

Original article

# Factors associated with the severity of positive and negative symptoms in inpatients with schizophrenia in Vietnam: A Cross-sectional Study

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## Abstract

**Background:** Schizophrenia is a complex, debilitating disorder imposing a substantial global burden. Its symptomatic heterogeneity has prompted a shift from traditional subtypes towards a dimensional understanding, validating the positive-negative dichotomy as two core domains with divergent neurobiological substrates. While this structure is established, the specific clinical, functional, and sociodemographic factors modulating each domain's severity can vary across populations. In Vietnam, despite schizophrenia being a significant public health concern, a critical gap exists. There is a lack of comprehensive investigations concurrently examining a broad range of associated factors for both symptom domains in an inpatient setting.

**Objectives:** To identify factors independently associated with the severity of positive and negative symptoms among inpatients with schizophrenia in Vietnam.

**Materials and methods:** A cross-sectional study was conducted with 121 inpatients (ICD-10 diagnosis) at Hue Psychiatric Hospital from September 2024 to April 2025. Data were collected on sociodemographic, clinical, and functional characteristics. Symptom severity was assessed using the Positive and Negative Syndrome Scale (PANSS). Cognitive and social functioning were measured with the Mini-Mental State Examination (MMSE) and Social Functioning Questionnaire (SFQ), respectively. Two separate multiple linear regression models were constructed to identify independent associated factors for PANSS positive and negative subscale scores.

**Results:** The model for positive symptoms demonstrated a modest fit (Adjusted  $R^2 = .126$ ,  $p < 0.001$ ), identifying general polypharmacy ( $\geq 3$  medications) as the sole independent factor associated with higher severity. The model for negative symptoms demonstrated a substantial fit (Adjusted  $R^2 = .392$ ,  $p < 0.001$ ), where higher severity was independently associated with lower cognitive (MMSE) scores, poorer social functioning, and the absence of substance use history.

**Conclusion:** The determinants of positive and negative symptoms in schizophrenia are markedly distinct. Positive symptoms were primarily associated with clinical-diagnostic features and treatment complexity, while negative symptoms were strongly linked to cognitive and functional impairments. These findings highlight the need for personalized, dimension-specific therapeutic strategies to improve patient outcomes in Vietnam.

**Keywords:** Schizophrenia; Positive symptoms; Negative symptoms; Cognitive dysfunction; Social functioning; Vietnam; Inpatients.

## 1. INTRODUCTION

Schizophrenia is a complex and debilitating mental disorder that imposes a substantial global health burden, affecting approximately 1% of the world's population and ranking among the leading causes of disability worldwide [1, 2].

The pronounced heterogeneity in the clinical presentation of schizophrenia has prompted a shift away from traditional, less stable nosological subtypes toward a dimensional understanding of its psychopathology [3]. Analyses have robustly validated the positive-negative symptom dichotomy

as two core, longitudinally stable domains with divergent neurobiological substrates [3]. Clinically, positive symptoms reflect an excess or distortion of normal functions, including delusions (fixed false beliefs), hallucinations (perceptual abnormalities), and disorganized speech or behavior. Conversely, negative symptoms represent a diminution or loss of normal functions, characterized by blunted affect, avolition (poverty of speech), avolition (lack of motivation), anhedonia, and social withdrawal. While positive symptoms often lead to hospitalization, negative symptoms are frequently

associated with long-term functional disability. This perspective is clinically critical, as positive and negative symptoms are associated with different underlying neurochemical dysfunctions and often respond differently to treatment [4], necessitating the identification of specific associated factors for each domain.

Furthermore, while the relationship between symptoms and functioning is complex and bidirectional, cognitive impairment is increasingly recognized as a core, stable trait (endophenotype) that may underlie symptom expression rather than merely resulting from it [5-8]. Therefore, examining cognitive and social functioning as correlates of symptom severity is crucial for identifying high-risk patient subgroups [9].

While this structure is recognized, the factors modulating symptom severity can vary significantly across populations. Although prior research in Vietnam has provided valuable insights into specific facets such as volitional disturbances [10], medication efficacy on symptom clusters [11], or the correlation between poor insight and negative symptoms [12], a significant research gap remains. A comprehensive investigation concurrently examining a broad range of associated factors—spanning demographic, clinical, cognitive, and social functioning—for both symptom domains within a multivariable model in an inpatient setting is lacking. Therefore, the primary objective of this study was to identify factors independently associated with the severity of positive and negative symptoms, as measured by the Positive and Negative Syndrome Scale (PANSS), among inpatients at Hue Psychiatric Hospital.

## 2. RESEARCH METHODS

### 2.1. Study Design, Setting, and Participants

A cross-sectional descriptive study was conducted at Hue Psychiatric Hospital from September 2024 to April 2025. A total of 121 inpatients with an ICD-10 diagnosis of schizophrenia (F20) were recruited via convenience sampling.

Regarding sample size and model specification, we applied two distinct statistical criteria. First, an a priori power analysis (G\*Power 3.1; F-test, linear multiple regression, medium effect size  $f^2=0.15$ , power=80%,  $\alpha=0.05$ ) indicated that a minimum sample of 85 participants would be sufficient for hypothesis testing. Second, to ensure model stability and prevent overfitting given the multifactorial nature of schizophrenia, we adhered to the conservative heuristic recommended by Babyak (2004) [13], maintaining a minimum subject-to-variable ratio

of 15:1. With a final sample of 121 participants, our models were restricted to a maximum of 4 predictors, achieving a ratio of approximately 30:1. This approach prioritizes the reliability of coefficient estimates over model complexity.

**Inclusion Criteria:** (1) Age  $\geq 18$ ; (2) Met full ICD-10 F20 (schizophrenia) criteria; (3) Capable and willing to provide voluntary informed consent.

**Exclusion Criteria:** (1) Organic brain disease or intellectual disability; (2) Substance-induced psychotic disorder within one month prior; (3) Inability to cooperate sufficiently for scale completion.

### 2.2. Procedures and Ethical Considerations

All researchers were trained in standardized procedures for clinical interviewing and scale administration. The study adhered to the Declaration of Helsinki and was approved by the Ethics Committee in Biomedical Research of the University of Medicine and Pharmacy, Hue University (H2024/540; August 20, 2024). Written informed consent was obtained from all participants (or legal guardians if capacity was compromised).

### 2.3. Variables and Measurement Instruments

#### 2.3.1. Outcome Variable

The primary dependent variable, the burden of schizophrenic symptoms, was quantified using the Vietnamese version of the Positive and Negative Syndrome Scale (PANSS) [14]. The PANSS is a 30-item, semi-structured clinical interview in which each item is rated on a 7-point Likert scale (from 1 = absent to 7 = extreme) based on manifestations within the preceding week. Although more complex 5-factor models have been proposed [15], this study employed the original 3-subscale structure due to its robust reliability, validity, and sensitivity in clinical settings [16].

#### 2.3.2. Associated factors

Associated factors were collected via patient/relative interviews and medical records:

##### A. Sociodemographic Characteristics

Age (years), gender, highest education level, prospective discharge destination (home/social support center), and employment ('Employed' = holding a job with full salary in last 12 months, versus "Unemployed").

##### B. Clinical Characteristics

Age of onset (first psychotic symptoms), illness duration, prior relapses (total previous acute hospitalizations, excluding current), ICD-10 subtype, typical antipsychotics (AP) use, and treatment adherence ('Adherent' if the patient had used at least 80% of their total prescribed

medication over the last 12 months (or a shorter period if treatment duration was less). Alcohol and substance use within the past year were assessed using specific criteria.

**General Polypharmacy (Total Medication Load):** Defined as the total count of distinct pharmaceutical agents concurrently prescribed in the patient's daily regimen. This variable encompasses not only antipsychotics but also concomitant medications such as mood stabilizers, benzodiazepines, anticholinergics (for extrapyramidal side effects), somatic/supportive medications, etc. This variable was dichotomized into ' $\leq 2$  types' and ' $\geq 3$  types' to differentiate between standard regimens and complex multidrug regimens reflecting high treatment burden.

Alcohol/substance use was a merged binary variable due to low prevalence (Illicit substance use = any reported in past 12 months; Alcohol misuse =  $\geq 1$  standard drink/day for  $\geq 3$  days/week for females, or  $\geq 2$  standard drinks/day for  $\geq 3$  days/week for males).

### C. Psychosocial and Functional Characteristics

Family attitude ('Very supportive' = consistent medication reminders and active care involvement), physical exercise ('Regular':  $\geq 30$  minutes of activity per day, for  $\geq 5$  days a week; and 'Irregularly/No' for those not meeting these criteria). social functioning via the Social Functioning Questionnaire (SFQ) ( $\geq 10$  = significant impairment, functioning rated based on the last stable period prior to acute admission) [17], and global cognitive functioning via the Mini-Mental State Examination (MMSE) [18] (categorized for bivariate analysis: 'No impairment' 24–30, 'Mild' 18–23, 'Severe' 0–17) [19].

### 2.4. Statistical Analysis

All data were processed and analyzed using IBM SPSS 26.0,  $p < 0.05$ , two-tailed hypothesis tests.

Descriptive statistics included frequencies/percentages (categorical), mean and standard deviation (SD) if normally distributed, and median and interquartile range (IQR) for skewed data, based on Shapiro-Wilk tests for assessing the normality of data distributions.

For bivariate analysis, we used Pearson correlation ( $r$ ), Independent Samples T-test (Welch's T-test if Levene's test significant), and one-way ANOVA (Welch's F-test/Games-Howell post-hoc if variances unequal). Effect sizes (Cohen's  $d$  and Partial Eta Squared ( $\eta_p^2$ )) were reported to complement inferential tests. Specifically regarding cognitive assessment, cognitive functioning (MMSE) was

analyzed as a categorical variable (Normal/Mild/Severe) in bivariate comparisons to facilitate clinical interpretation of symptom burden across severity levels, but was entered as a continuous variable in the multivariable regression models to preserve statistical power and precision.

Two separate multiple linear regression models were constructed to identify independent associated factors for PANSS Positive and Negative scores. Diagnostic subtypes (e.g., Paranoid, Undifferentiated) were explicitly excluded from the multivariable models to avoid tautological bias, as these categories are defined by the symptom clusters being predicted. Multicollinearity was assessed using the Variance Inflation Factor (VIF), with all values in the final models  $< 2.0$ , indicating no significant multicollinearity.

## 3. RESULTS

A total of 121 inpatients were invited to participate in the study. Data was collected between September 2024 and April 2025. The final dataset contained no missing values.

### 3.1. Sociodemographic and Clinical Characteristics of the Study Sample

The sociodemographic, clinical, and functional characteristics of the 121 participants are presented in Tables 1a and 1b. The median age of the sample was 39.00 years (IQR 30.00 - 49.00), and the majority were male (64.5%). The median age of onset was 28.00 years (IQR 23.00 - 35.00), the median duration of illness was 8.0 years (IQR 4.0–16.0), and the median number of previous relapses was 3.0 (IQR 2.0- 7.0). The median MMSE score for the sample was 23.00 (IQR 20.00 - 26.00).

Clinically, the mean PANSS positive score was 23.11 ( $\pm 8.13$ ), and the median PANSS negative score was 19.00 (IQR 14.00 - 24.00). The Paranoid subtype (F20.0) was the most prevalent diagnosis, accounting for 56.2% of cases. The rate of treatment non-adherence was high at 58.7%.

Functionally, a significant portion of the sample faced considerable challenges: 51.2% of patients were unemployed, 63.6% exhibited poor social functioning (defined as an SFQ score  $\geq 10$ ), and 55.4% presented with cognitive impairment (defined as an MMSE score  $< 24$ ). Specifically, 44.6% of patients showed no cognitive impairment (MMSE 24-30), 36.4% had mild (18-23), and 19.0% had severe (0-17) cognitive impairment. Detailed characteristics are presented in Tables 1a and 1b.

**Table 1a.** Categorical Characteristics of the Study Sample (N = 121)

Characteristic	Subgroup	n	%
Sex	Male / Female	78 / 43	64.5 / 35.5
Employment Status	Employed / Unemployed	59 / 62	48.8 / 51.2
Discharge Destination	Home / Social Support Center	107 / 14	88.4 / 11.6
Subtype (ICD-10)	F20.0 (Paranoid)	68	56.2
	F20.3 (Undifferentiated)	40	33.1
	Other	13	10.7
Alcohol/Substance Use	Yes / No	11 / 110	9.1 / 90.9
Number of Medications	≤ 2 types / ≥ 3 types	68 / 53	56.2 / 43.8
Typical AP Use	Yes / No	37 / 84	30.6 / 69.4
Treatment Adherence	Adherent / Non-adherent	50 / 71	41.3 / 58.7
Family Attitude	Very supportive / Less/Not supportive	68 / 53	56.2 / 43.8
Education Level	Primary School	20	16.5
	Lower Secondary School	49	40.5
	High School	42	34.7
	College/University	10	8.3
Social Functioning (SFQ)	Good (< 10) / Poor (≥ 10)	44 / 77	36.4 / 63.6
Cognitive Impairment (MMSE)	Normal (24 - 30)	54	44.6
	Mild (18 - 23)	44	36.4
	Severe (< 18)	23	19

Note: AP: Antipsychotic

**Table 1b.** Quantitative Characteristics of the Study Sample (N = 121)

Variable	Mean ± SD / Median [IQR]
Age (years)	39.00 [30.00 - 49.00]
Age of Onset (years)	28.00 [23.00 - 35.00]
Duration of Illness (years)	8.00 [4.00 - 16.00]
Number of Prior Relapses	3.00 [2.00 - 7.00]
PANSS Positive Score	23.11 ± 8.13
PANSS Negative Score	19.00 [14.00 - 24.00]
MMSE Score	23.00 [20.00 - 26.00]
SFQ Score	10.56 ± 3.92

Note: Values are presented as Mean ± SD for normally distributed data and Median [IQR] for skewed data, based on the Shapiro-Wilk test ( $p < 0.05$ ).

### 3.2. Bivariate Analysis: Factors Associated with Symptom Burden

#### 3.2.1. Correlations Between Continuous Variables and PANSS Scores

Pearson correlation analysis revealed no statistically significant associations between either the positive or negative PANSS subscale scores and key illness history variables, including patient age, age at onset, duration of illness, or the number of previous relapses (all  $p > 0.05$ ).

Conversely, significant and clinically relevant correlations were identified for cognitive and functional measures:

**Cognitive Function:** The MMSE score demonstrated a strong, statistically significant negative correlation with the negative PANSS subscale score ( $r = -0.493, p < 0.001$ ). This indicates that a greater degree of cognitive impairment is robustly associated with more severe negative symptoms. No such relationship was observed with

the positive subscale score ( $r = -0.047, p = 0.607$ ).

**Social Function:** The SFQ score, a measure of social disability, was strongly and positively correlated with the negative PANSS subscale ( $r = 0.587, p < 0.001$ ) and showed a moderate positive correlation with the positive subscale ( $r = 0.306, p = 0.001$ ). This suggests that poorer social functioning is linked to a higher severity of both core symptom domains.

### 3.2.2. Group Comparisons of Mean PANSS Scores

The results of group comparisons for mean PANSS scores are detailed in Table 2. Statistically significant differences were noted for the following variables:

**For the Negative Symptom Subscale,** significantly higher mean scores (indicating greater severity) were observed in patients who were: female (vs. male,  $p = 0.017$ ), unemployed (vs. employed,  $p = 0.005$ ), perceived as having less family support ( $p = 0.011$ ), did not exercise regularly ( $p = 0.009$ ), were discharged to a social protection center ( $p = 0.009$ ), exhibited poor social functioning ( $p < 0.001$ ), and patients with

mild (Mean = 19.30, SD = 7.20) and severe (Mean = 25.83, SD = 8.53) cognitive impairment compared to those without impairment (Mean = 16.04, SD = 6.20) ( $p < 0.001, \eta_p^2 = 0.209$ ). Furthermore, a significant difference was found across diagnostic subtypes ( $p = 0.004$ ), where the 'Other' subtype group (Mean = 25.77, SD=6.10) showed significantly higher negative symptom severity compared to the Paranoid and Undifferentiated subtypes. Interestingly, patients with a history of substance use had significantly lower mean negative PANSS scores compared to those without such a history ( $p < 0.001$ ).

**For the Positive Symptom Subscale,** significantly higher mean scores were associated with: general polypharmacy (receiving  $\geq 3$  medications vs.  $\leq 2, p < 0.001$ ), current use of a typical antipsychotic ( $p = 0.012$ ), and poor social functioning ( $p = 0.032$ ). Furthermore, a one-way ANOVA revealed a significant difference in positive symptom severity across diagnostic subtypes ( $p < 0.001$ ), with the Paranoid subtype (F20.0) exhibiting the highest mean score.

**Table 2.** Comparison of Mean PANSS Positive and Negative Scores by Participant Characteristics

Variable	Subgroup (n)	Positive Mean (SD)	Negative Mean (SD)	p (Pos)	p (Neg)	ES (Pos)	ES (Neg)
Gender	Female (43)	23.63 (9.27)	21.60 (9.29)	0.603	0.017	0.1	0.51
	Male (78)	22.82 (7.48)	17.69 (6.61)				
Employment	Unemployed (62)	23.55 (8.46)	21.03 (8.61)	0.543	0.005	0.11	0.52
	Employed (59)	22.64 (7.82)	17.03 (6.45)				
Substance Use	Yes (11)	24.18 (8.22)	11.45 (5.54)	0.648	< 0.001	0.15	1.12
	No (110)	23.00 (8.15)	19.85 (7.67)				
Adherence	Non-adherent (71)	24.21 (8.31)	20.06 (8.23)	0.075	0.105	0.33	0.3
	Adherent (50)	21.54 (7.68)	17.70 (7.16)				
Family Attitude	Low support (53)	23.23 (8.19)	21.13 (7.91)	0.888	0.011	0.03	0.48
	Supportive (68)	23.01 (8.15)	17.49 (7.50)				
Medication Load	$\geq 3$ types (53)	26.43 (8.04)	20.09 (8.07)	< 0.001	0.213	0.78	0.23
	$\leq 2$ types (68)	20.51 (7.26)	18.29 (7.67)				
Social Function	Poor (77)	24.26 (8.41)	21.73 (7.78)	0.039	< 0.001	0.4	1.03
	Good (44)	21.09 (7.28)	14.45 (5.58)				
Exercise	Irregular/No (58)	23.53 (9.16)	21.00 (8.21)	0.586	0.009	0.1	0.48
	Regular (63)	22.71 (7.11)	17.32 (7.15)				
Discharge Place	Social Center (14)	23.79 (5.10)	23.93 (6.45)	0.634	0.014	0.11	0.71
	Home (107)	23.02 (8.46)	18.45 (7.83)				
Typical AP Use	Yes (37)	25.89 (7.85)	18.78 (8.10)	0.012	0.783	0.5	-0.06
	No (84)	21.88 (7.99)	19.21 (7.80)				

Cognitive (MMSE)	Normal (54)	23.26 (8.80)	16.04 (6.20)	0.848	< 0.001	0.003 <sup>†</sup>	0.21 <sup>†</sup>
	Mild (44)	22.59 (7.77)	19.30 (7.20)				
	Severe (23)	23.74 (7.43)	25.83 (8.53)				
Subtype (ICD-10) <sup>^</sup>	F20.0 Paranoid (68)	26.43 (7.38)	18.51 (7.30)	< 0.001	0.004	0.22 <sup>†</sup>	0.09 <sup>†</sup>
	F20.3 Undiff. (40)	19.00 (6.76)	17.88 (8.38)				
	Other (13)	18.38 (8.10)	25.77 (6.10)				

**Notes:** SD: Standard Deviation; ES = Effect Size (Cohen's *d* for *t*-tests; <sup>†</sup>Partial Eta Squared for ANOVA); Pos = Positive Scale; Neg = Negative Scale; AP: Antipsychotic. *p*-values for comparisons involving more than two groups were derived from one-way ANOVA. *p*-values for two-group comparisons were derived from Welch's *t*-test when Levene's test for equality of variances was significant (*p* < 0.05). <sup>^</sup> Diagnostic subtypes are included here for descriptive characterization of the sample but were excluded from multivariable regression models to avoid tautology

### 3.3. Results of Multivariable Regression Analysis

To address potential tautological overlaps between diagnostic subtypes and symptom dimensions, and to optimize statistical power relative to the sample size, diagnostic subtypes were excluded from the final regression models.

The model for positive symptoms (Adjusted  $R^2 = .126$ ,  $F(3, 117) = 6.78$ ,  $p < 0.001$ ) identified general polypharmacy ( $\geq 3$  medications) as the sole significant independent factor associated with higher symptom severity ( $B = 5.16$ , 95% CI: 1.74 – 8.58,  $p = 0.003$ ). Other variables, including typical antipsychotic use and social functioning, did not reach statistical significance in this adjusted model ( $p > 0.05$ ).

The model for negative symptoms demonstrated a robust fit, explaining 39.2% of the variance (Adjusted  $R^2 = .392$ ,  $F(4, 116) = 20.36$ ,  $p < .001$ ). Higher negative symptom severity was strongly and independently associated with lower cognitive scores (MMSE,  $B = -0.48$ ,  $p < .001$ ) and poor social functioning (SFQ  $\geq 10$ ,  $B = 5.33$ ,  $p < .001$ ). Additionally, the absence of substance use history was a significant predictor of greater negative symptom burden ( $B = -5.43$ ,  $p = .008$ ). Although female patients exhibited higher negative scores in bivariate analysis, gender did not reach statistical significance in the final multivariable model ( $B = -1.98$ ,  $p = .103$ ), suggesting its effect may be mediated by other functional variables.

**Table 3:** Multivariable Regression Models Predicting PANSS Positive and Negative Scores

Predictor Variables	Positive Symptom Model		Negative Symptom Model	
	B (95% CI)	p	B (95% CI)	p
(Constant)	19.25 (16.79, 21.72)	< 0.001	27.78 (22.61, 32.95)	< 0.001
MMSE Score	—	—	-0.48 (-0.68, -0.28)	< 0.001
Social Functioning (Poor vs. Good)	2.16 (-0.74, 5.06)	0.143	5.33 (2.94, 7.72)	< 0.001
Polypharmacy ( $\geq 3$ vs. $\leq 2$ Meds)	5.16 (1.74, 8.58)	0.003	—	—
Typical AP Use (Yes vs. No)	0.72 (-2.91, 4.34)	0.695	—	—
Substance Use (Yes vs. No)	—	—	-5.43 (-9.42, -1.44)	0.008
Gender (Male vs. Female)	—	—	-1.98 (-4.36, 0.41)	0.103
Model Fit	Adj. $R^2 = .126$	< 0.001	Adj. $R^2 = .392$	< 0.001

Note: *B* = Unstandardized Beta Coefficient; *CI* = Confidence Interval; *Ref* = Reference category. The analysis was performed using Multiple Linear Regression (Enter method). Variables with “—” were not included in the final model. Variables included in the initial model but removed due to non-significance included: Employment, Family Attitude, Exercise, etc. Diagnostic subtypes were excluded to avoid tautology. Non-significant results among entered variables (e.g., Gender in the negative model) are reported for transparency.

## 4. DISCUSSION

This study provides one of the first detailed multivariable analyses to identify independent associated factors for the two core symptom domains of schizophreniapositive and negative—within an

inpatient population in Vietnam. Our results identify two almost entirely disparate sets of prognostic factors, strongly endorsing the dimensional approach in modern psychiatry. Specifically, the burden of positive symptoms was predominantly

driven by clinical-diagnostic features, whereas negative symptoms were associated with a complex network of cognitive impairment, social dysfunction, and demographic factors. This underscores the necessity of viewing positive and negative symptoms as distinct therapeutic targets.

#### **4.1. Associated factors of Positive Symptoms**

In our refined multivariable model, general polypharmacy (defined as the concurrent use of  $\geq 3$  medications) emerged as the primary independent factor associated with the severity of positive symptoms. While one might intuitively suspect that multiple medications could contribute to side effects, the association with symptom severity in this context is most likely a reflection of “confounding by indication.” Patients with refractory positive symptoms—such as persistent hallucinations or treatment-resistant delusions—often require complex pharmaceutical regimens. These regimens frequently necessitate high-dose antipsychotics, augmentation strategies with mood stabilizers, or the addition of benzodiazepines for acute agitation [20]. Thus, a higher number of medications in this context should be viewed as an indicator of a ‘difficult-to-treat’ clinical profile (reverse causality) rather than suggesting that polypharmacy itself worsens symptoms.

#### **4.2. Associated factors of Negative Symptoms**

By excluding diagnostic subtypes from the multivariable analysis—thereby removing the potential confounding effect of tautological diagnostic criteria—our model clearly isolates the functional and demographic drivers of the deficit syndrome. The substantial fit (Adjusted  $R^2 \approx 40\%$ ) without the inclusion of ‘Subtype’ variables strongly suggests that negative symptoms are primarily ecologically determined by cognitive and social deficits rather than merely being artifacts of nosological classification. The model for negative symptoms demonstrated superior explanatory power, robustly supporting the “deficit syndrome” model. The most critical finding is the tight linkage of the “deficit triad”: cognitive impairment, social and the negative symptom burden. This interconnection suggests they are not discrete entities but rather an interacting system where intervening in one domain may yield cascading benefits for the others. A recent study in male patients similarly confirmed that a deficit syndrome group exhibited more severe impairments in both cognitive and social functioning compared to a non-deficit group [8].

#### **4.3. The inverse relationship with substance use**

Our finding that patients without a history of substance use exhibited significantly more severe

negative symptoms warrants careful interpretation. This should not be interpreted as a protective effect of substances. Instead, it likely reflects the “avolition hypothesis.” Patients with severe primary negative symptoms suffer from profound reward-processing deficits (anhedonia) and lack of motivation (avolition), which may reduce the drive to seek out illicit substances [21, 22]. Conversely, substance-using patients may represent a subgroup with preserved volitional drive and higher social engagement, albeit pathological.

#### **4.4. Clinical Implications**

These findings suggest that clinical management should move beyond symptom reduction alone. For patients with prominent negative symptoms, our data highlight the critical need for early screening of cognitive and social deficits. Such phenotypic profiling may assist clinicians in identifying patients who could benefit from more comprehensive functional rehabilitation programs.

#### **4.5. Limitations**

This study has several limitations. First, the cross-sectional design precludes causal inference. While we identified factors independently associated with symptom severity, the directionality of these relationships—particularly regarding social functioning—cannot be definitively established. Second, the use of the SFQ in an inpatient setting may reflect acute distress rather than baseline functioning. Third, the single-center setting and the use of consecutive convenience sampling limit the generalizability of our findings. Our sample likely reflects a patient subgroup with higher acuity and chronicity compared to community-dwelling outpatients in Vietnam.

Fourth, regarding model specification, we faced an inherent methodological trade-off. To maintain a conservative subject-to-variable ratio ( $\sim 30:1$ ) and prevent model overfitting, we deliberately constrained the number of predictors in our multivariable analyses. While this enhances the stability of the reported associations, we explicitly acknowledge the risk of omitted variable bias. Potentially relevant confounders such as the duration of untreated psychosis (DUP), cumulative antipsychotic dosage, or genetic family history were not captured. Consequently, our findings should be interpreted as identifying dominant independent factors within a stable, parsimonious model, rather than providing an exhaustive causal explanation. Future research utilizing larger, probabilistically sampled cohorts ( $N > 300$ ) is recommended to accommodate high-dimensional models.

## 5. CONCLUSION

Our study has demonstrated that the associated factors for positive and negative symptoms in Vietnamese patients with schizophrenia are markedly distinct. These insights drive a shift from a “one-size-fits-all” treatment strategy toward more personalized, tailored, and effective care regimens aimed at improving quality of life and reducing the burden imposed by this disorder.

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