# Negative symptoms in schizophrenia: An observational study of patient characteristics, cost and healthcare resource utilisation from a US healthcare database.

EPH169

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## Introduction

**1 Context**

Negative symptoms (NS) are common in patients living with schizophrenia (SCZ) and are characterised by reduced motivation, diminished emotional expression and social withdrawal. These symptoms significantly impair daily functioning and quality of life.[1,2]

**2 Unmet need**

Current pharmacological options offer limited efficacy in addressing NS, and no treatments are specifically approved for their management. As a result, many patients with SCZ continue to experience persistent NS despite receiving antipsychotic treatment.[1,2]

NS remains a major and under-addressed clinical challenge, contributing to long-term disability and a substantial burden on patients and the health care system. This includes increased healthcare resource utilisation (HCRU) and associated costs.[3]

## Aim

To identify patients with SCZ treated with antipsychotics and who suffer from NS, using United States (U.S) electronic health records (EHRs) and claims data, and to describe their clinical and demographic characteristics, HCRU, and associated costs.

## Methods

### Study design

This was an observational, non-interventional study using de-identified EHR and administrative claims data from the Optum Market Clarity Integrated Clinical + Claims Database. Patients with and without NS were identified and compared.

- Study Period: July 2018 – September 2023.
- Index Date: Randomly selected medical claim with a SCZ diagnosis during the identification period (Jan 1, 2019 – Sep 30, 2022).
- Baseline: 6 months prior to index date.
- Follow-up: 12 months on and after index date.

**Inclusion Criteria**

Population: Adults with ≥1 SCZ diagnosis (ICD-10: F20.*)

Continuous claims-based enrollment during baseline and follow-up

EHR data of ≥2 records, ≥1 during baseline and ≥1 during follow-up period

≥90 days of antipsychotic supply during baseline and at index date

### Outcomes

Patients with NS:

- Were identified within ±6 months of the index period using natural language processing of EHR data (e.g., loss of interest in usual activities, flat affect, anhedonia) and diagnosis codes (e.g., indicating lack of energy, lethargy, flat affect or feeling lonely).

Overall mortality was analysed using a Cox proportional hazards model adjusting for multiple covariates including age, sex, substance abuse and comorbidity index score.

Treatment change was defined as the initiation of an antipsychotic or mood stabiliser not present at the index date during the follow-up period.

HCRU and standardised related costs: all cause (not limited to mental health), mental health-related and SCZ-related.

### Abbreviations

CI, confidence interval; EHR, electronic health record; HCRU, healthcare resource utilisation; HR, hazard ratio; ICD, international classification of diseases; MDD, major depressive disorder; NS, negative symptoms; SCZ, schizophrenia; SD, standard deviation; U.S, United States.

### References

1. Galderisi S, Kaiser S, Bitter I, *et al*. EPA guidance on treatment of negative symptoms in schizophrenia. *Eur Psychiatry*. 2021;64:e21.
2. Sabé M. Combating negative symptoms in schizophrenia: Updated treatment approaches. *Psychiatric Times*. 2024;41(12):20–21.
3. Correll CU and Schooler NR. Negative symptoms in schizophrenia: A review and clinical guide for recognition, assessment, and treatment. *Neuropsychiatr Dis Treat*. 2020;16:519–534.
4. Charlson ME, Pompei P, Ales KL, *et al*. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373–383.

### Disclosures

JZ, LZ and CH are full-time employees of Boehringer Ingelheim. WBH is an employee of Optum Life Sciences.

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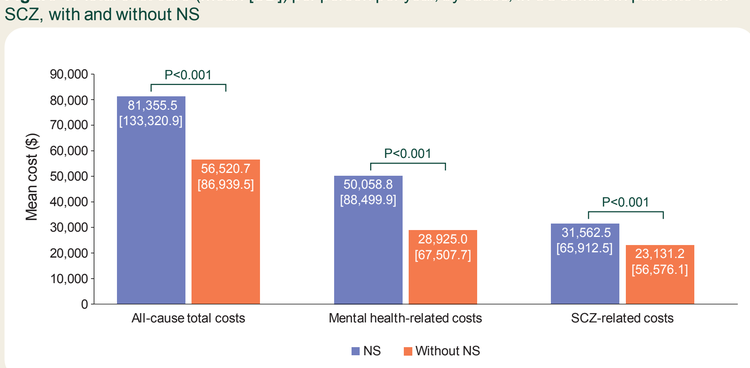
## Key Conclusions

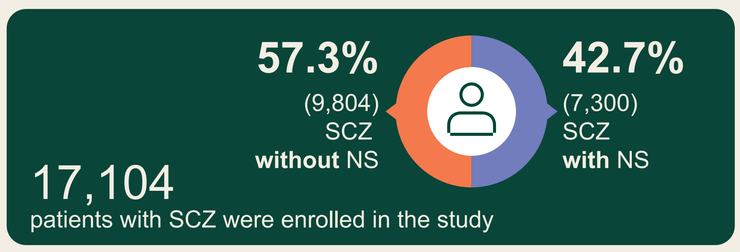
- In this US-based observational study of 17,104 patients with SCZ, 43% exhibited NS, highlighting the substantial burden within this population.
- NS was associated with increased HCRU, particularly in emergency visits, inpatient stays, and mental health-related services, which translated into substantially higher standardised healthcare costs across all domains.
- Patients with NS incurred higher total cost of care, including higher total mental-health-related and SCZ-related cost of care (**Figure 1**), indicating a significant economic burden.
- To optimise outcomes for patients with SCZ, it is essential for the healthcare system to prioritise the recognition and diagnosing of NS and advance treatment approaches.

**Figure 1.** Total cost care (mean [SD]) per person per year, by cause, in US dollars in patients with SCZ, with and without NS




## Results

### Study population




Demographic characteristics were numerically similar between patients with and without NS. (Full patient demographics are shown in **Table 1**).

**Table 1**. Patient demographics in patients with SCZ with and without NS

| Characteristic | SCZ with NS | SCZ without NS |
|---|---|---|
| Mean age, yrs (SD) | 49 (15) | 48 (15) |
| **Sex** | | |
| Female | 3,442 (47.1) | 4,755 (48.5) |
| Male | 3,858 (52.8) | 5,049 (51.5) |
| **Race** | | |
| Caucasian | 4,434 (60.7) | 5,695 (58.0) |
| Black | 2,149 (29.4) | 2,827 (28.8) |
| Asian | 94 (1.2) | 181 (1.8) |
| **Insurance** | | |
| Commercial | 2,797 (38.3) | 3,363 (34.3) |
| Medicaid | 2,357 (32.2) | 2,921 (29.7) |
| Medicare | 1,627 (22.2) | 2,118 (21.6) |
| Medicare patients <65 years old | 1,222 (75.1) | 1,542 (72.8) |
| Missing | 238 (3.2) | 1,026 (10.4) |
| Other | 171 (2.3) | 223 (2.2) |
| Uninsured | 110 (1.5) | 153 (1.5) |

Results are shown as n (%) unless otherwise stated

### Study outcomes

The Charlson Comorbidity Index was analysed, and the most frequent mental health comorbidities are shown in **Table 2**.

**Table 2**. The five most common comorbidities at index date and during follow up in patients with SCZ, with and without NS

| Baseline characteristic | NS (n=7,300) | Without NS (n=9,804) |
|---|---|---|
| **Comorbidity, n (%)** | | |
| Alcohol or substance abuse* | 3,185 (43.6%) | 2,861 (29.1%) |
| Adjustment disorder* | 2,084 (28.5%) | 1,993 (20.3%) |
| Anxiety disorder* | 4,230 (57.9%) | 4,658 (47.5%) |
| Bipolar disorder* | 3,474 (47.5%) | 3,783 (38.5%) |
| MDD* | 4,091 (56.0%) | 4,358 (44.4%) |
| Charlson Comorbidity Index, mean (SD)* | 1.52 (2.0) | 1.33 (1.8) |

*P<0.0001 for all variables tested

**Mortality Risk Factor in SCZ**

**NS** were associated with a 35% increased risk of death

HR = 1.35, 95% CI:1.14–1.59; P<0.001; model adjusted for demographics, baseline comorbidities, medication usage

**Table 3**. Antipsychotic treatment patterns in patients with SCZ, with and without NS

| SCZ treatment use at index date | With NS (%) | Without NS (%) |
|---|---|---|
| First generation antipsychotics | 26.8 | 19.4 |
| Second generation antipsychotics | 72.8 | 80.0 |
| Antipsychotic monotherapy | 66.3 | 83.1 |
| Dual combination antipsychotic therapy | 30.1 | 15.8 |
| Triple combination antipsychotic therapy | 3.5 | 0.9 |
| **SCZ treatment use at follow-up** | | |
| Changed the SCZ treatment†* | 34.0 | 21.0 |
| Discontinued antipsychotic medication* | 27.6 | 23.8 |

NS, negative symptoms; SCZ, schizophrenia.

*P<0.0001;†Treatment change was defined as the initiation of an antipsychotic or mood stabiliser not present at the index date during the follow-up period

**Table 4**. HCRU during 1-year-follow-up in patients with SCZ, with and without NS

| | NS | Without NS | P-value |
|---|---|---|---|
| **All-cause HCRU** | | | |
| Number of visits, mean (SD) | | | |
| Outpatient | 8.5 (20.1) | 7.6 (18.5) | 0.002 |
| Emergency services | 3.1 (5.7) | 1.8 (3.6) | <0.001 |
| Inpatient | 2.0 (3.7) | 0.9 (2.3) | <0.001 |
| Length of inpatient stay, days (SD) | 7.8 (21.8) | 7.6 (33.9) | 0.760 |
| **Mental health-related HCRU** | | | |
| Number of visits, mean (SD) | | | |
| Outpatient | 4.9 (16.6) | 4.2 (15.6) | 0.005 |
| Emergency services | 1.7 (3.8) | 0.8 (2.2) | <0.001 |
| Inpatient | 1.6 (3.1) | 0.7 (2.0) | <0.001 |
| Length of inpatient stay, days (SD) | 8.6 (23.8) | 8.6 (35.9) | 0.930 |
| **SCZ-related HCRU** | | | |
| Number of visits, mean (SD) | | | |
| Outpatient | 1.9 (11.3) | 2.1 (11.9) | 0.285 |
| Emergency services | 0.6 (1.8) | 0.3 (1.0) | <0.001 |
| Inpatient | 0.7 (1.9) | 0.3 (1.3) | <0.001 |
| Length of inpatient stay, days (SD) | 9.3 (27.8) | 9.7 (42.7) | 0.691 |

Patients with NS incurred substantially higher healthcare costs across several categories. Differences between patients with NS and those with no NS were driven by medical cost. Pharmacy cost did not differ significantly (**Table 5**).

**Table 5**. Standardised healthcare costs during 1-year-follow-up in patients with SCZ with and without NS

| | NS | Without NS | P-value |
|---|---|---|---|
| **All-cause costs** | | | |
| Outpatient | 7,501.6 (26,773.3) | 6,151.2 (20,660.2) | <0.001 |
| Emergency services | 10,692.0 (24,652.6) | 5,324.5 (14,083.1) | <0.001 |
| Inpatient | 29,973.8 (69,131.4) | 14,314.2 (49,447.7) | <0.001 |
| Medical | 64,828.4 (99,740.7) | 40,149.7 (75,562.7) | <0.001 |
| Pharmacy | 16,527.1 (86,616.4) | 16,371.0 (38,459.5) | 0.874 |
| **Mental health related costs** | | | |
| Outpatient | 4,152.1 (20,730.5) | 3,276.6 (16,993.3) | 0.002 |
| Emergency services | 6,891.7 (19,926.9) | 2,912.2 (10,588.5) | <0.001 |
| Inpatient | 27,828.9 (66,272.1) | 13,108.3 (47,769.2) | <0.001 |
| Medical | 48,690.2 (88,176.5) | 27,567.9 (67,154.3) | <0.001 |
| Pharmacy | 1,368.6 (4,842.5) | 1,357.0 (5,249.6) | 0.883 |
| **SCZ-related costs** | | | |
| Outpatient | 1,875.6 (16,555.4) | 1,753.8 (15,460.5) | 0.621 |
| Emergency services | 2,577.4 (10,074.3) | 1,224.2 (4,673.8) | <0.001 |
| Inpatient | 12,931.8 (41,414.8) | 6,678.1 (36,258.5) | <0.001 |
| Medical | 22,695.3 (59,651.3) | 14,653.9 (52,276.9) | <0.001 |
| Pharmacy | 8,867.2 (27,336.1) | 8,477.3 (20,517.6) | 0.287 |

Data shown as mean (SD). Costs are shown as US$

## Additional Conclusions

- In addition to the higher HCRU and standardised related costs demonstrating the economic burden of NS in patients with SCZ, the higher prevalence of comorbidities and more frequent switching or discontinuation of drug treatment confirms the patient burden of NS.

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