Clinical Characteristics of Patients with Cognitive Impairment Associated with Schizophrenia

Theresa Cassidy[1], Kira Griffiths[2], Min Min Chan[2], Mayowa Oyesanya[2], Rifqi Alkhatib[2], Suzanne St Rose[3], Rashmi Patel[4]

[1]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; [2]Holmusk Technologies Inc, Real World Evidence, Singapore & New York, NY, USA;
[3]Boehringer Ingelheim, Ingelheim am Rhein, Germany; [4]King's College London, Institute of Psychiatry, Psychology & Neuroscience, London, UK
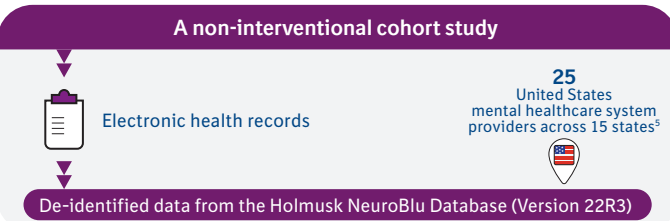
INTRODUCTION

1 CONTEXT
- Schizophrenia is a complex psychiatric illness characterised by positive, negative and cognitive symptoms[1,2]
- Cognitive impairment associated with schizophrenia (CIAS) is common, with around 90% of patients having some level of symptoms[3]
  - One study reported a 16-point decline in IQ from premorbid status[4]

2 UNMET NEED
- Cognitive deficits vary across patients with schizophrenia[4] and may cause limitations with attention, memory, language and visuospatial skills[3]
- Despite being a main feature of schizophrenia,[4] no specific treatment for CIAS exists[2]

AIM

Analysis of real-world data to characterise patients with schizophrenia with and without CIAS to improve the understanding of cognitive symptom burden and unmet patient needs within routine mental healthcare

METHODS

STUDY DESIGN AND PATIENTS

A non-interventional cohort study

- Electronic health records
- **25** United States mental healthcare system providers across 15 states[5]
- De-identified data from the Holmusk NeuroBlu Database (Version 22R3)

KEY INCLUSION CRITERIA
- Patients were ≥18 years of age with ≥2 diagnoses of schizophrenia between 1999 and 2021 using International Statistical Classification of Diseases (ICD) diagnostic codes including ICD-9 295.0–295.65, 295.80–295.95 or ICD-10 F20.0–20.9

KEY EXCLUSION CRITERIA
- Diagnosis of bipolar disorder I or bipolar disorder II, or any neurological disease that may lead to cognitive impairment

Study definitions
- Index was defined as the first recorded diagnosis of schizophrenia in the NeuroBlu Database
- Baseline period was defined as +/- 14 days from Index

Analyses performed
- Features of cognitive dysfunction recorded within +/- 14 days of the first recorded schizophrenia diagnosis were derived from free text documented during the mental status examination (MSE) and extracted using natural language processing models[6]
- MSE features indicative of CIAS were identified through clinical review (Table 1)

Table 1. MSE labels indicative of CIAS

MSE category	Label	Example of raw text strings mapped to label
Cognition	General issues	"impaired cognition", "limited", "poor", "unable to spell name"
Cognition	Issues with attention	"impaired attention"
Cognition	Issues with concentration	"impaired concentration"
Attention/ Concentration	General issues	"mild/moderate difficulty with attention/focus", "seems distracted", "short attention span", "concentration poor"
Executive functioning	Some impairment	"slow cognitively", "impaired by lower cognitive functioning", "impaired"
Reasoning	Impaired reasoning	"impaired", "unable to repeat back concrete instruction", "limited reasoning ability"
Fund of knowledge	Issues with fund of knowledge / generally limited	"deficits in fund of knowledge", "impaired", "limited"
Cognition	Issues with fund of knowledge	"fund of knowledge, impaired"

CIAS, cognitive impairment associated with schizophrenia; MSE, mental status examination.

Demographic and baseline clinical features of patients with and without at least one recorded MSE clinical feature indicative of CIAS were compared

Clinical features included:
- Comorbid psychiatric disorders
- Pharmacological treatments
- Disease severity (based on the Clinical Global Impressions-Severity [CGI-S] score)
- Functioning (based on the Global Assessment of Functioning [GAF] score)
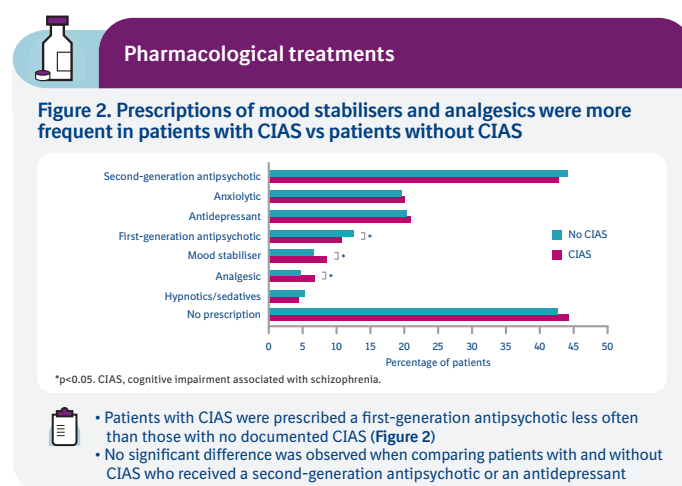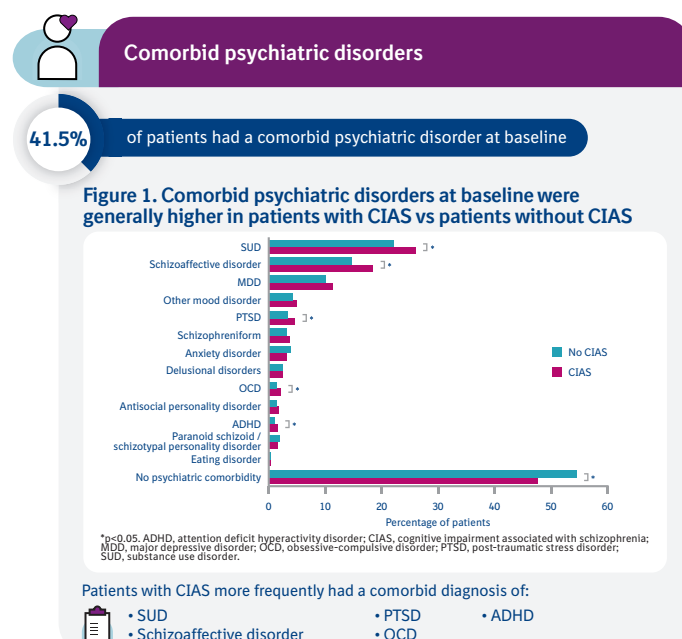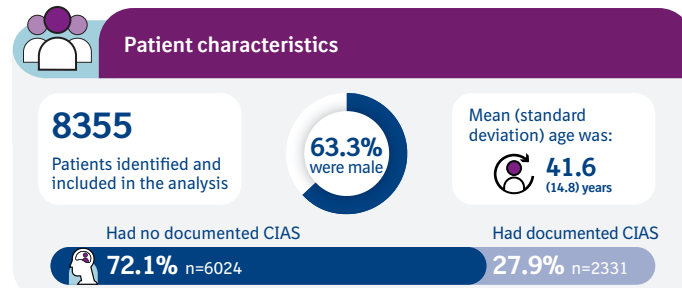- Social factors

KEY CONCLUSIONS

- The proportion of patients with CIAS in this study was lower than reported in the literature,[3] suggesting under-recognition and recording in routine clinical practice
- An opportunity exists to improve detection and management of CIAS through:
  - Clinician education
  - Digital approaches
  - Additional therapeutics

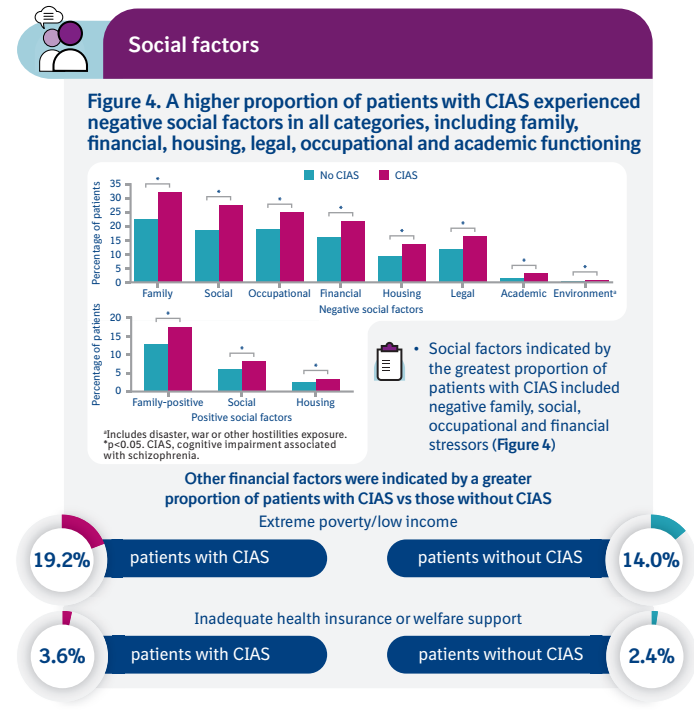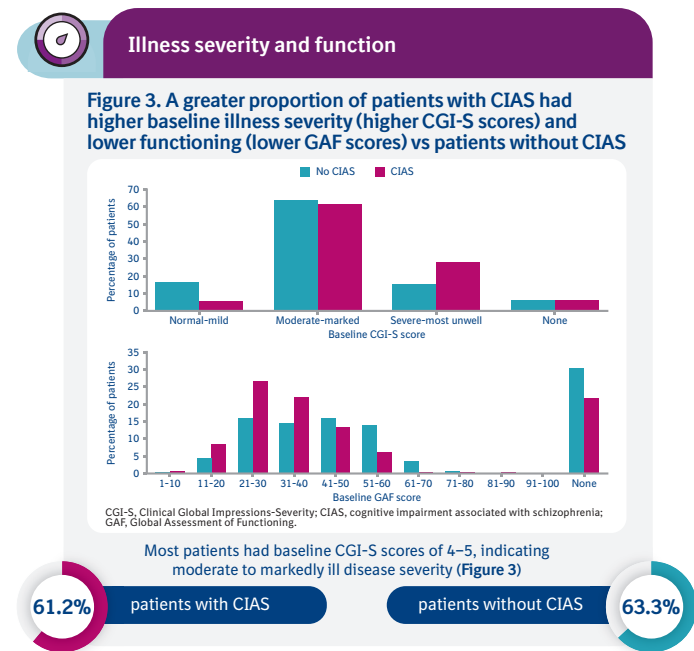CIAS, cognitive impairment associated with schizophrenia.

CIAS
- Comorbid psychiatric disorders were more common
- Prescribed mood stabilisers and analgesics more frequently
- Higher baseline illness severity and lower functioning
- Increased emergency department visits, inpatient visits and outpatient visits
- More likely to experience negative social factors

RESULTS

Patient characteristics

8355 Patients identified and included in the analysis

63.3% were male

Mean (standard deviation) age was: **41.6** (14.8) years

Had no documented CIAS **72.1%** n=6024
Had documented CIAS **27.9%** n=2331

Comorbid psychiatric disorders

41.5% of patients had a comorbid psychiatric disorder at baseline

Figure 1. Comorbid psychiatric disorders at baseline were generally higher in patients with CIAS vs patients without CIAS

*p<0.05. ADHD, attention deficit hyperactivity disorder; CIAS, cognitive impairment associated with schizophrenia; MDD, major depressive disorder; OCD, obsessive-compulsive disorder; PTSD, post-traumatic stress disorder; SUD, substance use disorder.

Patients with CIAS more frequently had a comorbid diagnosis of:
- SUD
- Schizoaffective disorder
- PTSD
- OCD
- ADHD

Pharmacological treatments

Figure 2. Prescriptions of mood stabilisers and analgesics were more frequent in patients with CIAS vs patients without CIAS

*p<0.05. CIAS, cognitive impairment associated with schizophrenia.

- Patients with CIAS were prescribed a first-generation antipsychotic less often than those with no documented CIAS (Figure 2)
- No significant difference was observed when comparing patients with and without CIAS who received a second-generation antipsychotic or an antidepressant

Psychotherapy

Patients with CIAS received psychotherapy significantly less often than patients without CIAS (p<0.001)

15.7% patients with CIAS
21.2% patients without CIAS

Illness severity and function

Figure 3. A greater proportion of patients with CIAS had higher baseline illness severity (higher CGI-S scores) and lower functioning (lower GAF scores) vs patients without CIAS

CGI-S, Clinical Global Impressions-Severity; CIAS, cognitive impairment associated with schizophrenia; GAF, Global Assessment of Functioning.

Most patients had baseline CGI-S scores of 4–5, indicating moderate to markedly ill disease severity (Figure 3)

61.2% patients with CIAS
63.3% patients without CIAS

Social factors

Figure 4. A higher proportion of patients with CIAS experienced negative social factors in all categories, including family, financial, housing, legal, occupational and academic functioning

*Includes disaster, war or other hostilities exposure.
*p<0.05. CIAS, cognitive impairment associated with schizophrenia.

- Social factors indicated by the greatest proportion of patients with CIAS included negative family, social, occupational and financial stressors (Figure 4)

Other financial factors were indicated by a greater proportion of patients with CIAS vs those without CIAS

Extreme poverty/low income
19.2% patients with CIAS
14.0% patients without CIAS

Inadequate health insurance or welfare support
3.6% patients with CIAS
2.4% patients without CIAS

Healthcare resource utilisation

Table 2. Patients with CIAS had significantly more emergency department visits, inpatient visits and less outpatient visits than those without CIAS

	Emergency*	Inpatient*	Outpatient*
Patients with CIAS (n=2331)	26.3% (n=614)	45.3% (n=1057)	61.1% (n=1425)
Patients without CIAS (n=6024)	18.8% (n=1135)	27.7% (n=1669)	71.4% (n=4304)

*p<0.001. CIAS, cognitive impairment associated with schizophrenia.

ADDITIONAL CONCLUSIONS

1 Patients with CIAS received psychotherapy less often, suggesting that CIAS may make it harder for patients to engage with psychotherapy

2 Higher prescribing of mood stabilisers and analgesic medications for patients with CIAS suggests additional illness-related features or physical comorbidities among these patients

3 CIAS was associated with meaningful differences in clinical presentation and other outcomes such as negative social factors, providing evidence to support associations between CIAS and higher illness burden

REFERENCES
1. Kahn RS, et al. Nat Rev Dis Primers 2015;1:15067. 2. McCutcheon RA, et al. JAMA Psychiatry 2019;77:201–10. 3. Goonathilake P, et al. BMC Psychiatry 2022;22(1):716. 4. Fujino H, et al. Psychiatry Clinical Neuroscience 2017;71(5):294–300. 5. Patel R, et al. BMJ Open 2022;12(4):e057227. 6. Mukherjee SS, et al. Computational Psychiatry 2020;4:76–106.

Boehringer Ingelheim