The association of comorbid substance use disorders with time to treatment discontinuation in patients with schizophrenia

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BACKGROUND

- Approximately 42% of patients with schizophrenia have a comorbid substance use disorder (SUD)[1] and are associated with higher risks of poor clinical outcomes and decreased treatment efficacy.[2]
- Time until first discontinuation of antipsychotic treatment may provide an indication of the effectiveness, safety, and tolerability of treatment.[3]
- Time until first discontinuation is assessed by duration between start and end date of first prescription of antipsychotic medication (prescription records of the same drug were combined if <30 days apart)
- **Objective:** Assess the associations between schizophrenia with versus without comorbid SUDs, and the associations of substance-specific SUDs with time to treatment discontinuation

METHOD

Data source: NeuroBlu database

Inclusion Criteria:

- Age 18 and above at time of first diagnosis of schizophrenia (ICD-10: F20*)
- Gender of patient known
- ≥ 1 antipsychotic prescribed for ≥ 7 days

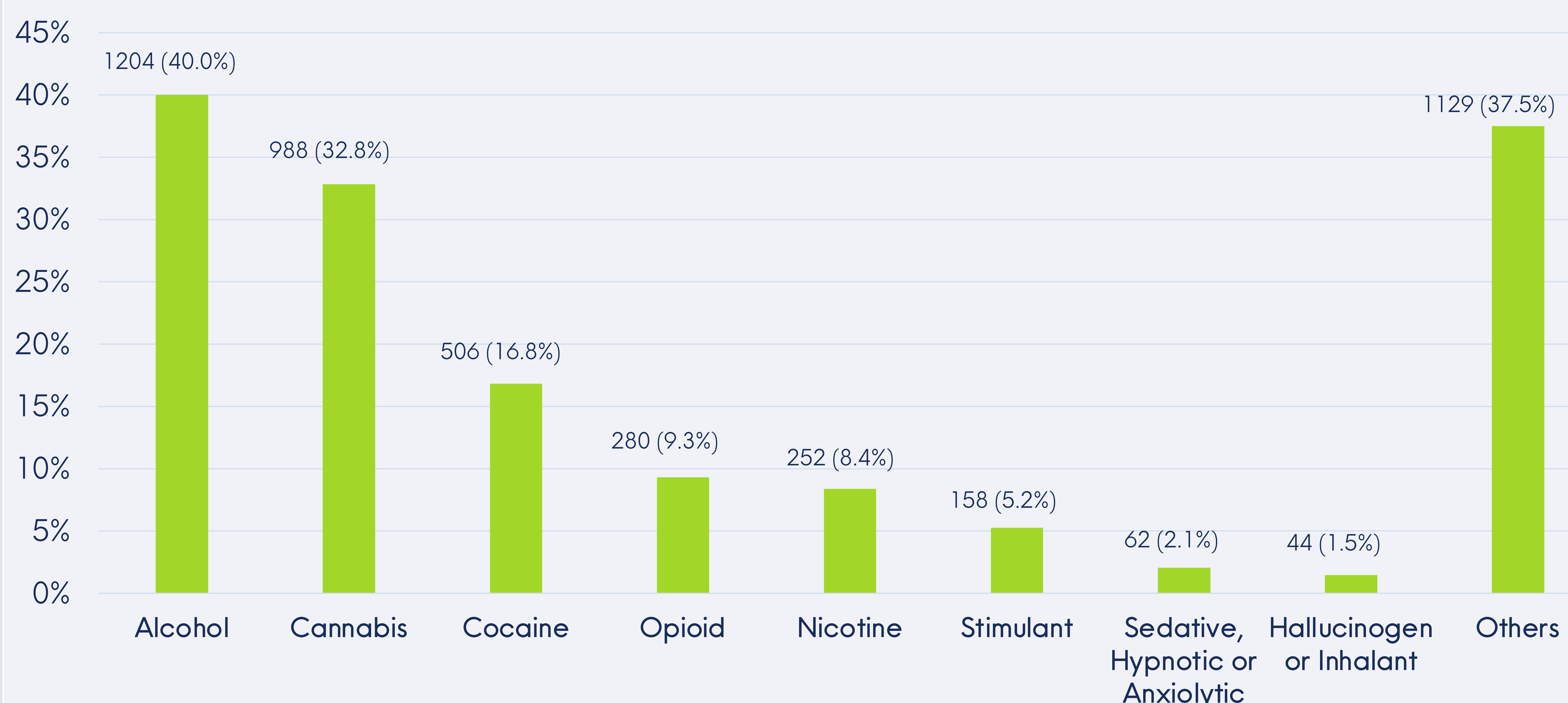
Analysis:

- Mann-Whitney U test: Compare time to first treatment discontinuation between schizophrenia with versus without comorbid SUDs.
- Cox proportional hazard (CoxPH) model: Assess the association of substance-specific SUDs with time to first treatment discontinuation.

RESULTS

- Of the total cohort (n=13,634; male=62.9%), 3,010 (22.1%) were identified as having comorbid SUDs. (see Figure 1)
- Patients with schizophrenia and comorbid SUD (M=36.5yrs, SD=13.0; male=77.1%) were younger than those without SUD
- (M= 42.9yrs, SD=15.2; male=58.8%).
- 69.7% (n=9,504) had 1 or more antipsychotic prescription of 7 or more days.
- Presence of comorbid SUDs was associated with shorter time to first antipsychotic discontinuation (M=176.8 days, SD=393.3) compared to the absence of comorbid SUDs (M=270.0 days, SD=538.1, U=1.44, p<.001).
- Comorbid cocaine use disorder, stimulant use disorder, and polysubstance use disorder were associated with shorter time to first antipsychotic discontinuation compared with schizophrenia without comorbid SUDs. (see Table 1)

Figure 1. Breakdown of types of comorbid SUD (n= 3,010)



Note: The total count is greater than total cohort size as patients may be diagnosed with more than 1 SUD and thus accounted for in multiple categories

Table 1. CoxPH model comparing time to first antipsychotic discontinuation between specific SUDs vs no SUD [a] (n=9,504)

Types of SUD	*n*	*Mean (SD)*	*Hazard Ratio*	*C.I.*	*p*
Alcohol	346	342.1 (535.8)	1.12	0.99-1.27	0.077
Cannabis	267	306.9 (486.7)	1.06	0.92-1.23	0.41
Opioid	82	333.1 (543.4)	1.21	0.95-1.56	0.13
Cocaine	**66**	**180.1 (356.4)**	**1.87**	**1.42-2.45**	**< 0.001**
Nicotine	48	488.0 (612.4)	0.93	0.67-1.28	0.64
Stimulant	**31**	**167.0 (333.8)**	**1.64**	**1.07-2.52**	**0.024**
Others	437	233.9 (440.5)	1.39	1.24-1.56	< 0.001
Polysubstance	**737**	**219.4 (385.3)**	**1.46**	**1.33-1.59**	**< 0.001**

[a] ref group: n=7,490, M=357.8, SD=579.6.
Note. CoxPH analyses only involved patients with records of antipsychotic prescriptions for ≥ 7 days.

DISCUSSION

- Patients with dual diagnoses are frequently excluded from studies and trials – real-world data generated from EHRs provide valuable insights into symptomatology, treatment efficacy, and behavioral patterns in complex patient sub-groups.
- Results of this study were aligned with previous research where schizophrenia with comorbid SUDs was related to poorer adherence to medications.[5]
- Our finding that comorbid use of cocaine was associated with shorter time to antipsychotic discontinuation was novel and aligned with dilemmas raised about treatment in this patient sub-group.[6]
- Chronic use of dopaminergic drugs like cocaine disrupts dopamine receptors, possibly resulting in poorer adherence to antipsychotics.[7]
- Mental health services should strive to provide holistic care by targeting symptoms of primary and comorbid conditions, to reduce treatment attrition of patients with dual diagnoses.
- One limitation of this study was that some other factors influencing the results of this study could not be controlled for – e.g., the dataset would not have contained a patient's full health records if they had accessed multiple providers.

Conflicts of Interest: All authors report current employment with Holmusk Technologies, Inc. RP reports equity ownership in Holmusk Technologies, Inc.

References:

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NeuroBlu™ database

50+ million rows of patient data

560K+ Patients

20+ years Longitudinal Data

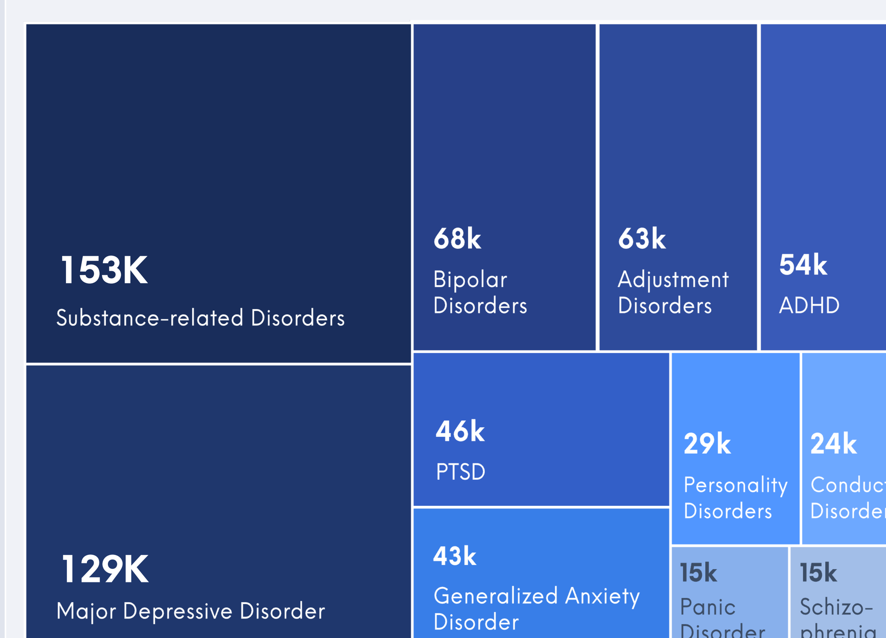

Figure 2. Overview of NeuroBlu Database (data source)

Structured Data

- Outcome Measures (e.g., CGI-S, GAF)
- Diagnosis Codes (ICD-9, ICE-10)
- Prescription Data
- Patient Demographics
- **Emergency Department, inpatient & outpatient data** across the same patients in 20 of 25 clinics

Unstructured Data

Mental State Examination (MSE)

- Categorized notes on patient's function, appearance and mood at a visit
- Holmusk developed >30 advanced Neural Network models to predict structured labels from MSE
- Created >300 psychiatry specific labels in collaboration with clinicians to track disease progression over time

External Stressors

Social, relational and occupational events that may affect the patient's mental health

Data Source of US Health Facilities

De-identified EHR data were obtained from U.S. mental health services that use the MindLinc EHR system. The data were analysed in NeuroBlu, a secure Trusted Research Environment (TRE) that enables data assembly and analysis using an R/Python code engine.