Associations Between Negative Symptoms in Schizophrenia, Psychotherapy Exposure, and Healthcare Resource Utilisation and Clinical Outcomes: A Non-Interventional Observational Study

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Aims

This study examined:

- Associations between negative symptoms (primary study exposure) and HCRU, treatment continuity and functioning (using the GAF)
- Outcomes related to outpatient psychotherapy exposure (excluding crisis intervention) in a separate analysis limited to patients with negative symptoms

Introduction

1 CONTEXT

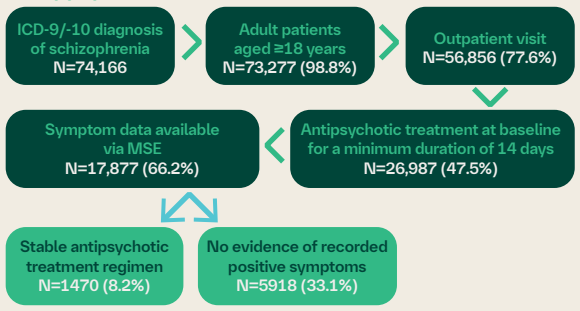
Negative symptoms of schizophrenia often persist despite antipsychotic treatment and even after other symptoms have fully or partially resolved, and they can be associated with substantial functional impairment[1,2]

2 UNMET NEED

There is a need to characterise the real-world experience of patients with stable schizophrenia and evidence of negative symptoms, investigate associations between clinical presentation, longitudinal illness course and HCRU, and to better understand psychotherapy use in these patients

Results

Study population

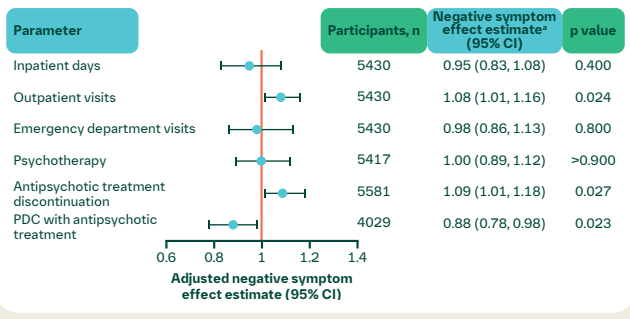


- Of 5918 patients with stable schizophrenia (no evidence of recorded acute positive symptoms), 5430 were included in the HCRU analyses; of these, 36% (n=1956) had documented negative symptoms

Negative symptom exposure and HCRU

- Negative symptoms were associated with more outpatient visits and a higher risk of antipsychotic discontinuation during the 12-month follow-up period (**Figure 2**)
  - The adjusted estimated mean rate of outpatient visits was 21.99 per year for patients with negative symptoms and 17.78 per year for those without
  - By 12 months, the cumulative risk of treatment discontinuation increased to 60% (95% CI: 57, 62) for patients with negative symptoms and 49% (95% CI: 47, 51) for those without
- There was no statistically significant difference in estimated mean rate of inpatient days per year between patients with negative symptoms and those without (1.19 vs 1.26)
- The mean (SD) proportion of days covered with antipsychotic treatment was lower in patients with negative symptoms (0.64 [0.38]) versus those without (0.71 [0.37])

Figure 2. Associations between negative symptoms and clinical outcomes



[a]These were risk ratios for inpatient days, outpatient visits, emergency department visits and psychotherapy, hazard ratio for antipsychotic treatment discontinuation, and odds ratio for proportion of days covered with antipsychotic treatment.
CI, confidence interval; PDC, proportion of days covered.

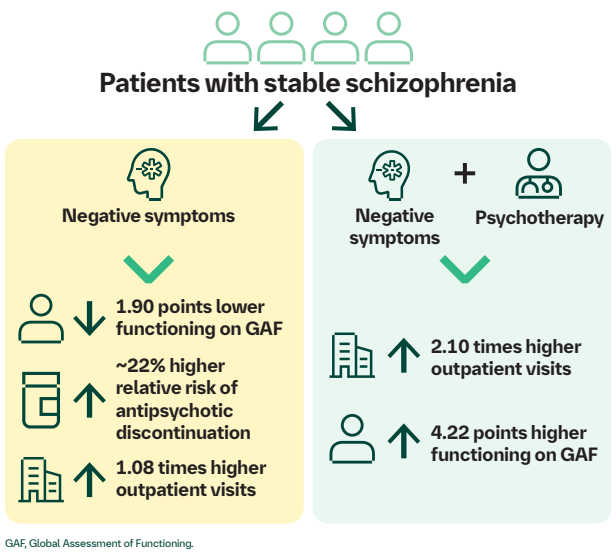
Negative symptom exposure and functioning

- GAF scores (range: 0–91) were significantly lower in those with baseline negative symptoms, albeit a small effect estimate (Beta= −1.90 [95% CI: −2.90, −0.85], p<0.001)

Key Conclusions

- Negative symptoms pose significant challenges for patients with schizophrenia, including greater number of outpatient visits, reduced adherence to antipsychotics and lower overall functioning (**Figure 1**)
- Among patients with negative symptoms, psychotherapy exposure was associated with greater outpatient engagement reflected by higher visit frequency and better functioning, suggesting potential benefits for sustained treatment participation and everyday outcomes (**Figure 1**)
- Functional burden associated with negative symptoms was partially mitigated by psychotherapy. The fact that only 14% of the sample had psychotherapy exposure at baseline underscores a critical clinical challenge: those who might benefit most from psychosocial interventions may face the greatest barriers to accessing such care

Figure 1. Impact of negative symptoms and psychotherapy exposure on clinical outcomes and functioning



GAF, Global Assessment of Functioning.

Psychotherapy exposure and HCRU

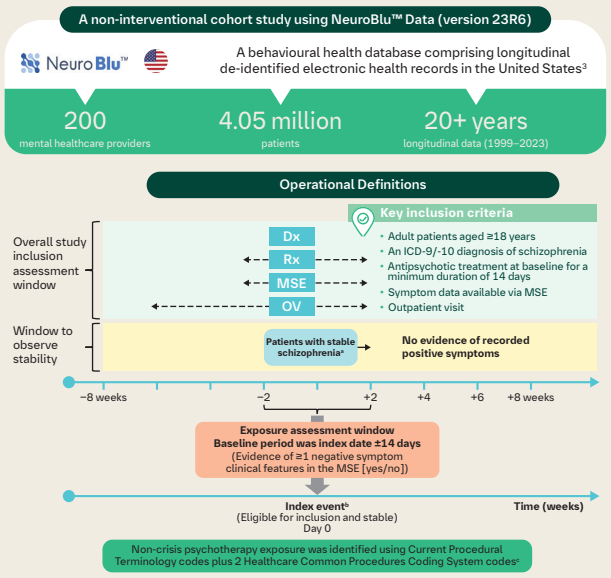
- Within the separate psychotherapy analysis among patients with negative symptoms (n=1603), 223 (14%) had psychotherapy exposure at baseline
- At baseline, a smaller proportion of patients with psychotherapy exposure had indicators of experiential negative symptoms and motivational deficits versus those without

	Patients with psychotherapy exposure	Patients without psychotherapy exposure
Experiential negative symptoms	24.2%	49.2%
Motivational deficits	7.2%	35.0%

- The adjusted estimated mean rate of outpatient visits was 42.75 per year (95% CI: 24.25, 75.39) for patients with psychotherapy exposure at baseline and 20.35 per year (95% CI: 11.96, 34.62) for those without (**Figure 3**)
- A significant association between baseline psychotherapy exposure and emergency department visit rate (**Figure 3**) may suggest that such visits flag patients with greater clinical need, who are subsequently more likely to be referred to psychotherapy
- There was no evidence of an association between baseline psychotherapy exposure and either the PDC with antipsychotic treatment or the number of inpatient days (**Figure 3**)

Methods

Study design, key inclusion criteria and operational definitions



[a]Two definitions of stability in patients with schizophrenia were considered for this study: Definition 1 included those with stable antipsychotic medication prescribing and definition 2 included those without recorded positive symptoms. While the overall results were similar between the 2 groups, the results presented in this poster are based on patients included based on definition 2 due to two reasons. First, its larger sample size and second, this data source did not capture dosing, and stable antipsychotic prescribing may include dosing adjustments.
[b]Index date was defined as the first diagnosis with schizophrenia within the NeuroBlu™ data with symptom records available. Follow-up time began at the end of the inclusion, stability and exposure assessment windows (index event +2 weeks) to mitigate against immortal time bias. Study rules were applied to each patient and arranged in event time anchored at cohort entry.
[c]Crisis sessions or those that occurred within the context of an inpatient setting were not included.

Data analyses performed

- Patients with negative symptoms versus without were compared to examine associations with HCRU, treatment adherence and functioning
- Outcomes associated with psychotherapy exposure were evaluated among the subset of patients with negative symptoms for whom psychotherapy exposure could be assessed
- Associations between exposures and outcomes were examined using multivariable regression models adjusted for demographic and clinical covariates; effect estimates were reported with 95% CIs
- A linear mixed-effects model was used to examine the association between negative symptoms (yes/no) and GAF scores over time

Study outcomes over the 12-month follow-up period

Primary outcome

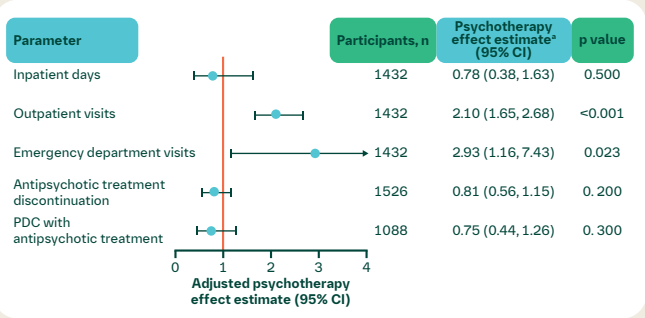
- Total number of inpatient days

Secondary outcomes

- Total number of outpatient visits
- Total number of emergency department visits
- Sum of number of non-crisis, outpatient psychotherapy sessions[a]
- PDC with any antipsychotic treatment
- Time to antipsychotic discontinuation
- Functioning assessed by GAF scores

[a]This was evaluated over a follow-up period of up to 36 months.

Figure 3. Association between psychotherapy exposure and clinical outcomes in patients with negative symptoms



[a]These were risk ratios for inpatient days, outpatient visits, emergency department visits and psychotherapy, hazard ratio for antipsychotic treatment discontinuation, and odds ratio for proportion of days covered with antipsychotic treatment.
CI, confidence interval; PDC, proportion of days covered.

Psychotherapy exposure and functioning

- GAF scores (range: 10–80) were significantly higher in those with baseline psychotherapy exposure, albeit with a small effect estimate (Beta= 4.22 [95% CI: 2.04, 6.40], p<0.001)
  - The results indicated those with psychotherapy had better functioning, with scores ~4-points higher versus those without psychotherapy; scores remained stable over follow-up

Additional Conclusions

- These results highlight the challenges negative symptoms pose and reinforce the need for targeted interventions to support patients and optimise outcomes in psychiatric care
- While GAF was used, due to being the most commonly used assessment measuring functioning, only a small proportion (26%) of patients had a GAF score in the baseline period, which may limit the generalisability of findings relative to the broader study population

Abbreviations

CI, confidence interval; Dx, diagnosis; GAF, Global Assessment of Functioning; HCRU, healthcare resource utilisation; ICD-9/-10, International Classification of Diseases Ninth and Tenth Revision; MSE, Mental Status Examination; OV, office visit; PDC, proportion of days covered; Rx, treatment; SD, standard deviation.

References

1. Fervaha G, et al. *Eur Psychiatry* 2014;29:449–55; **2.** Green MF, et al. *Schizophr Res* 2004;72:41–51; **3.** Patel R, et al. *BMJ Open* 2022;12:e057227.

Disclosures

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