Assessing Antipsychotic Adherence in People with Cognitive Impairment Associated with Schizophrenia: A US Non-Interventional Cohort Study of Real-World Data

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Introduction

1. **CONTEXT** ▸ Antipsychotics are the mainstay of pharmacologic treatment for schizophrenia, with non-adherence presenting a major risk factor for relapse and poor overall outcomes[1–3]

2. **UNMET NEED** ▸ Cognitive impairment is common in people with schizophrenia and presents a significant burden, contributing to overall morbidity and mortality.[3–6] However, there are currently no approved pharmacologic treatments for CIAS

3. **RATIONALE** ▸ Real-world data on antipsychotic use in people with schizophrenia may allow a better understanding of their needs through identification of characteristics related to adherence, such as the presence or absence of CIAS, length of continuous antipsychotic use, and the proportion of people who choose to switch antipsychotic treatments

Aims

To assess antipsychotic use and adherence in people with schizophrenia with and without CIAS

Methods

Study design

Non-interventional retrospective cohort study (October 1, 2016 – March 31, 2022)

Data source

Optum Market Clarity database (Q2 2022 version)
US-based de-identified real-world data from linked administrative claims and electronic health records data

- 72 million enrollees
- 500,000 patients with schizophrenia
- >15 years of longitudinal data (January 1, 2007 – March 31, 2022)

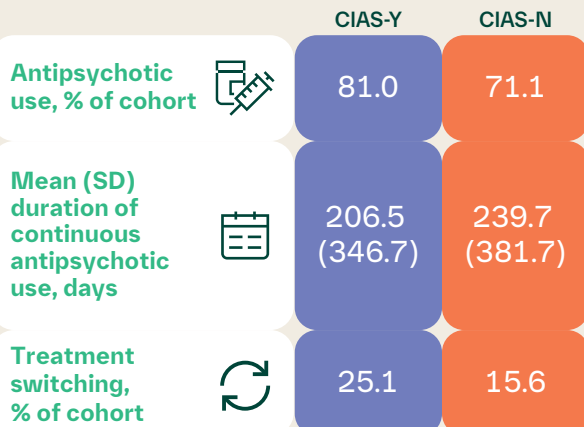| Baseline period	Index date	End of follow-up
12 months pre-index date	First observed diagnosis of schizophrenia during the study period	Date of last encounter, end of database or death

Inclusion criteria
- ≥18 years of age at index date
- ≥2 claims for diagnosis of schizophrenia during the study period (according to ICD-10 F20/ICD-9 295)
- ≥1 year of continuous enrollment during the baseline period

Exclusion criteria
- Presence of Alzheimer's disease, dementia, or epilepsy (during the baseline period); attention deficit hyperactivity disorder (≤1 year before or after index date); bipolar disorder I, bipolar disorder II, or intellectual disability (any time before index date)
- Use of central nervous system stimulants, ketamine, or electroconvulsive therapy procedures ≤6 months pre-index date
- Use of tricyclic antidepressants or transcranial magnetic stimulation ≤35 days pre-index date

Key Conclusions

- People with CIAS had greater antipsychotic use, shorter durations of continuous antipsychotic use, and were more prone to switching antipsychotic class than those without CIAS
  - Findings indicate people with CIAS experience greater treatment burden, highlighting an unmet need for more effective strategies to improve utilization of antipsychotic medication

	CIAS-Y	CIAS-N
Antipsychotic use, % of cohort	81.0	71.1
Mean (SD) duration of continuous antipsychotic use, days	206.5 (346.7)	239.7 (381.7)
Treatment switching, % of cohort	25.1	15.6

Outcomes

- Baseline demographics and antipsychotic use on the index date
- Antipsychotic use in the follow-up period
  - Overall and stratified by CIAS status (CIAS-Y; CIAS-N)
  - Stratified by class: FGA oral, FGA LAI, SGA oral, SGA LAI
    - Duration of continuous antipsychotic use
      - Created by linking prescriptions with allowed gap days (allowed gaps: 30 days for oral medication, 60 days for LAI medication)
      - Imputation days for missing days of supply was 30 for oral medication and 60 for LAI medication
        - Proportion of patients switching class of antipsychotic medication
- MPR: ratio of treated days with each class of antipsychotic medication to total treatment duration
- PDC: number of treated days with each class of antipsychotic medication over number of days from first day of treatment until the end of follow-up; overlapped days of supply were not counted twice

Data analysis

Patient CIAS status was determined by calculating a weighted sum score based on individual CIAS indicator scores (claims code and NLP measure) and absolute distance to any schizophrenia diagnosis date

Score >0	Patients with a history of CIAS or CIAS at follow-up (CIAS-Y)
Score ≤0	Patients with no history of CIAS or CIAS at follow-up (CIAS-N)

All outcomes were reported descriptively and stratified by CIAS status.

Results

Study population

183,483 adult patients with schizophrenia

- 24.1% (44,236) CIAS-Y
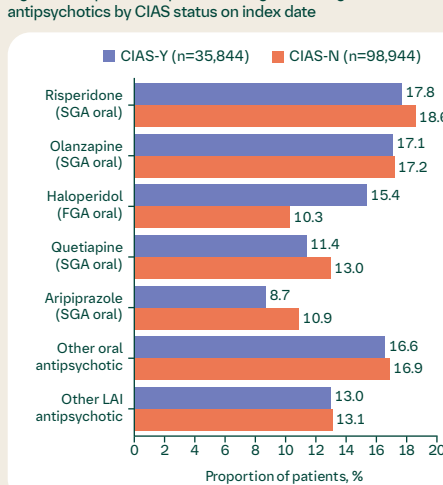- 75.9% (139,247) CIAS-N
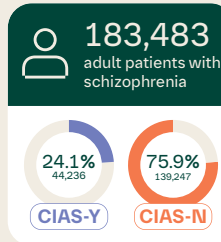
Baseline demographics

Table 1. Patient demographics in the overall study population and by CIAS status

	CIAS-Y (n=44,236)	CIAS-N (n=139,247)	Overall (N=183,483)
Mean (SD) age, years	52.2 (16.7)	46.5 (15.9)	47.8 (16.2)
Sex, n (%)			
Male	26,444 (59.8)	88,209 (63.3)	114,653 (62.5)
Race, n (%)			
Asian	577 (1.3)	2169 (1.6)	2746 (1.5)
Black	13,665 (30.9)	40,133 (28.8)	53,798 (29.3)
Caucasian	21,630 (48.9)	60,783 (43.7)	82,413 (44.9)

Antipsychotic use on index date

- Overall, 134,788 (73.5%) patients used antipsychotics, including 35,844 (81.0%) patients in the CIAS-Y group and 98,944 (71.1%) patients in the CIAS-N group in the form of either monotherapy or combination therapy (**Table 2**)
- On index the CIAS-Y group demonstrated a higher rate of haloperidol use compared with the CIAS-N group (**Figure 1**)

Figure 1. Proportion of patients using different generic antipsychotics by CIAS status on index date

CIAS-Y (n=35,844) ■ CIAS-N (n=98,944)

	CIAS-Y	CIAS-N
Risperidone (SGA oral)	17.8	18.6
Olanzapine (SGA oral)	17.1	17.2
Haloperidol (FGA oral)	15.4	10.3
Quetiapine (SGA oral)	11.4	13.0
Aripiprazole (SGA oral)	8.7	10.9
Other oral antipsychotic	16.6	16.9
Other LAI antipsychotic	13.0	13.1

Table 2. Number of generic antipsychotic prescriptions on index date by CIAS status

	CIAS-Y n=44,236	CIAS-N n=139,247
Number of generic antipsychotic prescriptions on index date, n (%)		
0	8392 (19.0)	40,303 (28.9)
1	32,330 (73.1)	91,767 (65.9)
2	3226 (7.3)	6696 (4.8)
3	264 (0.6)	441 (0.3)
≥4	24 (0.1)	40 (<0.1)
Monotherapy or combination therapy on index date, n (%)		
Monotherapy	32,330 (73.1)	91,767 (65.9)
Combination therapy, ≥2 generic antipsychotic prescriptions	3514 (7.9)	7177 (5.2)
None	8392 (19.0)	40,303 (28.9)

Antipsychotic use in the follow-up period

- During the follow-up period, a higher proportion of patients in the CIAS-Y group were prescribed 3 or more antipsychotic medications compared with the CIAS-N group (**Figure 2**)

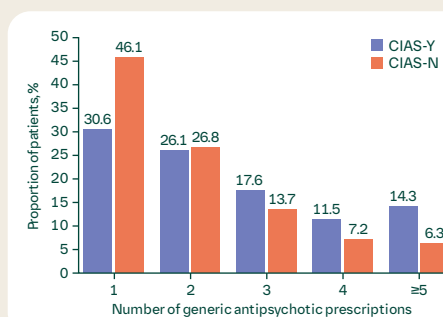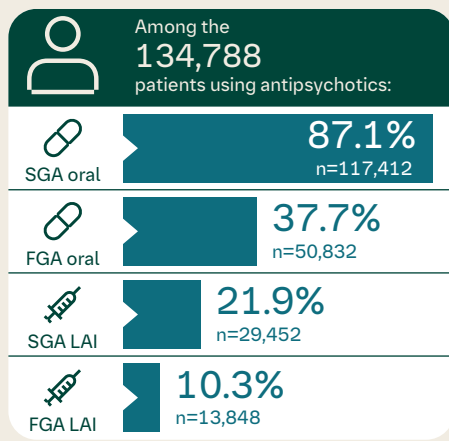Figure 2. Proportion of patients receiving generic antipsychotic prescriptions during the follow-up period

■ CIAS-Y ■ CIAS-N

Number of generic antipsychotic prescriptions	CIAS-Y	CIAS-N
1	30.6	46.1
2	26.1	26.8
3	17.6	13.7
4	11.5	7.2
≥5	14.3	6.3

Antipsychotic use by class in the follow-up period

Among the **134,788** patients using antipsychotics:

- SGA oral: **87.1%** n=117,412
- FGA oral: **37.7%** n=50,832
- SGA LAI: **21.9%** n=29,452
- FGA LAI: **10.3%** n=13,848

As patients may switch antipsychotic class, percentages do not total 100%.

Duration of continuous antipsychotic use

Mean (SD) duration of continuous antipsychotic use, days

CIAS-Y	CIAS-N
206.5 (346.7)	239.7 (381.7)
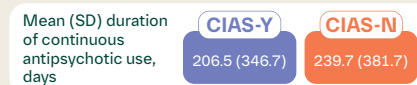
Antipsychotic treatment switching

- For those receiving monotherapy, treatment-switching between the different antipsychotic classes during the first continuous exposure period was generally more common in the CIAS-Y group than the CIAS-N group across all antipsychotic classes (**Figure 3**)

Figure 3. Proportion of patients switching treatments between the 4 antipsychotic classes during the first continuous exposure period

■ CIAS-Y ■ CIAS-N

Antipsychotic class	CIAS-Y	CIAS-N
Overall antipsychotic use	25.1	15.6
FGA oral	35.5	24.7
FGA LAI	43.0	34.3
SGA oral	18.6	10.6
SGA LAI	43.0	32.9
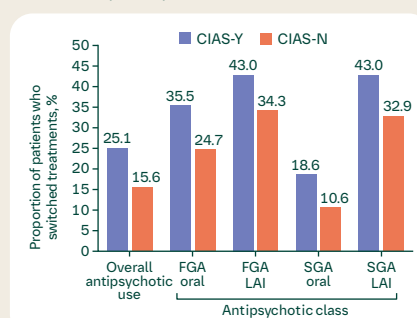
A total of 32,783 patients in the CIAS-Y group vs 95,593 patients in the CIAS-N group had continuous exposure with 1 of the 4 antipsychotic classes and were included in the switching analysis: FGA oral CIAS-Y (n=6825), CIAS-N (n=13,718); FGA LAI CIAS-Y (n=1439), CIAS-N (n=3649); SGA oral CIAS-Y (n=21,898), CIAS-N (n=67,925); SGA LAI CIAS-Y (n=2621), CIAS-N (n=8301).

MPR and PDC in the follow-up period

- For each of the 4 classes of antipsychotics, the mean MPR and mean PDC in the CIAS-Y and CIAS-N groups are described in **Table 3**

Table 3. MPR and PDC by CIAS status and antipsychotic class in the follow-up period

	CIAS-Y	CIAS-N
Medication possession ratio (MPR), mean (SD)		
FGA oral	0.67 (0.33) n=11,084	0.71 (0.31) n=20,594
FGA LAI	0.70 (0.29) n=4247	0.73 (0.27) n=7991
SGA oral	0.66 (0.31) n=31,426	0.69 (0.30) n=82,247
SGA LAI	0.77 (0.26) n=3081	0.79 (0.24) n=7341
Proportion of days covered (PDC), mean (SD)		
FGA oral	0.30 (0.32) n=12,998	0.35 (0.34) n=24,940
FGA LAI	0.33 (0.31) n=4905	0.40 (0.33) n=9232
SGA oral	0.45 (0.32) n=32,998	0.47 (0.34) n=88,694
SGA LAI	0.34 (0.32) n=3606	0.41 (0.34) n=8413

Additional Conclusions

- Patterns of antipsychotic treatment vary between CIAS-Y and CIAS-N groups, with the CIAS-Y group having a higher rate of haloperidol use than the CIAS-N group on index date
- The observation of a higher proportion of patients in the CIAS-Y group switching antipsychotics compared with the CIAS-N group was also reflected in each of the 4 classes of antipsychotics, which may suggest CIAS status is a potential contributory factor in changing treatments. Future studies that capture patients' reasons for switching would be of interest

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