Healthcare Resource Utilization Among Patients With Schizophrenia and Negative Symptoms: A Real-World Data Study

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Introduction

- Negative symptoms in schizophrenia (NSS), including avolition, anhedonia, and reduced emotional expression,[1] affect approximately 60% of individuals and are associated with significant functional impairment[2-4]
- Understanding the impact of negative symptoms on healthcare resource utilization (HRCU) in patients with schizophrenia is crucial for healthcare systems to optimize resource allocation and develop targeted interventions

Objective

- To estimate the association between negative symptoms features and the number of psychiatry-related and non-psychiatric inpatient, outpatient, and emergency visits among patients with schizophrenia within a 12-month follow-up

Methods

Study design and data source

- This retrospective cohort study analyzed electronic health records (EHRs) from NeuroBlu Data (V24R5) linked with Inovalon MORE2 Registry® of Closed Claims and the 100% Medicare Fee-for-Service databases
- NeuroBlu Data is a de-identified, longitudinal, behavioral health, real-world database comprising structured and unstructured patient-level records from US mental healthcare providers spanning 1999 to 2024. Inovalon is a real-world database that includes medical and pharmacy closed claims between 2019 and 2024

Study population

- Patients were included if further conditions were met:
  – A recorded diagnosis of schizophrenia in NeuroBlu Data
  – At least 1 record for the following: a mental status examination (MSE), negative symptoms label extracted via Natural Language Processing (NLP), or Brief Negative Symptoms Assessment (BNSA) within ± 14 days of a diagnosis of schizophrenia
  – Aged ≥18 years at the time of the MSE/NLP/BNSA assessment
  – A record of payer plan period throughout the 12-month follow-up in Inovalon claims dataset

Exposure

- The exposure of interest was NSS. Patients were classified as having evidence of negative symptoms if any of the following conditions were met: (1) BNSA total score ≥9 points, (2) NLP label indicating presence of negative symptoms, or (3) MSE documentation of negative symptoms
- All conditions were assessed within a time window of ±14 days around a diagnosis of schizophrenia to ensure clinical relevance of recorded symptoms; if multiple conditions were met, the earliest record by date was selected as the index event

Outcomes

- The study outcomes were counts of healthcare visits (inpatient, outpatient, and emergency department) during the 12-month follow-up period, stratified into psychiatry-related and non-psychiatry-related visits. Psychiatry-related visits included those occurring in a psychiatric setting (departments or with psychiatric provider specialties) or having associated psychiatric diagnostic codes, procedures, prescriptions, or clinical measurements. Non-psychiatry-related visits encompassed all other healthcare activity

Covariates

- Potential confounders, used in both propensity score assessment and regression adjustment, included demographic (age, sex, race, and ethnicity) and clinical characteristics (care setting, psychiatric and medical comorbidities, presence of positive symptoms, cognitive impairment, psychopharmacological treatments, and insurance type)

Statistical analysis

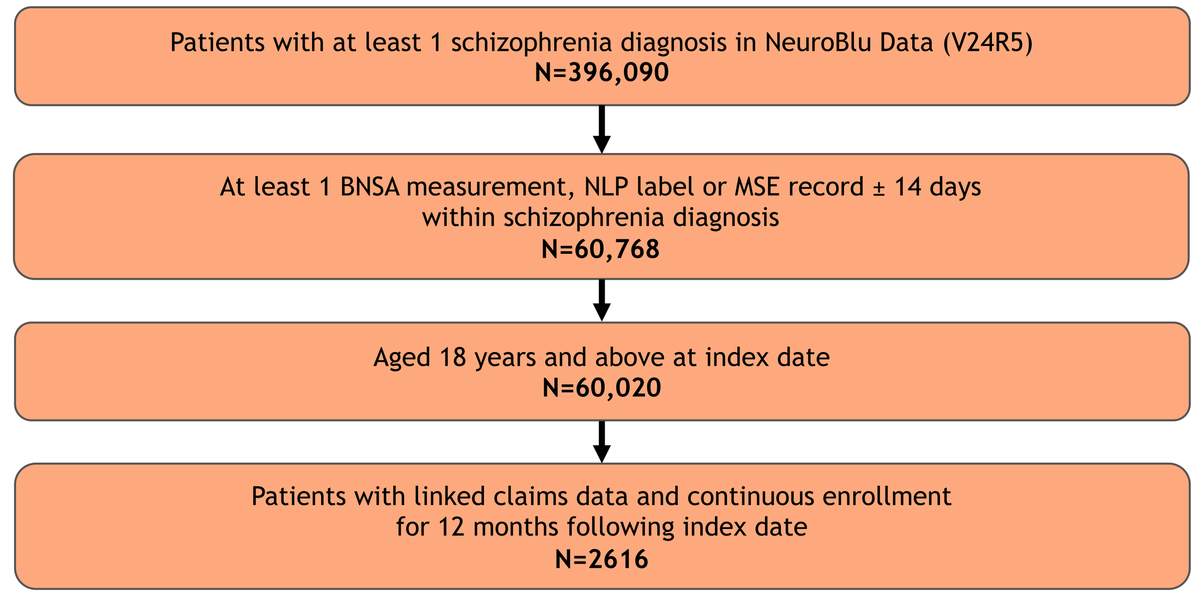
- Descriptive statistics were calculated for all variables, with continuous variables summarized using medians and interquartile range, and categorical variables summarized using absolute counts and percentages
- Stabilized inverse probability treatment weighing (IPTW) was used to create balanced cohorts between patients with and without negative symptoms. Propensity scores were estimated using logistic regression and included all listed covariates
- Extreme weights below the 1st percentile or above the 99th percentile were trimmed to prevent disproportionate influence of outlier observations
- Covariate balance was assessed using standardized mean differences (SMDs) for continuous variables and raw mean differences (RMDs) for categorical variables, with differences ≤0.1 considered adequately balanced
- Negative binomial regression was used to assess the relationship between negative symptoms and HCRU outcomes. Zero-inflated negative binomial regression was applied when data was zero-inflated. Double-robust adjustment was performed by including all propensity score covariates into regression models. Additional covariates, not used in the weighing, were adjusted for in the regression (payor type, LAI prescription at baseline, psychotherapy at baseline, data source) to further control for potential confounding
- Outcome results are presented as incidence rate ratios (IRRs) with 95% confidence intervals, where IRR >1.0 indicates higher service use among patients with negative symptoms, IRR <1.0 indicates lower service use, and IRR=1.0 indicates no difference compared with patients without negative symptoms

Results

Study population

- The linked claims cohort included 2616 adults (1774 [68%] with NSS) (**Figure 1**). After IPTW, the cohort had an effective sample size (ESS) of 1676 patients (1282 [77%] with NSS). The ESS for the weighted analysis is lower than the nominal population size, meaning the propensity score weighted analyses have approximately the same statistical power as an unweighted sample with 1676 individuals

Figure 1. Study population flowchart



MSE, Mental Status Examination; BNSA, Brief Negative Symptoms Assessment; NLP, Natural Language Processing.

Descriptive characteristics

- **Table 1** shows baseline population characteristics after applying IPTW. The ESS represents the number of independent observations required by an unweighted sample to obtain the same level of precision achieved after applying IPTW. It is a measure of statistical information rather than a participant count, and therefore subgroup ESS values do not sum to the total

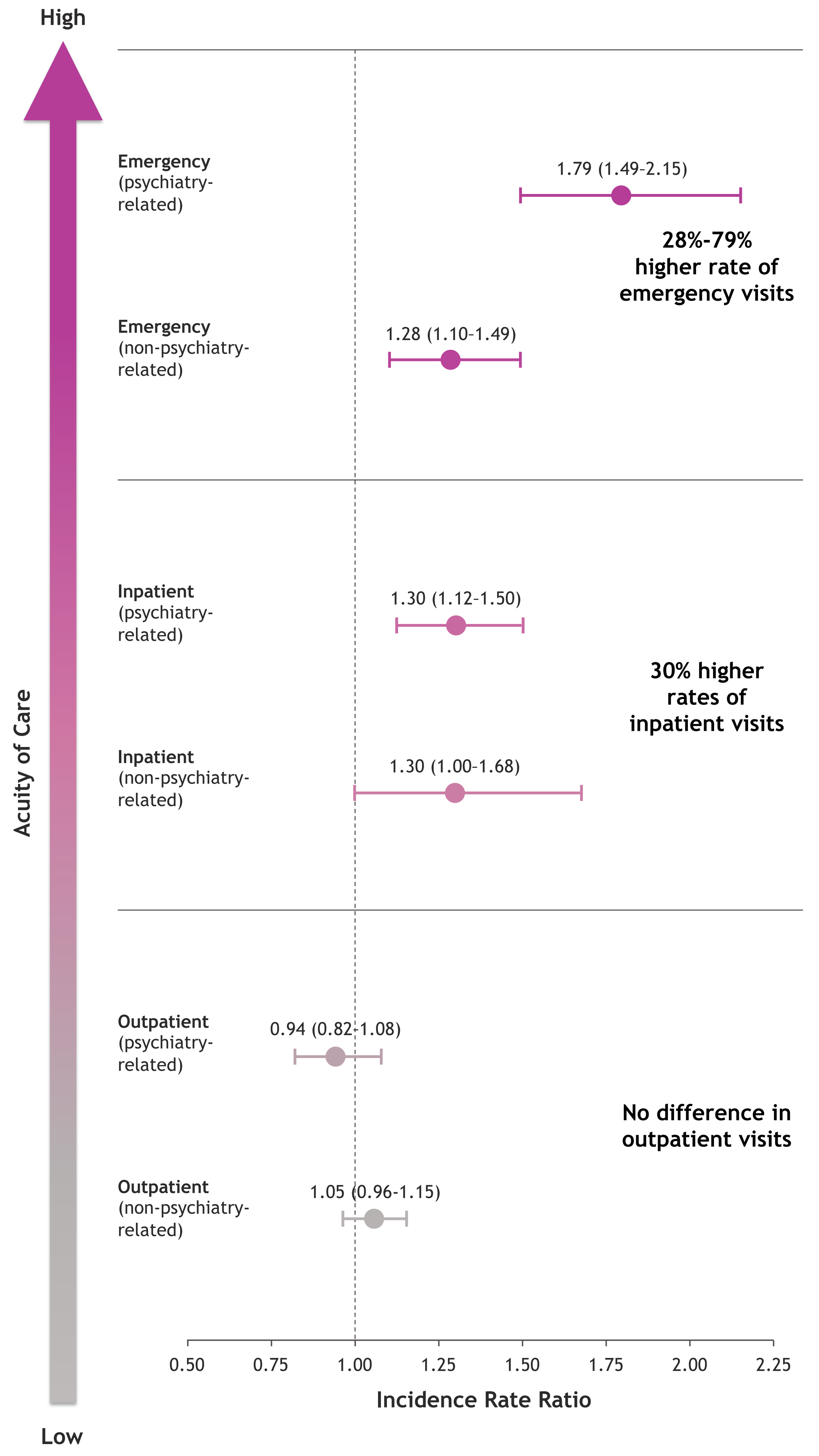
Table 1. Population characteristics after weighting

Variable		With NSS (ESS=1282)	Without NSS (ESS=394)	SMD/ RMD
Age at baseline, years	Median [Q1, Q3]	38 [28, 54]	39 [27, 52]	
Sex, n (%)	Female	714.03 (40.4%)	319.5 (42.8%)	0.02
	Male	1051.5 (59.6%)	427.52 (57.2%)	
Race, n (%)	White	650.67 (36.9%)	247.05 (33.1%)	0.03
	Black or African American	879.72 (49.8%)	396.39 (53.1%)	<0.01
	Other race	110.98 (6.3%)	48.75 (6.5%)	<0.01
	Unknown	124.17 (7%)	54.82 (7.3%)	0.04
Ethnicity, n (%)	Hispanic or Latino	68.15 (3.9%)	26.92 (3.6%)	<0.01
	Not Hispanic or Latino	1031.58 (58.4%)	428.47 (57.4%)	0.01
	Unknown	665.79 (37.7%)	291.62 (39%)	0.01
Clinical setting at index date, n (%)	Inpatient visit	471.87 (26.7%)	130.04 (17.4%)	0.09
	Outpatient visit	1093.97 (62%)	418.43 (56%)	0.06
	Emergency room visit	502.14 (28.4%)	267.64 (35.8%)	0.07
	Other setting	994.45 (56.3%)	490.47 (65.7%)	0.09
Symptoms, n (%)	Positive symptoms	937.27 (53.1%)	345.96 (46.3%)	0.07
	Cognitive impairment symptoms	1017.62 (57.6%)	389.04 (52.1%)	0.06
Comorbidities and treatment at baseline, n (%)	Attention deficit hyperactivity disorder	80.21 (4.5%)	36.85 (4.9%)	<0.01
	Bipolar I or II disorder	161.27 (9.1%)	77.18 (10.3%)	0.01
	Borderline personality disorder	39.25 (2.2%)	13.99 (1.9%)	<0.01
	Generalized anxiety disorder	44.97 (2.5%)	13.7 (1.8%)	0.01
	Major depressive disorder	252.25 (14.3%)	88 (11.8%)	0.03
	Obsessive compulsive disorder	17.85 (1%)	8.72 (1.2%)	<0.01
	Posttraumatic stress disorder	137.38 (7.8%)	56.32 (7.5%)	<0.01
	Schizoaffective disorder	329.82 (18.7%)	112.25 (15%)	0.04
	Substance use disorder (or treatment)	886.57 (50.2%)	341.37 (45.7%)	0.05
	Cardiovascular disorders (or cardiovascular treatment)	713.32 (40.4%)	283.51 (38%)	0.05
	Diabetes mellitus (or hypoglycemic treatment)	261.09 (14.8%)	118.88 (15.9%)	0.01
	Antidepressants	885.59 (50.2%)	332.16 (44.5%)	0.06
	First-generation antipsychotics	611.92 (34.7%)	241.08 (32.3%)	0.02
	Second-generation antipsychotics	1083.47 (61.4%)	422 (56.5%)	0.05
Payor source, n (%)	Medicaid	54.48 (3.1%)	23.98 (3.2%)	<0.01
	Medicare	100.53 (5.7%)	53.62 (7.2%)	0.02
	Commercial	1630.63 (92.4%)	676.76 (90.6%)	0.02

ESS, effective sample size; NSS, negative symptoms in schizophrenia; SMD, standard mean difference; RMD, raw mean difference.

- Negative symptoms in schizophrenia were associated with higher utilization of crisis-based services (**Figure 2**)

Figure 2. Association between negative symptoms in schizophrenia and HCRU (psychiatry-related and non-psychiatry-related)



The figure shows incidence rate ratios and 95% confidence intervals.
HRCU, healthcare resource utilization.

Discussion

- Healthcare utilization analyses revealed that negative symptoms were associated with substantial increases in emergency and inpatient care utilization. Critically, these increases occurred without corresponding changes in outpatient utilization, suggesting a potential breakdown in preventive care
- These findings may reflect the motivational and volitional deficits inherent to negative symptoms that impair patients' capacity to maintain regular outpatient appointments and engage proactively with healthcare services, leading to clinical deterioration requiring acute intervention. The consistency of this pattern across both psychiatry-related and non-psychiatry-related settings suggests that negative symptoms create barriers to healthcare engagement that transcend specialty boundaries

Limitations

- This study has constraints including potential unmeasured confounding, low linkage rate between EHR and claims data that may limit study generalizability, and reliance on multiple routine assessments rather than a single scale (eg, MSE rather than formal assessments such as Positive and Negative Syndrome Scale).

Conclusions

- NSS were associated with substantially increased crisis-driven HCRU across both psychiatry-related and non-psychiatry-related services
- These findings highlight opportunities for targeted interventions addressing negative symptoms in schizophrenia to potentially improve care coordination, reduce healthcare costs, and enhance patient outcomes

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Disclosures

- **NL, JY, LH, EOCP, and SS:** Employment and equity ownership: KKT Technologies, Pte. Ltd. or its subsidiaries
- **MS:** Employee at the time the analysis was conducted: Bristol Myers Squibb
- **KG:** Employee: Bristol Myers Squibb

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