Illness severity associated with comorbid substance use disorders in schizophrenia: an electronic health record study

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BACKGROUND

Approximately 50% of schizophrenia patients have comorbid substance use disorder (SUD).¹ Patients with dual diagnoses of schizophrenia and SUDs have poorer outcomes, such as higher rates of relapse and rehospitalizations.²

OBJECTIVE

To investigate the association between illness severity in schizophrenia patients and the prevalence of comorbid SUD using a largescale electronic health record (EHR) dataset.

METHOD

Cohort	Adults with a diagnosis of schizophrenia (ICD
Index	Date of Schizophrenia diagnosis
Exposure	The presence of a comorbid SUD (F10* alcoh cannabis, F14* cocaine, F15* stimulant, F17* i
Outcome	Clinical Global Impression - Severity (CGI-S) and 5-7) documented within 30 days of inde
Covariate	Age, gender, race, marital status, employme schizophrenia diagnosis – multivariable logisti

Neuro **Bu**[™] database

50+ million	560K+	2

20+ years

Longitudinal Data

Patient volume by disease

rows of patient data

153K Substance-related Disorders	68k Bipolar Disorders	63k Adjus Disor	stment	4k DHD
	46k PTSD		29k Persona Disorde	24k Conduct Disorders
129K Major Depressive Disorder	43k Generalized Any Disorder	kiety	15k Panic Disorde	15k Schizo- phrenia

Patients

Structured Data



Outcome Measures (e.g., CGI-S, GAF)



Prescription Data



Unstructured Data



Mental Status Examination (MSE)
Categorized notes on patient's function 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

Figure 1. NeuroBlu Database overview

D-10 F20*).

- phol, F11^{*} opioid, F12^{*} nicotine.)
- score (2 categories 1-4 ex date.
- ent status and year of tic regression analysis.



Diagnosis Codes (ICD-9, ICD-10)

Patient Demographics

Emergency Department, inpatient and outpatient data across the same patients in 20 of 25 clinics

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.

- documented CGI-S score.
- Comorbid cannabis use disorder (F12^{*}) was associated with greater illness severity (mean CGI-S (SD): 4.89(1.14); OR: 1.68, 95% CI 1.32 to 2.14, p<0.001)
- Comorbid opioid use disorder (F11^{*}) was associated with lower illness severity (mean CGI-S (SD): 4.23(1.23); OR: 0.56, 95% CI 0.37 to 0.83, p=0.004) compared to patients without comorbid SUD (mean CGI-S (SD): 4.57(1.23)).
- The associations between demographic and diagnostic factors and CGI-S scores are illustrated in Table 1.

Alcohol only2Cannabis only3Opioid only1Cocaine only1Nicotine only1Nicotine only2Others only2Polysubstance1Gender4Reference: Female4Male7,9Age5,9Reference: Age < 405,9Age 40 and above6,7Race7Reference: Black3,8White4,8Others9Unknown2,9Marital status7,9Reference: Divorced/Separated1,Single8,Married/Engaged/In a relationship9	N (%) 883 (78.0) 492 (3.9) 336 (2.7) 111(0.9) 104 (0.8) 55 (0.4) 42 (0.3) 55 (0.4) 42 (0.3) 542 (5.1) ,011(8.0) 737(37.4) 737(37.4) 737(37.4) 739 (62.6) 951 (46.9) 725 (53.1) 848 (30.4) 890 (38.6) 88 (7.8)	Mean (SD) 4.57 (1.23) 4.42 (1.45) 4.89 (1.14) 4.23 (1.23) 4.63 (1.17) 4.64 (1.39) 4.98 (0.91) 4.95 (1.10) 4.95 (1.10) 4.69 (1.20) 4.50 (1.20) 4.60 (1.20) 4.61 (1.24)	Odds Ratio 0.93 1.68 0.56 1.15 1.32 2.05 1.67 1.22 0.97 0.83	0.77 to 1.12 1.32 to 2.14 0.37 to 0.83 0.77 to 1.71 0.76 to 2.30 1.03 to 4.07 1.40 to 1.99 1.06 to 1.40 0.90 to 1.05	p 0.44 < 0.001 0.004 0.50 0.32 0.04 < 0.001 0.005 0.45 < 0.001
Reference: No SUD9,8Alcohol only2Cannabis only3Opioid only3Cocaine only1Nicotine only1Stimulant only6Others only6Polysubstance1Gender4,Male7,5Age6,7Reference: Female4,Male7,5Age 40 and above6,7Race6,7Reference: Black3,8White4,8Others5,9Unknown2,9Marital status7,9Reference: Divorced/Separated1,Single8,Married/Engaged/In a relationship5,9	492 (3.9) 336 (2.7) 111(0.9) 104 (0.8) 55 (0.4) 42 (0.3) 542 (5.1) ,011(8.0) 737(37.4) 737 (37.4) 739 (62.6) 751 (46.9) 725 (53.1) 848 (30.4) 390 (38.6)	$\begin{array}{c} 4.42 (1.45) \\ 4.89 (1.14) \\ 4.23 (1.23) \\ 4.63 (1.17) \\ 4.64 (1.39) \\ 4.98 (0.91) \\ 4.98 (0.91) \\ 4.95 (1.10) \\ 4.69 (1.20) \end{array}$ $\begin{array}{c} 4.58 (1.22) \\ 4.62 (1.24) \\ 4.62 (1.24) \\ 4.50 (1.25) \\ 4.60 (1.20) \end{array}$	1.68 0.56 1.15 1.32 2.05 1.67 1.22	1.32 to 2.14 0.37 to 0.83 0.77 to 1.71 0.76 to 2.30 1.03 to 4.07 1.40 to 1.99 1.06 to 1.40 0.90 to 1.05	< 0.001 0.004 0.50 0.32 0.04 < 0.001 0.005
Alcohol only 2 Cannabis only 3 Opioid only 3 Cocaine only 1 Nicotine only 1 Stimulant only 2 Others only 2 Polysubstance 1 Gender 4, Male 7,5 Age 5, Reference: Female 4, Male 7,5 Age 40 and above 6,5 Reference: Black 3,8 White 4,8 Others 5 Unknown 2,5 Marital status 7 Reference: Divorced/Separated 1, Single 8, Married/Engaged/In a relationship 5	492 (3.9) 336 (2.7) 111(0.9) 104 (0.8) 55 (0.4) 42 (0.3) 542 (5.1) ,011(8.0) 737(37.4) 737 (37.4) 739 (62.6) 751 (46.9) 725 (53.1) 848 (30.4) 390 (38.6)	 4.89 (1.14) 4.23 (1.23) 4.63 (1.17) 4.64 (1.39) 4.98 (0.91) 4.95 (1.10) 4.69 (1.20) 4.58 (1.22) 4.62 (1.24) 4.72 (1.20) 4.50 (1.25) 4.60 (1.20) 	1.68 0.56 1.15 1.32 2.05 1.67 1.22	1.32 to 2.14 0.37 to 0.83 0.77 to 1.71 0.76 to 2.30 1.03 to 4.07 1.40 to 1.99 1.06 to 1.40 0.90 to 1.05	< 0.001 0.004 0.50 0.32 0.04 < 0.001 0.005
Cannabis onlySOpioid onlyICocaine onlyINicotine onlyIStimulant onlyOthers onlyOthers onlyIGenderIReference: Female4,Male7,9AgeIReference: Age < 40	111(0.9) 104 (0.8) 55 (0.4) 42 (0.3) 542 (5.1) ,011(8.0) 737(37.4) 737 (62.6) 751 (46.9) 725 (53.1) 848 (30.4) 890 (38.6)	 4.23 (1.23) 4.63 (1.17) 4.64 (1.39) 4.98 (0.91) 4.95 (1.10) 4.69 (1.20) 4.62 (1.24) 4.72 (1.20) 4.50 (1.25) 4.60 (1.20) 	0.56 1.15 1.32 2.05 1.67 1.22 0.97	0.37 to 0.83 0.77 to 1.71 0.76 to 2.30 1.03 to 4.07 1.40 to 1.99 1.06 to 1.40 0.90 to 1.05	0.004 0.50 0.32 0.04 < 0.001 0.005
Cocaine only1Nicotine onlyStimulant onlyOthers onlyCPolysubstance1Gender4,Reference: Female4,Male7,5Age5,5Age 40 and above6,7Race6,7Race3,8White4,8Others5,7Unknown2,7Marital status7,9Reference: Divorced/Separated1,Single8,Married/Engaged/In a relationship9	104 (0.8) 55 (0.4) 42 (0.3) 542 (5.1) ,011(8.0) 737(37.4) 737 (62.6) 751 (46.9) 725 (53.1) 848 (30.4) 890 (38.6)	4.63 (1.17) 4.64 (1.39) 4.98 (0.91) 4.95 (1.10) 4.69 (1.20) 4.69 (1.20) 4.62 (1.24) 4.72 (1.20) 4.50 (1.25) 4.60 (1.20)	1.15 1.32 2.05 1.67 1.22	0.77 to 1.71 0.76 to 2.30 1.03 to 4.07 1.40 to 1.99 1.06 to 1.40 0.90 to 1.05	0.50 0.32 0.04 < 0.001 0.005
Nicotine onlyStimulant onlyOthers onlyPolysubstance1GenderReference: FemaleMale7,9AgeReference: Age < 40	55 (0.4) 42 (0.3) 542 (5.1) ,011(8.0) 737(37.4) 737 (62.6) 725 (53.1) 848 (30.4) 890 (38.6)	4.64 (1.39) 4.98 (0.91) 4.95 (1.10) 4.69 (1.20) 4.58 (1.22) 4.62 (1.24) 4.72 (1.20) 4.50 (1.25) 4.60 (1.20)	1.32 2.05 1.67 1.22 0.97	0.76 to 2.30 1.03 to 4.07 1.40 to 1.99 1.06 to 1.40 0.90 to 1.05	0.32 0.04 < 0.001 0.005
Stimulant only Others onlydePolysubstance1Gender4,Reference: Female4,Male7,9Age7,9Age6,7Race6,7Race8Reference: Black3,8White4,9Others9Unknown2,9Marital status8,7Reference: Divorced/Separated1,8Single8,7Married/Engaged/In a relationship9	42 (0.3) 542 (5.1) ,011(8.0) 737(37.4) 739 (62.6) 725 (53.1) 848 (30.4) 890 (38.6)	 4.98 (0.91) 4.95 (1.10) 4.69 (1.20) 4.58 (1.22) 4.62 (1.24) 4.72 (1.20) 4.50 (1.25) 4.60 (1.20) 	2.05 1.67 1.22 0.97	1.03 to 4.07 1.40 to 1.99 1.06 to 1.40 0.90 to 1.05	0.04 < 0.001 0.005 0.45
Others onlyOthers onlyPolysubstance1Gender4,7Reference: Female4,7Male7,9Age7,9Age5,9Age 40 and above6,7Race6,7Race3,8White4,8Others9Unknown2,9Marital status8,7Reference: Divorced/Separated1,Single8,7Married/Engaged/In a relationship9	542 (5.1) ,011(8.0) 737(37.4) 739 (62.6) 725 (53.1) 848 (30.4) 890 (38.6)	 4.95 (1.10) 4.69 (1.20) 4.58 (1.22) 4.62 (1.24) 4.72 (1.20) 4.50 (1.25) 4.60 (1.20) 	1.67 1.22 0.97	1.40 to 1.99 1.06 to 1.40 0.90 to 1.05	< 0.001 0.005 0.45
Polysubstance1GenderReference: Female4,7Male7,9Age7,9Age 40 and above6,7Race6,7Reference: Black3,8White4,8Others9Unknown2,9Marital status8,7Reference: Divorced/Separated1,5Single8,7Married/Engaged/In a relationship9	,011(8.0) 737(37.4) 739 (62.6) 725 (53.1) 848 (30.4) 890 (38.6)	 4.69 (1.20) 4.58 (1.22) 4.62 (1.24) 4.72 (1.20) 4.50 (1.25) 4.60 (1.20) 	1.22 0.97	1.06 to 1.40 0.90 to 1.05	0.005 0.45
GenderReference: Female4,7Male7,9Age7,9Age8Reference: Age < 40	737(37.4) 739 (62.6) 751 (46.9) 725 (53.1) 848 (30.4) 890 (38.6)	4.58 (1.22) 4.62 (1.24) 4.72 (1.20) 4.50 (1.25) 4.60 (1.20)	0.97	0.90 to 1.05	0.45
Reference: Female4,Male7,9Age7,9Age5,9Age 40 and above6,7Race6,7Reference: Black3,8White4,8Others9Unknown2,9Marital status8,7Reference: Divorced/Separated1,5Single8,7Married/Engaged/In a relationship9	939 (62.6) 951 (46.9) 725 (53.1) 848 (30.4) 890 (38.6)	4.62 (1.24) 4.72 (1.20) 4.50 (1.25) 4.60 (1.20)			
Male7,9AgeReference: Age < 40	939 (62.6) 951 (46.9) 725 (53.1) 848 (30.4) 890 (38.6)	4.62 (1.24) 4.72 (1.20) 4.50 (1.25) 4.60 (1.20)			
AgeReference: Age < 40	951 (46.9) 725 (53.1) 848 (30.4) 890 (38.6)	4.72 (1.20) 4.50 (1.25) 4.60 (1.20)			
Reference: Age < 40	725 (̀53.1)́ 848 (30.4) 890 (38.6)	4.50 (1.25) 4.60 (1.20)	0.83	0.77 to 0.90	< 0.001
Age 40 and above6,7Race3,8Reference: Black3,8White4,8Others9Unknown2,9Marital status2,9Reference: Divorced/Separated1,Single8,Married/Engaged/In a relationship9	725 (̀53.1)́ 848 (30.4) 890 (38.6)	4.50 (1.25) 4.60 (1.20)	0.83	0.77 to 0.90	< 0.001
Race3,8Reference: Black3,8White4,8Others9Unknown2,9Marital status2,9Reference: Divorced/Separated1,Single8,7Married/Engaged/In a relationship9	848 (30.4) 890 (38.6)	4.60 (1.20)	0.83	0.77 to 0.90	< 0.001
Reference: Black3,8White4,8Others9Unknown2,9Marital status2,9Reference: Divorced/Separated1,Single8,7Married/Engaged/In a relationship9	390 (38.6)				
White4,8Others9Unknown2,9Marital status2,9Reference: Divorced/Separated1,9Single8,9Married/Engaged/In a relationship9	390 (38.6)				
Others9Unknown2,9Marital status1Reference: Divorced/Separated1Single8,9Married/Engaged/In a relationship9		A = A = A = A = A = A = A = A = A = A =			
Unknown 2,9 Marital status Reference: Divorced/Separated 1, Single 8,7 Married/Engaged/In a relationship 9)	4.61 (1.24)	1.10	1.01 to 1.20	0.038
Marital status Reference: Divorced/Separated Single Married/Engaged/In a relationship	288 (7.8)	5.06 (1.10)	1.91	1.63 to 2.23	< 0.001
Reference: Divorced/Separated1,Single8,Married/Engaged/In a relationship9	950 (23.3)	4.39 (1.26)	0.92	0.83 to 1.02	0.12
Single 8, Married/Engaged/In a relationship 9					
Married/Engaged/In a relationship	,068 (5.5)	4.40 (1.33)			
	123 (42.1)	4.73 (1.17)	1.42	1.24 to 1.62	< 0.001
Widowed	281 (4.4)	4.36 (1.22)	0.93	0.78 to 1.11	0.44
	208 (0.9)	4.42 (1.17)	1.32	0.97 to 1.78	0.075
	935 (40.4)	4.39 (1.33)	0.67	0.59 to 0.77	< 0.001
Employment status					
	,000 (7.9)	4.80 (1.08)	0.01		0.41
	534 (4.2)	4.78 (1.17)	0.91	0.73 to 1.14	0.41
	207 (17.4)	4.94 (1.09)	1.27	1.08 to 1.49	0.004
Student/Retired			0 (7		0.001
	935 (70.5)	4.49 (1.26)	0.67	0.59 to 0.77	< 0.001
Year of Schizophrenia diagnosis					
	216 (1.7)	4.77 (0.92)	1.00		0.00
· ·	290 (26.0)	4.83 (1.16)	1.00	0.75 to 1.34	0.99
	560 (51.8) 610 (20.6)	4.53 (1.27) 4.49 (1.19)	0.66 0.57	0.49 to 0.87 0.43 to 0.77	0.004 < 0.001

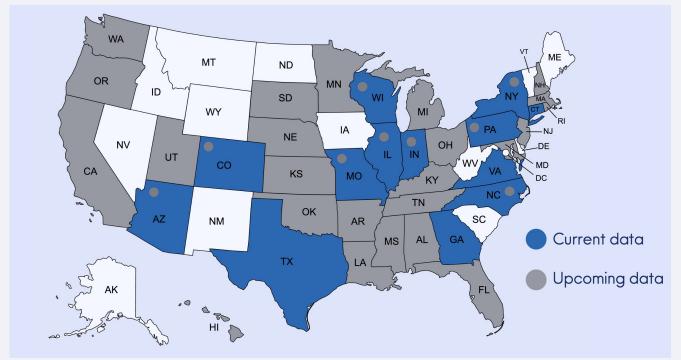


Figure 2. State specific data source for NeuroBlu

RESULTS

• A total of 13,634 adults with schizophrenia were included of which 12,676 (93.0%) had a

and is Culaster as I les Dissuelans (CLD, p. 10(74)

Comorbidity of SUD and CGI-S Score

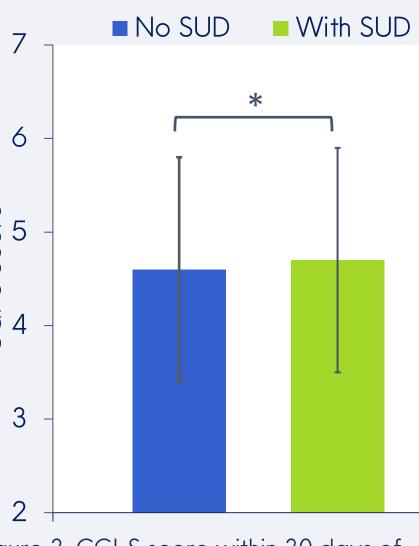


Figure 3. CGI-S score within 30 days of schizophrenia diagnosis of patients with (n = 2,793 and without (n = 9,883) comorbid SUDs. Data presented as Mean and Standard deviation. Analyzed with Mann-Whitney U tests with a significance threshold of < 0.05 (U = 1.48e⁷, p < 0.001).

the most prevalent.

- with schizophrenia.

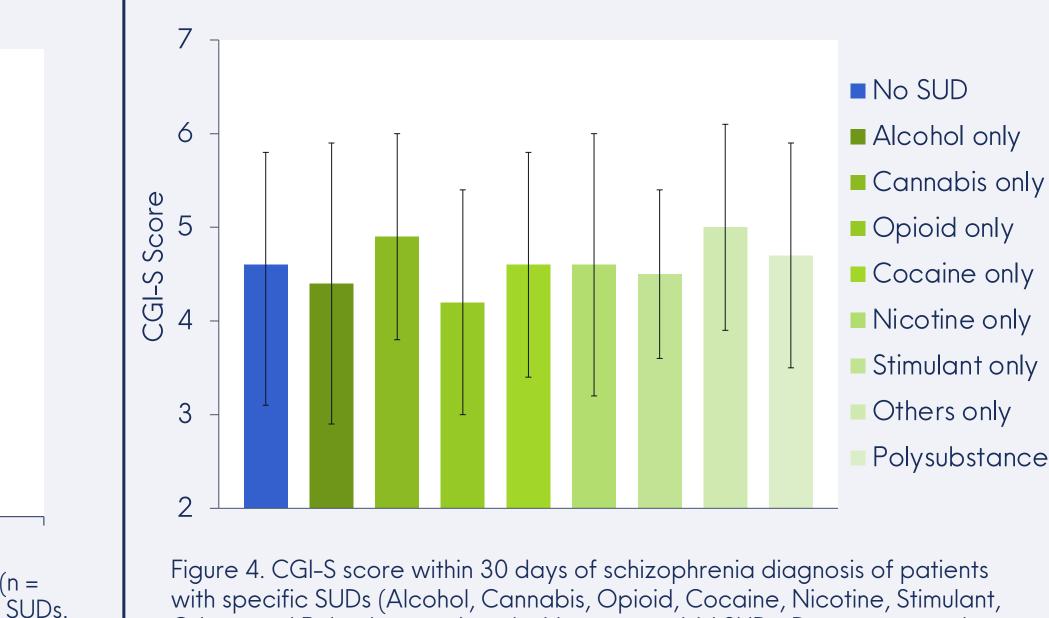
- substances.
- clinical outcomes.

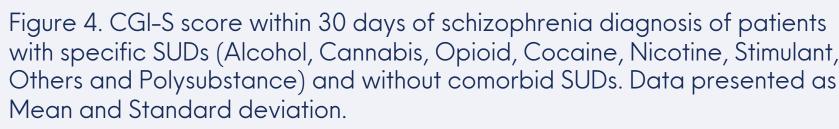
Conflicts of Interest: All authors report current employment with Holmusk Technologies, Inc. RP, MV, and SK report equity ownership in Holmusk Technologies, Inc.

References:

CGI-S Score of schizophrenia patients with specific SUDs

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CONCLUSION

• Amongst patients with comorbid SUDs, Polysubstance use disorder was

• Comorbid SUDs are associated with increased illness severity in patients

• Comorbid SUDs vary in their associations with illness severity.

• Comorbid cannabis use disorder is associated with greatest illness

severity consistent with its potential etiological role in schizophrenia.

• Conversely, opioid use disorder is associated with least illness severity. • This could reflect differences in the clinical characteristics and functioning of individuals who use opioids compared to those who use other

• Further analyses of healthcare service utilization could address the degree to which different comorbid SUDs are associated with worse

1. Hunt GE, Large MM, Cleary M, Lai HMX, Saunders JB. Prevalence of comorbid substance use in schizophrenia spectrum disorders in community and clinical settings, 1990–2017: Systematic review and meta-analysis. Drug Alcohol Depend. 2018;191:234-258. doi: 10.1016/j.drugalcdep.2018.07.011 2. Kessler T, Lev-Ran S. The associations between comorbid psychiatric diagnoses and hospitalizationrelated factors among individuals with schizophrenia. Compr Psychiatry. 2019;89:7-15. doi:10.1016/j.comppsych.2018.12.004

