

A 2-year retrospective study of predictors of relapse in chronic schizophrenia

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BACKGROUND

- A majority of subjects diagnosed with schizophrenia experience multiple relapses during the course of the illness. Relapse may have serious implications. Moreover, there is a biological risk associated with relapse. Active psychosis illustrates a period of disease progression as subjects may not return to their previous level of functioning and symptoms of treatment refractory illness may appear.
- In recognition of the associated risks, improving treatment adherence and relapse prevention have been emphasized as key components of the management of schizophrenia. However, there remain many unanswered questions regarding the nature of relapse making further study of this component of the illness imperative.
- Research has shown that costs associated with treatment received following relapse may constitute the largest share of treatment costs psychiatric illnesses. Although, demographic and clinical characteristics associated with relapse have been examined in previous research, information about potential predictors of relapse are limited.

OBJECTIVE

Prevention of relapse or recurrence is a primary treatment objective in the management of symptoms. The aim of this study was to evaluate the effect of patient and disease characteristics on relapse following discharge from an inpatient facility within two years while receiving optimal treatment.

DEFINITION OF RELAPSE

To determine factors predicting relapse in subjects with chronic schizophrenia, a Cox regression survival analysis with backward elimination modeling was performed. Time to first relapse within the first two years of follow-up was included as the dependent variable, and it was defined as:

- Arrest/Incarceration
- Psychiatric Hospitalization
- Suicide/Self-Harm
- Discontinuation of Antipsychotic medication that leads to hospitalization
- Treatment supplementation with another antipsychotic that leads to hospitalization
- Increase in the level of psychiatric services in order to prevent imminent psychiatric hospitalization

PREDICTORS OF RELAPSE INCLUDED IN THE MODEL

Predictors of Relapse was assessed using a linear regression model. A backward elimination method was used to identify the best predictive model according to best R² value. Two models were developed:

Model 1 (Predictors of Treatment Failure/Relapse at year 2)

- Age
- Age at onset of illness
- Years of substance use at baseline
- Number and length of prior hospitalizations
- Scores on PANSS Positive Symptom Domain at baseline and 3-month follow-up
- PANSS Negative and Disorganized Domains at baseline and 3-month follow-up
- PANSS Item G12 (Lack of Judgment and Insight) at baseline and 3-month follow-up
- MCCB cognitive domain and composite scores
- Personal and Social Performance Scale (PSP) total score.

Model 2 (Predictors of decline in functional outcomes as measured by the total score on the Personal and Social Performance Scale (PSP) at year 1 as the dependent variable):

- Age
- Age at onset of illness
- Years of substance use at baseline
- Number and length of prior hospitalizations,
- baseline PSP total score,
- PANSS Positive, Negative and Disorganized domains scores at baseline
- PANSS Item G12 Lack of judgment and Insight

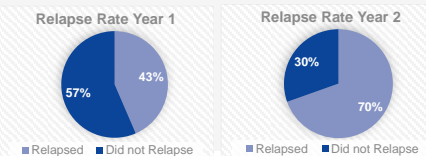
SAMPLE POPULATION

This study is retrospective study evaluating the 2-year outcome of 138 subjects with schizophrenia receiving rehabilitative intervention in an inpatient psychiatric facility (Manhattan Psychiatric Center, New York, NY) who were discharged to an outpatient psychiatric clinic.

SAMPLE CHARACTERISTICS

	N = 138
	Mean (SD)
Age (years)	42.12 (7.23)
Education (years)	11.36 (3.68)
Age of onset (years)	20.11 (3.22)
Substance abuse prior to admission (years)	10.36 (4.68)
Number of previous hospitalization	9.16 (6.43)
Length of stay (prior to discharge) (months)	12.01 (6.23)
	%
Gender	
Male	87.68%
Female	12.32%
Antipsychotic Treatment	
Oral antipsychotics ^a	58.70%
Intramuscular depot ^b	41.30%
Ethnicity	
African American	55.07%
Asian	3.62%
Caucasian	21.01%
Hispanic	20.29%
Baseline Symptoms	Mean (SD)
PANSS Positive Subscale	18.03 (4.69)
PANSS Negative Subscale	21.36 (5.67)
PANSS Total Score	78.22 (12.48)
Clinical Global Impression Scale - Severity	4.1 (0.98)
Cognitive Symptoms	Mean (SE)
Speed of Processing	14.15 (1.01)
Attention/Vigilance	18.53 (1.56)
Working Memory	10.69 (1.35)
Verbal Learning	26.45 (0.49)
Visual Learning	23.48 (0.79)
Reasoning & Problem Solving	29.35 (0.62)
Global Composite T Score	18.69 (36.44)
Functional Outcomes	

RELAPSE RATE AFTER 1 YEAR and 2 YEARS



CONCLUSIONS

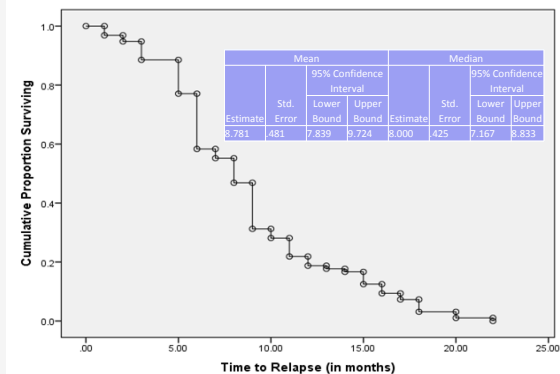
- The major findings from this study suggest that the PANSS item Lack of Judgment and Insight is the strongest predictor of relapse, followed by Average years of Substance Use prior to relapse.
- When assessing functional outcomes, PANSS Negative Symptom factor and Lack of Judgment and Insight were the only significant predictors of functioning at one year follow-up.
- The study overall suggests that there are a number of baseline factors that can be associated with treatment failure or relapse in this population.
- Knowledge of these factors has significant clinical implications and could aid in treatment and prevention strategies in schizophrenia.

DISCLOSURES AND CONTACT INFORMATION

A Khan is an employee of NeuroCog Trials, Durham, NC, USA, and currently or in the past 3 years has received support from National Institute of Mental Health, Celgene, Teva Pharmaceuticals, and Stanley Medical Research Foundation. AS Atkins is a full-time employee of NeuroCog Trials, Durham, NC, USA, and has received support from National Institute of Mental Health. RSE Keefe currently or in the past 3 years has received investigator-initiated research funding support from the Department of Veteran's Affairs, Feinstein Institute for Medical Research, GlaxoSmithKline, National Institute of Mental Health, Novartis, Psychogenics, Research Foundation for Mental Hygiene, Inc., and the Singapore National Medical Research Council. He currently or in the past 3 years has received honoraria, served as a consultant, or advisory board member for AbbVie, Akebia, Amgen, Aurobindo, AvNeuro/ChemRx, BiolineRx, Biogen Idec, Biomarin, Boehringer-Ingelheim, Eli Lilly, EnVivo/FORUM, GW Pharmaceuticals, Janssen, Lundbeck, Merck, Minerva Neurosciences, Inc., Mitsubishi, Novartis, NY State Office of Mental Health, Otsuka, Pfizer, Reviva, Roche, Sanofi/Aventis, Shire, Sunovion, Takeda, Targacept, and the University of Texas South West Medical Center. Dr. Keefe receives royalties from the BACS testing battery, the MATRICS Battery (BACS Symbol Coding) and the Virtual Reality Functional Capacity Assessment Tool (VRFCAT). He is also a shareholder in NeuroCog Trials and Sengenix. P Harvey has served as a consultant to AbbVie, Allergan, Akli, Boehringer Ingelheim, Forum Pharmaceuticals, Genentech, Lundbeck Pharmaceuticals, Otsuka Digital Health, Roche Pharma, Sanofi, Sunovion, and Takeda Pharmaceutical for the past 3 years.

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RELAPSE AFTER 2 YEARS OF OPTIMAL TREATMENT



30.43% (n=42) of the population had multiple relapses (defined as >2 relapses in 2 years)

PREDICTORS OF RELAPSE

Relapse Rate

The backward elimination method to identify the best Cox regression model according to likelihood ratio criteria (seventh step, $-2 \log \text{likelihood} = 189.59$, $\chi^2 = 9.01$, $df = 2$, $p = .021$) showed that the best predictive variables for relapse:

	B	SE	p	Exp B
PANSS Item G12 Lack of Judgment and Insight	0.20	0.09	0.011	1.36
Average Years of Substance Use	0.16	0.11	0.029	1.33
PANSS Marder Disorganization Factor	0.15	0.12	0.031	1.56
Number of Previous Hospitalizations	0.13	0.11	0.048	1.23

Functioning

Total scores on the PSP at two-years were only available for 91 of the original 138 subjects. Cumulative rates of relapse for the 91 subjects were 71.43% (N=68 of 91) at two years. PSP scores were only available for Year 1 with the best predictors as:

	B	SE	P	Exp B
PANSS Marder Negative Symptom Factor	0.21	0.10	0.043	1.53
PANSS Item G12 Lack of Judgment and Insight	0.19	0.11	0.048	1.35