Predictors of Benzodiazepine Re-Prescription Among U.S. Veterans with a History of Chronic Benzodiazepine Use

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Abstract

Objective: Given difficulty in discontinuing prescribed benzodiazepines and potential harms to people from chronic benzodiazepine use, it is important to understand medical and mental health conditions associated with re-prescription. This study sought to estimate benzodiazepine re-prescription incidence rates among Veterans in the United States Veterans Health Administration (VHA) and identify predictors of re-prescription among Veterans who discontinued benzodiazepines. **Methods:** This longitudinal study used VHA administrative data from patients' electronic health records in Fiscal Year 2019. Patients with chronic (>30 days) benzodiazepine prescriptions who were not prescribed benzodiazepines continuously for the entire year were identified based on pharmacy records (n=151,777). We used Kaplan-Meier methods and a Cox proportional hazards model to estimate benzodiazepine re-prescription incidence rates. Unadjusted and adjusted hazard ratios were used to examine demographic and clinical characteristics as predictors of benzodiazepine re-prescription. **Results:** Among 151,777 patients who did not refill a benzodiazepine prescription for [?]30 days, 50% were re-prescribed benzodiazepines within 2.5 months. Benzodiazepine re-prescription was associated with mental health conditions (e.g., anxiety, PTSD). Patients were less likely to be re-prescribed benzodiazepines if they had a history of an alcohol or drug use disorder, neurological disorder other than paralysis, chronic heart failure, dementia, and hospice care. **Conclusions:** The short gap between benzodiazepine prescriptions ending and being re-prescribed suggests patients have difficulty discontinuing prescribed benzodiazepines. More investigations are needed on the medical necessity of chronic benzodiazepines and strategies for increasing guideline concordant care.

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Methods: This longitudinal study used VHA administrative data from patients' electronic health records in Fiscal Year 2019. Patients with chronic (>30 days) benzodiazepine prescriptions who were not prescribed benzodiazepines continuously for the entire year were identified based on pharmacy records (n=151,777). We used Kaplan-Meier methods and a Cox proportional hazards model to estimate benzodiazepine re-prescription incidence rates. Unadjusted and adjusted hazard ratios were used to examine demographic and clinical characteristics as predictors of benzodiazepine re-prescription.

Results: Among 151,777 patients who did not refill a benzodiazepine prescription for [?]30 days, 50% were re-prescribed benzodiazepines within 2.5 months. Benzodiazepine re-prescription was associated with mental health conditions (e.g., anxiety, PTSD). Patients were less likely to be re-prescribed benzodiazepines if they had a history of an alcohol or drug use disorder, neurological disorder other than paralysis, chronic heart failure, dementia, and hospice care.

Conclusions: The short gap between benzodiazepine prescriptions ending and being re-prescribed suggests patients have difficulty discontinuing prescribed benzodiazepines. More investigations are needed on the medical necessity of chronic benzodiazepines and strategies for increasing guideline concordant care.

Key Words: Benzodiazepine, Prescription, Incidence, Hazard Model, Associated Conditions, US Veterans.

KEY POINTS

1. Using VHA administrative data from patients' electronic health records, this longitudinal study was conducted to estimate benzodiazepine re-prescription incidence rates.
2. One-half of patients were re-prescribed benzodiazepines within 2.5 months after discontinuation.

3. Anxiety, PTSD, sleep apnea, and oncology conditions were associated with higher benzodiazepine re-prescription.
4. Psychoses, alcohol and drug use disorders, insomnia, dementia, and hospice were associated with lower benzodiazepine re-prescription.
5. The challenges of chronic benzodiazepine use, and re-prescription remain high among patients, and it is critical to develop strategies to increase guideline concordant care.

Plain Language Summary

We used VHA administrative data from patients' electronic health records to estimate benzodiazepine re-prescription incidence rates and identify predictors of re-prescription among Veterans who discontinued benzodiazepines. Among patients who did not refill a benzodiazepine prescription for [?]30 days (at risk for benzodiazepine refill), 50% were re-prescribed benzodiazepines within 2.5 months. While Benzodiazepine re-prescription was associated with mental health conditions such as anxiety, and PTSD; Benzodiazepine re-prescription was less likely if patients had a history of an alcohol or drug use disorder, neurological disorder other than paralysis, chronic heart failure, dementia, and hospice care.

Introduction

Benzodiazepines are considered safe and effective for short-term use (about 2-4 weeks) to treat anxiety disorders, alcohol withdrawal, insomnia, muscle-stretching, and seizures [1-3], but lack long-term effectiveness and can have harmful effects (e.g., increased risk of falls in older patients) [4]. However, healthcare providers are prescribing benzodiazepines for longer periods[1,5]. Longer-term prescribing is a growing public health problem [5,6] because it goes against clinical guidelines and contributes to benzodiazepine-related overdose deaths and emergency room visits [7]. Benzodiazepines are the third most common illicit or misused prescription substance among adults and adolescents [7].

There is no consensus in the literature for defining chronic or long-term benzodiazepine use, which ranges from >30 to >120 days of benzodiazepine supply [8-10]. It takes about a month to become physically dependent on benzodiazepines, even on small, therapeutic doses [11]and clinical guidelines advise against using benzodiazepines for more than 4 weeks [12,13]. Benzodiazepine treatment for insomnia should not exceed 2 weeks, as studies show sleep patterns return to pre-treatment levels after only a few weeks of regular use[14,15]. For anxiety, continuing beyond 2 weeks results in reduced effectiveness, increased tolerance or dependence, withdrawal symptoms, persistent adverse effects, and interference with counseling effectiveness [15,16]. Addressing the reasons benzodiazepines are re-prescribed early could avoid normalizing long-term benzodiazepine use.

Due to physical dependence and subsequent withdrawal symptoms, discontinuing benzodiazepines can be challenging for patients and contribute to re-prescription after discontinuation. Depending on the type of benzodiazepine (short or long-acting), dose, and duration, withdrawal symptoms typically last for up to 2-3 weeks following discontinuation [17]. However, benzodiazepine craving may last for 6 months and is an independent factor in relapse after discontinuation of long-term benzodiazepine use [18]. A prior Veterans Health Administration (VHA) study indicated a short benzodiazepine re-prescription period ranged from 1.62 to 8.17 days without any dose changes [19]. Benzodiazepine discontinuation difficulties among Veteran patients could be explained by a combination of factors including benzodiazepine overprescribing and misuse [20].

Benzodiazepine discontinuation difficulties among patients can be difficult to distinguish from undertreated mental health or medical conditions [20]. Given the harms of benzodiazepine use, it is important to identify the most common mental health and medical conditions among patients who are re-prescribed a benzodiazepine after not refilling their benzodiazepine prescription for at least 30 days. Identifying these mental health and medical conditions could help suggest better treatment strategies and prevent longer-term prescribing. This study's objectives were to estimate the incidence rate for benzodiazepine re-prescription and identify predictors of re-prescription among Veteran patients who had discontinued benzodiazepines for at least 30 days.

Methods

Data Source and Study Cohort

After Institutional Review Board approval, outpatient benzodiazepine use was obtained from VHA's Corporate Data Warehouse (CDW) for VHA-enrolled patients in Fiscal Year (FY) 2019 (10/1/2018-9/30/2019)[1]. CDW outpatient pharmacy files included benzodiazepine type and quantity prescribed, dose, number of days supplied, and pharmacy release date.

Although there are varying definitions of chronic benzodiazepine use, we defined chronic benzodiazepine use as >30 consecutive days supply during FY2019 to be consistent with clinical guidelines[1,4,21]. The number of days a patient was prescribed benzodiazepines was identified based on pharmacy fills beginning 3 months prior to FY2019 to ensure the study accounted for benzodiazepine prescriptions dispensed before the FY began [8]. Patients who were prescribed benzodiazepines for 12 consecutive months (continuous prescription group) were excluded from study (Figure 1). We used benzodiazepine dispensed date and days supply to expand the dataset at a daily level and identified how many days patients were on and off benzodiazepines in FY2019.

[Figure 1]

We estimated "time to re-prescription" based on a period of discontinuation due to not refilling a 30-day prescription. Benzodiazepine re-prescription incidence rate was the proportion of people with chronic benzodiazepine use who were re-prescribed any benzodiazepine after >30 days of discontinuation during FY2019. We considered the first benzodiazepine re-prescription among patients who met these re-prescription criteria multiple times during FY2019. We used >30 days of benzodiazepine discontinuation prior to re-prescription for three reasons: 1) To avoid administrative error related to undocumented prescriptions or inclusion of patients with only minor delays in a prescription refill or reporting of prescriptions from alternative sources (usually benzodiazepines are prescribed in a monthly pattern); 2) To increase the likelihood that patients no longer had benzodiazepines from previous prescriptions; and 3) To increase the likelihood that patients were no longer experiencing withdrawal symptoms when re-prescribed [11].

Demographics, Benzodiazepine History, and Health Conditions

Patients' demographic characteristics at baseline (10/1/2018), obtained from VA CDW, are detailed in Appendix 1, and include sex, age, race and ethnicity, and marital status. Benzodiazepine history was captured by total number of years patients were prescribed benzodiazepines since enrolled in VHA. Benzodiazepine dose for FY2019 was calculated by estimating daily diazepam-equivalent (DDE) for all benzodiazepines[8]. Health conditions (listed on Table 1) were determined by ICD-10 diagnosis codes based on the conditions that benzodiazepines are most likely to be used to treat and conditions where they are contraindicated or may cause adverse effects (Appendix 1).

Analysis

The demographic and clinical characteristics of Veteran patients with benzodiazepine re-prescriptions in FY2019 are in Table 1. We compared characteristics of patients with continuous benzodiazepine prescriptions, which is excluded, to those with benzodiazepine re-prescriptions to assess the patients at risk for benzodiazepine re-prescriptions (Appendix 2). We estimated overall benzodiazepine re-prescription incidence rates and risk-specific subgroups (defined by demographic characteristics and health conditions) using Kaplan-Meier methods. We used Cox proportional hazards models to calculate unadjusted and adjusted hazard ratios (HR) for benzodiazepine re-prescription incidence, controlling for demographics (age, sex, marital status, insurance, and death in FY2019), years of benzodiazepine prescription in VA, and DDE average dose. Finally, using adjusted Cox proportional hazards models, we conducted sensitivity analyses to compare patient subgroups with different lengths of discontinuation (< 3 months vs. [?] 3 months) before benzodiazepine re-prescription to assess early benzodiazepine remission (other than craving), which is defined as a period [?]3 months but <12 months without benzodiazepine use [22].

Results

Benzodiazepine Re-prescription

During FY2019, a total of 211,714 patients enrolled in VHA health care were prescribed benzodiazepines for >30 days in the outpatient setting, and 71.69% (n=151,777) of these patients were identified as subsequently discontinuing benzodiazepines for at least 30 days. As shown in Table 1, Veterans who were at risk for benzodiazepine re-prescription were mostly men (84.48%), > 65 years old (47.70%), and white (72.67%). Of the patients with benzodiazepine re-prescriptions, 32% did not have any documented ICD codes of anxiety disorders, PTSD, sleep disorders, and alcohol use disorder, as primary indicators for benzodiazepine prescription, in FY2019 (data not shown).

[Table 1]

Re-prescription Incidence Rate Overall and by Demographic Subgroups

Among 151,777 Veterans who were identified as discontinuing chronic benzodiazepine use for at least 30 days, the re-prescription incidence rate was 19.77 (95% confidence interval [CI]: 19.65, 19.9) per 100 person-months of observations (PMO) during FY2019 (Table 2). Benzodiazepine re-prescription incidence among younger Veterans (<45 years old) was 17.97 (CI95%: 17.71, 18.24) per 100 PMO, which was significantly lower compared to older Veterans (45-65 YO: 20.62 [CI95%: 20.4, 20.84]; >65 YO: 19.93 [CI95%: 19.75, 20.11]). Benzodiazepine re-prescription incidence (per 100 PMO) among Hispanic or Latino Veterans was 21.66 (CI95%: 21.22, 22.11), which was significantly higher compared to Whites (19.61 [CI95%: 19.47, 19.76]). We observed higher benzodiazepine re-prescription incidence among Veterans who were married, were government insurance holders (Medicare/Medicaid/supplementary), had a DDE average dose of >30 mg/day, and were prescribed benzodiazepines for >3 years. No sex differences were found for benzodiazepine re-prescription incidence (Table 2).

[Table 2]

Figure 2 illustrates that 25%, 50%, and 75% of patients were re-prescribed a benzodiazepine after 1.35, 2.37, and 9.40 months of discontinuation, respectively. Only 22% of Veterans who discontinued benzodiazepines for at least 30 days were not re-prescribed a benzodiazepine through the end of the follow-up period (FY2019).

[Figure 2]

Health Conditions and Benzodiazepine Re-prescription

Table 3 summarizes associations between health conditions and benzodiazepine re-prescription, controlling for demographic characteristics and prescription duration and dose. Table 3 provides sensitivity analysis results comparing benzodiazepine discontinuation subgroups at <3 months (n=94,821) or [?]3 months (n=56,002), and notes how benzodiazepine re-prescription varied by discontinuation length among Veterans with psychosis, bipolar disorder, insomnia, and opioid prescription.

[Table 3]

Mental Health Disorders. After adjusting for demographic characteristics, both anxiety and PTSD were associated with higher rates of re-prescription (HR=1.08 (CI 95%: 1.07, 1.1); Table 3). Patients with psychosis had a 2% higher hazard of re-prescription within 3 months of discontinuation and a 10% lower hazard for re-prescription after at least 3 months of discontinuation. Also, a diagnosis of bipolar disorder was associated with an 8% decrease in re-prescription hazard after discontinuation of [?]3 months. Alcohol and drug use disorders were associated with a reduced hazard of benzodiazepine re-prescription. Opioid prescriptions were also associated with a 19% decrease in re-prescription after [?]3 months of benzodiazepine discontinuation.

Sleep disorders. As shown in Table 3, insomnia was associated with a 7% decrease in benzodiazepine re-prescription after [?]3 months of discontinuation. We observed a 2% higher rate of benzodiazepine re-prescription among Veterans with sleep apnea regardless of the length of discontinuation.

Other Medical Conditions. Benzodiazepine re-prescription was 8% less likely among patients with neurological disorders other than paralysis, compared to those without these disorders. Oncology clinic patients were 21% more likely to be re-prescribed a benzodiazepine after ≥3 months discontinuation. However, we observed a 15% lower benzodiazepine re-prescription rate in patients receiving hospice and a 20% lower benzodiazepine re-prescription rate in patients with dementia.

Discussion

Among Veteran patients with a history of chronic benzodiazepine use in FY2019, one-half were re-prescribed benzodiazepines within 2.5 months of discontinuing. Only 22% of patients who discontinued benzodiazepines for at least 30 days were not re-prescribed benzodiazepines through the end of the follow-up period (FY2019), and re-prescription incidence rates were 20 per-100-PMO in the VHA. Results, together with previous findings from Voshaar's randomized controlled trial [10]on benzodiazepine abstinence, support implementation of VHA's initiatives to help identify how clinicians can better manage benzodiazepine withdrawal and train providers to offer Cognitive Behavioral Therapy (CBT). CBT has an important role in treating several mental health and medical conditions associated with long-term benzodiazepine use including anxiety, insomnia, and PTSD [23-27]. Like Voshaar's trial[10], our study found benzodiazepine discontinuation was associated with a lower daily benzodiazepine dosage (<10 mg of diazepam equivalent). This result suggests preventative strategies are needed to keep patients on lower benzodiazepine dosages for shorter durations which could help avoid re-prescription.

Despite known risks of benzodiazepine use among older people, including risk of falls [28], older Veterans (i.e., [?]45 years old) were more likely to be continuously prescribed [1,5] as well as re-prescribed benzodiazepines. However, benzodiazepine re-prescription incidence rates among patients older than 65 were slightly lower compared with those of patients aged 45-65 years old. Our previous study showed that compared to Veteran patients who discontinued benzodiazepines, Veteran patients who continued were more often White or Hispanic [1]. The present study found Hispanic patients were more likely to be re-prescribed benzodiazepines after discontinuation compared to Whites. Although the present study did not observe any sex difference in benzodiazepine re-prescription, it observed higher rates of benzodiazepine re-prescription in Veterans who were married (vs. not married), had other governmental insurance (Medicare/Medicaid/supplementary), and had been taking benzodiazepines for a longer duration and at a higher dose.

Mental Health Disorders

This study provides new insights on benzodiazepine re-prescription by considering the role of different medical and mental health conditions, not previously studied in-depth. Consistent with previous studies[29], our results suggest Veteran patients diagnosed with anxiety have a higher chance of benzodiazepine re-prescription and may benefit from additional/alternative treatment for managing anxiety such as non-benzodiazepine anxiolytics and CBT [30]. We also observed a higher likelihood of benzodiazepine re-prescription among Veterans with PTSD despite VHA/DoD's (Department of Defense) 2017 practice guidelines that do not recommend routine use of benzodiazepines for these patients due to negative impacts on trauma recovery and treatment [27]. A systematic review [24]found benzodiazepines are ineffective for PTSD treatment and contribute to worsened symptom severity, psychotherapy outcomes, aggression, depression, and substance use [24]. Factors contributing to benzodiazepine re-prescription in patients with PTSD should be studied further to better understand clinical indications against benzodiazepine prescription or discontinuation and to minimize negative side-effects.

The results also suggest some conditions may be differentially associated with hazard of benzodiazepine re-prescription depending on length of discontinuation. In psychosis, higher rates of benzodiazepine re-prescription after short-term discontinuation (i.e., <3 months) could be explained by unplanned or temporary benzodiazepine treatment. But in the long-term (i.e., at least 3 months of discontinuation), we observed lower benzodiazepine re-prescription rates for Veteran patients with psychosis and bipolar disorders. Benzodiazepines may be prescribed for acute psychosis-induced aggression or agitation, although its use for this purpose is not universally agreed upon [31]. Fewer benzodiazepine re-prescriptions in the long-term could be

explained by providers' agreement on the short-term advantage of benzodiazepines and no longer prescribing benzodiazepines after stabilizing a patient's mood or psychosis [32]. Our findings also indicate less benzodiazepine re-prescription in Veterans with opioids and alcohol use disorder. Previous studies have shown co-prescription of opioids and benzodiazepines is associated with increased all-cause mortality and overdose death in VHA and in the U.S. overall [33,34]. We found after long-term benzodiazepine discontinuation ([?]3 months), Veterans with prior opioid prescriptions were 19% less likely to be re-prescribed benzodiazepines, which is consistent with VA/DoD clinical practice guidelines discouraging co-prescribing benzodiazepines and opioids [35].

Sleep disorders

Benzodiazepines used to be first-choice hypnotics for treating insomnia[36]. However, currently, CBT for insomnia is the first-line therapy, and using pharmacologic agents as adjuvant therapy in the short-term has been found unsuccessful[25,26,37,38]. Our observation that insomnia was not associated with short-term re-prescription, and was associated with a lower likelihood of longer-term re-prescription, is consistent with recommended guidelines

Other Medical Conditions

Patients with prior cancer care had higher rates of benzodiazepine re-prescription after longer-term discontinuation, whereas patients in hospice care had an overall reduced rate of re-prescription. Nausea, pain, and anxiety may be treated simultaneously with benzodiazepines in patients receiving chemotherapy and patients with end stage cancer may develop delirium during their final days of life [39], which may account for higher re-prescription rates for patients receiving cancer care [40]. The reasons for fewer benzodiazepine re-prescriptions among Veterans receiving hospice care should be further investigated. However, reduced benzodiazepine re-prescriptions could be due to Veterans in hospice care receiving high amounts of opioids for pain [41].

The benzodiazepine re-prescription rate was lower in Veterans with than without dementia. A meta-analysis found benzodiazepines significantly increase risk of dementia in the elderly population and worsens dementia symptoms [42]. Accordingly, clinicians usually avoid prescribing benzodiazepines to older people with dementia[43].

Limitations

The data are limited to the VHA and FY2019. The electronic health record (EHR) system in VHA allowed us to include reliable study measures, including benzodiazepine prescription frequency and intervals, however patients may receive additional medications or treatment outside the VHA system. Results are limited to characteristics and conditions within EHRs, which means we were unable to identify reasons for failed benzodiazepine discontinuation and re-prescription in VHA (administrative error; provider discontinued and re-prescribed benzodiazepine; or the patient missed a prescription, received it from another sources, as needed (PRN) or used medications left over from a previous prescription). We focused on demographic characteristics and mental health and medical conditions predicting benzodiazepine re-prescription, and further study with chart review, in-depth interviews, and/or surveys are needed to investigate reasons for discontinuation and re-prescription and factors increasing benzodiazepine re-prescription. Such studies should include provider and patient perspectives and other biological, social, and structural factors.

Conclusions

This study found that 50% of Veteran patients with chronic benzodiazepine prescriptions were re-prescribed benzodiazepines within 2.5 months of discontinuation. The medical necessity of benzodiazepine use for about one-third of patients in our cohort is not clear since they did not have a history of anxiety disorders, PTSD, sleep disorders, or alcohol use disorders, which are the most common indications for benzodiazepines [2]. The short time between benzodiazepine discontinuation and re-prescription suggests; 1- providers may have difficulty discontinuing patients, or 2- patients may be experiencing benzodiazepine dependence or cravings[18,20]. Given that patients with anxiety disorders or sleep disorders [44], may be highly susceptible to

long-term benzodiazepine use, non-benzodiazepine alternative treatments (i.e., Z-drugs or Buspirone) should be offered for sleep problems[45] and anxiety [30,45]. Benzodiazepine re-prescription could be attributable to continuation of care for flare-ups of symptoms and re-initiation of benzodiazepine treatment in mental health conditions such as anxiety and PTSD [29]. Consistent with VHA's Whole Health approach to care[46], VHA has lower benzodiazepine re-prescription rates among Veterans with alcohol or drug use disorder (than those without these disorders), dementia (than among patients without dementia), and receiving hospice (than those not in hospice). However, benzodiazepine re-prescription is more likely among Veteran patients who are >45 years old, Hispanic, married, and have been taking higher doses for longer durations. Tailored provider and patient support after benzodiazepine discontinuation may reduce benzodiazepine re-prescription [47]. Successful benzodiazepine discontinuation regimens should be co-designed with patients and emphasize that benzodiazepines should not continue indefinitely[48].

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Figure 1. Study flow chart.

Table 1: Demographic and clinical characteristics of Veteran patients with benzodiazepine re-prescriptions (more than 30 days) in 2019 (N=151,777).

Age
Sex (male)
Race/Ethnicity
Marital Status
Insurance
Anxiety disorders
PTSD
Psychoses
Depression
Bipolar Disease
Alcohol Abuse
Drug Abuse
Any Opioids prescriptions 2019
Insomnia
Sleep Apnea
Valvular Disease
Pulmonary Circulation Disease
Peripheral Vascular Disease
Congestive Heart Failure
Chronic Pulmonary Disease
Diabetes (without chronic complication)
Diabetes (with chronic complication)
Renal Failure
Liver Disease
Dementia
Paralysis
Other Neurological Disorder
Oncology
Hospice
Benzodiazepine Day Supply>120
Daily diazepam-equivalent average dose mg/day

Total Number of Elixahuser Conditions

years of benzodiazepine prescription

Abbreviations: daily diazepam-equivalent (DDE), PPO= Preferred provider organization, HMO= Health maintenance orga

Table 2: Benzodiazepine re-prescription incidence rate (per 100 person-month), and crude hazard rate ratio of demographic and clinical characteristics in patients with history of discontinued benzodiazepine prescriptions (more than 30 days) in FY2019.

		Person-Time	IRR per 100 PMO	95% CI	Crude HR	95% CI	p
Overall		503101.7	19.77	19.65-19.9			
Age	<45	98649.7	17.97	17.71-18.24			
	45-65yo	165610.9	20.62	20.4-20.84	1.14	1.12-1.17	<.001
	>65	238841.1	19.93	19.75-20.11	1.12	1.1-1.14	<.001
Sex	Female	79076.12	19.77	19.46-20.08			
	Male	424025.6	19.77	19.64-19.91	1.01	1-1.03	.123
Race/Ethnicity	White	365672.8	19.61	19.47-19.76			
	African American	58454.86	19.56	19.21-19.93	.99	.97-1.01	.164
	Hispanic or Latino	41761.5	21.66	21.22-22.11	1.08	1.06-1.1	<.001
	Other	37212.58	19.54	19.1-20	.99	.96-1.01	.297
Marital Status	Married	275154.6	20.26	20.09-20.43			
	Single	64958.8	19.32	18.98-19.66	.96	.94-.97	<.001
	Widowed/Separated/	155010.5	19.35	19.13-19.57	.97	.95-.98	<.001
	Unknown	7977.89	14.92	14.09-15.79	.72	.68-.76	<.001
Insurance	Medicare/Medicaid/Supplemental	260871.9	20.34	20.16-20.51			
	Major Medical/HMO/PPO	85520.53	19.34	19.05-19.64	.94	.92-.95	<.001
	Other/Unknown	156709.3	19.07	18.85-19.29	.93	.92-.94	<.001
Anxiety	No	212940.3	17.62	17.45-17.8			
	Yes	284898	21.61	21.44-21.79	1.19	1.18-1.21	<.001

		Person-Time	IRR per 100 PMO	95% CI	Crude HR	95% CI	p
PTSD	No	319842.5	18.47	18.32-18.62			
	Yes	177995.7	22.49	22.28-22.72	1.19	1.17-1.2	<.001
Psychoses	No	421353	19.66	19.52-19.79			
	Yes	76485.32	21.29	20.97-21.62	1.08	1.06-1.1	<.001
Depression	No	355122.3	19.71	19.56-19.85			
	Yes	142716	20.41	20.17-20.64	1.03	1.01-1.04	<.001
Bipolar	No	461965.3	19.85	19.73-19.98			
	Yes	35872.96	20.61	20.14-21.08	1.04	1.01-1.06	.002
Alcohol Abuse	No	476503.6	20.14	20.01-20.27			
	Yes	21334.72	14.75	14.24-15.28	.75	.73-.78	<.001
Drug Abuse	No	479895.9	20.16	20.03-20.28			
	Yes	17942.35	13.26	12.74-13.81	.68	.65-.71	<.001
Any Opioids prescriptions 2019	No	364753	20.4	20.26-20.55			
	Yes	138348.8	18.11	17.89-18.34	.9	.89-.92	<.001
Insomnia	No	380856.3	20.02	19.87-20.16			
	Yes	116982	19.55	19.3-19.81	.97	.96-.99	<.001
Sleep Apnea	No	414201.4	19.8	19.67-19.94			
	Yes	83636.89	20.42	20.12-20.73	1.02	1.01-1.04	.004
Pulmonary Circulation Disease	No	494605.9	19.94	19.81-20.06			
	Yes	3232.36	15.44	14.14-16.85	.78	.72-.86	<.001
Peripheral Vascular Disease	No	480190.7	19.96	19.83-20.08			
	Yes	17647.54	18.57	17.94-19.22	.94	.9-.97	<.001

		Person-Time	IRR per 100 PMO	95% CI	Crude HR	95% CI	p
Congestive Heart Failure	No	476503.9	20.07	19.94-20.2			
	Yes	21334.4	16.26	15.72-16.81	.83	.8-.86	<.001
Chronic Pulmonary Disease	No	438343.7	20.03	19.89-20.16			
	Yes	59494.55	19.04	18.69-19.39	.96	.94-.98	<.001
Diabetes (without chronic complication)	No	416745.9	19.73	19.59-19.86			
	Yes	81092.41	20.83	20.52-21.15	1.05	1.03-1.07	<.001
Diabetes (with chronic complications)	No	435847.9	19.88	19.75-20.02			
	Yes	61990.38	20.09	19.74-20.44	1.01	.99-1.03	.18
Renal Failure	No	476706.4	20	19.87-20.12			
	Yes	21131.87	17.91	17.35-18.49	.91	.88-.94	<.001
Liver Disease	No	481630.6	19.96	19.83-20.09			
	Yes	16207.69	18.37	17.73-19.05	.93	.89-.96	<.001
Dementia	No	480942.3	20.13	20-20.26			
	Yes	16896.03	13.62	13.07-14.19	.7	.67-.73	<.001
Paralysis	No	490770	19.89	19.76-20.01			
	Yes	7068.27	21.26	20.22-22.37	1.07	1.01-1.12	.014
Other Neurological Disorder	No	453542	20.11	19.98-20.25			
	Yes	44296.26	17.79	17.4-18.19	.9	.88-.92	<.001
Oncology	No	495971.7	19.82	19.7-19.95			
	Yes	7130.06	16.14	15.24-17.1	.82	.77-.87	<.001
Hospice	No	488557.2	20.09	19.97-20.22			
	Yes	14544.51	9.08	8.61-9.59	.48	.46-.51	<.001

		Person-Time	IRR per 100 PMO	95% CI	Crude HR	95% CI	p
Benzodiazepine Day Supply>120	No	305681.1	8.66	8.56-8.76			
	Yes	197420.6	36.98	36.71-37.25	4.04	3.98-4.1	<.001
The daily diazepam-equivalent average dose mg/day	0-9.99	167068.1	16.63	16.44-16.83			
	10-19.99	177716.7	19.41	19.21-19.62	1.16	1.14-1.18	<.001
	20-29.99	87666.66	21.55	21.25-21.86	1.29	1.26-1.31	<.001
	[?] 30	70650.3	25.89	25.52-26.27	1.55	1.52-1.58	<.001
Total Number of Elixahuser Conditions	0	121011.8	18.3	18.06-18.55			
	1 or 2	259519.5	20.96	20.78-21.13	1.13	1.11-1.14	<.001
	[?]3	122570.5	18.71	18.47-18.96	1.02	1-1.04	.015
Years of benzodi-azepine prescription	< 3	102164.8	12.26	12.05-12.48			
	[?] 3 years	400937	21.69	21.54-21.83	1.75	1.71-1.78	<.001

		Person-Time	IRR per 100 PMO	95% CI	Crude HR	95% CI	p
Abbreviations: IRR= Incidence rate ratio, PMO= Person Month of observations, CI= Confidence interval, PPO= Preferred provider organization, HMO= Health maintenance organization.	Abbreviations: IRR= Incidence rate ratio, PMO= Person Month of observations, CI= Confidence interval, PPO= Preferred provider organization, HMO= Health maintenance organization.	Abbreviations: IRR= Incidence rate ratio, PMO= Person Month of observations, CI= Confidence interval, PPO= Preferred provider organization, HMO= Health maintenance organization.	Abbreviations: IRR= Incidence rate ratio, PMO= Person Month of observations, CI= Confidence interval, PPO= Preferred provider organization, HMO= Health maintenance organization.	Abbreviations: IRR= Incidence rate ratio, PMO= Person Month of observations, CI= Confidence interval, PPO= Preferred provider organization, HMO= Health maintenance organization.	Abbreviations: IRR= Incidence rate ratio, PMO= Person Month of observations, CI= Confidence interval, PPO= Preferred provider organization, HMO= Health maintenance organization.	Abbreviations: IRR= Incidence rate ratio, PMO= Person Month of observations, CI= Confidence interval, PPO= Preferred provider organization, HMO= Health maintenance organization.	Abbreviations: IRR= Incidence rate ratio, PMO= Person Month of observations, CI= Confidence interval, PPO= Preferred provider organization, HMO= Health maintenance organization.

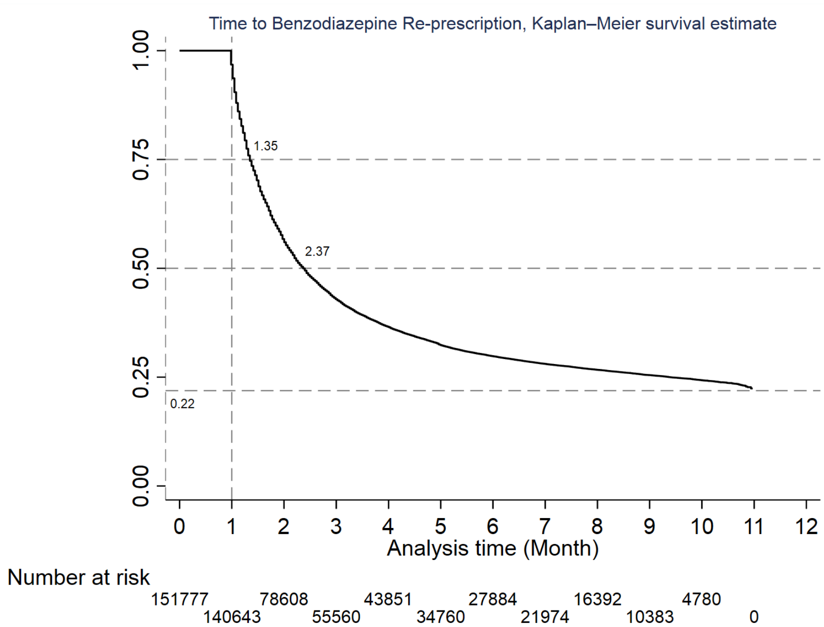

Figure 2. Time to benzodiazepine re-prescription, Kaplan-Meier survival estimate, in Veteran patients with chronic benzodiazepine prescriptions in FY2019. About 25% and 50% of Veteran patients were prescribed benzodiazepine again after 1.35 and 2.37 months after benzodiazepine discontinuation.

Table 3: Adjusted hazard rate ratio of benzodiazepine re-prescriptions of selected medical conditions in veteran patients after benzodiazepine discontinuation for 30 days in FY2019.

Anxiety	Anxiety
PTSD	PTSD
Psychoses	Psychoses
Depression	Depression
Bipolar Disease	Bipolar Di
Alcohol Abuse	Alcohol Ab
Drug Abuse	Drug Abus
Prescribed Opioids VA FY2019	Prescribed
Insomnia	Insomnia
Sleep Apnea	Sleep Apne
Pulmonary Circulation Disease	Pulmonary
Chronic Pulmonary Disease	Chronic Pu
Peripheral Vascular Disease	Peripheral
Congestive Heart Failure	Congestive
Diabetes (without chronic complications)	Diabetes (w
Diabetes (with chronic complications)	Diabetes (w
Renal Failure	Renal Failu
Liver Disease	Liver Disea
Dementia	Dementia
Paralysis	Paralysis
Other Neurological Disorder	Other Neu
Oncology	Oncology
Hospice	Hospice
Abbreviations: aHR= Adjusted Hazard ratio, CI= Confidence interval, PTSD= post-traumatic stress disorder	*Abbreviatio*