The Relationship of Post-traumatic Stress Disorder to End-of-life Care Received by Dying Veterans: a Secondary Data Analysis

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BACKGROUND: Post-traumatic stress disorder (PTSD) can be exacerbated by subsequent trauma, but it is unclear if symptoms are worsened by impending death. PTSD symptoms, including hyperarousal, negative mood and thoughts, and traumatic re-experiencing, can impact end-of-life symptoms, including pain, mood, and poor sleep. Thus, increased symptoms may lead to increased end-of-life healthcare utilization.

OBJECTIVES: To determine if veterans with PTSD have increased end-of-life healthcare utilization or medication use and to examine predictors of medication administration.

DESIGN: Secondary analysis of a stepped-wedge design implementation trial to improve end-of-life care for Veterans Affairs (VA) inpatients. Outcome variables were collected via direct chart review. Analyses included hierarchical, generalized estimating equation models, clustered by medical center.

SUBJECTS: Veterans, inpatient at one of six VA facilities, dying between 2005 and 2011.

MAIN MEASURES: Emergency room (ER) visits, hospitalizations, and medication administration in the last 7 days of life.

KEY RESULTS: Of 5341 veterans, 468 (8.76%) had PTSD. Of those, 21.4% (100/468) had major depression and 36.5% (171/468) had anxiety. Veterans with PTSD were younger (mean age 65.4 PTSD, 70.5 no PTSD, $p < 0.0001$) and had more VA hospitalizations and ER visits in the last 12 months of life (admissions: PTSD 2.8, no PTSD 2.4, $p < 0.0001$; ER visits: 3.2 vs 2.5, $p < 0.0001$). PTSD was associated with antipsychotic administration (OR 1.52, 95% CI 1.06–2.18). Major depression (333/5341, 6.2%) was associated with opioid administration (OR 1.348, 95% CI 1.129–1.609) and benzodiazepines (OR 1.489, 95% CI 1.141–1.943). Anxiety disorders (778/5341, 14.6%) were only associated with benzodiazepines (OR 1.598, 95% CI 1.194–2.138).

CONCLUSIONS: PTSD's association with increased end-of-life healthcare utilization and increased antipsychotic

administration in the final days of life suggests increased symptom burden and potential for terminal delirium in individuals with PTSD. Understanding the burden of psychiatric illness and potential risks for delirium may facilitate the end-of-life care for these patients.

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KEY WORDS: PTSD; end of life care; utilization; mental health; veterans.

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INTRODUCTION

Despite its inevitability, death is often considered a poor outcome in medicine and in society. Accepting a poor prognosis and navigating the last months of life can be challenging for anyone¹ and is potentially harder for individuals predisposed to depression or anxiety.²

Generally, individuals with psychiatric illness have higher healthcare utilization,^{3–6} lower quality of life and functional status,^{7–10} and worse medical outcomes^{10, 11} than the general population. Individuals with psychiatric illness may have difficulty coping with life stressors¹² and are at risk for relapse or worsening symptoms during major life changes, such as retirement, divorce, or death.^{13, 14} Individuals with post-traumatic stress disorder (PTSD) may be specifically at risk for relapse or worsening symptoms as their own death approaches because PTSD requires exposure to a trauma, specifically near death or threatened death.¹⁵ Due to the traumatic encoding of memories in PTSD,¹⁶ reminders of one's own death may consciously or unconsciously trigger reminders of prior trauma. Thus, in terminal illness, any reminders of impending death could be re-traumatizing or exacerbate the symptoms of patients with PTSD. However, the effects of PTSD on symptom burden and healthcare utilization in the last months of life have not been well studied.

Diagnostically, PTSD consists of four clusters, re-experiencing, avoidance, negative cognitions and mood, and increased arousal.¹⁵ PTSD frequently co-exists with other

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psychiatric illness, such as mood or substance use.^{17, 18} PTSD also negatively affects pain sensation and interpretation,^{19–21} causes poor sleep,¹⁵ and can lead to somatization.^{22, 23} PTSD's course can be chronically symptomatic, resolving over time, remitting and relapsing, or with late onset.^{24–29} Trajectories vary depending on trauma type, treatment, and other factors.^{25–27, 30–32} Life stressors, such as retirement or death of loved ones, have been correlated with PTSD relapse or worsening symptoms.^{32–36} Specifically, the theory of later-adulthood trauma re-engagement describes later-life worsening of PTSD symptoms as a part of life reminiscence, which is triggered by common older life events, such as physical or cognitive decline, role transitions, or deaths of loved ones.^{37, 38} However, it is unclear how often PTSD symptoms occur or if they impact medical care in the final months and days of life, as death nears.

United States (US) PTSD prevalence rates are 3.5% current and 6.8% lifetime, but as low as 2.5% in the older population.^{39–42} Studies have quoted increased PTSD rates in various life-threatening medical conditions: 2.3–18% in cancer,^{43–45} 30–54% in human immunodeficiency virus (HIV),^{46, 47} and in 3.7–59% of patients admitted to the intensive care unit (ICU).^{48–50} These rates vary, as different tools and time periods were used to diagnose PTSD. The gold standard for PTSD diagnosis is a structured clinical interview, and symptoms must persist for at least one month.¹⁵ PTSD rates are lower when using these criteria.^{45, 48}

PTSD is often studied within Veterans Affairs (VA), due to combat trauma exposure. VA is also the largest national health-care system to routinely screen all patients for PTSD.⁵¹ Outside of VA, PTSD screening varies and is often under-diagnosed.^{52–54} Therefore, to test our hypothesis that PTSD symptoms worsen at the end of life, manifested by increased healthcare utilization or increased medication use, we sought to study PTSD in VA. We conducted an exploratory, secondary analysis of data describing end-of-life care received by veterans, dying in VA medical centers from the Best Practices for End-of-Life Care for Our Nation's Veterans (BEACON) trial.⁵⁵

METHODS

Description of the Primary Study

The BEACON study has been previously described.⁵⁵ It was a multisite, stepped-wedge implementation trial of a multicomponent intervention to improve the quality of end-of-life care in VA medical centers, including ensuring that routinely prescribed medications and comfort-focused practices were ordered for dying inpatients via implementation of a Comfort Care Order Set. Additional details in online Appendix 1 (online).

BEACON Data Collection

A standardized chart abstraction tool was used to record the primary terminal diagnosis of each veteran and the end-of-life care process outcomes in the last 7 days of life, including

administration of opioids, benzodiazepines, or antipsychotics; presence of an intravenous line or nasogastric tube at the time of death; location of death; and record of an advanced directive or a do not resuscitate (DNR) order. Inter-rater reliabilities were established between the chart abstractor and the Director of Palliative Care at the coordinating center.

Demographic data, including race, and medical and psychiatric comorbidities were obtained from the VA National Data Sets in Austin, Texas. The first 15 comorbidities indicated by International Statistical Classification of Diseases, 9th edition (ICD-9) code in each veterans' electronic medical record problem list were included.

Secondary Analysis

Chi-square was used to compare categorical values and Student's *t* test to compare continuous values between participants with and without PTSD. A Bonferroni correction was used to account for the multiple comparisons, yielding $\alpha = 0.05/32 = 0.0016$ for the *p* value for these comparisons only.

Primary outcomes were VA emergency room (ER) visits, admissions, and administration of each medication class (opioids, benzodiazepines, antipsychotics, and all three classes together). Models used generalized estimating equations (GEE) to account for the clustering of patients within sites⁵⁶ and were adjusted to account for the small number of clusters.^{57–60} Poisson and logistic models were used for count (ER visits and VA admissions) and binary (administration of medication) data, respectively. Predictors were added hierarchically to examine potential moderating effects of each group of predictors. These predictors were (1) PTSD alone; (2) demographics (year of death, race, age, gender, intervention arm); (3) psychiatric comorbidities (anxiety disorders, any dementia diagnosis, major depression, alcohol use disorder, schizophrenia, non-nicotine drug use disorder); and (4) terminal diagnosis of cancer (no/yes). The categorical intervention variable denoted whether the patient died before or after the BEACON intervention⁵⁵ was implemented at that VA facility to account for temporal trends from the primary intervention.

RESULTS

Patient Characteristics

Of the 5341 veterans included in this analysis, 1946 (36.4%) had at least one psychiatric illness and 468 (8.76%) had a diagnosis of PTSD (Appendix Table 5—online). Table 1 characterizes the demographic differences between veterans with and without PTSD. The cohort was predominantly male (98.2%) and was 31.6% African-American, reflecting the racial distribution of the participating VA medical centers. Veterans with PTSD were significantly younger at death than those without PTSD, with mean ages of 65.4 and 70.1, respectively ($p < 0.0001$). Psychiatric comorbidities were statistically more prevalent in veterans with PTSD, 36.5% with anxiety disorder and 21.4% with major depressive disorder.

Table 1 Demographic Characteristics of 5341 Veterans in the BEACON Intervention Trial Who Died as Inpatients in One of 6 VA Medical Facilities, Stratified by PTSD Diagnosis

Characteristics	PTSD diagnosis		Total (n = 5341)	Chi-square, p value
	Yes (n = 468)	No (n = 4873)		
Male gender	462 (98.7)	4784 (98.2)	5246 (98.2)	0.39
Race				0.058
Black	171 (36.5)	1519 (31.2)	1690 (31.6)	
White	261 (55.8)	2940 (60.3)	3201 (59.9)	
Other	36 (7.7)	414 (8.5)	450 (8.4)	
Mean age at death in years (SD)*	65.4 (10.4)*	70.5 (11.5)*	70.1 (11.5)*	< 0.0001*†
Timing of death				< 0.0001†
Before intervention	196 (41.9)	2720 (55.8)	2916 (54.6)	
After intervention	272 (58.1)	2153 (44.2)	2425 (45.4)	
Study site				< 0.0001†
1	45 (9.6)	993 (20.3)	1038 (19.4)	
2	67 (14.3)	808 (16.6)	875 (16.4)	
3	125 (26.7)	739 (15.2)	864 (16.2)	
4	49 (10.5)	564 (11.6)	613 (11.5)	
5	87 (18.6)	1018 (20.9)	1105 (20.7)	
6	95 (20.3)	751 (15.4)	846 (15.9)	
Psychiatric comorbidities (could have one or more)				
Anxiety disorders	171 (36.5)	607 (12.5)	778 (14.6)	< 0.0001†
Any dementia	45 (9.6)	526 (10.8)	571 (10.7)	0.43
Major depression	100 (21.4)	233 (4.8)	333 (6.2)	< 0.0001†
Alcohol use disorder	50 (10.7)	165 (3.4)	215 (4.0)	< 0.0001†
Schizophrenia	29 (6.2)	179 (3.7)	208 (3.9)	0.007
Drug use disorder (non-nicotine)	55 (11.8)	139 (2.9)	194 (3.6)	< 0.0001†
Primary terminal diagnosis				0.0004†
Cancer	146 (31.2)	1445 (29.7)	1591 (29.8)	
Dementia	28 (6.0)	415 (8.5)	443 (8.3)	
Lung disease	40 (8.6)	392 (8.0)	432 (8.1)	
Heart disease	70 (15.0)	1018 (20.9)	1088 (20.4)	
Kidney disease	30 (6.0)	252 (5.2)	282 (5.3)	
Liver disease	47 (10.4)	272 (5.6)	319 (6.0)	
Brain (stroke or neurological)	28 (6.0)	354 (7.3)	382 (7.2)	
HIV	5 (1.1)	77 (1.6)	82 (1.5)	
Acute illness	32 (6.8)	294 (6.0)	326 (6.1)	
Unexpected or none	42 (9.0)	354 (7.3)	396 (7.4)	

135 patients had missing data and were not included. Data presented as number (column %), unless otherwise indicated

BEACON Best Practices for End-of-Life Care for Our Nation's Veterans, VA Veterans Affairs, PTSD post-traumatic stress disorder, SD standard deviation, HIV human immunodeficiency virus

*Continuous variable, t test for statistical significance

†Statistically significant after Bonferroni correction, $p < 0.0016$

The most common primary terminal diagnosis was cancer, followed by heart disease, regardless of PTSD diagnosis.

Care Patterns in Veterans With and Without PTSD

Table 2 describes the differences in outcomes for veterans with and without PTSD. Patients with PTSD had significantly more VA hospital admissions and ER visits than those without PTSD (admissions: PTSD 2.8, no PTSD 2.4, $p < 0.0001$; ER visits: 3.2 vs 2.5, $p < 0.0001$). Patients with PTSD were significantly more likely to have an advanced directive, 48.1% vs 37.9% ($p < 0.0001$). However, there was a trend towards fewer DNR orders in patients with PTSD, 66.5% vs 71.0% ($p = 0.037$). During the final admission, for veterans with PTSD, there was a trend towards any ICU use (49.6% vs 42.7%, $p = 0.004$), but deaths in the medical or cardiac ICU were less likely. There were no statistically significant differences noted in length of stay or use of invasive treatments. However, there were significant differences in administration of symptom-relieving medications in the last 7 days of life.

Patients with PTSD were more likely to have received an opioid, benzodiazepine, or an antipsychotic at any time during the last 7 days of life and were also more likely to have received each medication class in both the last 48 h of life and in the time period from 49 h to 7 days before death.

Predictors of Medication Administration Throughout the Last 7 Days of Life

To model our assumption that patients with PTSD were more symptomatic, and thus consistently requiring symptom-relieving medication, we chose the data category of “both” observed time periods (receiving medication in the last 48 h of life and in the time period from 49 h to 7 days before death) for our GEE drug class models. As opioids, benzodiazepines, and antipsychotics tend to be used for different symptom clusters, we examined predictors of administration for each drug class separately and for all three classes combined using hierarchical GEE models (Appendix Table 6—online). PTSD was significant in the univariate models. However, in fully adjusted models, PTSD was only significant in the antipsychotic model (Table 3).

Table 2 Process of Care Outcomes of 5341 Veterans in the BEACON Intervention Trial Who Died as Inpatients in at One of 6 VA Medical Facilities, Stratified by PTSD Diagnosis

Outcomes	PTSD diagnosis		Total (n = 5341)	Chi-square, p value
	Yes (n = 468)	No (n = 4873)		
Mean number of VA admissions				
In last 12 months of life (SD)*	2.8 (2.1)*	2.4 (1.8)*	2.4 (1.8)*	< 0.0001* [†]
Mean number of ER visits				
In last 12 months of life (SD)*	3.2 (3.7)*	2.5 (2.8)*	2.6 (2.9)*	< 0.0003* [†]
Events—any time prior to death				
Advanced directive documented	225 (48.1)	1847 (37.9)	2072 (38.8)	<0.0001 [†]
Do not resuscitate order present	311 (66.5)	3462 (71.0)	3773 (70.6)	0.037
Events—Final Inpatient Admission				
Mean length of stay in days (SD)*	11.3 (78.6)*	21.4 (146.9)*	23.1 (172.4)*	0.143*
Mean days of IV infusion (SD)*	5.0 (2.5)*	5.0 (2.5)*	5.0 (2.5)*	0.85*
Palliative care consult	88 (18.8)	787 (16.2)	875 (16.3)	0.139
Any time spent in ICU	232 (49.6)	2080 (42.7)	2312 (43.3)	0.004
Pastoral care note (during last 7 days)	289 (61.8)	2821 (57.9)	3110 (58.2)	0.106
IV infusing at death	334 (71.4)	3444 (70.7)	3778 (70.7)	0.75
Nasogastric or feeding tube at death	188 (40.2)	1904 (39.1)	2092 (39.2)	0.64
In restraints at death	77 (16.5)	801 (16.4)	878 (16.4)	0.99
Family present at death	201 (42.9)	2095 (43.0)	2296 (43.0)	0.99
Location of death				0.006
Medical/Cardiac ICU	138 (29.5)	1873 (38.4)	2011 (37.7)	
Emergency room or urgent care	5 (1.1)	82 (1.7)	87 (1.6)	
Medical ward	185 (39.5)	1685 (34.6)	1870 (35.0)	
Surgical ICU	47 (10.0)	395 (8.1)	442 (8.3)	
Surgical ward	27 (5.8)	219 (4.5)	246 (4.6)	
Palliative care unit	25 (5.3)	196 (4.0)	221 (4.1)	
Other	41 (8.8)	423 (8.7)	464 (8.7)	
Medications given in last 7 days				
Opioids				
Ever given	343 (73.3)	3328 (68.3)	3671 (68.7)	0.026
When given				0.004
Never	125 (26.7)	1545 (31.7)	1670 (31.3)	
0–48 h only	114 (24.4)	1283 (26.3)	1397 (26.2)	
49 h–7 days only	42 (9.0)	502 (10.3)	544 (10.2)	
Both time periods	187 (40.0)	1543 (31.7)	1730 (32.4)	
Benzodiazepines				
Ever given	222 (47.4)	1936 (35.6)	2158 (40.4)	0.0012 [†]
When given				0.0008 [†]
Never	246 (52.6)	2937 (60.3)	3183 (59.6)	
0–48 h only	74 (15.8)	769 (15.8)	843 (15.8)	
49 h–7 days only	58 (12.4)	524 (10.8)	582 (11.0)	
Both time periods	90 (19.2)	643 (13.2)	733 (13.7)	
Antipsychotics				
Ever given	123 (26.3)	763 (17.8)	886 (16.6)	< 0.0001 [†]
When given				< 0.0001 [†]
Never	345 (73.7)	4110 (84.3)	4455 (83.4)	
0–48 h only	32 (6.8)	217 (4.5)	249 (4.7)	
49 h–7 days only	44 (9.4)	260 (5.3)	304 (5.7)	
Both time periods	47 (10.0)	286 (5.9)	333 (6.2)	

135 patients had missing data and were not included. Data presented as number (column %), unless otherwise indicated

BEACON Best Practices for End-of-Life Care for Our Nation's Veterans, VA Veterans Affairs, PTSD post-traumatic stress disorder, SD standard deviation, ER emergency room, IV intravenous, ICU intensive care unit

*Continuous variable, t test for statistical significance

[†]Statistically significant after Bonferroni correction, $p < 0.0016$

Table 4 illustrates the full models from Table 3, including covariates. Year of death was significant in each model. Older age was also significant, associated with a 13% lower likelihood of receiving opioids, a 15% lower likelihood of receiving benzodiazepines, and a 24% lower likelihood of receiving all three drug classes together.

Cancer and major depression were significant in both the opioid and benzodiazepine models. Patients with depression were 39% more likely to receive opioids and 49% more likely to receive benzodiazepines. In the benzodiazepine model, significant predictors included year of

death, age, race, anxiety, alcohol use disorder, drug use disorder, and cancer. PTSD was only significant in the antipsychotic model, along with year of death and schizophrenia.

To examine if PTSD remained a significant predictor of VA ER visits or hospitalizations in the last 12 months of life, we also created GEE relative risk models with the same covariates as the drug class models. A PTSD diagnosis was associated with 1.09 times more admissions (95% CI 1.03–1.16, $p = 0.034$) and 1.10 times more ER visits (95% CI 0.98–1.24, $p = 0.17$).

Table 3 Generalized Estimating Equation (GEE) Models for Odds of PTSD Associated with Administration of Each Listed Medication Class in Both Time Periods (in the Last 48 h of Life and in the Last 2–7 Days of Life)

Model	Odds ratio (95% confidence interval)	p value
Opioids		
PTSD alone	1.36 (1.04–1.79)	0.034
Full model*	1.18 (0.89–1.55)	0.192
Benzodiazepines		
PTSD alone	1.50 (1.20–1.18)	0.006
Full model*	1.06 (0.75–1.49)	0.703
Antipsychotics		
PTSD alone	1.75 (1.40–2.19)	0.001
Full model*	1.52 (1.06–2.18)	0.030†
All three drug classes		
PTSD alone	2.34 (1.11–4.95)	0.032
Full model*	1.62 (0.48–5.46)	0.358

All models included clustering by medical center

PTSD post-traumatic stress disorder

*Full models adjusted for year of death, in intervention phase of primary study, age at death, race, gender, anxiety, dementia, major depression, non-nicotine drug use disorder, alcohol use disorder, schizophrenia, and a primary terminal diagnosis of cancer

†Statistically significant in full model, $p < 0.05$

DISCUSSION

Our findings provide new empirical evidence supporting the hypothesis that individuals with PTSD have increased symptom burden in the final months and days of life. In comparing veterans with and without PTSD dying in a VA medical facility, those with PTSD were more likely to have previously been admitted to a VA facility in the past 12 months and were more likely to have received antipsychotics in the last 7 days of life. PTSD, by definition, requires exposure to a traumatic event involving near death or threatened death.¹⁵ Subsequent trauma can cause a recurrence or worsening of PTSD symptoms.^{61, 62} Therefore, we hypothesized that as death nears, PTSD symptoms would worsen. Obtaining evidence that PTSD impacts the end of life will facilitate future work exploring this impact and developing interventions to improve the end-of-life experience.

Because prospective data collection in hospice and palliative care populations can be challenging,^{63, 64} we used medications and healthcare utilization as proxies for PTSD symptom burden. Patients with psychiatric illness typically have increased healthcare utilization.^{3–6} Those in mid-life with PTSD may have the highest utilization.⁶⁵ Because this utilization is associated with symptom burden,^{65–67} we hypothesized that continued or worsening PTSD symptoms would thus contribute to increased end-of-life healthcare utilization.

Moving beyond symptoms, because PTSD is frequently comorbid with other psychiatric illnesses,^{17, 18, 68} we needed to determine if PTSD was a separately detectable issue at the end-of-life. Importantly, we found that only PTSD and schizophrenia were associated with administration of antipsychotics in the last 7 days of life. The schizophrenia finding was unsurprising, as the data did not consider medications prior to the last 7 days of life. While patients with schizophrenia would continue to receive antipsychotics in the final days of life, antipsychotics

are not recommended for PTSD treatment⁶⁹ nor are they routinely prescribed for PTSD in the VA setting.^{70, 71}

For example, antipsychotic prescription rates in PTSD in VA in 2009 were 5.1% for second-generation antipsychotics in veterans age 65 and older⁷¹ and 13.9% for any antipsychotic overall.⁷⁰ Our data was collected between 2005 and 2011, and the rates of receiving any antipsychotic in the last 7 days of life with and without PTSD were 26.3% and 15.6%, respectively. Antipsychotics have been associated with PTSD in patients with dementia.⁷¹ However, we controlled for dementia, and it was not associated with antipsychotic administration.

Antipsychotics are commonly prescribed in palliative care and hospice settings^{72, 73} and are recommended for short-term treatment of delirium.^{74, 75} However, black box warnings recommend against the long-term use of antipsychotics in elderly patients or those with dementia.^{76, 77} Antipsychotics are less commonly prescribed upon hospice admission than opioids or benzodiazepines.^{73, 78} However, prescriptions increase as death nears,^{73, 78} initiated an average of 2–5 days prior to death.⁷³ For additional context, in veterans receiving palliative care, but not actively dying, there was no difference in antipsychotic prescription rates between patients with or without PTSD.⁷⁹ We cannot be certain, but these studies suggest that the antipsychotics provided to veterans with PTSD in our study were newly ordered in response to symptoms in the imminently dying.

To potentially explain our observed association with PTSD and antipsychotics, PTSD has been associated with anesthesia emergence delirium^{80–82} and ICU delirium.^{83, 84} However, to date, PTSD has not been identified as a risk factor for terminal delirium,^{85, 86} which is treated first-line with antipsychotics.⁷⁴ A detailed discussion about the psycho-neuro-pathophysiology of PTSD and how it may predispose to delirium is beyond the context of this paper but has been described elsewhere.^{87–91} Briefly, in a semi-conscious state, an unknown stimulus, such as monitor beeping, is often interpreted as something dangerous, something to fear, especially in patients with PTSD. Generally, patients with PTSD are also less able to extinguish a fear response. Therefore, it is more likely that the continued fear response signal will cause physical agitation, such as pulling at tubes or lines. While some literature suggests that ICU exposure causes PTSD and not the opposite,^{48, 50} controlling for pre-existing PTSD or psychiatric illness removes this association.^{84, 92, 93}

Due to the high psychiatric comorbidity in PTSD and in our study, it was unsurprising that PTSD was not associated with the administration of opioids or with benzodiazepines in the last 7 days of life. By controlling for comorbid psychiatric diagnoses, we were attempting to isolate the effects of PTSD on end-of-life medication administration. However, in patients with multiple psychiatric diagnoses, attributing one specific symptom to one specific diagnosis can be challenging.^{94, 95} Still, we feel that the correlations observed between opioids and depression and benzodiazepines with depression and anxiety suggest that in the final days of life, psychiatric illness may contribute to symptom burden.

Table 4 Full Generalized Estimating Equation (GEE) Models, Including Covariates, for Odds of PTSD Associated with Administration of Each Listed Medication Class in Both Time Periods (in the Last 48 h of Life and in the Last 2–7 Days of Life)

Variables	Drug class GEE models							
	Opioids		Benzodiazepines		Antipsychotics	All three drug classes		
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
PTSD	1.18 (0.89–1.55)	0.192	1.06 (0.75–1.49)	0.703	1.52 (1.06–2.18)	0.030*	1.62 (0.48–5.46)	0.358
Year (vs 2011)		< 0.001 [†]		< 0.001 [†]		< 0.001 [†]		0.0046*
2005	0.93 (0.56–1.54)		0.80 (0.45–1.40)		0.62 (0.44–0.88)		0.32 (0.02–4.28)	
2006	0.78 (0.47–1.31)		0.69 (0.41–1.16)		0.59 (0.37–0.93)		0.24 (0.02–2.69)	
2007	0.73 (0.48–1.11)		0.79 (0.43–1.47)		0.41 (0.28–0.60)		0.10 (0.02–0.41)	
2008	0.80 (0.54–1.17)		0.77 (0.55–1.08)		0.48 (0.33–0.68)		0.22 (0.03–1.63)	
2009	0.90 (0.55–1.48)		0.90 (0.52–1.55)		0.53 (0.44–0.65)		0.41 (0.10–1.74)	
2010	0.95 (0.65–1.39)		0.92 (0.61–1.39)		0.55 (0.36–0.85)		0.36 (0.11–1.21)	
Non-intervention arm	0.89 (0.69–1.15)	0.298	1.19 (0.95–1.49)	0.098	0.75 (0.45–1.25)	0.21	1.05 (0.12–9.21)	0.954
Older age (by decade)	0.87 (0.81–0.93)	< 0.001 [†]	0.85 (0.80–0.91)	< 0.001 [†]	1.08 (0.96–1.21)	0.193	0.76 (0.61–0.95)	0.015*
White race	0.79 (0.62–1.02)	0.067	0.78 (0.66–0.92)	0.012*	0.92 (0.66–1.28)	0.53	0.99 (0.37–2.65)	0.97
Female gender	1.14 (0.57–2.26)	0.652	0.83 (0.39–1.74)	0.54	0.75 (0.35–1.62)	0.385	1.73 (0.34–8.96)	0.429
Anxiety	1.07 (0.84–1.37)	0.51	1.60 (1.19–2.14)	0.009*	1.12 (0.77–1.64)	0.472	1.42 (0.46–4.44)	0.462
Dementia	0.92 (0.59–1.43)	0.646	0.68 (0.48–0.95)	0.032*	1.65 (0.99–2.73)	0.052	2.03 (0.83–4.98)	0.099
Major depression	1.35 (1.13–1.61)	0.0075*	1.49 (1.14–1.94)	0.012*	1.49 (0.78–2.85)	0.178	1.27 (0.54–3.01)	0.506
Alcohol use disorder	0.98 (0.54–1.78)	0.943	2.15 (1.50–3.07)	0.003*	0.99 (0.43–2.29)	0.982	1.34 (0.29–6.24)	0.645
Schizophrenia	0.89 (0.58–1.37)	0.513	0.91 (0.59–1.39)	0.579	4.35 (2.42–7.81)	0.0013*	1.88 (0.34–10.49)	0.39
Drug use disorder	1.51 (1.002–2.27)	0.049*	1.45 (1.08–1.95)	0.022*	1.45 (0.55–3.79)	0.371	1.94 (0.80–4.73)	0.112
Non-cancer terminal diagnosis [‡]	0.45 (0.38–0.53)	< 0.001 [†]	0.85 (0.74–0.98)	0.032*	0.77 (0.52–1.15)	0.159	0.53 (0.28–1.004)	0.0509

PTSD post-traumatic stress disorder; CI confidence interval

*p value is statistically significant, $p < 0.05$

[†]p value < 0.0001 and statistically significant

[‡]Non-cancer terminal diagnosis includes all primary terminal diagnoses other than a cancer diagnosis

We also considered that symptom burden may lead to increased healthcare utilization. We found that VA hospitalizations in the last 12 months of life were increased in comparing patients with and without PTSD; ER visits were not statistically different. Generally, patients with psychiatric illness, including those with PTSD, have increased healthcare utilization,^{65–67} if they have adequate healthcare access and do not feel stigmatized.^{96, 97} As VA provides expertise in veteran issues, especially in PTSD,⁵¹ veterans may feel less stigma and more comfortable seeking VA care.^{98, 99} In contrast, in Washington state, patients with psychiatric illness had decreased inpatient and ICU utilization, with increased ER use in the last 30 days of life.¹⁰⁰ However, all psychiatric illnesses in this study were grouped together, which may not be ideal, as end-of-life care patterns can be more nuanced. For example, pre-existing depression was associated with earlier hospice use and less acute care in patients with lung cancer.¹⁰¹ A similar study found that patients with pre-existing depression or post-cancer depression both were more likely to use hospice than those without depression.¹⁰² However, patients with lung cancer and increased depression or anxiety symptoms were more likely to receive chemotherapy in the last 14 days of life.¹⁰³ Thus, further study of psychiatric illness and its impact on end-of-life healthcare utilization is needed.

It was unexpected that advanced directive documentation was more common in veterans with PTSD, because we had

hypothesized that avoidant coping in PTSD¹⁵ would decrease advance care planning (ACP). However, it is possible that repeated health system contact via higher utilization led to this finding.^{104, 105} In contrast, there was a trend towards veterans with PTSD being less likely to have a DNR order. Thus, it is difficult to discern the care choices made, or if PTSD impacted these choices. It is also possible that the BEACON intervention itself, emphasizing ACP and decreasing unwanted aggressive end-of life care, impacted our ACP findings.

We acknowledge that defining PTSD based on the patient problem list is a limitation. Our PTSD rate was 8.7%, with a median age of 65 for those patients, compared to lifetime PTSD prevalence of 3.7% for US veterans age 65 or older.⁶⁸ In VA, using ICD-9 codes to detect PTSD has a 72–84% positive predictive value.¹⁰⁶ Also, using ICD-9 codes for PTSD has been demonstrated to adequately separate patients with the most PTSD symptoms (true positives) from those with the least symptoms (true negatives),¹⁰⁷ symptoms being a dimension of interest in our study. However, without further information, PTSD rates using the problem list would be less than lifetime rates. Thus, our PTSD rate is likely an underestimate. However, an underestimate would bias the findings toward the null.

Further, our study focused on predominantly male veterans, dying within VA medical centers. Our findings only generalize

to similar settings, as patients dying at home may have different end-of-life symptoms and utilization patterns. Non-VA healthcare use was unaccounted for and could have influenced our utilization findings. Additionally, descriptions of patient symptoms, rationales for medication administration, and PTSD severity were lacking. Other possible confounders, such as chronic pain, traumatic brain injury, or socioeconomic disadvantage, could not be accounted for. The strengths of this study include its large sample size and detailed information about end-of-life care processes metrics. Also, with 31.6% African-Americans, this sample was more racially representative than other VA-based studies, important because of the higher PTSD rates noted in minorities.^{18, 68}

In conclusion, our findings provide new evidence suggesting increased symptom burden for individuals with PTSD at the end-of-life and that PTSD may be a separate risk factor for terminal delirium. Future studies should examine the impact of PTSD and other psychiatric illnesses on the end-of-life experience in all patient populations, not only veterans. The impact of symptom severity, prior treatment for psychiatric illness, physical and psychiatric comorbidities, and type of trauma experienced should also be considered.

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