

BACKGROUND & OBJECTIVE

- Benzodiazepine (BZD) are commonly prescribed for anxiety, insomnia, and related conditions
- Clinical guidelines discourage long-term BZD therapy (LTBT) and recommend gradual tapering
- Little is known about whether BZD discontinuation patterns are associated with suicide- and/or drug overdose-related outcomes in the U.S.
- Objective:** To identify the BZD use trajectory post-LTBT using machine learning and assess their associations with outcomes

METHODS

- Design:** Retrospective cohort study
- Source:** Electronic health records (EHR) data from the *All of Us* dataset, U.S. (2014-2024)
- Cohort:**
 - Excluded BZD prescriptions of liquid, injectables, nasal sprays, rectal gels, combination products, or not sold in the U.S.
 - Non-cancer adults initiating LTBT (≥ 3 BZD orders/fills at least 21 days apart with ≥ 84 total days supplied)
- Exposure:**
 - BZD use trajectory group
 - 12-month follow-up after meeting criteria for LTBT
 - Using group-based trajectory model according to Nagin's model adequacy criteria
- Main outcome measures:**
 - Composite suicide- and/or drug overdose-related risks in emergency department (ED) visits or hospitalizations

Outcome Conditions	ICD-10 codes
All drug overdose	F11-16, F18-20, T36-T50
Suicide attempts/behaviors	T14.19, T36-T71, X60-70, Y10-Y34

- Statistical analysis:**
 - Applied inverse probability of treatment weighting (IPTW) to balance baseline characteristics measured during the 3 months before the index date
 - Absolute standardized mean difference (ASMD) was used to verify the balance before and after IPTW
 - Weibull accelerated failure time (AFT) model:** compared time to outcomes across trajectory groups
 - Time ratio (TR) quantifies acceleration or deceleration in time to first event (value less than 1 indicating shorter time)

RESULTS

Table 1. Baseline characteristics of LTBT study cohort

Baseline Characteristics	Group A (n=1177)	Group B (n=731)	Group C (n=1235)	Group D (n=1228)	Group E (n=1192)	Group F (n=3870)	ASMD†
Age ≥ 65 years, %	15.8	18.1	18.3	19.2	21.4	19.1	0.01
Female, %	69.9	74.8	73.0	74.8	74.9	71.3	0.01
Race, %							
White	67.2	72.8	70.8	73.1	73.6	73.6	0.01
Mental health disorder, %							
Anxiety	39.8	31.7	35.9	38.4	35.7	32.2	0.02
Depression	40.7	29.7	33.2	36.0	33.1	34.5	0.01
Substance use disorder, %							
Alcohol	2.6	< 2.7	2.8	2.9	< 1.7	> 1.0	0.01
Opioid	3.7	< 3.4	2.1	1.6	1.8	> 1.0	0.01
Medication-related, %							
Any Opioid: nonIV, nonOUD	38.2	34.2	32.7	31.0	33.4	34.7	0.01
Any non-BZD anxiolytics	8.8	16.4	14.4	11.2	12.7	9.1	0.01
Chronic conditions, %							
COPDB	4.0	2.8	1.9	3.0	2.4	1.6	0.01
Outpatients visits, %							
≥ 9	51.6	39.4	42.4	49.5	46.5	46.3	0.02

† ASMD: Absolute standardized mean difference after IPTW adjusted; SMD >0.1 was considered as having non-negligible differences; COPDB: Chronic Obstructive Pulmonary Disease and Bronchiectasis; IV: intravenous; OUD: Opioid Use Disorders

Figure 1. Post-LTBT trajectory groups based on the proportion of days covered by benzodiazepine use during 12-month follow-up period

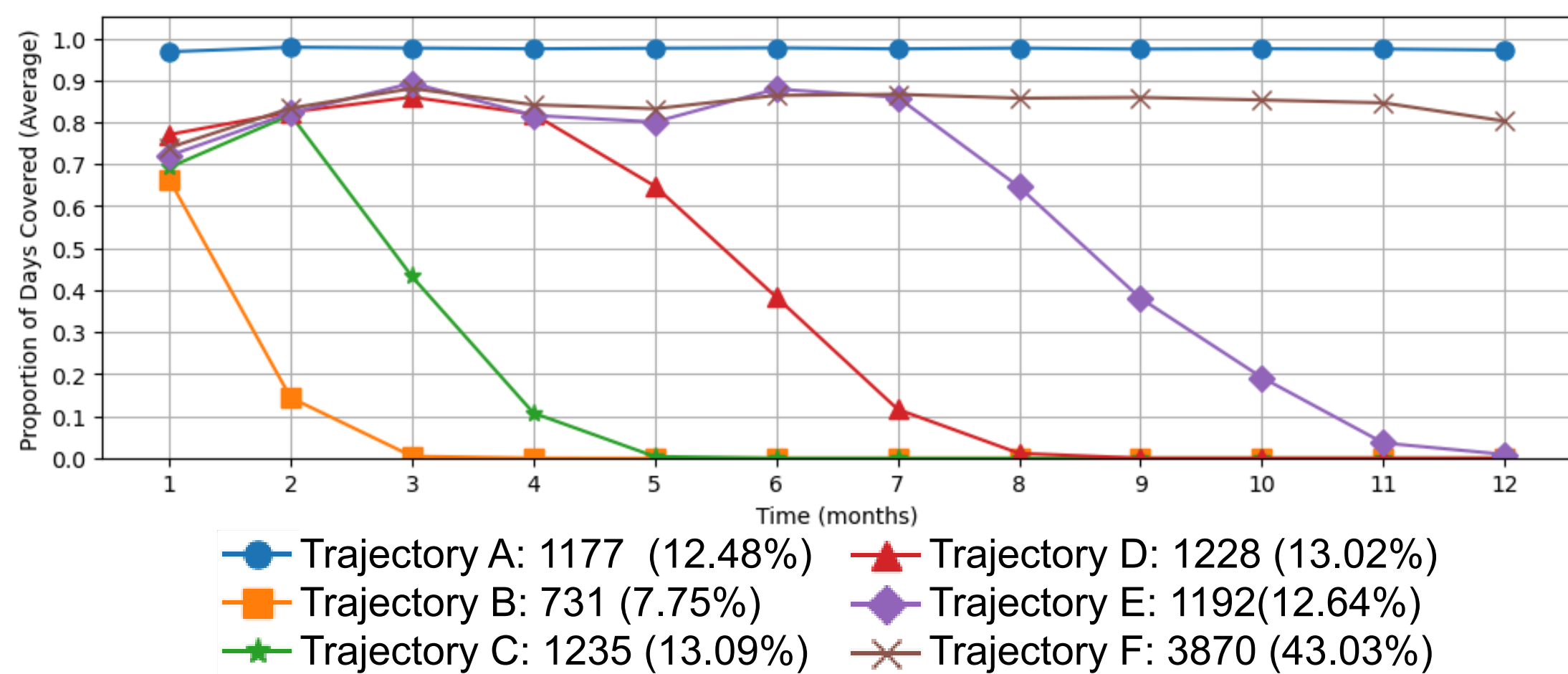


Table 2. Risk of suicide- and/or drug overdose-related using AFT model

Trajectory groups	Composite suicide- and/or drug overdose-related risk (n=186, 2.0% of the cohort)	
	%	Adjusted time ratio (95% CI)
Group A (n=1177)	1.7	reference
Group B (n=731)	3.0	0.51 (0.27, 0.98)
Group C (n=1235)	2.7	0.62 (0.34, 1.14)
Group D (n=1228)	2.8	0.56 (0.31, 1.00)
Group E (n=1192)	1.1	1.41 (0.69, 2.88)
Group F (n=3870)	1.7	0.87 (0.52, 1.47)

DISCUSSION & CONCLUSIONS

- BZD utilization patterns among post-LTBT in the *All of Us* cohort from 2014 to 2024
 - Six distinct trajectories were identified by GBTM: high-adherence persistent use (12.5%), discontinuation within 90 days (7.8%), discontinuation 60-150 days (13.1%), discontinuation 120-240 days (13.0%), discontinuation 210-360 days (12.6%) and Moderate-adherence persistent use (43.0%)
- Early discontinuation within 90 days was associated with a significantly faster risk of suicide- and drug overdose-related ED visits/hospitalizations than later discontinuations during the 12-month trajectory period
- The timing of BZD deprescribing may be important in future studies of patient safety