

# Long-term Patient Functioning and Illness Burden Associated with Cognitive Impairment and Negative Symptoms in Schizophrenia

Poster  
F147

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## INTRODUCTION

- CONTEXT**
  - Cognitive impairment and negative symptoms (NS) are core features of schizophrenia.<sup>1,2</sup> However, there are few effective treatments for these symptom domains<sup>3</sup>
  - Cognitive impairment associated with schizophrenia (CIAS) is linked to poor functional outcomes such as treatment resistance, as well as poor social determinants of health including unemployment, sociality, finances, and inability to live independently, all of which lead to greater healthcare resource utilisation (HCRU)<sup>4-6</sup>
- UNMET NEED**
  - In patients with schizophrenia, increased awareness of CIAS and NS and their association with poor clinical outcomes may improve access to novel treatment approaches
  - Real-world data (RWD) reporting CIAS and NS can provide further insights into patients with schizophrenia who have these symptoms, including clinical presentation, symptom burden and their association with long-term clinical outcomes

**AIM**

Analysis of RWD from electronic health records (EHR) to investigate associations between clinician-reported CIAS and NS with clinical outcomes in a large and representative sample of patients with schizophrenia

## METHODS

### STUDY DESIGN AND PATIENTS

A non-interventional cohort study

Electronic health records

25 United States mental healthcare system providers across 15 states<sup>7</sup>

De-identified data from the Holmusk NeuroBlu Database (Version 22R3)

The main cohort comprised patients ≥18 years of age with ≥2 recorded 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

### Study definitions

- Index date was defined as the first-recorded schizophrenia diagnosis in the NeuroBlu Database and baseline variables were extracted at index +/-14 days
- Presence of CIAS, NS or positive symptoms was defined as having one or more clinician-documented symptoms
- Natural language processing models were used to transform clinician-documented free text from the mental state examination (MSE) into structured MSE features<sup>8</sup>
- Clinical features indicative of CIAS, NS and positive symptoms were identified via clinical review (Table 1)

Table 1. MSE features reflecting each domain

COGNITIVE SYMPTOMS					
MSE Category	Cognition	Attention/Concentration	Executive functioning	Reasoning	Fund of knowledge
MSE label	General issues Issues with attention Issues with concentration Issues with fund of knowledge	General issues	Some impairment	Impaired reasoning	Issues with fund of knowledge/generally limited
NEGATIVE SYMPTOMS					
MSE Category	Affect	Appearance	Language	Psychomotor	Speech
MSE label	Blunted/restricted affect	Issues with grooming/hygiene Issues with eye contact Issues with dress	Non-verbal/mute Minimally verbal Impaired language	Retarded; slow Declined psychomotor Catatonic	Impoverished Mute, non-verbal
POSITIVE SYMPTOMS <sup>a</sup>					
MSE Category	Abnormal or psychotic thoughts				
MSE label	Delusions (not specified) Delusions/abnormal thoughts (paranoia) Delusions/abnormal thoughts (grandeur) Delusions/abnormal thoughts (obsessions) Delusions/abnormal thoughts (persecution) Delusions/abnormal thoughts (religious) Delusions/abnormal thoughts (sexual) History of delusions/abnormal thoughts			History of hallucinations (not specified) Auditory hallucinations Tactile hallucinations Olfactory hallucinations Responding to internal stimuli	

<sup>a</sup>Additional MSE label of "Tangential Loose" belonged to the category of "Association". MSE, Mental state examination.

### Statistical analysis

- The primary exposure variables of interest were presence of CIAS (yes/no) and presence of NS (yes/no)
- Cox and negative binomial regression models were used to investigate associations between baseline symptom presentation and:
  - Time to first psychiatric hospitalisation
  - Data were censored at 18 months
  - The number of unique inpatient visits
  - Patients with follow-up <3 months were excluded and an offset term was included in each model whereby the follow-up duration for a patient was defined as time from index to last recorded visit date
  - The total duration of inpatient days
  - For descriptive statistics, the duration of inpatient visits was defined as the total duration of days spent in an inpatient setting calculated from the mean length of inpatient hospitalisation by averaging the annualised cumulated length of stay across all patients
- Covariates included presence of positive symptoms, age, gender, race, year of index, clinic type, plus baseline psychotherapy exposure, illness severity based on the Clinical Global Impression-Severity (CGI-S) score, functioning based on the Global Assessment of Functioning (GAF) score, pharmacological prescriptions, psychiatric comorbidities, and social features

## KEY CONCLUSIONS

- CIAS and NS were independently associated with greater HCRU after adjusting for multiple baseline variables
- The relationship between CIAS or NS and HCRU in schizophrenia supports the growing body of evidence that implicates these symptom domains in the long-term disease burden and highlights the need for adequate detection to better identify patient subgroups for treatment
- The independent real-world association between CIAS and HCRU provides additional evidence that CIAS is a specific symptom domain requiring improved identification and specifically targeted treatments in patients with schizophrenia
- Additional research into the relationship between CIAS and psychotherapy exposure is needed to better understand why CIAS may restrict access to psychotherapy, and how access can be promoted

Increased risk of psychiatric hospitalisations

HR: 1.19 (95% CI: 1.04, 1.37)

1.16 times higher rate of inpatient visits  
IRR: 1.16 (95% CI: 1.01, 1.34)

1.23 times higher rate of total number of inpatient days  
IRR: 1.23 (95% CI: 1.06, 1.43)

Increased risk of psychiatric hospitalisations

HR: 1.61 (95% CI: 1.37, 1.89)

1.55 times higher rate of inpatient visits  
IRR: 1.55 (95% CI: 1.32, 1.83)

1.59 times higher rate of total number of inpatient days  
IRR: 1.59 (95% CI: 1.35, 1.89)

## RESULTS

**Baseline patient characteristics**

Figure 1. Patient attrition

8355 patients with a diagnosis of schizophrenia were identified in the NeuroBlu Database (Figure 1)

4469 included for time to first psychiatric hospitalisation analyses

3799 included for number of inpatient visits and total number of inpatient days analyses

Patients identified in NeuroBlu Database with a diagnosis of schizophrenia (N=8355)

Patients received care at clinical sites with both inpatient and outpatient units (n=7051)

Patients had visit data through 78 weeks post index and included in time-to-event analyses; for time to first psychiatric hospitalisation (n=4469)

Patients had ≥3 months of post-index visit data included in the count analyses; frequency and duration of inpatient days across follow-up (n=3799)

Baseline demographic and clinical characteristics for the broader NeuroBlu schizophrenia population (N=8355) are presented separately (see poster S152 at this congress)

Patients were seen in the following settings:

32.6% (n=2726) Inpatient\*

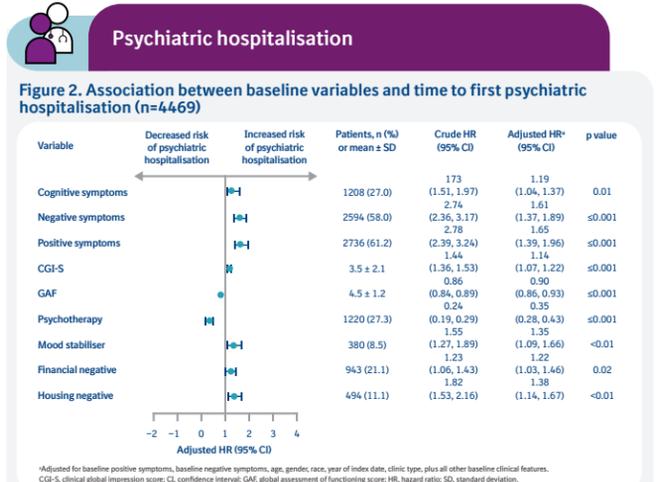
20.9% (n=1749) Emergency department\*

68.6% (n=5729) Outpatient\*

Baseline mean (standard deviation [SD]) CGI-S was 4.51 (1.15)

Baseline mean (SD) GAF was 39.3 (13.4)

\*Categories are not mutually exclusive and a patient may have multiple visits recorded during the baseline period



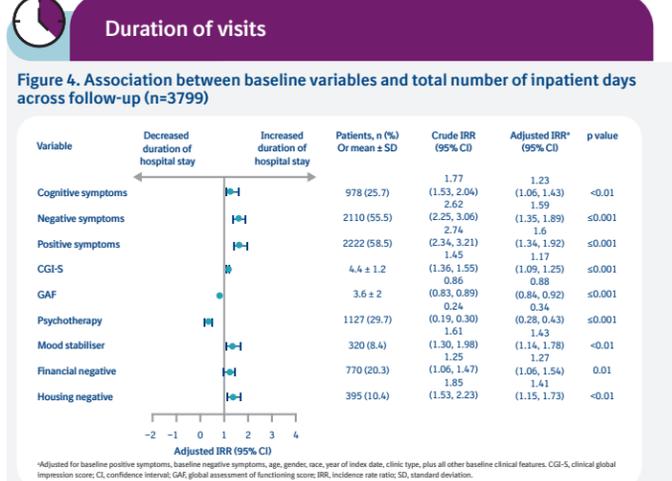
Adjusted hazard ratio (HR) demonstrated that patients with documented CIAS or NS were at higher risk of hospitalisation than patients without these symptoms documented

Presence of positive symptoms, Negative housing features, Prescription of a mood stabiliser, Negative financials

were also associated with increased risk of hospitalisation (Figure 2)

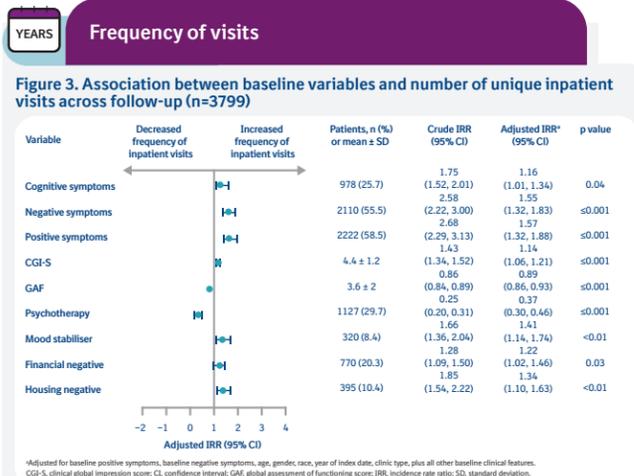
19% Higher risk of psychiatric hospitalisation across follow-up for patients with documented CIAS versus patients without documented CIAS

Exposure to psychotherapy at baseline was associated with substantially reduced risk of psychiatric hospitalisation



## ADDITIONAL CONCLUSIONS

- CIAS and NS in schizophrenia are likely underreported in RWD, although NS are more commonly reported compared with CIAS
- Treatments which target CIAS and NS could potentially reduce the personal and economic burden associated with schizophrenia
- Exposure to psychotherapy was associated with substantially reduced risk of hospitalisation, that may reflect a cohort of patients who are less unwell and therefore less likely to experience an exacerbation in illness across follow-up versus patients who did not receive psychotherapy; psychotherapy may also provide these patients with a possible protective effect against clinical deterioration, thus reducing hospitalisation



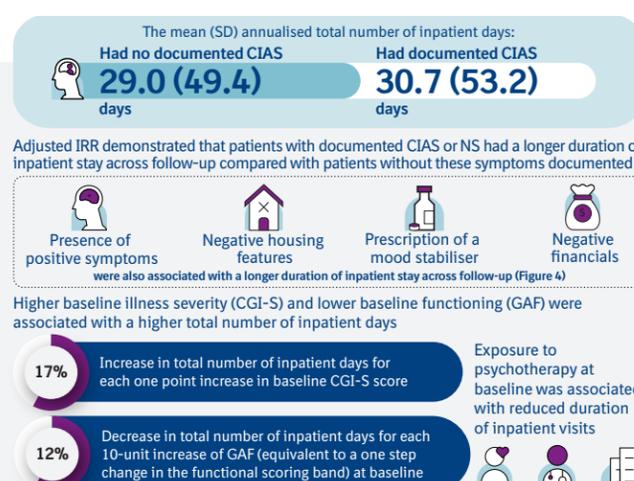
Adjusted incidence rate ratio (IRR) demonstrated that patients with documented CIAS or NS experienced higher number of inpatient visits than patients without these symptoms documented

Presence of positive symptoms, NS and CIAS, Higher baseline illness severity (CGI-S), Lower baseline functioning (GAF)

were also associated with increased number of inpatient visits across follow-up (Figure 3)

1.16 Times higher rate of inpatient visits for patients with CIAS at baseline compared to patients who did not have CIAS at baseline

Exposure to psychotherapy at baseline was associated with reduced number of unique inpatient visits



## REFERENCES

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## DISCLOSURES

TC and SR are employees of Boehringer Ingelheim. KG, MMC, MO are employees of Holmusk Technologies Inc. RA was previously employed by Holmusk Technologies Inc. RP has received grant funding from the National Institute for Health and Care Research (NIHR/S030590). The Medical Research Council (MR/S00318/1), the Academy of Medical Sciences (SLG15/1020) and Janssen, and consulting fees from Holmusk, Akkriva Health, Columbia Data Analytics, Boehringer Ingelheim and Otsuka.

## ACKNOWLEDGEMENTS

The authors meet the criteria for authorship as recommended by the International Committee of Medical Journal Editors. This study was funded by Boehringer Ingelheim (1346-0067). Writing, editorial support, and formatting assistance for the poster were provided by Sharon Bryant, DPT, of Fishback Communications Ltd, part of Avaree Health, funded by Boehringer Ingelheim International GmbH. Funding for the studies presented was provided by Boehringer Ingelheim.

