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Long-term Outcomes of People With DSM Psychotic Disorder NOS

Line Widing[1,*], Carmen Simonsen[1,2], Thomas Bjella[1], Magnus Johan Engen[3], Camilla Bärthel Flaaten[1,4], Erlend Gardsjord[5], Beathe Haatveit[1], Elisabeth Haug[6], Siv Hege Lyngstad[3], Ingrid Hartveit Svendsen[7], Ruth Kristine Vik[1], Kristin Fjelnseth Wold[1], Gina Åsbø[1,4], Torill Ueland[1,4], and Ingrid Melle[1]

[1]NORMENT, Norwegian Centre for Mental Disorders Research, Division of Mental Health and Addiction, Oslo University Hospital and University of Oslo, Oslo, Norway; [2]Early Intervention in Psychosis Advisory Unit for South East Norway, Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway; [3]Nydalen District Psychiatric Centre, Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway; [4]Department of Psychology, University of Oslo, Oslo, Norway; [5]Unit for Early Intervention in Psychosis, Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway; [6]Division of Mental Health, Department of Child and Adolescent Psychiatry, Innlandet Hospital Trust, Gjøvik, Norway; [7]Department for competence and education, Innlandet Hospital Trust, Brumunddal, Norway

[*]To whom correspondence should be addressed; Psychosis Research Unit/TOP, Division of Mental Health and Addiction, Oslo University Hospital HF, P.O. Box 4956 Nydalen, N-0424 Oslo, Norway; tel: +47 93405699, e-mail: l.h.widing@studmed.uio.no

***Introduction*: The Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV diagnostic category "Psychotic disorder not otherwise specified" (PNOS) is seldom investigated, and we lack knowledge about long-term outcomes. We examined long-term symptom severity, global functioning, remission/recovery rates, and diagnostic stability after the first treatment for PNOS. *Methods*: Participants with first-treatment PNOS (n = 32) were reassessed with structured interviews after 7 to 10 years. The sample also included narrow schizophrenia spectrum disorders (SSD, n = 94) and psychotic bipolar disorders (PBD, n = 54). Symptomatic remission was defined based on the Remission in Schizophrenia Working Group criteria. Clinical recovery was defined as meeting the criteria for symptomatic remission and having adequate functioning for the last 12 months. *Results*: Participants with baseline PNOS or PBD had lower symptom severity and better global functioning at follow-up than those with SSD. More participants with PNOS and PBD were in symptomatic remission and clinical recovery compared to participants with SSD. Seventeen (53%) PNOS participants retained the diagnosis, while 15 participants were diagnosed with either SSD (22%), affective disorders (19%), or substance-induced psychotic disorders (6%). Those rediagnosed with SSD did not differ from the other PNOS participants regarding baseline clinical characteristics. *Conclusions*: Long-term outcomes are more favorable in PNOS and PBD than in SSD. Our findings confirm diagnostic instability but also stability for a subgroup of participants with PNOS. However, it is challenging to predict diagnostic outcomes of PNOS based on clinical characteristics at first treatment.**

Key words: psychosis NOS/schizophrenia/bipolar/diagnostic stability/remission/recovery

Introduction

The clinical characteristics of psychotic disorders do not always fit neatly with the criteria-based diagnostic categories. For clinical presentations where information is either lacking, contradictory, or does not meet the criteria of any specified diagnosis, the diagnosis "Psychotic disorder not otherwise specified" (PNOS) was used in Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV[1] and previous editions[2] of the diagnostic manual. PNOS is now replaced by "Other specified schizophrenia spectrum disorder and other psychotic disorder" (OSSPD) and "Unspecified schizophrenia spectrum disorder and other psychotic disorder".[3] The first is intended for conditions that do not meet the full criteria for any other specific disorder and the latter is for conditions that cannot be specified due to missing information. The OSSPD includes the diagnosis of "Attenuated psychotic syndrome," but outside of this, the 2 DSM-5 categories combined essentially correspond to DSM-IV PNOS.

Approximately 7%–12% of first-episode psychosis patients (FEP) are initially classified as PNOS.[4–7] Because it is a "diagnosis of exclusion" without specific criteria, PNOS captures a wide range of heterogeneous psychotic conditions.[8] They are thus often excluded from research studies and, when included, reported with brief psychotic disorder and delusional disorder as "other psychotic disorders." Given the high prevalence of PNOS diagnoses

in FEP, we need more knowledge on the course and outcome to ensure that new patients receive appropriate information and to plan their treatment.

The few cross-sectional studies that have examined PNOS specifically indicate that people with PNOS as a group have milder psychotic symptoms and better global functioning than people with narrow schizophrenia spectrum disorders (SSD; schizophrenia, schizoaffective disorder, schizophreniform disorder),[8–10] but more severe symptoms and poorer global functioning than those with psychotic bipolar disorders (PBD).[8] As a group, people with PNOS have similar neurocognitive profiles to those with schizophrenia (SZ), with milder deficits in the affected domains.[10,11] Furthermore, findings indicate that the PNOS group has as poor premorbid academic functioning in childhood as SSD but is intermediate between PBD and SSD in their premorbid social functioning.[12] Taken together, the available evidence suggests that PNOS is intermediate between PBD and SSD in severity assessments over the short term.

There are few longitudinal studies of PNOS, those published are mainly short term and are focused on diagnostic stability.[4,6,10,13] The proportion of PNOS retaining their initial diagnosis in these studies varies between 27 and 78%,[4,6,10,13] compared to 90% for SZ and 56% for brief psychotic disorder.[13] Meta-analyses indicate 34%–46% of diagnostic transitions from PNOS are to SSD[13,14] and 7% to affective psychoses.[13] Thus, for a significant proportion of the patients, the PNOS criteria define a diagnostically stable psychotic condition in the short term. For others, the condition can be considered as a precursor to SSD or PBD. To what extent diagnostic transitions are limited to the first years of illness or continue over time is not fully known, as a minimal number of studies have investigated the longer-term stability of PNOS diagnoses in FEP. The studies comprise a catchment area-based study that reports diagnostic stability after 6 years of follow-up in a total of 4 PNOS participants out of baseline 13[7] and a larger UK study that reports ten years of stability in 8 out of 30 PNOS participants.[5] In the latter, only 219 out of the total 403 participants with different types of first-episode psychoses were reinterviewed,[15] and the remaining diagnoses were based on chart reviews.

A diagnosis is also not a precise indication of outcome. Many patients with psychotic disorders experience stable remission of psychotic symptoms and even clinical recovery.[16,17] There are also differences in remission and recovery rates within the psychosis spectrum, with PBD having better rates than SSD.[16,18] A limited number of studies have investigated other short-term outcomes than diagnostic stability in PNOS. The exception is 2 recent follow-up studies that found higher remission rates in participants with PNOS compared to participants with SZ after 1-[10] and 3-year[19] follow-ups. The rates of full recovery were also higher in PNOS than in SZ after 1 year,[10] but not after 2 and 3 years.[19] There are, to the best of our knowledge, no studies investigating the long-term clinical outcome of FEP patients diagnosed with PNOS. We thus aimed to investigate the long-term clinical outcome of PNOS participants recruited during their first year of treatment and followed up after 7 to 10 years, compared to PBD and SSD. We here focus on the following outcomes:

1) Clinical symptomatology as measured with structured clinical scales.
2) Remission and recovery rates using consensus criteria.
3) Diagnostic stability using structured diagnostic interviews.

Methods

Participants

Participants coming to their first treatment for a psychotic disorder were recruited to the ongoing Thematically Organized Psychosis study (TOP) between 2003 and 2012. Patients were referred to the TOP study from inpatient and outpatient services of hospitals in the catchment areas of Oslo and Innlandet Hospital Trust. They were invited to follow-up assessments after 10 years in Oslo and after 7 years at Innlandet, and the reassessments were carried out between 2015 and 2021. Subjects included in the present study were 18–65 years old and had a DSM-IV diagnosis of SSD, PBD, or PNOS at baseline. The participants were recruited within 1 year after starting their first adequate treatment for a psychotic disorder (defined as hospital treatment for psychosis or treatment with antipsychotic medication/mood stabilizing medication in a recommended dose) or, in some cases, before adequate treatment was started. Participants who met the criteria for a substance-induced psychotic disorder or attenuated psychosis syndrome were excluded from the study as these are not defined as primary psychotic disorders. Other exclusion criteria were IQ below 70, severe brain damage, or not speaking a Scandinavian language.

A total of 189 of the 431 participants assessed at baseline took part in the follow-up assessment, resulting in a retention rate of 43.9% (Figure 1). Nine participants were omitted from the current analyses due to incomplete datasets at follow-up (missing data for both Global Assessment of Functioning [GAF] and Positive and Negative Syndrome Scale [PANSS]). The final sample thus consisted of 180 participants, 131 assessed in Oslo and 49 at Innlandet Hospital Trust. The diagnostic distribution of the participants at baseline was as follows (*n* (%)): SZ 65 (36.1%), schizoaffective disorder 17 (9.4%), schizophreniform disorder 12 (6.7%), bipolar disorder type I 51 (28.3%), bipolar disorder not otherwise specified (NOS) 3 (1.7%), and PNOS 32 (17.8%).

The study was conducted in accordance with the Helsinki Declaration of ethics in medical research

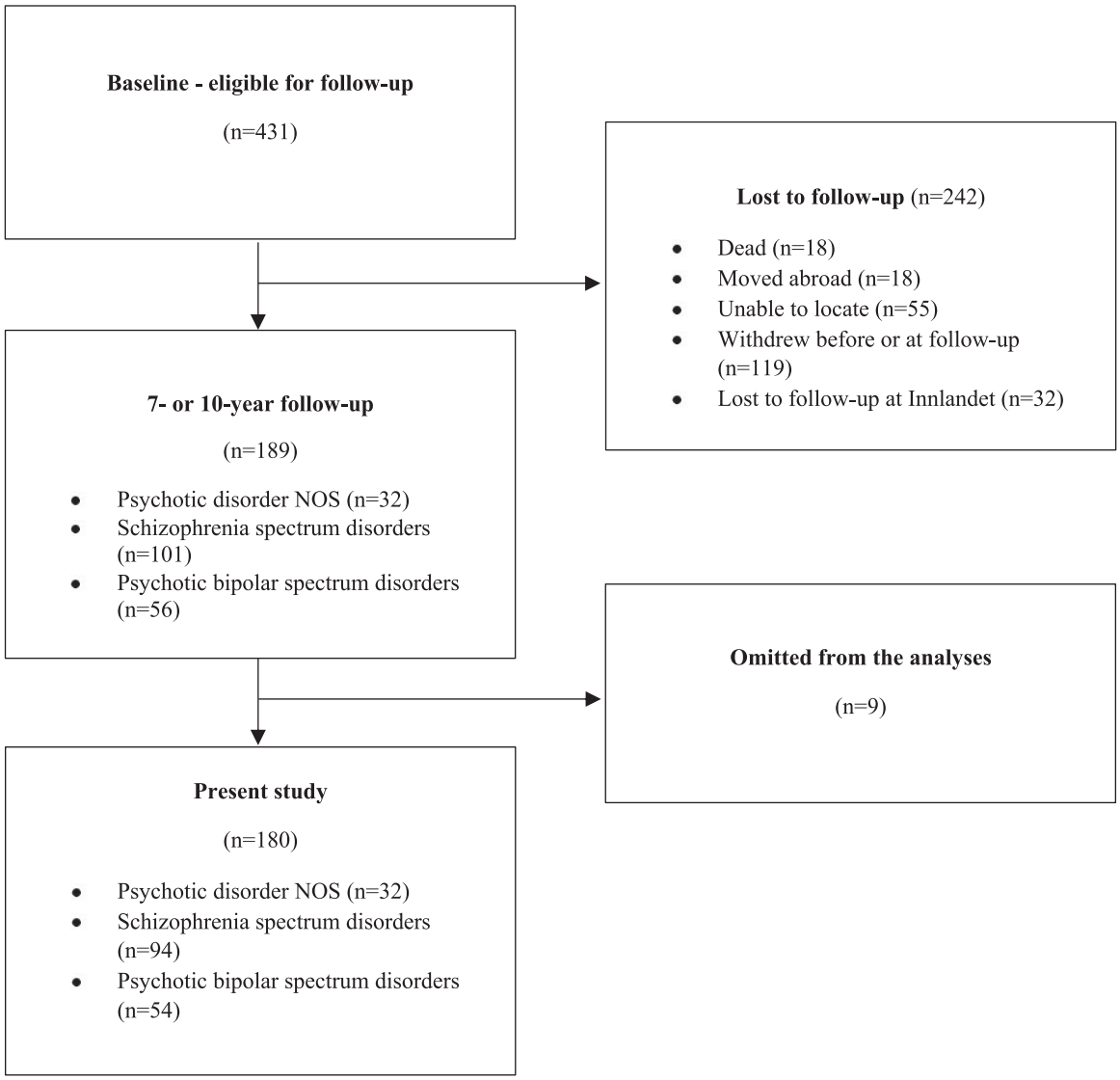

Fig. 1. Participation in 7- or 10-year follow-up.

and approved by the Regional Committee for Medical Research Ethics (REK# 22265) and the Norwegian Data Inspectorate. We obtained written informed consent from all participants before the assessments.

Clinical Assessments

The participants underwent a comprehensive clinical assessment performed by trained clinical psychologists or physicians, supervised by experienced consultant clinical psychologists and psychiatrists. At the Innlandet Hospital Trust, parts of the follow-up assessments were carried out by a trained psychiatric nurse. We obtained demographic data and a complete medical history through a comprehensive clinical interview supplemented with information from the participants' clinical records. DSM-IV diagnoses for all diagnostic categories were made using the Structural Clinical Interview for DSM-IV Axis I Disorders, module A-E (SCID-I).[20] The interviewers received training in accordance with a program developed at University of California, Los Angeles, USA before conducting the assessments. Diagnostic reliability in the TOP study has been found to be satisfactory, with an overall kappa score varying between 0.92 and 0.99 across different assessment teams.[21] Since the SCID for DSM-IV does not directly differentiate between psychotic and nonpsychotic forms of bipolar disorder, we classified patients as having PBD at baseline if they reported symptoms that met the criteria for a psychotic episode during the SCID-I interview and/or during the assessment of current psychotic symptoms.

We used the Structured Clinical Interview for Positive and Negative Syndrome Scale (SCI-PANSS)[22] to assess current psychotic symptoms. The PANSS items were grouped according to Wallwork's five-factor model as this has better psychometric properties in FEP samples

than the original three-factor model.[23,24] Psychosis was defined as having a score of 4 or higher on PANSS items P1, P3, P5, P6, or G9. Global functioning was assessed with the GAF, split version.[25] We used the Alcohol Use Disorder Identification Test (AUDIT)[26] and the Drug Use Disorders Identification Test (DUDIT)[27] to measure the amount and pattern of alcohol and drug use over the past 12 months. The clinical assessment with SCID-I, GAF, PANSS, and AUDIT/DUDIT was conducted at baseline and at follow-up.

Illness Course

We obtained information on the number of participants who went into stable remission during the first year after adequate treatment, the total duration of psychotic episodes, and the total duration of hospital admissions. Due to different follow-up lengths in the Oslo region and the sample from Innlandet Hospital trust, the duration of psychotic episodes and the duration of hospital admissions were divided by the number of follow-up years for the analyses and expressed in analyses as weeks per year. The participants' use of psychotropic medication and antipsychotic medication was recorded at baseline and at follow-up.

Remission and Clinical Recovery

Psychotic symptomatic remission was defined based on the Remission in Schizophrenia Working Group's international consensus definition,[28] with scores of 3 (mild) or less on the following PANSS items: positive symptoms (P1 delusions, P3 hallucinatory behavior, and G9 unusual thought content), disorganized symptoms (P2 conceptual disorganization, G5 mannerisms, and posturing), and negative symptoms (N1 blunted affect, N4 passive-apathetic social withdrawal, N6 lack of spontaneity, and flow of conversation). *Adequate functioning* was defined similarly as in a previous large Norwegian 10-year follow-up study[29] and required full-time occupational functioning (work, studies, or equivalent), social functioning (equivalent to meeting a friend in person once a week or more), and independent living (living without supervision at home and maintain daily activities [ADL]). Participants were in *clinical recovery* if they met the criteria for symptomatic remission from psychosis and adequate functioning for the last 12 months.

Diagnostic Stability

Diagnostic stability was determined as the percentage of participants who retained the same diagnosis at follow-up. We classified the participants with baseline PNOS into subcategories according to the symptomatology that provided the basis of their diagnosis, as described previously.[8] The subcategories were defined as follows: (1) Psychotic symptomatology that *does not meet the criteria* for any specific diagnosis, (2) Psychotic symptomatology about which there is *contradictory information* to make a specific diagnosis, and (3) Psychotic symptomatology about which there is *inadequate information* to make a specific diagnosis.

Statistical Analyses

Statistical Package for the Social Sciences (SPSS), also known as IBM SPSS, version 27, was used for statistical analyses. The threshold for statistical significance was set at $P < .05$. Group differences were examined with Chi-Square tests/Fisher's exact test for categorical variables and Analyses of variance (ANOVAs) for continuous variables. For continuous variables with unequal variances, Welch's ANOVAs were used. Statistically significant results were interpreted using Bonferroni (ANOVA, Chi-square) and Games-Howell (Welch ANOVA) post hoc tests. Mann-Whitney-U test and Kruskal Wallis test were used for non-normally distributed continuous variables.

Results

Demographic and Baseline Clinical Characteristics

The participants who completed the reassessment and those who were lost to follow-up did not differ regarding demographic and clinical data, except for more females (49.7% vs 37.2%, $\chi^2(1, N = 431) = 6.83$, $P = .009$) and participants with a PBD diagnosis (29.6% vs 19.4%, $\chi^2(1, N = 431) = 6.13$, $P = .047$) among the completers (supplementary table 1). There were no significant differences between the completers and non-completers for any baseline variables within the 3 diagnostic groups.

The baseline demographic and clinical characteristics of the follow-up study participants are presented in table 1. The participants with PBD, PNOS, and SSD did not differ regarding age or gender. There were no differences between the 3 groups in the proportion of participants belonging to an ethnic minority or the proportion of participants who were first-generation immigrants. The PNOS and PBD groups had lower levels of positive and negative symptoms at baseline than the SSD group. There were no differences between the 3 groups for the PANSS excited and depressed factors at baseline. The participants with PNOS and PBD also had better global functioning than those with SSD. There were no differences in AUDIT scores between the 3 groups, but the PNOS group had higher DUDIT scores than the PBD group.

Clinical Characteristics at Follow-up

Clinical characteristics at follow-up are presented in table 2. Participants with baseline PNOS or PBD had less positive ($F = 16.57_{2, 174}$, $P < .001$) and disorganized symptoms ($F = 12.77_{2, 71.8}$, $P < .001$) than those with baseline SSD.

Table 1. Clinical Characteristics at Baseline, By Baseline Diagnosis

	1. PBD $n = 54$	2. PNOS $n = 32$	3. SSD $n = 94$	F/χ^2	df	*P*	Post hoc
Demographics:							
Age, mean (SD)	28.94 (8.13)	25.22 (8.81)	25.86 (7.26)	3.34	2,177	.038	n.s.
Gender, female (%)	32 (59.3)	14 (43.8)	43 (45.7)	3.01	2	.222	n.s.
Ethnic minority, *n* (%)	5 (9.3)	6 (18.8)	11 (11.7)	1.74	2	.420	n.s.
First generation immigrant, *n* (%)	10 (21.3)	5 (19.2)	12 (13.3)	1.57	2	.456	n.s.
Clinical:							
PANSS:							
Positive, mean (SD)	7.11 (3.97)	9.28 (3.09)	11.83 (4.28)	24.35	2, 177	<.001	PBD < PNOS < SSD
Negative, mean (SD)	9.11 (4.05)	11.31 (5.22)	14.49 (6.57)	18.81	2, 84.6	<.001	PBD, PNOS < SSD
Disorganized, mean (SD)	4.51 (1.87)	5.31 (2.15)	6.18 (2.86)	7.23	2, 177	<.001	PBD < SSD
Excited, mean (SD)	5.37 (1.81)	5.81 (2.38)	6.31 (2.49)	2.94	2, 177	.055	n.s.
Depressed, mean (SD)	8.24 (3.27)	8.84 (2.93)	9.01 (3.10)	1.06	2, 177	.349	n.s.
GAF:							
Symptoms, mean (SD)	52.50 (13.20)	45.94 (11.75)	38.54 (11.63)	23.14	2,177	<.001	SSD < PNOS < PBD
Functioning, mean (SD)	49.06 (12.90)	51.91 (14.19)	40.05 (10.32)	15.72	2, 71.1	<.001	SSD < PBD, PNOS
AUDIT, median (IQR)	7 (11)	9 (11)	5 (10)	4.20	2	.122	n.s.
DUDIT, median (IQR)	0 (0)	2 (10)	0 (4)	10.17	2	.006	PBD < PNOS
Medical treatment at baseline:							
Psychotropic medication, *n* (%)	44 (83.0)	21 (65.6)	79 (84.0)	5.47	2	.065	n.s.
Antipsychotic medication, *n* (%)	38 (71.7)	18 (56.3)	73 (77.7)	5.44	2	.066	n.s.

Note: PBD, psychotic bipolar disorder; PNOS, psychotic disorder not otherwise specified; SSD, schizophrenia spectrum disorder; PANSS, Positive and Negative Syndrome Scale; GAF, Global Assessment of functioning; AUDIT, Alcohol Use Disorder Identification Test; DUDIT, Drug Use Disorders Identification Test; n.s, non-significant.

The SSD group also had more negative symptoms ($F = 5.99_{2, 78.9}$, $P = .004$) than the PBD group and more excitatory symptoms than the PNOS group ($F = 4.27_{2, 89.3}$, $P = .017$). There were no differences between the 3 groups regarding depressive symptoms at follow-up. The participants with PNOS and PBD had higher GAF-F scores ($F = 10.61_{2, 177}$, $P < .001$) than those with SSD. The 3 groups still did not differ significantly for AUDIT scores, but the PNOS group and the SSD group had higher DUDIT scores than the PBD group at follow-up ($\chi^2 = 9.22$, $P = .010$). Outcomes split by research site are reported in supplementary table 2. There were no significant outcome differences across sites.

Illness Course

As shown in table 2, a higher proportion of the participants with baseline PNOS (40%) and PBD (44%) experienced stable remission from psychotic symptoms already from the first year after starting the first treatment, compared to participants with baseline SSD (10.1%, $\chi^2 = 23.45$, $P < .001$). The PNOS group was intermediate between the other 2 groups regarding the total duration of psychotic episodes ($\chi^2(2, N = 169) = 46.07$, $P < .001$), here the PBD group had the shortest duration of psychosis, and the SSD group had the longest. The PNOS group, however, had a shorter total duration of hospitalizations during the follow-up period compared to the other 2 groups ($\chi^2(2, N = 165) = 24.46$, $P < .001$). There were no differences between the 3 groups in the proportion of participants who used psychotropic medication at follow-up. However, significantly more of the participants with baseline SSD were treated with antipsychotics at follow-up compared to the participants with baseline PBD and PNOS ($\chi^2(2, N = 179) = 13.46$, $P < .001$).

Remission and Recovery Rates at Follow-up:

Presented in table 2, the rate of psychotic remission at follow-up was significantly higher in participants with baseline PNOS (75.0%) and PBD (83.3%) than in participants with baseline SSD (44.1%, $\chi^2(2, N = 180) = 25.23$, $P < .001$). Significantly more of the participants with PNOS (40.6%) and PBD (50%) also met the criteria for adequate functioning compared with SSD (20.2%, $\chi^2(2, N = 180) = 14.90$, $P < .001$) and the clinical recovery rates were thus significantly higher among participants with PNOS (40.6%) and PBD (48.1%) than among those with SSD (17.0%, $\chi^2(2, N = 180) = 21.08$, $P < .001$).

Diagnostic Stability

The diagnostic stability was highest for SZ (92.3%) and bipolar I disorder (86.3%), followed by schizoaffective disorder (70.6%) and PNOS (53.1%) (table 3). The least stable diagnoses were schizophreniform disorder (8.3%) and bipolar NOS (0.0%). Bipolar NOS, however, accounted for only 3 participants at baseline. Of the 32 participants with initial PNOS, 15 (47%) received a different diagnosis at 10 years of follow-up. Of these, 6

Table 2. Follow-up Clinical Characteristics by Baseline Diagnosis

	1. PBD *n* = 54	2. PNOS *n* =32	3. SSD *n* = 94	F/χ^2	*df*	*P*	Post hoc
Demographics:							
Age, mean (SD)	38.63 (8.69)	34.91 (9.03)	34.89 (7.48)	3.98	3	.020	SSD < PBD
Gender, female, *n* (%)	32 (59.3)	14 (43.8)	43 (45.7)	3.01	2	.222	n.s.
Clinical:							
PANSS							
Positive, mean (SD)	5.55 (2.55)	6.30 (2.83)	8.85 (4.42)	16.57	2, 174	<.001	PBD, PNOS < SSD
Negative, mean (SD)	8.31 (3.99)	9.27 (4.87)	11.08 (5.63)	5.99	2, 78.9	.004	PBD < SSD
Disorganized, mean (SD)	3.54 (0.84)	3.83 (1.72)	4.93 (2.39)	12.77	2, 71.8	<.001	PBD, PNOS < SSD
Excited, mean (SD)	4.50 (0.98)	4.30 (0.95)	4.98 (1.62)	4.27	2, 89.3	.017	PNOS < SSD
Depressed, mean (SD)	6.70 (3.78)	6.03 (2.81)	6.76 (2.89)	0.75	2, 72.6	.476	n.s.
GAF-S, mean (SD)	66.17 (14.10)	63.25 (16.09)	53.15 (16.04)	13.39	2,177	<.001	SSD < PBD, PNOS
GAF-F, mean (SD)	67.02 (17.68)	65.78 (16.95)	55.12 (16.00)	10.61	2, 177	<.001	SSD < PBD,PNOS
AUDIT, median (IQR):	3 (7)	5 (5)	4 (6)	1.42	2	.491	n.s.
DUDIT, median (IQR):	0 (0)	0 (2)	0 (2)	9.22	2	.010	PBD < PNOS, SSD
Illness course:							
Stable psychotic remission within 1st year of treatment, *n* (%):	22 (44.0)	12 (40.0)	9 (10.1)	23.45	2	<.001	SSD < PBD, PNOS
Total duration psychotic episodes/ follow-up year, weeks, median (IQR):	0.73 (1.65)	4.58 (16.74)	21.00 (45.97)	46.42	2	<.001	PBD<PNOS<SSD
Total duration of hospitalizations/ follow-up year, median (IQR):	1.27 (2.95)	0.12 (0.93)	2.45 (7.66)	26.46	2	<.001	PNOS<PBD<SSD
Medication at follow-up:							
Psychotropic medication, *n* (%)	36 (66.7)	14 (46.7)	62 (66.0)	4.09	2	.129	n.s.
Antipsychotic medication, *n* (%)	17 (31.5)	8 (25.8)	53 (56.4)	13.46	2	.001	PBD,PNOS < SSD
Outcome:							
Remission, psychosis, *n* (%):	45 (83.3)	24 (75.0)	41 (44.1)	25.23	2	<.001	SSD < PBD,PNOS
Adequate functioning, n (%):	27 (50.0)	13 (40.6)	19 (20.2)	14.90	2	<.001	SSD < PBD,PNOS
Clinical recovery, *n* (%):	26 (48.1)	13 (40.6)	16 (17.0)	21.08	2	<.001	SSD < PBD,PNOS

Note: PBD, psychotic bipolar disorder; PNOS, psychotic disorder not otherwise specified; SSD, schizophrenia spectrum disorder; GAF, Global Assessment of functioning; PANSS, Positive and Negative Syndrome Scale; AUDIT, Alcohol Use Disorder Identification Test; DUDIT, Drug Use Disorders Identification Test; n.s, non-significant.

(19%) participants were diagnosed with SZ, 1 (3%) participant with schizoaffective disorder, 1 (3%) participant with bipolar I disorder, 2 (6%) participants with bipolar II disorder, 1 (3%) participant with bipolar NOS, 2 (6%) participants with major depressive disorder and 2 (6%) participants with a substance-induced psychotic disorder.

The participants with a baseline PNOS diagnosis who either retained their PNOS (*n* = 17) or were rediagnosed with either affective disorder (*n* = 6) or substance-induced psychotic disorder (*n* = 2) at follow-up did not differ from the baseline PNOS participants who were rediagnosed as SSD (*n* = 7) for any baseline clinical characteristics, except for lower PANSS excitatory symptoms in the rediagnosed SSD group ($F_{1, 30}$ = 7.20, *P* = .012). However, the groups differed significantly in their course of illness. Those rediagnosed as SSD at follow-up experienced statistically significantly longer durations of psychotic symptoms (*U* = 142.00, *P* = .011) and longer duration of hospitalizations per follow-up year than the other group (*U* = 122.00, *P* = .001). None of those rediagnosed with SSD experienced stable remission within the first year of treatment, compared to 56% of the other baseline PNOS participants (*P* = .01, Fisher's exact test), and they also had significantly lower rates of symptomatic remission at follow-up (28.6% vs 92.0%, *P* = .005, Fisher's exact test). Among those rediagnosed with SSD, 28.6% were in clinical recovery vs 44.0% among the other baseline PNOS participants; however, this difference did not reach statistical significance.

Of the PNOS participants with psychotic symptomatology that did not meet the criteria for any specific diagnosis, 11 out of 17 (65%) retained the PNOS diagnosis, 2 (12%) changed to SSD, and 4 (24%) to affective disorders (table 4). For PNOS participants with contradictory information at baseline, 3 (30%) retained the PNOS

Table 3. Stability and Change of Baseline Diagnoses

	Baseline diagnosis						
Follow-up diagnosis	Schizophrenia	Schizophreniform disorder	Schizoaffective disorder	Bipolar I disorder	Bipolar disorder NOS	Psychotic disorder NOS	Total
Schizophrenia	**60 (92.3%)**	8	4	2	0	6	80
Schizophreniform disorder	0	**1 (8.3%)**	0	0	0	0	1
Schizoaffective disorder	3	1	**12 (70.6%)**	4	0	1	21
Bipolar I disorder	1	0	0	**44 (86.3%)**	2	1	48
Bipolar disorder NOS	0	0	0	0	**0 (0%)**	1	1
Bipolar II disorder	0	0	0	1	1	2	4
Psychotic disorder NOS	1	2	1	0	0	**17 (53.1%)**	21
Major depressive disorder	0	0	0	0	0	2	2
Substance-induced psychotic disorder	0	0	0	0	0	2	2
Total	**65**	**12**	**17**	**51**	**3**	**32**	**180**

Note: NOS, not otherwise specified.

Table 4. Diagnostic Stability and Change By Baseline PNOS Subgroup

	PNOS-retained $n = 17$	PNOS-SSD $n = 7$	PNOS-other $n = 8$	Total ~~$n =$~~ 32
1. Psychotic symptomatology that does not meet the criteria for any specific psychotic disorder, *n* (%)	**11 (64.7)**	**2 (11.8)**	**4 (23.5)**	**17 (100)**
a.Persistent non-bizarre delusions with periods of overlapping mood episodes that have been present for a substantial portion of the delusional disturbance	3	1	1	5
b.Hallucinations as the only psychotic symptom	2	0	1	3
c.Meets Criterion A for Schizophrenia, but functioning is not markedly impaired	4	0	1	5
d.Meets Criterion A for Delusional Disorder, but functioning is markedly impaired	2	1	1	4
2. Psychotic symptomatology about which there is contradictory information, *n* (%)	**3 (30)**	**4 (40)**	**3 (30)**	**10 (100)**
a.Meets Criterion A for Schizophrenia, but Substance-Induced Psychotic Disorder cannot be ruled out	3	2	1	6
b.Meets Criterion A for Delusional Disorder, but Substance-Induced Psychotic Disorder cannot be ruled out	0	1	1	2
c.Other cases where there is contradictory information	0	1	1	2
3. Psychotic symptomatology about which there is inadequate information to make a specific diagnosis, *n* (%)	**3 (60)**	**1 (20)**	**1 (20)**	**5 (100)**
a.Participant unable to provide sufficiently detailed information about symptomatology to make a specific diagnosis	1	1	1	3
b.Vague psychotic symptomatology	2	0	0	2

Note: PNOS, psychotic disorder not otherwise specified; PNOS-retained, participants with baseline PNOS retaining the diagnosis at follow-up; PNOS-SSD, participants with baseline PNOS diagnosed with SSD at follow-up; PNOS-other, participants with baseline PNOS diagnosed with affective disorder or substance-induced psychotic disorder at follow-up.

diagnosis, 4 (40%) were rediagnosed with SSD, 1 (10%) with PBD, and 2 (20%) were rediagnosed with a substance-induced psychotic disorder. Finally, for participants with inadequate information to make a specific diagnosis, 3 out of 5 (60%) retained the PNOS diagnosis, 1 (20%) shifted towards SSD, and 1 (20%) towards PBD.

Discussion

The main findings of this study are that participants with a baseline PNOS diagnosis have long-term clinical and functional outcomes that are intermediate between participants with PBD and SSD. The poorest outcomes are found in the SSD group. Half of the participants

with a baseline PNOS diagnosis retained the diagnosis at follow-up. This confirms that the diagnostic category includes not only clinical syndromes that are precursors to other psychotic disorders, but also conditions that still do not meet the criteria for a specific DSM diagnosis even 10 years after the first treatment.

To the best of our knowledge, comprehensive information on the long-term illness course of PNOS as a separate diagnostic group, including remission and recovery rates, has not been reported previously. Our results add new information about stability to earlier findings from cross-sectional and short-term studies showing milder psychotic symptoms[8,9] and less severe courses of illness[9,10] in PNOS compared to SSD. The remission and recovery rates for PNOS in the current sample are almost equal to PBD and higher than what is found in diagnostically broad FEP[16] and first-episode SZ in other studies using the same outcome criteria.[16,30]

However, the intermediate outcomes of the PNOS group comprise different illness developments. Although 50% of the baseline PNOS group retained their diagnosis, about 1/5 were rediagnosed with SSD at follow-up. This group had a more severe illness course with longer periods of psychosis and significantly lower remission rates at follow-up than the others, contributing to the diagnostic change. On the other hand, of those who did not transition to SSD, 92% were in symptomatic remission and 44% in clinical recovery at follow-up. The proportion rediagnosed with an affective disorder (19%) was almost as large as that of SSD (22%). This underlines the heterogeneous structure of the PNOS group. While identifying individuals at risk of developing SSD is important, PNOS diagnoses are not primarily precursors to SSD.

The diagnostic stability of 53% in our study was somewhat higher than what was found in the meta-analysis of short-term studies by Fusar-Poli et al.[13] (36%). Furthermore, the transition to affective disorders was higher (19% vs 7%), while the diagnostic shift to SSD was somewhat lower (22% vs 34%). These dissimilarities may be due to differences in recruitment between studies. The current study included SSD and bipolar spectrum disorders broadly. This may have led to the inclusion of PNOS participants clinically closer to the bipolar spectrum.

Few studies have been large enough to divide the PNOS group in line with the DSM-5 categories.[8,10] For conditions that did not meet the full criteria for any specific disorder (OSSPD), Li et al. found that 84% retained the diagnosis at 1-year follow-up.[10] In comparison, the long-term diagnostic stability for the equivalent group in the current study was 65% (11 out of 17 participants). Furthermore, the group given a PNOS diagnosis because of inadequate information had diagnostic stability of 50% in Li et al.'s study[10] and 60% in the current study (3 out of 5 participants). A PNOS diagnosis may be used as a place-holder diagnosis at first contact in a clinical setting, and the proportion of PNOS diagnoses made due to inadequate information will likely be even higher and less stable in a clinical population[31] than in a research study where all participants have undergone a structured diagnostic assessment. The DSM-5-based subcategories did, however, not predict who was later rediagnosed as SSD, as these cases were distributed between several subcategories, and we did not find any other significant differences in demographic, illness history, or clinical baseline characteristics for the participants who transitioned to SSD compared to those who did not. Predicting the outcome of PNOS based on characteristics at first treatment is thus challenging.

The high diagnostic stability in the current sample shows that some psychotic disorders do not meet the criteria for any specified psychotic disorder, even after 10 years of observation. Our finding aligns with the current understanding of psychotic disorders as constituting a psychosis spectrum without clear boundaries between diagnoses and disorders,[32] where some clinical syndromes will not fit into the predefined categories. The higher diagnostic stability for the PNOS subcategory with precise information that however does not meet the full criteria for any specified disorder, implies that it comprises different but distinct clinical syndromes.[10] Although the traditional diagnostic categories are still maintained in the DSM-5, it is explicitly stated in its preface that the current classification is not ideal for clinical phenomena that are not categorical in nature, that such categorization consequently leads to the frequent use of imprecise diagnoses[3] and that further subtyping to achieve diagnostic homogeneity is not fruitful.

Our finding of better long-term outcomes in the group with baseline PNOS compared to participants with baseline SSD suggest that a distinction between the 2 may be appropriate in clinical practice even if only a few studies have investigated etiologic and neurobiological differences between PNOS and SSD. There is a substantial overlap in polygenic risk scores between SSD and PNOS,[33] and both commonalities and differences in neuronal connectivity[34] in line with studies comparing PBD and SSD.[35–37] The absence of clear etiological differences combined with the finding of a poor outcome sub-group transitioning to SSD suggest that PNOS patients should be offered the same comprehensive treatment as SSD until stable remission is achieved.

The strength of this study is the large sample of first-treatment psychotic disorders recruited continuously from a large catchment area with a public health system available to everyone regardless of socio-economic status, maintaining representativeness of the study sample. The comprehensive clinical characterization and the long follow-up period are also strengths.

The main limitation is the low retention rate. Due to increased mobility and privacy legislation, attrition is an increasing challenge in conducting longitudinal studies. Attrition rates of up to 90% have recently been reported

for 1-year follow-up studies from experienced research sites.[38] The only previous 10-year follow-up study that reported on PNOS outcomes had a similar attrition rate as the current study, as only 219 (43%) participants of the 505 participants eligible for follow-up were actually reinterviewed.[5,15] An ongoing Australian long-term follow-up also reports difficulties locating and contacting cohort proportions due to changes in privacy legislation.[39] We found no differences in demographic and clinical data between completers and noncompleters, except for a greater retention of participants with baseline PBD and thus more females in those interviewed due to higher rates of females in the baseline PBD group. This may indicate a potentially better outcome across diagnostic groups for the group of completers across diagnoses but should not influence the PNOS-specific findings.

To conclude, our findings indicate that most participants with a first-treatment PNOS diagnosis have significantly better outcomes than those with an initial SSD diagnosis. A subset of the PNOS participants with a more severe illness course after baseline were rediagnosed with SSD at follow-up but these did not differ significantly from the other PNOS participants at baseline. This indicates that predicting diagnostic outcomes of PNOS based on clinical characteristics at first treatment can be challenging.

Supplementary Material

Supplementary data are available at *Schizophrenia Bulletin Open* online.

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