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# Prospective 2-Year Study of Emergency Department Patients With Early-Phase Primary Psychosis or Substance-Induced Psychosis

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### Abstract

**Objective**—The authors examined treatment utilization and outcomes over 2 years among patients admitted to emergency departments with early-phase primary or substance-induced psychosis. The main hypothesis was that patients with substance-induced psychosis would have a more benign course of illness than those with primary psychosis.

**Method**—Using a prospective naturalistic cohort study design, the authors compared 217 patients with early-phase primary psychosis plus substance use and 134 patients with early-phase substance-induced psychosis who presented to psychiatric emergency departments at hospitals in Upper Manhattan. Assessments at baseline and at 6, 12, 18, and 24 months included psychiatric diagnoses, service use, and institutional outcomes using the Psychiatric Research Interview for Substance and Mental Disorders; psychiatric symptoms using the Positive and Negative Syndrome Scale; social, vocational, and family functioning using the World Health Organization Psychiatric Disability Assessment Schedule; and life satisfaction using the Quality of Life Interview. Longitudinal analyses were conducted using generalized estimating equations.

**Results**—Participants with primary psychosis were more likely to receive antipsychotic and mood-stabilizing medications, undergo hospitalizations, and have out-patient psychiatric visits; those with substance-induced psychosis were more likely to receive addiction treatments. Only a minority of each group received minimally adequate treatments. Both groups improved significantly over time on substance dependence, psychotic symptoms, homelessness, and psychosocial outcomes, and few group-by-time interactions emerged.

**Conclusions**—Patients presenting to Upper Manhattan emergency departments with either early-phase primary psychosis or substance-induced psychosis improved steadily over 2 years despite minimal use of mental health and substance abuse services.

Patients frequently present to emergency psychiatric settings with early-phase primary psychosis complicated by substance use or with early-phase substance-induced psychosis (1). In this study, we examined service use and outcomes naturalistically for both these groups over 2 years to investigate the hypothesis that patients with substance-induced psychosis would experience a more benign course of illness than patients with primary psychosis and concurrent substance use.

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The early course of primary psychosis, especially in schizophrenia and schizoaffective disorder, has been studied extensively in recent years (2, 3). Several consistent findings have emerged. Up to 80% of people with a first episode of psychosis respond well to antipsychotic medication, usually at low dosages, in terms of remission of positive psychotic symptoms (4). However, psychosocial functioning remains poor for approximately 80% of such patients (5). One common problem is that the majority of early-psychosis patients present with concurrent substance use (and often substance use disorders), which can complicate treatment response, medication adherence, and course of illness (6). Another is that over 50% of patients discontinue their medication within the first year, thereby significantly increasing their risk of relapse (7). Minimal treatment recommendations therefore include maintenance of medications and treatment relationships, substance abuse treatment, and psychosocial interventions.

Substance-induced psychosis is also a common clinical presentation in hospitals, crisis centers, and other emergency settings, but research on its treatment and longitudinal course is much less extensive than for primary psychosis (8). The psychosis-producing properties of several ingested substances have been known since prehistorical times (9), and numerous studies have confirmed the existence of drug-induced psychotic states that persist beyond the physiological presence of the substance in otherwise nonpsychotic individuals, especially with cannabis, amphetamines, and other stimulants (10-13). The diagnosis of substance-induced psychotic disorder entered DSM in 1994 with the fourth edition (14). The DSM-IV diagnostic criteria include prominent hallucinations or delusions that arise during or within 1 month of substance intoxication or withdrawal, that persist beyond the expected reactions to the substance, and that are not better accounted for by a primary psychotic disorder. People who experience a substance-induced psychosis have high rates of substance dependence and are vulnerable to subsequent psychotic episodes and more chronic psychotic states, especially in relation to cannabis use (15). Although longitudinal studies of substance-induced psychosis tend to focus on individuals who predominantly use one drug, many patients are polysubstance abusers, which can increase the risk of developing psychotic syndromes (16). Treatment guidelines for early-phase substance-induced psychosis, such as the duration of treatment with antipsychotic medication, are less clear than guidelines for early-phase primary psychosis (17). Nevertheless, substance abuse treatment and psychiatric monitoring for persistent or recurrent psychotic symptoms represent minimal treatment recommendations.

This 2-year prospective study of early-phase psychosis and substance use has illuminated several aspects of co-occurring psychosis and substance use by incorporating real-world heterogeneity and naturalistic follow-up (18, 19). In the present study, we compared treatment utilization and outcomes over 2 years for patients with either early-phase primary psychosis plus concurrent substance use or substance-induced psychosis, predicting that those with substance-induced psychosis would experience greater improvements.

## Method

## **Participants**

All participants were recruited from emergency psychiatric departments in five Upper Manhattan hospitals (18). Of 499 patients who met study criteria and were approached for baseline interviews, 38 declined, 58 initially agreed but could not be located for interviews, two were excluded because of dangerousness, and one died. Of the 400 who gave consent and were interviewed, 14 were excluded because they did not meet study criteria, yielding a baseline study group of 386 patients. We obtained data on the 386 participants at baseline, on 319 participants at 1 year, and on 273 participants at 2 years. Of the 67 participants who were never interviewed after baseline, 31 were lost to follow-up, 16 left the region and could

not be interviewed, 11 were incarcerated and could not be interviewed, eight declined to continue participating, and one died.

The study group for this analysis consisted of 351 patients who were interviewed at baseline, who had research diagnoses of early-phase primary psychosis plus substance use (N=217) or early-phase substance-induced psychosis (N=134), and for whom some follow-up data were available. We excluded the 34 of 168 (20.2%) patients whose baseline diagnoses changed from substance- induced psychosis to primary psychosis at the 12-month follow-up (19). No diagnostic changes occurred between months 12 and 24. Early phase of psychosis was defined as having neither hospitalizations nor untreated psychosis for more than 6 months prior to emergency department admission (20). Participants spoke English or Spanish, were between the ages of 17 and 45 years, had at least one psychotic symptom at the baseline assessment, had used alcohol or drugs within the past 30 days, and were free of delirium.

The institutional review boards of the New York State Psychiatric Institute/Columbia University Medical Center and the other participating institutions approved and monitored the research protocol. All participants gave written informed consent.

#### Measures

Participants reported their age, sex, marital status, ethnicity, education, and work status in response to questions on the Community Care Schedule (21).

**Diagnoses**—Research interviewers established diagnoses at baseline using the Psychiatric Research Interview for Substance and Mental Disorders (PRISM; 22), which was specifically developed to assess psychiatric and substance use comorbidity according to DSM-IV criteria (14). According to DSM-IV, a psychotic symptom must be persistent or repetitive and not an isolated experience, and a primary diagnosis of psychosis is given only if there is no evidence of heavy substance use or withdrawal, if the full psychiatric syndrome is established prior to heavy substance use, or if the syndrome persists more than 4 weeks after the cessation of acute intoxication or withdrawal. In contrast, a diagnosis of substance-induced psychosis is given for disorders that occur only during periods of heavy substance use or soon afterward. The substance used must have been capable of causing the psychotic symptoms. During these periods, the psychotic symptoms must exceed the expected effects of intoxication or withdrawal and be sufficiently severe to warrant independent clinical attention. DSM-IV lists the expected intoxication and withdrawal symptoms for each class of drug. For substance-induced psychotic disorders, DSM-IV does not include minimum duration or symptom requirements as it does for primary psychotic disorders.

Data for the PRISM included patient self-reports obtained during the interview, observations and diagnostic assessments of clinical staff, hospital medical records, collateral reports of patterns of substance use and onset of psychosis, and results of urine toxicology screens conducted routinely on all emergency department admissions. The reliability of the PRISM diagnoses relevant to this study (substance dependence for most substances, psychotic disorders, and substance-induced psychotic disorders) has been good to excellent (kappa values >0.6) (22). Further details of PRISM diagnostic procedures are available elsewhere (22, 23).

**Psychiatric symptoms**—Psychiatric symptoms were assessed at each interview with the Positive and Negative Syndrome Scale (PANSS; 24). The alpha coefficients of reliability for the PANSS scores reported here were 0.78 for the positive symptom scale and 0.81 for the negative symptom scale.

Psychosocial adjustment—Current employment (yes/no), social functioning, and family functioning were assessed with the World Health Organization Psychiatric Disability Assessment Schedule (WHO/DAS; 25), which contains ratings on a 5-point scale ranging from 1 (no disability) to 5 (gross disability). The WHO/DAS items include underactivity; social withdrawal; household participation; marital, sexual, and parental relationships and functioning; and occupational role performance. WHO collaborators have reported high levels of interrater agreement on ratings of major social roles covered in WHO/DAS, with kappa values 0.7 in 86% of comparisons and 0.8 in 60% (25). Overall life satisfaction was assessed twice, at the beginning and end of interviews, using the Lehman Quality of Life Interview (26).

**Utilization of institutions and services**—Episodes of treatment, hospitalization, incarceration, and homelessness were assessed at each interview using a timeline follow-back calendar as part of the PRISM interview. We examined the use of 10 dichotomously rated treatments (yes/no) at each 6-month follow-up: antidepressant medications, antipsychotic medications, mood-stabilizing medications, addiction medications, outpatient mental health treatment, outpatient addiction treatment, outpatient dual diagnosis treatment, hospitalization, visits to an outpatient psychiatrist, and visits to other physicians.

#### **Procedures**

Patients were recruited for the study after assessment, treatment, and stabilization in emergency departments. For about three-quarters of participants, recruitment occurred after transfer to an inpatient service; for the others, recruitment occurred before discharge after treatment in the emergency department for up to 72 hours. Baseline assessments were completed in one or two sessions within 2 weeks. Interviewers assessed diagnoses, including alcohol and drug dependence, at baseline, at 12 months, and at 24 months using DSM-IV criteria and the PRISM interview. The same interviewers conducted all interviews and were therefore not blind to previous interviews. Participants were paid for interviews. We focused on substance dependence because the reliability of abuse diagnoses has generally been lower and much more variable than that of dependence, which has been excellent (27). Researchers administered all other interviews at baseline and at 6, 12, 18, and 24 months.

### **Data Analysis**

To compare the primary psychosis and the substance-induced psychosis groups on the longitudinal course of treatments and outcomes, we used generalized estimating equations (GEE; 28) implemented in SAS GENMOD (29). We examined service use for the two diagnostic groups separately as time-varying covariates in GEE models. GEE allows analysis of both continuous and categorical variables in the same procedure. It includes participants with missing data or attrition, and inferences are valid if data are missing completely at random. To check for the effects of missing data, we repeated the analyses with dropouts excluded. The results were similar and are therefore not reported here. GEE tests multiple variables simultaneously in a single model.

## **Results**

Of the 351 participants at baseline, 284 (80.9%) were interviewed at 6 months, 260 (74.1%) at 12 months, 253 (72.1%) at 18 months, and 239 (68.1%) at 24 months. As described above, reasons for attrition were moves, refusals, incarceration, death, and loss to follow-up. Of baseline demographic and diagnostic variables, only drug dependence predicted attrition ( $^2$ =5.44, df=1, p=0.02).

## **Participants**

As shown in Table 1, at baseline the 351 participants were predominantly young, male, from minority backgrounds, single, minimally educated, and unemployed. Those with primary psychosis were younger and more likely to be single than those with substance-induced psychosis.

Among the 217 with a diagnosis of primary psychotic disorder, the diagnoses were schizophrenia (N=80, 36.9%), psychotic mood disorder (N=73, 33.6%, including 34 with depressed mood only, 24 with mania only, and 15 with mixed mania and depression), psychotic disorder not otherwise specified (N=32, 14.7%), schizophreniform disorder (N=18, 8.3%), schizoaffective disorder (N=8, 3.9%), and delusional disorder (N=6, 2.8%). The most common substances used by the primary psychotic disorder group were cannabis (N=120, 55.3%), alcohol (daily or near-daily use for at least 1 month) (N=50, 23.0%), cocaine (N=35, 16.1%), and hallucinogens (N=11, 5.1%).

Among the 134 patients with a substance-induced psychotic disorder, the specific diagnoses were psychosis induced by two or more substances (most commonly cannabis and one other drug) (N=54, 40.3%), alcohol-induced psychosis (N=25, 18.7%), cocaine-induced psychosis (N=24, 17.9%), cannabis-induced psychosis (N=18, 13.4%), hallucinogen-induced psychosis (N=5, 3.7%), sedative-induced psychosis (N=3, 2.2%), heroin-induced psychosis (N=2, 1.5%), stimulant-induced psychosis (N=1, 0.7%), and uncertain (N=2, 1.5%).

#### **Service Utilization**

Table 2 provides a longitudinal comparison of service use by the two groups over 2 years. Patients with primary psychosis were more likely to use antipsychotic medications, mood-stabilizing medications, hospitals, and out-patient psychiatrists; those with substance-induced psychosis were more likely to use outpatient substance abuse treatments and medications for addictions. The use of antipsychotic medications decreased over time, whereas the use of outpatient dual disorders programs, outpatient psychiatrist visits, and other outpatient physician visits increased over time. The only interaction between group and treatment showed that patients with primary psychosis increased participation in outpatient mental health treatments over time, while those with substance-induced psychosis decreased such treatments. Seeing an outpatient psychiatrist was correlated with using an antidepressant medication (r=0.35), with using an antipsychotic medication (r=0.31), and with using outpatient mental health treatment (r=0.35). Other correlations among treatment variables were weak (r=0.30).

Table 2 also shows that overall use of specific services was low for both groups. We defined minimally adequate treatment for patients with primary psychosis as taking a medication, participating in outpatient mental health treatment, and visiting a psychiatrist or other doctor. After baseline, patients with primary psychosis achieved this level of treatment at the following rates: 19% at 6 months, 21% at 12 months, 25% at 18 months, and 26% at 24 months (data not shown in table). Similarly, we defined participating in some form of substance abuse treatment and seeing a doctor for monitoring as minimal treatment for patients with substance-induced psychosis. After baseline, 8% achieved this level of treatment at 6 months, 9% at 12 months, 12% at 18 months, and 9% at 24 months (data not shown in table).

## **Outcomes at 2 Years**

Table 3 summarizes the longitudinal data for 10 outcomes. The primary psychosis group consistently had higher rates of positive and negative symptoms of psychosis, and the substance-induced psychosis group consistently had higher rates of alcohol dependence,

drug dependence, and homelessness. Several outcomes improved over time for both groups: alcohol and drug dependence, positive and negative symptoms of psychosis, homelessness, employment, family relations, and social relations. A small number of group-by-time interactions indicated that the number of incarcerations declined more in the primary psychosis group than in the substance-induced psychosis group, while employment and family relations improved more over time in the substance-induced psychosis group than in the primary psychosis group.

Several outcomes were intercorrelated. Positive symptoms were correlated with negative symptoms (r=0.50) and inversely correlated with family relationships (r=-0.44) and social relationships (r=-0.55). Negative symptoms were inversely correlated with family relationships (r=-0.40) and social relationships (r=-0.55). Family and social relationships were correlated (r=0.72). Life satisfaction was correlated with family relationships (r=0.37) and social relationships (r=0.35). Other correlations among outcomes were weak (<0.30).

## **Discussion**

We compared the longitudinal course of patients with emergency department admissions for substance-induced psychosis and those from the same settings with primary psychosis plus concurrent substance use. Having identified these patients in crisis, we expected longitudinal improvements in both groups as a result of fluctuating illnesses, treatments, and regression to the mean. Both groups did in fact improve over time in several areas: reductions in positive and negative symptoms of psychosis, decreased rates of alcohol and drug dependence, and better social functioning. Consistent with baseline diagnostic distinctions, patients with primary psychosis consistently reported more psychotic symptoms, and those with substance-induced psychosis reported greater substance dependence longitudinally.

The hypothesis that patients with substance-induced psychosis would improve more than those with primary psychosis was not generally supported. The observed longitudinal differences between diagnostic groups largely reflected baseline values. Only three interactions between diagnostic group and outcomes emerged, showing greater psychosocial gains but also greater rates of incarceration by the patients with substance-induced psychosis.

Both diagnostic groups decreased their levels of substance dependence by approximately 50%, despite relatively low levels of substance abuse treatments. Previous research on early psychosis has shown similar rates of remission of substance use disorders after the initial psychotic episode without specific substance abuse treatments (30, 31). The same trend may be true for patients with substance-induced psychosis as well. Several explanations are possible: the experience of psychosis, education about the relationships between substance use and psychosis, treatment of psychotic symptoms, interruption of social relationships, or other factors may motivate patients to decrease their substance use after an initial psychotic episode.

Both groups also experienced marked decreases in psychotic symptoms after the baseline assessment. The use of antipsychotic medication early on undoubtedly contributed to this finding, but relatively few participants continued to take antipsychotics over time. For the primary psychosis group, the approximately 50% use of antipsychotics may be partly explained by diagnostic heterogeneity. For the substance-induced psychosis group, less than 20% were using antipsychotics at each follow-up after the first 6 months. Although these data support the view that most patients with substance-induced psychosis do not need long-term antipsychotic medication, this conclusion should be tempered by the rediagnoses in our sample: we excluded approximately one-fifth of the patients who were initially diagnosed as

having substance-induced psychosis and subsequently were rediagnosed as having primary psychosis. All of these rediagnosed patients experienced persistent or recurrent psychotic symptoms while abstinent from substances of abuse and needed ongoing antipsychotic medication (19). Our earlier analyses (19) showed that the key factors predicting such rediagnoses were poor premorbid functioning, lack of awareness of psychosis, and family history of mental illness. Patients who have one or more of these risk factors need continued clinical follow-up and probably need continued antipsychotic medication for several months. Because evidence-based guidelines for duration of antipsychotic medication treatment after a substance-induced psychosis do not exist, however, studies of adaptive treatment strategies are needed.

Only a small minority of patients in each diagnostic group received treatments reflecting minimal standards of adequacy. These findings are consistent with epidemiologic data on serious mental illness (32). In our study, the rates of service use for patients with substance-induced psychosis were even lower than those for patients with primary psychosis, possibly because of lack of insurance, awareness, or need.

Several limitations of this study warrant mention. The patients with substance-induced psychosis often had polysubstance use disorders and complex clinical and psychosocial presentations that seriously confounded diagnosis (8). In addition to using multiple drugs, their clinical presentations were sometimes obfuscated by psychosocial stressors, cognitive problems, legal entanglements, trauma histories, poverty, or other factors. Furthermore, many patients were unable to give any recent history of significant intervals without exposure to psychoactive drugs. Although this patient group is complex, its heterogeneity reflects the nature of real-world emergency department patients in large cities. Finally, the study was limited by reliance on self-report for some of the measures.

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TABLE 1

Baseline Characteristics of 351 Patients With Early-Phase Primary Psychosis or Substance-Induced Psychosis Treated in Emergency Psychiatric Departments

Characteristic	Primary Psych	osis (N=217)	Substance-Induced	Psychosis (N=134)
	Mean	SD	Mean	SD
Age <sup>a</sup> (years)	27.2	8.1	30.4	8.3
	N	%	N	%
Male	152	70	100	75
Race				
Black	95	44	57	43
Hispanic	84	39	63	47
White or other	38	17	14	10
Marital status <sup>b</sup>				
Single	174	81	89	67
Married	15	7	23	17
Separated	25	12	20	15
Completed high school	124	57	65	49
Employed	53	24	35	26

<sup>&</sup>lt;sup>a</sup>Significant difference between groups, p<0.001.

 $<sup>^{</sup>b}$ Significant difference between groups, p=0.004.

TABLE 2

Service Utilization Over 2 Years by 351 Patients With Early-Phase Primary Psychosis or Substance-Induced Psychosis

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					Assessment	ment						ď	
	Bas	Baseline	9 W	Months	12 Months	nths	18 Months	onths	24 Months	onths	Groun Difference of		
Group and Treatment or Service	Z	%	Z	%	Z	%	Z	%	Z	%	Baseline	Average Time Trend	Group- by-Time Interaction
Primary psychosis group	217	100	186	98	173	80	171	62	162	75			
Substance-induced psychosis group	134	100	86	73	87	65	82	61	77	57			
Antidepressant medication											0.297	0.574	0.109
Primary psychosis group	99	30	53	28	62	36	09	35	99	35			
Substance-induced psychosis group	37	28	20	20	13	15	14	17	15	19			
Antipsychotic medication											<0.001	<0.001	0.139
Primary psychosis group	175	81	121	65	95	55	91	53	85	52			
Substance-induced psychosis group	19	50	30	31	14	16	13	16	10	13			
Mood-stabilizing medication											0.008	0.351	0.547
Primary psychosis group	55	25	45	254	34	20	40	23	39	24			
Substance-induced psychosis group	21	16	10	10	4	5	5	9	10	13			
Outpatient mental health treatment											0.079	0.232	0.004
Primary psychosis group	20	6	46	25	39	23	45	26	49	30			
Substance-induced psychosis group	∞	9	12	12	6	10	5	9	3	4			
Outpatient substance abuse treatment											0.016	0.057	0.531
Primary psychosis group	9	3	9	3	5	3	∞	S	5	3			
Substance-induced psychosis group	7	S	11	11	12	14	15	18	∞	10			
Outpatient dual disorders treatment											0.000	0.005	0.530
Primary psychosis group	18	∞	24	13	24	14	19	11	26	16			
Substance-induced psychosis group	4	ю	∞	∞	10	11	6	11	9	∞			
Psychiatric hospitalization											0.010	0.331	0.945
Primary psychosis group	6	4	27	15	15	6	19	11	18	11			
Substance-induced psychosis group	1	1	3	3	1	_	0	0	2	3			
Outpatient visits to a psychiatrist											<0.001	<0.001	0.534
Primary psychosis group	62	29	124	29	105	61	104	61	100	62			
Substance-induced psychosis group	16	12	25	26	20	23	20	24	20	26			

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				7	Assessment	nent						ď	
	Base	line	Baseline 6 Months		12 Months	ths	18 Months	ths	24 Months	ıths	Croun Difference of		
Group and Treatment or Service	Z	х % х	Z	%	Z	%	Z	%	% N % N % N	%	Baseline	Average Time Trend	Baseline Average Time Trend Group- by-Time Interaction
Outpatient visits to other physicians											0.136	<0.001	0.205
Primary psychosis group	37	37 17	35	19	39	23	40	24	43	27			
Substance-induced psychosis group 15 11	15	11	14	41	16	18	17	21	19	25			
Substance treatment medication											0.009	0.356	0.082
Primary psychosis group	S	2	ю	2	7	-	9	4	S	8			
Substance-induced psychosis group 12 9	12	6	9	9	8	3	2	2	3	4			

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TABLE 3

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Outcomes Over 2 Years for 351 Patients With Early-Phase Primary Psychosis or Substance-Induced Psychosis

					Assessment	nent						d	
Group and Variable	Ba	Baseline	9W 9	6 Months	12 Months	onths	18 Months	onths	24 Months	onths	Group Difference at Baseline	Average Time Trend	Group- by-Time Interaction
	z	%	z	%	z	%	z	%	z	%			
Primary psychosis group <sup>a</sup>	217	100	186	98	173	80	171	79	162	75			
Substance-induced psychosis group <sup>a</sup>	134	100	86	73	87	92	82	61	77	57			
Alcohol dependence											<0.001	<0.001	0.773
Primary psychosis group	55	25			25	14			19	12			
Substance-induced psychosis group	71	53			31	36			21	27			
Drug dependence											<0.001	<0.001	0.138
Primary psychosis group	59	27			33	19			23	14			
Substance-induced psychosis group	81	61			34	39			24	31			
Homelessness											0.002	<0.001	0.210
Primary psychosis group	22	10	17	6	14	∞	6	S	6	9			
Substance-induced psychosis group	27	20	18	18	14	16	5	9	4	5			
Incarceration											999:0	0.606	0.003
Primary psychosis group	19	6	13	7	6	S	7	4	9	4			
Substance-induced psychosis group	12	6	∞	∞	17	20	13	16	6	12			
Employment											0.584	<0.001	0.015
Primary psychosis group	53	24	65	35	59	34	54	32	51	31			
Substance-induced psychosis group	35	26	40	41	36	41	38	46	34	44			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Positive symptoms											<0.001	<0.001	0.096
Primary psychosis group	18.6	7.2	13.2	6.1	13.3	0.9	12.4	6.1	12.5	9.9			
Substance-induced psychosis group	13.9	5.4	10.5	4.2	9.6	3.8	9.2	2.5	9.4	2.4			
Negative symptoms											<0.001	<0.001	0.066
Primary psychosis group	14.2	6.2	12.8	5.6	12.4	5.9	11.7	5.2	11.6	4.8			
Substance-induced psychosis group	11.1	4.5	10.6	4.6	9.5	3.3	10.1	3.5	9.2	3.0			

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Group and Variable	Bas	Baseline	6 Mon	ths	12 Mon	ths	18 Mon	ths	6 Months 12 Months 18 Months 24 Months	Group Difference at Baseline	Average Time Trend	erence at Baseline Average Time Trend Group- by-Time Interaction
Family relationships										0.465	<0.001	0.003
Primary psychosis group	2.4	1.4	1.9	1.5	1.9 1.5 1.6 1.3		1.7 1.4	1.4	1.6 1.4			
Substance-induced psychosis group	2.6	1.5	1.5 1.3	1.3	1.3 1.2	1.2	1.2	1.2	9. 1.1			
Social relationships										0.231	<0.001	0.217
Primary psychosis group	2.9	1.4	2.4 1.5	1.5	2.3	1.4	1.9	1.3	1.9 1.4			
Substance-induced psychosis group	2.8	1.4	1.9	1.6	1.8	1.4	1.7	1.3	1.2 1.1			
Life satisfaction										0.201	0.339	0.464
Primary psychosis group			9.3	2.8	8.6	3.1	9.3	2.7	9.4 2.8			
Substance-induced psychosis group			6.6	2.8	9.9 2.8 10.4 2.4	2.4	9.7 2.8		10.6 2.4			

<sup>&</sup>lt;sup>4</sup>The Ns in these rows indicate the maximum numbers of participants at each time point; actual Ns may differ for different variables. The ranges of valid Ns across variables are 348–351 at baseline, 214–284 at 6 months, 201–260 at 12 months, 194–253 at 18 months, and 197–239 at 24 months.