

PROSPECTIVE FOLLOW-UP OF PATIENTS WITH SCHIZOPHRENIA – RESULTS FOR OUTCOME PREDICTORS

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Abstract

Schizophrenia is a heterogeneous disease with wide variation in the therapeutic response of patients – from good to treatment refraction and severe disability.

This study has naturalistic, non-interventional design, and includes one-year prospective follow-up. Schizophrenia patients are evaluated in three time points: at admission (T1), at discharge (T2), and one year after the hospitalization (T3). Psychopathology is assessed by the Positive and Negative Syndrome Scale (PANSS), negative symptoms – by the Scale for Assessment of Negative Symptoms (SANS), aggression – by the Modified Overt Aggression Scale (MOAS), and functioning – by the Global Assessment of Functioning (GAF) scale. Statistical analyses are performed using descriptive methods, Student's *t*-test, Wilcoxon Signed Ranks Test, and multiple regression. Ethical approval for the study has been obtained.

The sample consists of 108 patients with mean age of 39 (SD $\pm$ 12.7), and 89.8% ($N = 97$) of them were prospectively assessed after one year. All symptom dimensions in the 5-factor model – positive, negative, disorganized, manic, and depressive, measured by PANSS, as well as the negative symptoms (objectified by SANS) and aggression (objectified by MOAS) rates, are significantly lower after inpatient treatment. There is an improvement in functioning one year after admission ($z = -8.01$, $p < .001$), although both negative symptoms ($z = -2.45$, $p = 0.015$) and aggressive behaviour ($z = -4.260$, $p < .001$) are significantly higher as compared to discharge. From the multiple regression, at

T1, involuntary admission is a significant predictor for higher aggression and lower functioning ($p < .001$). The duration of hospitalization is longer with lower compliance ($p = .022$), and the treatment with atypical antipsychotics decreases the hospital stay ($p = .021$). One year after admission, employment serves as a positive predictive factor as it is significantly associated with drop of psychopathology ($p = .001$) and negative symptoms ($p < .001$), and with improvement of functioning ($p < .001$). Good compliance is a predictor for lower psychopathology ($p = .015$), less aggression and higher functioning ($p < .001$).

The inpatient treatment is efficacious in terms of psychopathology and aggression, and is linked to better functioning. The naturalistic design shows depletion of the positive effects of treatment in terms of negative symptoms and aggression probably due to incomplete medication compliance, which is a poor prognostic factor for functioning. This demonstrates the imperative need of continuity in mental health care and better psychoeducation after discharge.

Key words: schizophrenia, treatment, predictors, follow-up, outcome

Introduction. Schizophrenia is a heterogeneous disease with chronic course and is among the top-leading causes of disability in the world. The heterogeneity is observed not only in clinical picture but in different disease outcomes – from symptom remission and functional recovery to personality deterioration. Outcome and treatment response could be measured by different constructs – decrease in psychopathology, improvement in functioning, maintaining employment, or subjective well-being [1,2]. The assessment of treatment efficacy, objectified by different constructs, and follow-up of the changes longitudinally have important practical implication. They are useful for assessing both risk and protective factors which could guide clinical prognosis and treatment planning. The aim of the paper is to present findings for outcome predictors from a prospective study in patients with schizophrenia.

Materials and methods. The study is naturalistic, non-interventional, and includes one year prospective follow-up. The patients are evaluated in three time points: at admission (T1) in inpatient unit, at discharge (T2), and one year after the hospitalization (T3). The sample consists of patients with a diagnosis of schizophrenia according to both ICD-10 and DSM-5 criteria, with minimum age of 18 years, admitted at the Psychiatric Clinic of “Alexandrovska” University Hospital in Sofia. The exclusion criteria include severe decompensated somatic comorbidity, misuse of psychoactive substances and lack of consent to participate. The sample is heterogeneous, as each admitted patient who gives informed consent and meets the inclusion criteria is assessed. Validated semi-structured instruments are used for assessment of: psychopathology – by the Positive and Negative Syndrome Scale (PANSS), negative symptoms – by the Scale for the Assessment of Negative Symptoms (SANS), aggression – by the Modified Overt Aggression Scale (MOAS), and functioning – by the Global Assessment of Functioning (GAF) scale. In addition to structured assessment, all available data for thorough clinical and social evaluation is also used, i.e. medical history, infor-

mation from family members and hospital staff, clinical observation. A patient's questionnaire including socio-demographic variables, clinical characteristics and quality of remission indicators, is also completed.

Statistical analyses are performed using descriptive methods, Student's *t*-test, Wilcoxon Signed Ranks Test, and multiple regression in search of predictive factors.

Ethical approval of the study has been obtained and every patient has given written informed consent before study assessment. The patients' anonymity is preserved.

Results. The sample consists of 108 patients with mean age of 39 ($SD \pm 12.7$), and 89.8% ($N = 97$) of them were prospectively assessed after one year. 53.7% are males, 80.5% – not married, and 60.2% from the sample are with secondary education. The patients have 16.08 ($SD \pm 10.1$) median duration of illness in years, 51.9% of them have family history of psychiatric disorder, and 44.4% have somatic comorbidity.

In terms of psychopathology, PANSS scores at discharge (T2, $M = 86.02$) and after one year (T3, $M = 87.06$) are significantly lower than at admission (T1, $M = 112.86$), ($z = -9.02$, $p < 0.05$, and $z = -8.29$, $p < 0.05$, respectively). There are no significant differences between psychopathology scores at T2 and T3. This refers to all the symptom dimensions in the 5-factor model, i.e. positive, negative, disorganized, manic, and depressive. The negative symptoms measured by SANS are significantly lower at T2 ($M = 78.32$) ($z = -8.21$, $p < 0.05$) and T3 ($M = 81.31$) ($z = -5.05$, $p < 0.05$) in comparison to T1 (89.09), but they are significantly higher one year after discharge as compared to T2 ($z = -2.45$, $p = 0.015$). There is a significant decrease of aggression at T2 ($z = -7.34$, $p < 0.001$) and T3 ($z = -6.57$, $p < 0.001$), however, with rise of aggressive behaviour one year later as compared to T2 ($z = -4.260$, $p < 0.001$). And, there is significant improvement in functioning one year after admission ($M = 42.6$) ($z = -8.01$, $p < 0.001$).

From the multiple regression, at T1, involuntary admission is a significant predictor for higher aggression ($p < .001$, $R^2 = 0.294$) and lower functioning ($p < .001$, $R^2 = 0.249$) (Table 1). At T2, the duration of hospitalization is longer with lower compliance prior to admission ($p = .022$), and treatment with atypical antipsychotics decreases the hospital stay ($p = .021$, $R^2 = 0.183$) (Table 2).

One year after admission, employment serves as a positive predictive factor as it is associated with drop of psychopathology ($p = .001$, $R^2 = .358$) and negative symptoms ($p < .001$, $R^2 = .330$), and with improvement of functioning ($p < .001$, $R^2 = .521$). Good compliance is a predictor for lower psychopathology ($p = .015$, $R^2 = .358$), less aggression ($p < .001$, $R^2 = .267$) and higher functioning ($p < .001$, $R^2 = .521$) (Table 3).

Discussion. The study participants are patients with schizophrenia, admitted for inpatient treatment. The study design is naturalistic and close to the real

T a b l e 1

Multiple regression at T1 – status quo at admission

T1 independent variables	Outcome:MOAS			Outcome:GAF		
	B*	Std. Error	p-value	B*	Std. Error	p-value
(Constant)	1.648	2.050	.423	27.678	2.951	.000
Clozapine (yes)	.655	1.632	.689	1.148	2.349	.626
Admission (involuntary)	6.412	1.750	.000	−9.495	2.519	.000
Compliance (absent)	4.471	1.753	.012	−2.980	2.523	.240
Antipsychotic (atypical)	.991	2.193	.652	2.476	3.157	.435
Number antipsychotics (>/= 2)	1.460	1.825	.426	.028	2.628	.992
Medication form (oral)	−.944	2.003	.638	−.761	2.883	.792

*B – regression coefficient

T a b l e 2

Multiple regression at T2 – outcomes of the hospitalization

Predictors at T2	Outcome: Duration hospital stay		p-value
	B*	Std. Error	
(Constant)	32.531	4.435	.000
Clozapine (yes)	.713	3.531	.840
Admission (involuntary)	3.787	3.786	.320
Compliance (absent)	8.800	3.792	.022
Antipsychotic (atypical)	−11.165	4.744	.021
Number antipsychotics (>/= 2)	−2.999	3.949	.449
Medication form (oral)	10.761	4.333	.015

*B – regression coefficient

clinical practice as it includes patients consecutively, without subgrouping them on purpose by socio-demographic characteristics, clinical picture, or specific treatment – thus resulting in heterogeneous study population similar to the real life heterogeneity in schizophrenia. The choice of evaluation period is consistent with the chronic course and the dynamics of the disease suggesting one year as a minimal reasonable follow-up time span for assessment of exacerbations and quality of the remission after inpatient treatment.

In general, the results show that inpatient treatment is highly efficacious, with significant changes in psychopathology (and besides, across all symptoms domains), negative symptoms, aggression, and the level of functioning in schizophrenia. These results are consistent with findings from another naturalistic study with Bulgarian patients with schizophrenia demonstrating rates of treatment efficacy between 82% and 91% according to different clinical scales [3].

The regression model at admission finds that involuntary treatment is a

T a b l e 3
Multiple regression at T3 – outcomes of the follow-up

Predictors at T3	Outcome: PANSS ¹			Outcome: SANS ²			Outcome: MOAS ³			Outcome: GAF ⁴		
	B*	Std. Error	p-value	B*	Std. Error	p-value	B*	Std. Error	p-value	B*	Std. Error	p-value
(Constant)	100.041	5.474	.000	87.498	5.828	.000	5.19	1.13	.000	29.41	3.269	.000
Clozapine (yes)	7.583	3.481	.032	4.151	3.705	.266	.845	.720	.243	-4.29	2.078	.042
Employment (yes)	-15.230	4.283	.001	-21.191	4.559	.000	-.317	.886	.721	13.96	2.557	.000
Hospitalization (yes)	8.320	2.996	.007	6.117	3.189	.058	1.250	.619	.047	-5.576	1.789	.002
Compliance (yes)	-14.634	5.913	.015	-5.287	6.295	.403	-5.189	1.22	.000	14.19	3.531	.000
Type of antipsychotic (atypical)	-3.644	4.375	.407	-7.598	4.657	.106	.498	.905	.583	3.89	2.612	.140
Number antipsychotics (>/= 2)	-3.590	3.991	.371	-1.310	4.248	.759	-.591	.825	.475	2.083	2.383	.384
Medication form (oral)	-2.006	4.034	.620	2.110	4.295	.624	-.467	.834	.577	-0.397	2.409	.869

*B – regression coefficient

negative predictor for functioning and relates to higher rates of aggression. Between 30% and 50% of all involuntary admissions across Europe are attributed to schizophrenia [4], and these patients have higher readmission rates in the future [5]. Identified risk factors for readmission in the next one year after treatment are prior involuntary admission and shorter total hospitalization days [6]. In another study, reduction in the perceived coercion leads to better functioning and decrease in symptom severity [7]. A prospective study, based on assessment of coercion in Bulgarian sample, found that involuntary treatment is correlated with lower functioning and more serious psychopathology with higher positive and negative symptoms [8]. The results from our study are consistent with findings for risk factors for readmission in the literature. Furthermore, they have important practical implications as functional deterioration could be prevented by decreasing involuntary admission or reducing perceived coercion in the treatment process.

Not surprisingly, given the results of the efficacy of inpatient treatment, good compliance is a predictor for better outcome as it affects psychopathology and the functional domain. Insight is a replicable predictor for treatment compliance and is a challenging issue to address with schizophrenia patients [9]. Poor insight is linked to greater disease severity, continuous need for involuntary admissions, higher rates of aggression and functional disability, as well as worse quality of life [10,11]. On the contrary, good insight is associated with better psychosocial functioning [12]. A study by GARCÍA-CABEZA et al. [13] found that poor insight has major impact on disability in schizophrenia, and this effect is partially mediated by the impact of insight on treatment adherence. Our results are also consistent with the evidence for relationship between insight, treatment compliance and outcome. Lack of compliance as a predictor of longer inpatient stay has also economic impact. The positive predictive correlation between treatment with atypical antipsychotic and shorter hospitalization may be due both to their efficacy and to the lower rates of extrapyramidal side effects, although one year follow-up may be insufficient for assessment of the full range of the metabolic side effects of atypical medication in the longer run.

Data about the role of employment for better outcomes is controversial due to the potential vulnerability of people with severe mental illness to work stressors. A systematic review of longitudinal studies found that employment is not related to worse outcome, even though data was inconsistent regarding the association with symptom severity, life satisfaction, and global well-being [14]. In our sample, being employed one year after inpatient treatment is associated with reduction of overall psychopathology, especially the negative symptoms, and in improvement of global functioning. The findings from our study demonstrate not only the efficacy of psychiatric inpatient treatment but also the indispensable need of continuity with social services care for improving treatment compliance, finding and maintaining employment, and, consequently, for better outcomes and reduction of the economic burden of severe mental illness.

Strengths and limitations. This is a prospective study with naturalistic design, assessing different constructs of remission in patients with schizophrenia. The sample is formed by inpatients from one University hospital and may not be representative for the national inpatient population of persons with schizophrenia. This limitation is partially neutralized by the consecutive and no selection biased recruitment.

Conclusions. The inpatient treatment is efficacious in terms of psychopathology and aggression and is linked to better functioning. The naturalistic design shows depletion of the positive effects of treatment in terms of negative symptoms and aggression probably due to incomplete medication compliance, which is a poor prognostic factor for functioning. This demonstrates the imperative need of continuity in mental health care and better psychoeducation after discharge.

REFERENCES

- [1] LEUCHT S., R. LASSER (2006) The concepts of remission and recovery in schizophrenia, *Pharmacopsychiatry*, **39**(5), 61–70.
- [2] VITA A., S. BARLATI (2018) Recovery from schizophrenia: is it possible?, *Curr. Opin. Psychiatry*, **31**(3), 246–255.
- [3] IGNATOVA D., G. ONCHEV (2021) Observational follow-up study of the effectiveness of treating schizophrenia and affective disorders, *Bulg. Journal of Psychiatry*, **6**(1), 3–18, (in Bulgarian with English abstract).
- [4] DRESSING H., H. J. SALIZE (2004) Compulsory admission of mentally ill patients in European Union Member States, *Soc. Psychiatry Psychiatr. Epidemiol.*, **39**(10), 797–803.
- [5] KALLERT T. W., M. GLOCKNER, M. SCHUTZWOHL (2008) Involuntary vs. voluntary hospital admission. A systematic literature review on outcome diversity, *Eur. Arch. Psychiatry Clin. Neurosci.*, **258**(4), 195–209.
- [6] HUNG Y. Y., H. Y. CHAN, Y. J. PAN (2017) Risk factors for readmission in schizophrenia patients following involuntary admission, *PLoS One*, **12**(10), e0186768.
- [7] GOWDA G. S., N. KONDAPURAM, C. N. KUMAR, S. B. MATH (2017) Involuntary admission and treatment experiences of persons with schizophrenia: Implication for the Mental Health Care Bill 2016, *Asian J. Psychiatr.*, **29**, 3–7.
- [8] ONCHEV G. (2010) In book: *Coercion in Psychiatry: Empirical Data and Good Practice*, Sofia, Context, 81–91, (in Bulgarian).
- [9] BECK E. M., M. CAVELTI, S. KVRGIC et al. (2011) Are we addressing the ‘right stuff’ to enhance adherence in schizophrenia? Understanding the role of insight and attitudes towards medication, *Schizophr. Res.*, **132**, 42–49.
- [10] LINCOLN T. M., E. LÜLLMANN, W. RIEF (2007) Correlates and Long-Term Consequences of Poor Insight in Patients with Schizophrenia. A Systematic Review, *Schizophrenia Bulletin*, **33**, 1324–1342.

- [11] LYSAKER P. H., M. L. PATTISON, B. L. LEONHARDT et al. (2018) Insight in schizophrenia spectrum disorders: relationship with behavior, mood and perceived quality of life, underlying causes and emerging treatments, *World Psychiatry*, **17**(1), 12–23.
- [12] KLAAS H. S., A. CLEMMENCE, R. MARION-VEYRON et al. (2017) Insight as a social identity process in the evolution of psychosocial functioning in the early phase of psychosis, *Psychol. Med.*, **47**(4), 718–719.
- [13] GARCÍA-CABEZA I., C. M. DÍAZ-CANEJA, M. OVEJERO, E. DE PORTUGAL (2018) Adherence, insight and disability in paranoid schizophrenia, *Psychiatry Res.*, **270**, 274–280.
- [14] LUCIANO A., G. BOND, R. DRAKE (2014) Does employment alter the course and outcome of schizophrenia and other severe mental illnesses? A systematic review of longitudinal research, *Schizophr. Res.*, **159**(2–3), 312–321.

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