mavissakalian M, Feeny NC. Doubly randomized preference trial of prolonged exposure versus sertraline for treatment of PTSD. Am J Psychiatry. 2018;176(4):287–296. appiajp201817090995 [PubMed: 30336702]
45. Eftekhari A, Ruzek JI, Crowley JJ, Rosen CS, Greenbaum MA, Karlin BE. Effectiveness of national implementation of prolonged exposure therapy in Veterans Affairs care. JAMA Psychiat. 2013;70(9):949–955.
46. Department of Veterans Affairs. Agency information collection activity: the Veterans' Outcome Assessment (VOA). Fed Regist. 2017;82(121):28943–28944.

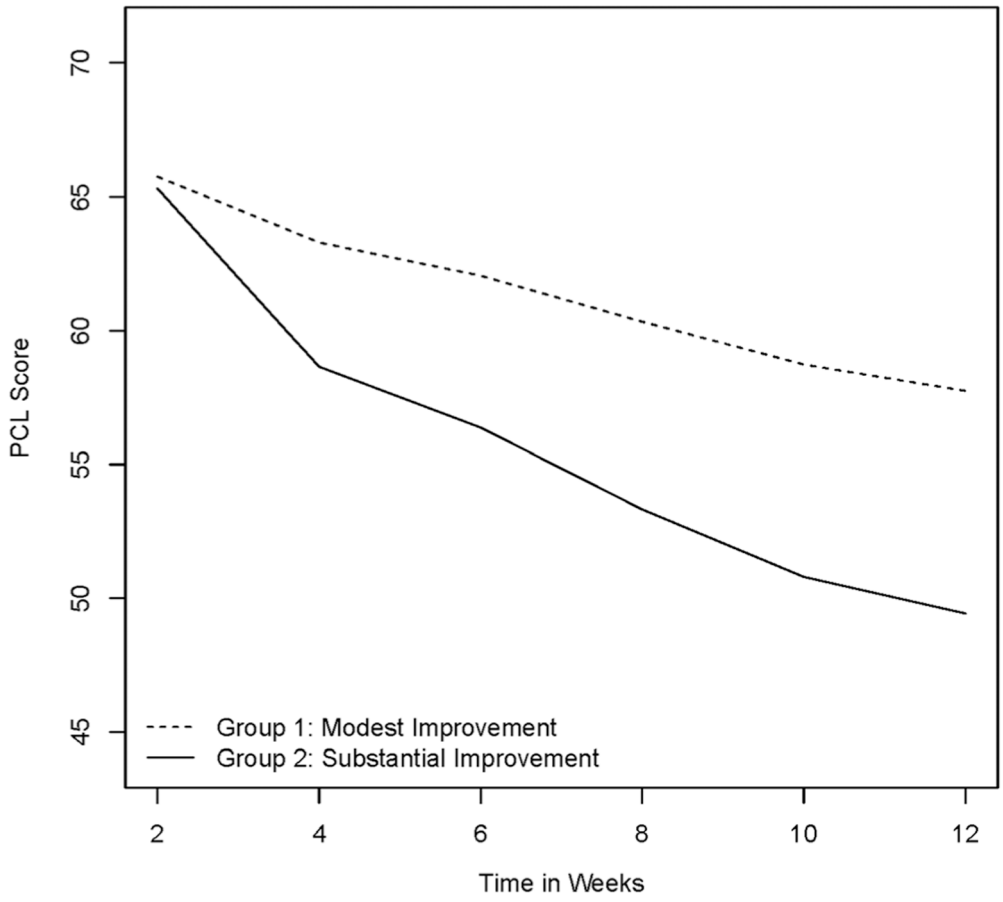

FIGURE 1.

Post-traumatic stress disorder (PTSD) symptoms scores based on the PTSD checklist (PCL) over time

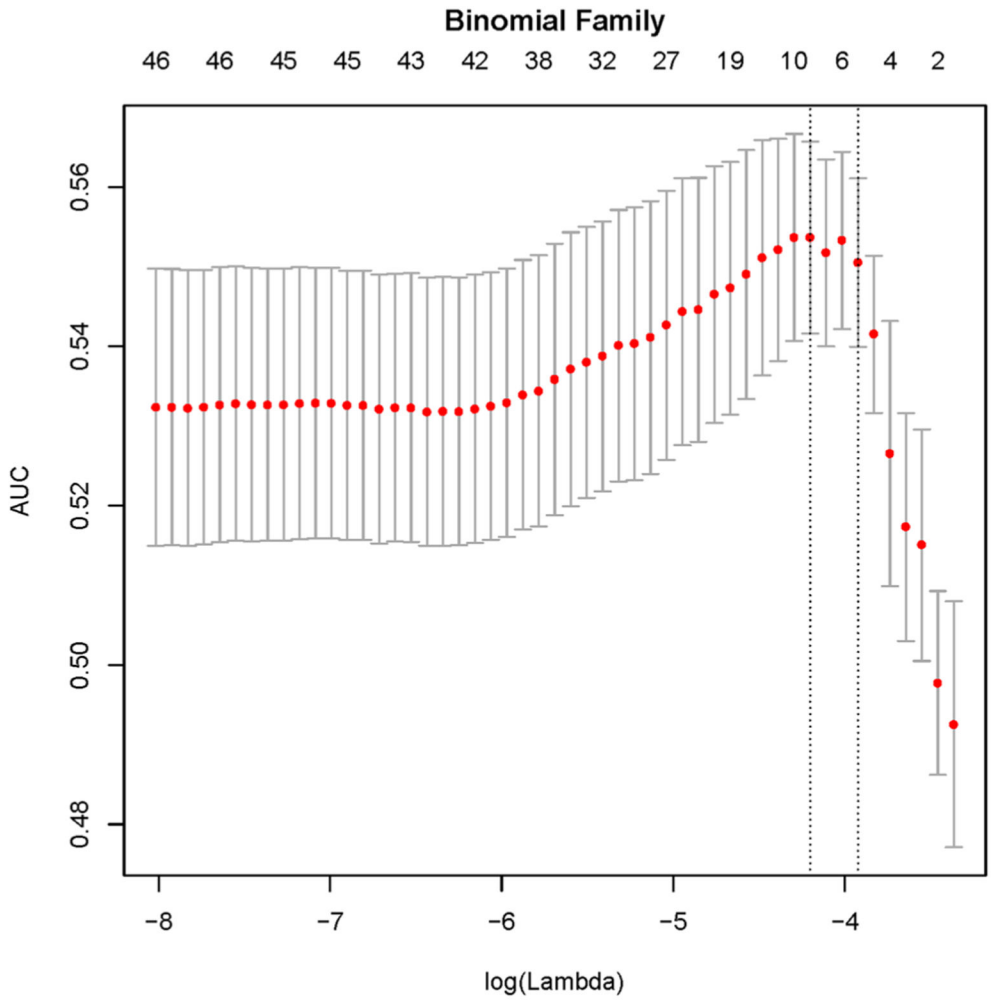

FIGURE 2.

Least absolute shrinkage and selection operator (LASSO) cross validation results. The y-axis represents the area under the curve, or AUC

TABLE 1

Characteristics of all VA patients with new episodes of PTSD care from 2008 to 2013 and final sample

	Overall (n = 491 040)		Final Sample (0.5%; n = 2,643)		
	M or %	SD or n	M or %	SD or n	*P*
Demographic characteristics at time of initial PTSD diagnosis					
Age, M, SD	48.55	16.00	47.09	14.74	<.001
Men, %, n	90.7	445 583	83.1	2195	<.001
Married, %, n	52.7	258 764	53.8	1422	.254
White non-Hispanic, %, n	63.5	311 756	60.3	1594	<.001
Black non-Hispanic, %, n	19.1	93 666	21.6	571	<.001
Hispanic, %, n	8.1	39 827	8.7	229	.296
OEF/OIF/OND veteran, %, n	34.9	171 364	38.4	1014	<.001
Rural, %, n	35.0	171 644	31.9	842	<.001
Homeless, %, n	5.4	26 574	7.5	199	<.001
Combat exposure, %, n	28.6	140 344	23.8	630	<.001
Sexual trauma while in military, %, n	9.3	45 803	17.2	455	<.001
VA disability level 70 or greater, %, n	55.7	273 242	55.6	1470	.978
Comorbid diagnoses in the year following initial PTSD diagnosis					
Pain disorder, %, n	64.9	318 802	68.8	1818	<.001
Headache disorder, %, n	25.1	123 441	31.9	842	<.001
Psychotic disorders, %, n	4.2	20 682	2.7	71	<.001
Bipolar mood disorders, %, n	6.2	30 560	5.4	143	.083
Depressive mood disorders, %, n	60.3	296 071	73.5	1943	<.001
Non-PTSD anxiety disorders, %, n	28.5	139 779	37.8	1000	<.001
TBI and cognitive disorders, %, n	13.4	65 834	14.8	391	.036
Personality disorders, %, n	3.9	18 959	4.2	110	.421
Nicotine dependence, %, n	39.0	191 712	33.7	891	<.001
Alcohol dependence, %, n	22.6	111 027	24.6	650	.015
Marijuana dependence, %, n	3.2	15 586	3.4	89	.570
Opioid dependence, %, n	3.2	15 903	3.5	92	.481
Service utilization during year following index PTSD diagnosis					

	Overall (n = 491 040)		Final Sample (0.5%; n = 2,643)		
	M or %	SD or n	M or %	SD or n	*P*
Any OP primary care visits, %, n	92.3	453 051	93.3	2466	.045
OP primary care visits, M, SD	5.52	5.63	6.12	5.24	<.001
Any OP general MH visits, %, n	99.9		99.9	2640	.928
OP general MH visits, M, SD	18.24	490 511 22.53	35.84	26.93	<.001
Any OP specialized PTSD visits, %, n	44.6		75.1	1986	<.001
OP specialized PTSD visits, M, SD	10.48	218 827 11.90	20.05	13.92	<.001
Any OP SA visits, %, n OP SA visits, M, SD	14.6	71 513	18.9	500	<.001
	18.88	28.59	22.80	26.11	.002
Any residential PTSD treatment, %, n	2.1	10 375	6.6	173	<.001
Days of residential PTSD, M, SD	60.49	56.15	65.47	46.15	.240
Any residential SA treatment, %, n	2.6	12 723	3.6	96	<.001
Days of residential SA, M, SD	69.74	69.72	88.90	77.56	.007
Any inpatient MH treatment, % (n)	7.0	34 386	8.0	210	.057
Days of inpatient MH, M, SD	20.58	39.49	21.27	35.00	.799
Evidence-based treatment for PTSD receipt during first year following index diagnosis					
Any PE, %, n	2.8	13 673	26.6	702	<.001
Sessions of PE, M, SD	5.51	4.41	7.42	4.61	<.001
Any individual CPT, %, n	6.6	32 311	54.4	1,438	<.001
Sessions of individual CPT, M, SD	5.44	4.70	8.12	4.99	<.001
Any group CPT, %, n	3.5	17 330	26.1	691	<.001
Sessions of CPT, M, SD	.37	5.29	8.52	4.91	<.001
Any fluoxetine, %, n	10.7	52 405	11.4	302	.208
Weeks supply of fluoxetine, M, SD	27.02	18.62	26.69	18.33	.755
Any paroxetine, %, n	5.8	28 628	6.7	176	.068
Weeks supply of paroxetine, M, SD	25.42	18.87	26.00	18.92	.691
Any sertraline, %, n	25.2	123 735	30.2	798	<.001
Weeks supply of sertraline, M, SD	26.5	18.5	29.2	18.7	<.001
Any venlafaxine, %, n	9.4	46 344	11.2	296	.002
Weeks supply of venlafaxine, M, SD	26.61	20.23	28.08	20.03	.209
Other mental health treatment receipt during year following index diagnosis					
Any non-PE/CPT individual therapy, %, n	86.1	422 545	95.7	2529	<.001
Any non-PE/CPT Group therapy, %, n	31.0	151 973	50.3	1330	<.001
Any non-F/S/P/V antidepressant, %, n	63.3	310 709	62.7	1656	.508
Any anticonvulsant, %, n	26.4	129.678	28.8	762	.005
Any sedative/hypnotics, %, n	39.7	194 690	35.2	930	<.001
Any opioid, %, n	37.2	182 514	35.0	926	.023

	Overall (n = 491 040)		Final Sample (0.5%; n = 2,643)		
	M or %	SD or n	M or %	SD or n	*P*
Any atypical antipsychotic, %, n	20.3	99 698	16.1	425	<.001
Any prazosin, %, n	18.6	91 551	26.8	708	<.001
Any nicotine replacement, %, n	11.2	54 777	11.9	315	.212
Any naltrexone or Acamprosate, %, n	1.2	5892	1.7	44	.028
Any opioid replacement therapy, %, n	0.7	3408	0.9	24	.184

Abbreviations: CPT, cognitive processing therapy; F/S/P/V, Fluoxetine/Sertraline/Paroxetine/Venlafaxine; M, mean; MH, mental health; OEF/OIF/OND, Operations Enduring Freedom/Iraqi Freedom/New Dawn; OP, outpatient; PE, prolonged exposure; PTSD, post-traumatic stress disorder; SA, substance abuse; SD, standard deviation; TBI, traumatic brain injury; VA, Department of Veterans Affairs.

TABLE 2

Symptomatic, demographic, diagnostic, and 12-week treatment characteristics by trajectory membership (n = 2645)

	Modest Improvement (74.1%; n = 1959)		Substantial Improvement (25.9%; n = 684)		
PTSD symptoms	**M or %**	**SD or n**	**M or %**	**SD or n**	***P***
Days from index diagnosis to PCL, M, SD	55.23	67.93	54.15	68.72	.721
Initial PCL score, M, SD	65.69	8.29	65.37	8.44	.397
Final PCL score, M, SD	57.60	14.40	49.13	15.42	<.001
Loss of PTSD diagnosis, %, n	16.8	329	39.0	267	<.001
Demographic, diagnostic, and 12-week treatment characteristics					
Age, M, SD	47.39	14.80	46.26	14.54	.085
Men, %, n	84.4	1,653	79.2	542	.002
Married, %, n	54.7	1,072	51.2	350	.109
White non-Hispanic, %, n	60.0	1,176	61.1	418	.619
Black non-Hispanic, %, n	21.6	424	21.5	147	.934
Hispanic, %, n	8.5	166	9.2	63	.555
OEF/OIF/OND, %, n	37.9	743	39.6	271	.433
Rural, %, n	31.3	614	33.3	228	.336
Homeless, %, n	7.7	150	7.2	49	.674
Combat exposure, %, n	24.3	476	22.5	154	.346
Sexual trauma while in military, %, n	16.1	315	20.5	140	.009
VA disability level 70 or greater, %, n	56.2	1101	54.0	369	.307
Pain disorder, %, n	69.1	1354	67.8	464	.534
Headache disorder, %, n	32.7	640	29.5	202	.130
Psychotic disorders, %, n	2.1	42	4.2	29	.004
Bipolar mood disorders, %, n	4.8	93	7.3	50	.011
Depressive mood disorders, %, n	73.3	1436	74.1	507	.676
Non-PTSD anxiety disorders, %, n	37.8	740	38.0	260	.912
TBI and cognitive disorders, %, n	15.4	301	13.2	90	.162
Personality disorders, %, n	3.7	72	5.6	38	.034
Nicotine dependence, %, n	33.6	659	33.9	232	.895
Alcohol dependence, %, n	23.3	456	28.4	194	.008
Marijuana dependence, %, n	3.4	66	3.4	23	.008

	Modest Improvement (74.1%; n = 1959)		Substantial Improvement (25.9%; n = 684)		
PTSD symptoms	**M or %**	**SD or n**	**M or %**	**SD or n**	***P***
Opioid dependence, %, n	3.3	64	4.1	28	.310
Any primary care visits, %, n	64.1	1,255	64.5	441	.847
Primary care visits, M, SD	2.32	1.85	2.42	1.89	.318
Any OP general MH visits, %, n	99.7	1,953	99.6	681	.609
OP general MH visits, M, SD	14.50	9.24	15.48	10.21	.021
Any outpatient SA visits, M, SD	13.4	262	16.4	112	053
Outpatient SA visits, M, SD	10.45	11.20	10.46	12.32	.997
Any residential PTSD treatment, %, n	5.1	99	6.7	46	.098
Days of residential PTSD, M, SD	51.34	16.36	52.30	18.11	.751
Any residential SA treatment, %, n	2.1	42	3.4	23	.077
Days of residential SA, M, SD	51.40	28.74	56.65	24.84	.464
Any inpatient MH treatment, %, n	1.7	33	3.4	23	.009
Days of inpatient MH treatment, M, SD	16.64	19.34	19.65	26.54	.625
Any PE, %, n	23.1	452	22.7	155	.825
Sessions of PE, M, SD	5.75	3.00	5.37	2.98	.172
Any individual CPT, %, n	49.9	977	46.2	316	.098
Sessions of individual CPT, M, SD	5.75	3.28	5.87	3.32	.564
Any group CPT, %, n	22.7	444	18.3	125	.016
Sessions of group CPT, M, SD	7.30	3.93	7.10	3.95	609
Any fluoxetine, %,	7.9	154	8.3	57	.695
n Weeks supply of fluoxetine, M, SD	9.42	4.50	9.22	4.89	.784
Any paroxetine, %, n	5.0	98	4.8	33	.854
Weeks supply of paroxetine, M, SD	8.76	4.97	9.80	4.78	.299
Any sertraline, %, n	22.7	445	23.3	159	.776
Weeks supply of sertraline, M, SD	9.21	4.88	10.37	4.92	.011
Any venlafaxine, %, n	7.2	140	8.2	56	.371
Weeks supply of venlafaxine, M, SD	10.35	5.14	10.48	6.10	.880
Any non-PE/CPT individual therapy, %, n	81.7	1601	84.7	579	.083
Any non-PE/CPT group therapy, %, n	32.6	638	33.8	231	.564
Any non-F/P/S/V antidepressant, %,n	50.9	997	51.5	352	.798
Any anticonvulsant, %, n	20.6	403	21.5	147	.610
Any sedative/hypnotics, %, n	24.1	472	27.6	189	.066
Any opioid, %, n	20.8	407	21.1	144	.878
Any atypical antipsychotic, %, n	9.2	181	14.6	100	<.001

	Modest Improvement (74.1%; n = 1959)		Substantial Improvement (25.9%; n = 684)		
PTSD symptoms	**M or %**	**SD or n**	**M or %**	**SD or n**	***P***
Any prazosin, %, n	19.1	375	18.6	127	.741
Any nicotine replacement, %, n	5.8	113	8.3	57	.019
Any naltrexone or Acamprosate, %, n	0.9	17	1.3	9	.307
Any opioid replacement therapy, %, n	0.6	11	0.9	6	.374

Abbreviations: CPT, cognitive processing therapy; F/S/P/V, Fluoxetine/Sertraline/Paroxetine/Venlafaxine; M, mean; MH, mental health; OEF/OIF/OND, Operations Enduring Freedom/Iraqi Freedom/New Dawn; OP, outpatient; PE, prolonged exposure; PTSD, post-traumatic stress disorder; SA, substance abuse; SD, standard deviation; TBI, traumatic brain injury.

TABLE 3

Classifiers in final LASSO model, with bootstrapped Cis

Variable	Odds Ratio	95% CI	
		Lower	Upper
Men	0.76	0.58	0.96
Homeless	0.76	0.49	1.00
Headache disorder	0.96	0.77	1.00
Alcohol dependence	1.15	1.00	1.48
Non-PE/CPT individual psychotherapy sessions	1.02	1.00	1.05
Atypical antipsychotic	1.33	1.00	1.80
Nicotine replacement	1.09	1.00	1.53

Abbreviations: CI, confidence interval; LASSO, least absolute shrinkage and selection operator; PE/CPT, prolonged exposure/cognitive processing therapy.