Suicide Among Veterans Health Administration Patients With Bipolar Disorder:

Evidence for Increased Risk Associated With Benzodiazepine Receipt

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Abstract

Objective: To evaluate factors associated with suicide mortality among Veterans Health Administration (VHA) patients with bipolar disorder.

Methods: VHA patients diagnosed with bipolar disorder in calendar year (CY) 2014 who utilized VHA health care services in CY2013 were included in the study cohort. Suicide mortality in the 5 years following the first documented bipolar disorder diagnosis during CY2014 was examined using Cox proportional hazards regression.

Results: 725 of 126,655 VHA patients who had a bipolar disorder diagnosis in CY2014 (0.6%) died by suicide in the following 5 CYs (2014–2019). Suicide was associated with suicide high-risk flags (hazard ratio [HR] = 2.21), prior year emergency department visit (HR = 1.25), having a new bipolar disorder diagnosis (HR = 1.23), and receiving a benzodiazepine prescription of ≥30 days of supply (HR = 1.58). Prescriptions of benzodiazepines of <30 days of supply, other anxiolytics (ie, buspirone), and sedatives were not significantly associated with suicide mortality in the multivariable model.

Conclusions: Among VHA patients diagnosed with bipolar disorder, receipt of a benzodiazepine prescription of ≥30 days was associated with increased suicide risk, even after controlling for clinical and demographic factors. Elucidating mechanisms through which benzodiazepine prescriptions increase suicide risk is an important avenue for future investigations. Additionally, VHA patients with newly diagnosed bipolar disorder may benefit from increased clinical attention, given the elevated suicide risk among this subgroup. Findings highlight targets for suicide prevention initiatives.

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The Veterans Health Administration (VHA) is the largest integrated health care system in the United States.[1] Suicide prevention is a top clinical priority of the Department of Veterans Affairs[2] with US Veterans having a higher suicide rate than non-Veteran US adults.[3] Veterans in VHA care with bipolar disorder diagnoses are at elevated risk for suicide (suicide rate of 131.0 per 100,000 in calendar year [CY] 2021) relative to all US Veterans (suicide rate of 33.9 per 100,000).[3] Given the consistently elevated suicide risk observed among VHA patients with bipolar disorder, it is not surprising that bipolar disorder diagnostic status is included in predictive models within VHA to identify patients at highest risk for suicide.[4,5] Despite the elevated suicide risk among VHA patients with bipolar disorder, prior VHA suicide risk evaluations have not identified factors within the disorder that are associated with suicide. There remains a need to identify subgroups of patients with bipolar disorder who experience especially heightened risk for suicide to assist clinical management and surveillance efforts.

Extant investigations have found that VHA patients with bipolar disorder experience elevated suicide risk even after controlling for demographic and medical characteristics.[6–10] There is also evidence that the association between bipolar disorder and suicide among VHA patients persists beyond the impact of other psychiatric comorbidities. In a national sample of 2,962,810 male VHA patients, the risk of suicide during a 7-year follow-up period among those with bipolar disorder did not significantly increase when considering the impact of comorbid posttraumatic stress disorder (PTSD), substance use, depression, anxiety, and schizophrenia.[11]

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Clinical Points

- Veterans Health Administration patients with bipolar disorder are at increased risk for suicide, but little is known about factors driving suicide risk among this group.
- For patients with bipolar disorder, longer-term benzodiazepine prescriptions may increase risk for suicide.
- Patients with newly documented bipolar disorder should be carefully evaluated for suicide risk.

Beyond psychiatric comorbidity, other studies have found mixed evidence for medication receipt influencing suicide risk among VHA patients with bipolar disorder. To date, we are only aware of 1 study that used a national cohort of VHA patients with bipolar disorder to examine medication receipt and suicide mortality. In that study of 21,194 VHA patients initiating lithium or valproate, there were not significant differences in suicide mortality during a 1-year follow-up period between patients who initiated lithium vs patients who initiated valproate.[12] Other studies examining medication receipt and suicide among Veterans with bipolar disorder have found inconsistent results. For example, an observational study suggested that lithium may be associated with reduced risk for suicide and suicide attempts among Veterans with bipolar disorder.[13] Conversely, a randomized clinical trial among 519 Veterans comparing lithium to placebo found that lithium augmentation did not reduce suicide-related behaviors (inclusive of suicide mortality) among Veterans with bipolar disorder or depression.[14] Given these inconsistencies and the paucity of identified factors associated with suicide among VHA patients with bipolar disorder, there remains a need to identify factors associated with suicide among patients with bipolar disorder.

The current evaluation was designed to identify factors associated with suicide risk among patients with bipolar disorder to inform VHA suicide surveillance and treatment protocols. VHA patients who received a bipolar diagnosis in CY2014 were followed using administrative records for 5 years to examine measures associated with suicide. Analyses examined demographic, diagnostic, clinical, and VHA health care utilization metrics as associated with suicide mortality.

METHODS

Patient Cohort

Data from the VHA Corporate Data Warehouse were used to identify all VHA patients with a bipolar disorder diagnosis received during a VHA encounter in CY2014. Patients were assigned an index date corresponding to their first encounter with a bipolar diagnosis in CY2014. Patients were excluded if they (1) did not have VHA encounters in CY2013, (2) had a date of death on or before the index date, (3) had indications of having died outside the United States, or (4) were missing data on covariates. Based on these criteria, the final cohort included 126,655 patients with bipolar disorder. This evaluation was conducted as part of VHA's ongoing quality improvement efforts and evaluation of Veteran suicide and was therefore exempt from Institutional Review Board approval.

Measures

Demographic characteristics derived from administrative data included age (categorized as 18–34 years, 35–54 years, and ≥55 years), sex (male, female), race (White, Black, other/unknown), ethnicity (Hispanic, non-Hispanic), and marital status (married, nonmarried). Clinical characteristics assessed from the year prior to the index date (inclusive of the index date) included mental health comorbidities (schizophrenia spectrum disorder, other psychotic disorder, substance use disorder, posttraumatic stress disorder, generalized anxiety disorder, insomnia, personality disorders; see Table 1), the presence of a bipolar disorder diagnosis in CY2013, medical comorbidities (calculated using a count of modified Elixhauser[15] medical morbidity conditions after removing mental health conditions), homelessness status (defined as the presence of 1 or more *ICD-9* homelessness diagnoses [V60.0] or an encounter with stop codes for services for homeless Veterans), and having a high rate of missed appointments in the past year (missed ≥25% of appointments[4]). The receipt of a suicide high-risk flag, a flag integrated with VHA's electronic health record that populates whenever a patient's record is accessed, was also examined. Indicators of a high-risk flag include a recent suicide attempt, current acute suicidal ideation, and the presence of warning signs (eg, making preparations for a suicide attempt).[16] Further, service-connected disability rating was used as a covariate. Service-connected ratings are assigned based on disability experienced due to illnesses or injuries received or aggravated during military service.[17] Service-connected disability ratings range from 0%–100% and were categorized as 0% or no service connection, 10%–40%, and 50%–100% for this evaluation.

VHA health care utilization was assessed over the year prior to the index date (inclusive of the index date). Primary care receipt, mental health service receipt, emergency department (ED) visits, and psychiatric inpatient stays were examined. The receipt of antipsychotic, mood stabilizer, sedative/anxiolytic, and antidepressant medications was also examined over the year prior to the index date (inclusive of the index date; see Supplemental Table). Information on days of medication supply was obtained using the longest single prescription fill supply length for the medication classes.

Suicide mortality data were obtained from the VA/Department of Defense (DoD) Mortality Data Repository

Table 1.
***International Classification of Diseases, Ninth Revision* (*ICD-9*) Diagnosis Codes**

Diagnosis	*ICD-9* codes
Bipolar disorder	F296.0, F296.1, F296.4, F296.5, F296.6, F296.7, F296.8
Schizophrenia spectrum disorder	F295.0, F295.1, F295.2, F295.3, F295.4, F295.6, F295.7, F295.8, F295.9
Other psychotic disorder	F297.0, F297.1, F297.2, F297.3, F297.8, F297.9, F298.0, F298.1, F298.2, F298.3, F298.4, F298.8, F298.9
Substance use disorder	F303, F304.0, F304.1, F304.2, F304.3, F304.4, F304.5, F304.6, F304.7, F304.8, F304.9
Posttraumatic stress disorder	F309.81
Generalized anxiety disorder	F300.02
Insomnia	F780.51, F780.52, F327.00, F327.01, F327.02, F327.09
Personality disorder	F301.0, F301.11, F301.12, F301.20, F301.22, F301.4, F301.50, F301.6, F301.7, F301.81, F301.82, F301.83

(MDR).[18] The MDR contains cause and date of death information for all Veterans and VHA patients. Mortality in the MDR is determined via annual searches of death certificate data from the Centers for Disease Control and Prevention's National Death Index. Suicide death was indicated by underlying cause of death *ICD-10* codes: X60-X84, Y87.0, and U03.

Data Analytic Plan

Chi-square tests were used to examine differences between suicide decedents and the remainder of the cohort. Cox proportional hazards regression was then used to examine risk for suicide mortality. Risk time for each patient began the day following their first encounter with a bipolar diagnosis in CY2014 (their index date) and went through the 5 years following that date (1,825 days). Risk time concluded at the date of death (suicide or nonsuicide) or 5 years following their index date, whichever occurred first. Given the large cohort size and the desire to balance statistically significant effects with operational utility, hazard ratios (HRs) greater than 1.20 or less than 0.80 were considered to be practically meaningful for the hazards regression model.[10] Only results that were statistically significant and practically meaningful were discussed. Cox proportional hazards models were estimated after accounting for clustering by facility.

For any significant effects of psychotropic medication receipt (ie, antipsychotic, mood stabilizer, anxiolytic/sedative) in the proportional hazards models, follow-up analyses were conducted after subdividing by medication class to identify potentially meaningful subgroups. The benzodiazepine receipt variable was further subdivided into 3 mutually exclusive categories reflecting no benzodiazepine receipt, benzodiazepine prescriptions of <30 days, and benzodiazepine prescriptions of ≥30 days. The updated medication variables were then entered into a final multivariable Cox proportional hazards regression model along with all other measures.

RESULTS

Descriptive Statistics

Of the 126,655 VHA patients who were diagnosed with bipolar disorder during an encounter in CY2014, had a VHA encounter in CY2013, and had complete covariate data, 725 (0.6%) died by suicide in the following 5 years. In unadjusted bivariate analyses (Table 2), VHA patients with bipolar disorder who died by suicide were more likely to be 18–34 or 35–54 years of age (relative to 55+ years of age, risk ratios [RRs] = 1.42 and 1.29, respectively), be male (RR = 1.43), be White (vs Black = 3.09), be non-Hispanic (RR = 1.56), be not married (RR = 1.35), and have 0 medical comorbidities (RR relative to 1–2 comorbidities = 1.16 to ≥3 comorbidities = 1.41) relative to those who did not die by suicide. Further, patients who died by suicide were more likely to have suicide high-risk flags (RR = 3.06), homelessness indicators (RR = 1.21), and frequent missed appointments (defined as missing ≥25% of appointments, RR = 1.26) and be diagnosed with other psychotic disorders (RR = 1.40) or substance use disorders (RR = 1.40). Regarding service utilization, VHA patients with bipolar disorder who died by suicide were more likely to have ≥4 mental health encounters (as compared to 0 mental health encounters; RR = 1.35), ED visits (RR = 1.38), and psychiatric inpatient stays (RR = 1.84) and be prescribed an antipsychotic (RR = 1.22), mood stabilizer (RR = 1.20), or anxiolytic/sedative (RR = 1.49).

Survival Analysis

In a multivariable Cox proportional hazards regression model, receipt of an anxiolytic/sedative was associated with increased suicide risk (HR = 1.40). To better characterize the risk between anxiolytic/sedative receipt and suicide, this variable was subdivided according to medication class, resulting in

Table 2.

Characteristics of VHA Patients With Bipolar Disorder in Calendar Year 2014 by Suicide Outcomes (N = 126,655)

	Suicide decedents (n = 725)		All other VHA patients (n = 125,930)				
Characteristic	n	%	n	%	RR	χ^2	*P*
Age						15.14	<.001
18–34 y	109	15.03	15,449	12.27	1.42		
35–54 y	298	41.10	46,362	36.82	1.29		
55+ y	318	43.86	64,119	50.92	ref		
Female sex	93	12.83	21,987	17.46	0.70	10.75	<.001
Race						52.12	<.001
White	623	85.93	96,536	76.66	ref		
Black	39	5.38	18,758	14.90	0.32		
Other/unknown	63	8.69	10,636	8.45	0.92		
Hispanic ethnicity	26	3.59	6,900	5.48	0.64	5.00	.03
Married	217	29.93	46,137	36.64	0.74	13.97	<.001
Past-year bipolar disorder diagnosis	544	75.03	97,317	77.28	0.88	2.07	.15
Service connection (SC)						5.73	.06
No SC or SC at 0%	327	45.10	51,401	40.82	ref		
SC at 10%–40%	141	19.45	25,488	20.24	0.87		
SC ≥50%	257	35.45	49,041	38.94	0.82		
Medical comorbidities[a]						11.72	.003
Medical comorbidities: 0	233	32.14	34,529	27.42	ref		
Medical comorbidities: 1–2	320	44.14	55,455	44.04	0.86		
Medical comorbidities: ≥3	172	23.72	35,946	28.54	0.71		
Suicide risk flag status	72	9.93	4,338	3.44	3.06	90.24	<.001
Homelessness status	140	19.31	20,791	16.51	1.21	4.10	.04
Missed appointments ≥25%	334	46.07	50,832	40.37	1.26	9.74	.002
Schizophrenia spectrum disorder	60	8.28	9,608	7.63	1.09	0.43	.51
Other psychotic disorder	56	7.72	7,091	5.63	1.40	5.93	.01
Substance use disorder	246	33.93	33,811	26.85	1.40	18.39	<.001
Posttraumatic stress disorder	249	34.34	42,486	33.74	1.03	0.19	.73
Generalized anxiety disorder	53	7.31	8,000	6.35	1.16	1.11	.29
Insomnia	80	11.03	11,868	9.42	1.19	2.19	.14
Personality disorder	53	7.31	7,251	5.76	1.29	3.20	.07
PC encounters (≥ 1 PC encounter)	643	88.69	113,434	90.08	0.86	1.55	.21
MH encounters						14.69	<.001
0 MH encounters	58	8.00	12,313	9.78	ref		
1–3 MH encounters	158	21.79	33,865	26.89	0.99		
≥4 MH encounters	509	70.21	79,752	63.33	1.35		
ED visit	327	45.10	46,960	37.29	1.38	18.81	<.001
Psychiatric inpatient stay	121	16.69	12,293	9.76	1.84	39.14	<.001
Antipsychotic	396	54.62	62,506	49.64	1.22	7.17	.01
Mood stabilizer	432	59.59	69,351	55.07	1.20	5.94	.01
Anxiolytic/sedative	455	62.76	66,684	52.95	1.49	27.82	<.001
Antidepressant	453	62.48	73,313	58.22	1.19	5.39	.02

[a]Medical comorbidities were assessed through a raw count of Elixhauser conditions after excluding mental health conditions.

Abbreviations: ED = emergency department, MH = mental health, PC = primary care, RR = risk ratio, VHA = Veterans Health Administration.

variables reflecting benzodiazepine receipt (a categorical variable with mutually exclusive categories reflecting no benzodiazepine receipt, benzodiazepine prescription of <30 days, and benzodiazepine prescription of ≥30 days), buspirone receipt, and sedative receipt. The updated medication variables were entered into a final multivariable Cox proportional hazards regression model along with all other variables (see Table 3).

In the multivariable Cox proportional hazards regression model, increased suicide risk was associated with male sex (HR = 1.49), White race relative to Black race (HR = 3.23), non-Hispanic ethnicity (HR = 1.85), nonmarried status (HR = 1.30), the absence of a prior-year diagnosis of bipolar disorder (HR = 1.23), 0 medical comorbidities relative to ≥3 comorbidities (HR = 1.33), suicide high-risk flags (HR = 2.21), ED utilization (HR = 1.25), and receiving a benzodiazepine prescription

Table 3.

Measures Associated With Suicide Among VHA Patients With Bipolar Disorder (N = 126,655)

Measures	HR	95% CI		P	Meaningful difference[a]
		LL	UL		
Age 18–34 (ref: ≥55 years)	1.15	0.89	1.47	.29	No
Age 35–54 (ref: ≥55 years)	1.15	0.98	1.35	.08	No
Female sex (ref: male)	0.67	0.54	0.83	<.001	Yes
Black race (ref: white)	0.31	0.22	0.44	<.001	Yes
Other/unknown race (ref: White)	0.96	0.76	1.22	.76	No
Hispanic ethnicity (ref: non-Hispanic)	0.54	0.35	0.84	.006	Yes
Married (ref: other)	0.77	0.65	0.91	.002	Yes
No past-year bipolar disorder diagnosis (ref: prior diagnosis)	1.23	1.06	1.43	.008	Yes
Service connection at 10%–40% (ref : 0% service connection)	0.86	0.69	1.08	.20	No
Service connection ≥50% (ref : 0% service connection)	0.84	0.69	1.02	.07	No
Medical comorbidities 1–2 (ref: 0)[b]	0.88	0.72	1.06	.17	No
Medical comorbidities ≥3 (ref: 0)	0.75	0.60	0.93	.009	Yes
Suicide risk flag status (ref: no flag)	2.21	1.68	2.92	<.001	Yes
Homelessness status (ref: no homelessness service use or diagnosis)	0.92	0.76	1.11	.37	No
Missed appointments ≥25% (ref: <25% missed appointments)	1.15	1.01	1.32	.04	No
Schizophrenia spectrum disorder (ref: no schizophrenia)	0.98	0.75	1.28	.88	No
Other psychotic disorder (ref: no other psychotic disorder)	1.18	0.90	1.54	.26	No
Substance use disorder (ref: no substance use disorder)	1.13	0.96	1.33	.14	No
PTSD (ref: no PTSD)	0.93	0.79	1.09	.37	No
GAD (ref: no GAD)	0.90	0.70	1.16	.43	No
Insomnia (ref: no insomnia)	1.01	0.80	1.28	.93	No
Personality disorder (ref: no personality disorder)	0.95	0.71	1.28	.73	No
≥ 1 PC visits (ref: 0 PC encounters)	0.92	0.72	1.17	.48	No
1–3 MH encounters (ref: 0 MH encounters)	0.84	0.61	1.16	.29	No
≥ 4 MH encounters (ref: 0 MH encounters)	0.95	0.69	1.30	.75	No
≥ 1 ED visits (ref: 0 ED visits)	1.25	1.05	1.49	.01	Yes
≥ 1 Psychiatric inpatient stays (ref: 0 inpatient stays)	1.12	0.88	1.42	.36	No
Antipsychotic (ref: no antipsychotic)	1.08	0.92	1.26	.35	No
Mood stabilizer (ref: no mood stabilizer)	1.11	0.95	1.30	.20	No
Benzodiazepine <30 days (ref: no benzodiazepine)	1.30	0.95	1.79	.10	No
Benzodiazepine ≥30 days (ref: no benzodiazepine)	1.58	1.35	1.85	<.001	Yes
Buspirone (ref: no buspirone)	1.06	0.79	1.42	.72	No
Sedative (ref: no sedative)	1.09	0.95	1.26	.21	No
Antidepressant (ref: no antidepressant)	1.04	0.91	1.19	.58	No

[a]Meaningful differences were defined as differences that were statistically significant ($P < .05$) with a relative probability value of at least 0.2 greater than/less than 1.
[b]Medical comorbidities were assessed through a raw count of Elixhauser conditions after excluding mental health conditions.
Abbreviations: ED = emergency department, GAD = generalized anxiety disorder, HR = hazard ratio, LL = lower limit, MH = mental health, PC = primary care, PTSD = posttraumatic stress disorder, UL = upper limit, VHA = Veterans Health Administration.

of ≥30 days relative to no benzodiazepine prescription (HR = 1.58). Receipt of benzodiazepine prescriptions of <30 days relative to no benzodiazepine receipt, buspirone, and sedatives were not significantly associated with suicide mortality in the multivariable Cox proportional hazards regression model.

Cause of Death

Additional analyses were conducted to explore the relationship between benzodiazepine receipt and method of suicide (ie, overdose, all other methods; Table 4). Of the 725 suicide decedents, 140 (19.31%) died via intentional overdose. There was a significant association between benzodiazepine receipt and method of suicide, with participants receiving benzodiazepine prescriptions of <30 days and participants receiving benzodiazepine prescriptions of ≥30 days being more likely to die by suicide via overdose (RRs = 2.09, 1.62, respectively).

DISCUSSION

Ongoing VHA suicide surveillance efforts have identified VHA patients with bipolar disorder as having increased risk of suicide.[3] Although previous research has found that VHA patients with bipolar disorder have increased risk for suicide after controlling for myriad factors,[6–9] there have not been any large-scale evaluations of risk factors associated with suicide among this population. The current evaluation of a national cohort of VHA patients diagnosed with bipolar disorder identified several patient subgroups based on demographic and care receipt indicators that experienced

Table 4.

Measures Associated With Cause of Suicide Death Among VHA Suicide Decedents With Bipolar Disorder (N = 725)

	Suicide cause of death						
	Overdose (n = 140)		All others (n = 585)				
	n	%[a]	n	%	RR	χ^2	*P*
Benzodiazepine prescription							
No	63	15.04	356	84.96	–	12.64	.002
Yes ≤29 d	11	31.43	24	68.57	2.09	–	–
Yes ≥30 d	66	24.35	205	75.65	1.62	–	–

[a]Row percents are displayed.
Abbreviations: RR = risk ratio, VHA = Veterans Health Administration.

heightened suicide risk. In the multivariable model, suicide risk was associated with demographic factors (ie, male sex, White race [vs Black race], non-Hispanic ethnicity, nonmarried status), clinical characteristics (ie, past-year bipolar disorder status, 0 medical comorbidities [relative to ≥3 comorbidities], suicide high-risk flags), and VHA service utilization (ie, ED utilization receiving a benzodiazepine prescription of ≥30 days). Previous investigations using national VHA cohorts have similarly found that male sex,[3,4,7,19] White race,[3,19] non-Hispanic ethnicity,[3] nonmarried status,[4] suicide high-risk flags,[16] and ED utilization[4] were associated with suicide mortality among VHA patients. Increased suicide rates among White, non-Hispanic, nonmarried males have been attributed to distress associated with economic and social hardship resulting in "deaths of despair,"[20–22] which could explain the elevated suicide risk associated with these variables in this evaluation. Regarding medical comorbidities, certain medical conditions are associated with *increased* suicide risk among Veterans (eg, chronic obstructive pulmonary disease, traumatic brain injury), and other conditions are associated with *decreased* suicide risk (eg, coronary artery disease, diabetes mellitus).[4] As the number of medical comorbidities was inversely related to suicide in this sample, future studies may benefit from examining the contribution of individual conditions on suicide risk among Veterans with bipolar disorder. Together, this evaluation is consistent with prior studies and extends those findings to VHA patients with bipolar disorder.

In multivariable analyses, receipt of an anxiolytic/sedative was associated with increased suicide risk. This finding is consistent with extant national evaluations of all VHA patients.[4,23] Among the medication classes that comprise anxiolytics and sedatives, the relations between benzodiazepine receipt and suicide has garnered particular attention. Research on benzodiazepines and suicide generally[24] and among VHA patients with PTSD,[25] women VHA patients ≥50 years of age,[26] Veterans with HIV,[27] and VHA patients using Home Based Primary Care services[28] suggests that benzodiazepine receipt is associated with an increased risk for suicide. Therefore, the results from the current evaluation are consistent with prior studies. More specifically, the current results suggest that the receipt of benzodiazepine prescriptions of ≥30 days is driving the relations between benzodiazepine receipt and suicide mortality among VHA patients with bipolar disorder. Further, VHA patients prescribed benzodiazepines (with prescriptions of any duration) were more likely to die by suicide via overdose relative to patients not prescribed benzodiazepines. Therefore, suicide safety planning practices among VHA patients with bipolar disorder who are prescribed benzodiazepines may benefit from safety planning related to substance use.

Recognizing the risk of benzodiazepine receipt on multiple deleterious outcomes, VHA has implemented benzodiazepine deprescribing practices.[29–31] Care should be made to ensure that deprescribing efforts extend to VHA patients with bipolar disorder, due to the elevated suicide risk associated with benzodiazepine receipt. Given evolving treatment guidelines, future work should evaluate whether changes in benzodiazepine prescribing results in changes in overall suicide risk among VHA patients with bipolar disorder. Consideration should also be made to evaluate possible fluctuations in the receipt of other pharmacologic treatments for anxiety (eg, buspirone) during the same period.

Patients who did not have a past-year diagnosis of bipolar disorder were also at heightened risk for suicide. This finding could potentially be due to increased psychosocial stress experienced by patients newly diagnosed with bipolar disorder. Qualitative findings suggest that patients with new-onset bipolar disorder experience multiple stressors, such as medication side effects, difficulties identifying warning signs and triggers for their symptoms, loss of autonomy, uncertainty about their future, and stigma.[32] However, some members of this cohort may have been diagnosed with bipolar disorder previously but were not identified due to low service

utilization during the period when covariates were identified. Given inconsistent patterns of health system retention for VHA patients with bipolar disorder,[33,34] VHA has implemented programs to enhance reengagement following loss to care among VHA patients with serious mental illness (inclusive of bipolar disorder).[35,36] The present work indicates that patients who were diagnosed with bipolar disorder without a past-year diagnosis (whether due to new-onset disease or gaps in service utilization) may warrant increased monitoring for suicide risk.

Notably, comorbid psychiatric diagnoses were not significantly associated with suicide in the current evaluation. This finding is consistent with analyses conducted by Conner et al[11] that found that comorbid psychiatric diagnoses did not significantly increase suicide risk among VHA patients with bipolar disorder. This was attributed to several mechanisms, including transdiagnostic processes that contribute to multiple forms of psychopathology, challenges with differential diagnosis, symptom interplay, and the increased clinical attention and service utilization of patients with greater disease burden.[11,37–39] The present work provides further indication that the presence of psychiatric comorbidities does not significantly alter suicide risk among VHA patients with bipolar disorder.

The current evaluation has several limitations. First, administrative health records were the sole source of data for this evaluation. Therefore, we were unable to identify diagnostic status using a standardized approach (eg, structured clinical interview). Given the observational nature of these findings, it is unclear if the increased suicide risk associated with benzodiazepine receipt is due to the medication itself or possible indications for medication prescriptions not consistently captured in the medical record (eg, agitation). Further, these analyses are constrained by limitations of administrative data, such as heterogeneous detection opportunities across levels of care. Therefore, it is likely that certain VHA patients who experienced bipolar disorder during this time period were not detected due to a lack of VHA service utilization. Additionally, the lack of available information on mental health and condition-specific severity limits interpretation of the impact of mental health conditions and suicide, given considerable variation in symptom presentation across bipolar disorder and other mental health covariates of interest.[40–42] Also, indicators of medication receipt were based on outpatient prescriptions dispensed to patients, and medication compliance data were not available. Finally, benzodiazepines are among the most commonly used drugs in suicides via overdose.[43] Therefore, access to benzodiazepines as a lethal mean for suicide, an independent suicide risk factor,[44] may contribute to the increased risk for suicide among VHA patients with bipolar disorder receiving benzodiazepines. Despite these limitations, the current work informs targets for suicide prevention initiatives to enhance care provided to VHA patients who are diagnosed with bipolar disorder.

This evaluation is the first to identify subgroups of VHA patients with bipolar disorder who experience particularly elevated suicide risk. Among patients with bipolar disorder, we found that male sex, White (relative to Black) race, non-Hispanic ethnicity, nonmarried status, lack of a past-year diagnosis of bipolar disorder, no recorded medical comorbidities (relative to ≥3 comorbidities), suicide high-risk flags, ED service utilization, and benzodiazepine prescription receipt of ≥30 days were associated with increased suicide risk. Efforts to decrease suicide among this high-risk population may benefit from providing additional support for patients with newly diagnosed bipolar disorder. Among patients prescribed longer-term benzodiazepines, careful clinical monitoring of suicide risk is warranted, and subsequent evaluations should seek to classify the multifactorial care pathways that result in benzodiazepine prescriptions among this population. Together, this evaluation elucidates potential targets for the advancement of suicide monitoring and prevention efforts for VHA patients diagnosed with bipolar disorder.

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Additional Information: Information on accessing the Veterans Health Administration Corporate Data Warehouse can be found at https://www.hsrd.research.va.gov/for_researchers/cdw.cfm.

Supplementary Material: Available at Psychiatrist.com.

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Supplementary Material

Article Title: Suicide Among Veterans Health Administration Patients With Bipolar Disorder: Evidence for Increased Risk Associated With Benzodiazepine Receipt

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LIST OF SUPPLEMENTARY MATERIAL FOR THE ARTICLE

1. Table 1 Medication Variable Definitions
2. Figure 1 Distribution of Suicide Deaths During the Follow-Up Period, per 91-Day Quarter

DISCLAIMER

This Supplementary Material has been provided by the authors as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary Table 1. Medication variable definitions

Medication class	Medications
Antipsychotic	aripiprazole, asenapine, chlorpromazine, clozapine, fluphenazine, haloperidol, iloperidone, loxapine, lurasidone, olanzapine, paliperidone, perphenazine, pimozide, prochlorperazine, quetiapine, risperidone, thioridazine, thiothixene, trifluoperazine, ziprasidone
Mood stabilizer	carbamazepine, divalproex, lamotrigine, lithium, oxcarbazepine, topiramate, valproic acid
Anxiolytic/sedative	
Benzodiazepine	alprazolam, chlordiazepoxide, clonazepam, clorazepate, diazepam, estazolam, flurazepam, halazepam, lorazepam, midazolam, oxazepam, prazepam, quazepam, temazepam, triazolam
Non-benzodiazepine anxiolytic	buspirone
Sedative	doxepin, eszopiclone, melatonin, ramelteon, trazodone, zaleplon, zolpidem
Antidepressant	amitriptyline, amoxapine, bupropion, citalopram, clomipramine, desipramine, desvenlafaxine, doxepin, duloxetine, escitalopram, fluoxetine, fluvoxamine, imipramine, isocarboxazid, levomilnacipran, maprotiline, mirtazapine, nefazodone, nortriptyline, paroxetine, phenelzine sulfate, protriptyline, selegiline, sertraline, tranylcypromine, trimipramine, venlafaxine, vilazodone, vortioxetine

Supplementary Figure 1. Distribution of suicide deaths during the follow-up period, per 91-day quarter