Diagnostic Stability 18 Months After Treatment Initiation for First-Episode Psychosis

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Objectives: (1) Assessment of diagnostic stability of psychotic disorders or psychotic mood disorders from 6 weeks to 18 months after initiation of treatment in a representative first-episode psychosis (FEP) sample. (2) Comparison between those patients who shifted from DSM-IV schizophreniform disorder to schizophrenia or schizoaffective disorder and those whose diagnosis of schizophreniform disorder remained stable.

Method: The Early Psychosis Prevention and Intervention Centre (EPPIC) in Australia admitted 786 FEP patients from January 1998 to December 2000. Data were collected from patients' medical records (MRs) using a standardized questionnaire. Seven hundred four MRs were available, 36 of which were excluded owing to nonpsychotic diagnoses or a psychotic disorder due to a general medical condition. Of the remaining 668 patients, 176 (26.3%) were lost to follow-up. Four hundred ninety-two subjects were analyzed. Strategies to assure validity and reliability of diagnoses were applied.

Results: The same diagnosis was made at baseline (≤ 6 weeks after admission into EPPIC) and 18 months for 69.9% of the patients. Among the most consistent diagnoses were schizophrenia (97.3%), schizoaffective disorder (94.1%), and bipolar disorder (83.2%); the least stable, as expected, was schizophreniform disorder (40.0%). In subjects with schizophreniform disorder at baseline, the best predictors of a shift from schizophreniform disorder to schizophrenia or schizoaffective disorder were a higher baseline Clinical Global Impressions-Severity of Illness scale score and lower premorbid Global Assessment of Functioning score, although the variance accounted for was small ($R^2 = .07$).

Conclusions: A longitudinally based diagnostic process in FEP samples is needed, especially in schizophreniform disorder and bipolar disorder. However, a thorough initial assessment of patient and family by a specialized team of investigators regarding the kind and duration of patient symptoms may lead to high diagnostic stability, especially in schizophrenia and schizoaffective disorder, even in a FEP sample with a relatively short duration of untreated psychosis.

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Diagnostic stability in patients with first-episode psychosis varies depending on psychosis subtype and diagnostic system used. Schizophrenia, especially since the introduction of the 6-month duration criterion with DSM-III, is reported to be the most stable diagnosis (about 90%) over a period of 6 months to 40 years.[1] Conversely, with diagnostic shifts varying from 10% to 50%, other psychotic disorders such as schizophreniform or schizoaffective disorder are reported to be less stable.[1–5] Important reasons for a diagnostic shift include a change of the clinical picture within the follow-up period, additional information on past symptomatic evolution, and an unreliability of assessment.

In recent prospective studies, the most frequent diagnostic shift was toward schizophrenia spectrum disorders. Schwartz et al.[1] investigated variables associated with a shift toward schizophrenia spectrum disorders. The best pretreatment predictors were poorer premorbid adjustment in adolescence and lack of lifetime substance use disorder.

This study is based on standardized medical records (MRs) of a representative first-episode psychosis (FEP) cohort assessed and treated for 18 months in a specialized early psychosis prevention and intervention center. Aims of the study were to assess diagnostic stability of psychotic disorders from 6 weeks to 18-month follow-up

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after the initiation of treatment and to compare those who shifted from schizophreniform disorder to schizophrenia or schizoaffective disorder with those whose diagnosis remained stable schizophreniform disorder at follow-up.

METHOD

Context and Sample

The initial sample comprises a population-based cohort of 786 subjects with FEP consecutively admitted to the Early Psychosis Prevention and Intervention Centre (EPPIC) in Melbourne, Australia, from January 1998 to December 2000. EPPIC covers a catchment area of approximately 880,000 people and has a mandate to treat all patients aged 15 to 29 years with FEP. In this catchment area, EPPIC is the only facility for the target population, with virtually no private psychiatrists and little, if any, movement into private facilities outside the area; as such, the study sample represents an epidemiologic cohort. The EPPIC program includes a comprehensive early-intervention treatment program with an episode of care of 18 months, which encompasses extensive psychiatric assessments, outpatient case management, cognitive-behavioral therapy, low-dose antipsychotic therapy, access to a specialized inpatient unit for acute care during crisis admissions, a mobile crisis intervention and community treatment team, group programs, family support groups, and a specialized consultation group for the treatment of enduring positive psychotic symptoms.

Seven hundred four (89.6%) of 786 MRs were assessed; 82 MRs (10.4%) were transferred to other services after patients were discharged from EPPIC and were not available for the study. The excluded patients did not differ in diagnostic distribution or available demographic variables (age and gender). Thirty-six MRs (5.1%) were excluded owing to a nonpsychotic diagnosis at baseline (≤ 6 weeks after admission into EPPIC) and after 18 months or owing to a psychotic disorder due to a general medical condition. Of the remaining 668 patients, 176 (26.3%) were lost to follow-up with diagnoses not available at 18 months. Subjects lost to follow-up had a higher prevalence of substance-induced psychotic disorder, psychotic disorder not otherwise specified, and delusional disorder than the rest of the cohort ($\chi^2 = 18.6$, df = 8, p = .017). Four hundred ninety-two patients were analyzed.

Procedure

Information on baseline, treatment, and outcome variables of each patient treated in EPPIC is documented in a standardized MR. Clinical initial assessments are partly based on the Royal Park Multidiagnostic Instrument for Psychosis.[6,7] Furthermore, treatment and its documentation in EPPIC are systematized according to the Australian Guidelines for Early Psychosis.[8] Therefore, each MR comprises information compiled during the 18-month treatment period from various sources using high-quality assessments carried out by trained clinicians. All MRs were assessed by 2 experienced psychiatrists well acquainted with EPPIC clinical service and treatment of FEP patients. The study is part of a large FEP outcome study and was approved by the local research and ethics committee.

Assessment of Diagnoses

Clinical diagnoses at EPPIC are assessed using DSM-IV criteria.[9] Baseline clinical diagnoses in MRs are the consensus result of an intensive diagnostic and treatment process within the first 6 weeks of admission by well-trained clinicians working in a specialized assessment and crisis intervention team. Discharge clinical diagnoses at 18 months documented in MRs are based on repeated clinical assessments made using various sources of information and performed by a treatment team consisting of a case manager, psychiatrist, and consultant psychiatrist responsible for a patient over the complete treatment period (on average, 94 treatment contacts with patient and/or family over 18 months). In isolated cases, this treatment team has already been involved in the initial diagnostic process.

Two research psychiatrists assessed all information available in MRs with respect to baseline and 18-month diagnoses. In the event of disagreement with clinical diagnoses, a consensus rating between both research psychiatrists and the case manager was performed. In addition, validity of these diagnoses was established by comparing MR diagnoses with diagnoses assessed by an independent research psychiatrist on a randomly selected subset of 115 patients who participated in other studies. These patients had been interviewed using a Structured Clinical Interview for DSM-IV (SCID-I/P)[10] within the first 6 weeks of admission to EPPIC. Research psychiatrists were blind to SCID-I/P diagnoses. The calculated kappa values yielded a good validity for both psychosis ($\kappa = 0.81$) and comorbid substance use disorder ($\kappa = 0.80$) as determined by MRs. Results on diagnostic stability based on the total sample were comparable to those from the subgroup with initial SCID diagnoses.

Diagnostic stability was considered to be present if information during the 18-month period subsequent to baseline diagnosis confirmed the original diagnosis, irrespective of whether the symptoms of the original diagnosis were actively present at follow-up assessment.[1]

Assessment of Baseline and Outcome Measures

Along with various clinical and sociodemographic characteristics, standardized measures extracted from MRs included the following. (1) Duration of untreated psychosis was assessed with the Duration of Untreated Psychosis scale.[6,7] (2) Level of functioning at baseline and

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follow-up was assessed with the Global Assessment of Functioning scale (GAF).[9] (3) Premorbid functioning was assessed with GAF. The Premorbid Adjustment Scale,[11] commonly used in prospective studies, was too complex to reliably extract data from MRs. Social personal adjustment, 1 item of the summary section of the Premorbid Adjustment Scale, was used to cross-validate GAF as a measure of premorbid functioning with satisfying correlation ($r = 0.6$). Furthermore, the assessment of premorbid functioning with the GAF had also been recommended by the Early Psychosis Association[12] for the definition of prodromal patients at high risk for transition to psychosis (reduction of GAF score of ≥ 30 points within 1 year). (4) Severity of illness at baseline and follow-up was assessed with the Clinical Global Impressions-Severity of Illness scale (CGI-S).[13] (5) Insight was assessed at baseline and endpoint. Administered at baseline, the EPPIC intake mental state examination contains a qualitative description of level of insight. Based on this description, level of insight was categorized into 1 of 3 groups: full, partial, or no insight. Level of insight at discharge was rated using inpatient and outpatient continuation notes and the final 18-month discharge summary. (6) Unemployment was defined according to Strakowski et al.[14] (vocation index) as not having a job or not being a student at school or university 4 weeks before entry into the program. (7) Suicide attempts were assessed and categorized according to ICD-10 diagnostic criteria. (8) Remission at follow-up was defined as no positive symptoms (no rating of more than 3 on any item of the Positive and Negative Syndrome Scale[15] positive scale) for at least the last 12 weeks. Interrater reliability was established for outcome measures such as CGI-S or GAF in 40 randomly selected MRs. Results revealed a very good reliability with a kappa of 0.80 to 0.90.

Data Analysis

Diagnostic stability between baseline and 18-month follow-up was summarized by a cross-tabulation of 9 different diagnostic categories (according to Schwartz et al.[1]). Two measures of stability are presented for each diagnosis. First, prospective consistency (positive predictive value) equals the proportion of subjects in a category at baseline who retained the same diagnosis at 18 months. The second measure, retrospective consistency (sensitivity), equals the proportion of subjects in an 18-month category who received the same diagnosis at baseline.

Baseline and outcome characteristics are summarized for the following 3 change groups: stable schizophrenia or schizoaffective disorder, stable schizophreniform disorder, and schizophreniform disorder at baseline shifting to schizophrenia or schizoaffective disorder at follow-up. Schizophrenia and schizoaffective disorder were grouped together since both disorders had comparable outcomes. Omitting schizoaffective disorder rendered similar results. Two comparative analyses were carried out. (1) Subjects shifting from schizophreniform disorder to schizophrenia or schizoaffective disorder (SZ/SA) were compared to those with stable schizophreniform disorder. This analysis identified factors predicting which subjects were subsequently reclassified as having SZ/SA. A direct logistic regression analysis was performed to assess prediction of shift from schizophreniform disorder to SZ/SA for those subjects initially diagnosed with schizophreniform disorder. (2) Subjects shifting from schizophreniform disorder to SZ/SA were compared to those with stable SZ/SA. Group differences were analyzed using a t test for continuous measures, the Mann-Whitney U test for nonparametric data, and the χ^2 test of independence for categorical measures.

RESULTS

Sample Characteristics

The 492 subjects were predominantly male (63.2%), 48.3% were unemployed, and 68.0% were living with family at entry. The mean age at baseline was 22.0 years (SD = 3.6), with 78.9% older than 18 years. The median duration of untreated psychosis was 82 days (range, 0–12.46 years). The premorbid GAF score was 70.2 (SD = 10.5), the GAF score at entry was 31.2 (SD = 9.7), and the CGI-S score at entry was 5.6 (SD = 0.8).

With regard to comorbidity, 291 subjects (59.1%) received a diagnosis of comorbid substance use disorder at baseline. One hundred fifty-one subjects (30.7%) received a non–substance use disorder comorbid diagnosis; most of them (N = 96) received a major depressive episode diagnosis (equivalent to 27.8% of the 345 subjects with nonaffective psychoses at baseline), and 13 subjects (2.6%) were diagnosed with anxiety disorders.

With regard to treatment details, 408 (82.9%) of 492 patients were hospitalized during treatment at least once, with no significant difference between the main diagnostic categories (schizophrenia spectrum disorders: 81.8%, psychotic mood disorders: 85.8%, other psychoses: 83.3%). Patients were treated with psychotropic drugs according to the Australian Guidelines.[16] On the basis of baseline diagnosis, patients with nonaffective psychosis were treated with low-dose antipsychotic monotherapy, patients with psychotic mood disorders were treated with antipsychotics plus a mood stabilizer, and, if indicated, additional antidepressant therapy was given to patients with psychotic mood disorders or comorbid major depressive episode. In this sample, only 5 subjects (1.5%) with schizophrenia spectrum disorders at baseline, 5 subjects (5.0%) with baseline bipolar disorder, and 1 subject (8.3%) with baseline major depressive disorder received no antipsychotic trial medication during treatment. As expected, 4 subjects (36.4%) with brief psychotic episode and 2 (22.2%) with substance-induced psychotic disorder did not receive antipsychotics during treatment.

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Stability of Diagnoses

Table 1 outlines a cross-tabulation of diagnoses at baseline and follow-up. The overall consistency was 69.9%; 344 of 492 subjects received the same diagnosis at both assessment time points. Schizophrenia and schizoaffective disorder, followed by delusional disorder and bipolar disorder, had among the highest prospective consistencies. The lowest prospective consistencies were observed for schizophreniform disorder and other nonaffective psychoses.

Schizophreniform and bipolar disorders, as well as major depressive disorder, had among the highest retrospective consistencies. The most frequent shifts resulted in a diagnosis of schizophrenia or schizoaffective disorder as indicated by retrospective consistency of 50.2% and 57.1%, respectively. The overall shift to schizophrenia spectrum disorders from non–schizophrenia spectrum disorders was low (retrospective consistency of 93.2%). The most frequent shift to schizophrenia was from schizophreniform disorder (52.6%), and the most frequent shift to schizoaffective disorder was from bipolar disorder (12.9%).

Baseline Differences Between Patients With Stable Schizophreniform Disorder and Those Shifting to Schizophrenia/ Schizoaffective Disorder and Prediction of Shift

Table 2 outlines baseline characteristics for the 3 diagnostic change groups (N = 330). Subjects shifting from schizophreniform disorder to SZ/SA compared to those with stable schizophreniform disorder had significantly lower premorbid and baseline GAF scores, had a significantly higher CGI-S score at baseline, and were significantly more likely to have attempted suicide before entry into treatment.

A direct logistic regression analysis was performed to assess prediction of change from schizophreniform disorder to SZ/SA. Independent variables were chosen according to their bivariate association with the dependent variable. All available baseline and pretreatment characteristics were tested (in addition to those mentioned in Table 1: comorbid depression, anxiety, and personality disorders). Only CGI-S score at baseline and premorbid GAF score fulfilled criteria for inclusion as independent variables. After deletion of

Table 1. Cross-Tabulation of Baseline and Endpoint (18-month) DSM-IV Diagnoses in First-Episode Psychosis Subjects (N = 492)

		Endpoint Diagnosis, N										
Diagnosis	Baseline Diagnosis, N	Schizophrenia Spectrum Disorder	Schizophrenia	Schizoaffective Disorder	Schizophreniform Disorder	Mood Disorder	Bipolar Disorder	MDD	Other Psychotic Disorder	Brief Psychotic Disorder	Psychotic Disorder NOS	Delusional Disorder	Substance-Induced Psychotic Disorder
Baseline													
Schizophrenia spectrum disorder	337	330				6			1				
Schizophrenia	113		110	3	0		0	0		0	0	0	0
Schizoaffective	34		2	32	0		0	0		0	0	0	0
Schizophreniform	190		100	7	76		6	0		0	0	1	0
Mood disorder	113	17				96			0				
Bipolar	101		4	13	0		84	0		0	0	0	0
MDD	12		0	0	0		0	12		0	0	0	0
Other psychotic disorder	42	7				3			32[a]				
Brief psychotic	11		0	1	1		0	0		8	0	0	1
Psychotic NOS	7		3	0	0		0	0		0	4	0	0
Delusional	15		0	0	0		2	0		0	0	13	0
Substance-induced psychotic	9		0	0	2		1	0		0	0	1	5
Total	492	354	219	56	79	105	93	12	33	8	4	15	6
Prospective consistency, %[b]		97.9	97.3	94.1	40.0	84.9	83.2	100	76.2	72.7	51.7	86.7	55.6
Retrospective consistency, %[c]		93.2	50.2	57.1	95.0	91.4	89.2	100	97.0	100	100	86.7	83.3

[a]Includes 2 subjects whose diagnoses changed between 2 of the "other" nonaffective psychoses.
[b]Percentage of patients at baseline with the same diagnosis at endpoint.
[c]Percentage of patients at endpoint with the same diagnosis at baseline.
Abbreviations: MDD = major depressive disorder, NOS = not otherwise specified.

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Table 2. Baseline and Pretreatment Characteristics of First-Episode Psychosis Subjects by Diagnostic Shift Groups (N = 330)

Characteristic	Stable SZ/SA (N = 147)	Stable Schizophreniform Disorder (N = 76)	Shift From Schizophreniform Disorder to SZ/SA (N = 107)
Baseline			
Age, mean (SD), y	22.0 (3.4)	22.1 (3.9)	21.3 (3.9)
Male, N (%)	101 (68.7)	46 (60.5)	64 (59.8)
Substance use disorder, N (%)	99* (67.3)	35 (46.1)	59 (55.1)
Living with family, N (%)	37 (25.2)	22 (28.9)	32 (29.9)
Unemployed, N (%)	89* (60.5)	31 (40.8)	48 (44.9)
No insight, N (%)[a]	91 (63.6)	38 (51.4)	71 (67.6)
GAF score, mean (SD)	29.7 (9.0)	33.8^{+} (10.0)	31.0 (8.8)
CGI-S score, mean (SD)	5.7 (0.7)	5.3^{++} (0.8)	5.6 (0.8)
Pretreatment			
Premorbid GAF score, mean (SD)	67.6 (9.7)	72.2^{+} (11.1)	68.8 (10.1)
Past psychiatric history, N (%)	71 (48.3)	32 (42.1)	50 (46.7)
Attempted suicide during lifetime, N (%)	26 (17.7)	1^{++} (1.3)	14 (13.1)
Family history of psychosis, N (%)	39 (26.5)	17 (22.4)	28 (26.2)
Age at onset, mean (SD), y	19.7** (3.7)	21.5 (3.8)	21.0 (3.3)
DUP, median (range), d	387*** (6–4549)	50 (6–385)	74 (3–178)

[a]Eight patients missing information.
*$p < .05$ for stable SZ/SA vs. shift from schizophreniform disorder to SZ/SA (χ^2 test, df = 1, N = 254).
**$p < .01$ for stable SZ/SA vs. shift from schizophreniform disorder to SZ/SA (t test, df = 251).
***$p < .001$ for stable SZ/SA vs. shift from schizophreniform disorder to SZ/SA (Mann-Whitney U test, N = 253).
$^{+}p < .01$ for stable schizophreniform disorder vs. shift from schizophreniform disorder to SZ/SA (t test, df = 180–181).
$^{++}p < .01$ for stable schizophreniform disorder vs. shift from schizophreniform disorder to SZ/SA (χ^2 test, df = 1, N = 183; t test, df = 181).
Abbreviations: CGI-S = Clinical Global Impressions-Severity of Illness scale, DUP = duration of untreated psychosis, GAF = Global Assessment of Functioning, SZ/SA = schizophrenia or schizoaffective disorder.

1 case with a missing value for premorbid GAF, data from 182 subjects were available for analysis: 76 subjects with stable schizophreniform disorder and 106 subjects changing from schizophreniform disorder to SZ/SA. A test of the full model against a constant-only model was statistically reliable ($\chi^2 = 21.6$, $p < .001$), indicating that the predictors, as a set, reliably distinguished between the group with stable schizophreniform disorder and those with schizophreniform disorder shifting to SZ/SA. The variance in group membership accounted for was small; $R^2 = .07$ (Nagelkerke).

Outcome Differences Between Patients With Stable Schizophreniform Disorder and Those Shifting to Schizophrenia/Schizoaffective Disorder

Subjects with stable schizophreniform disorder had better outcomes with respect to almost all variables assessed in this study. Besides better GAF and CGI-S scores at endpoint, the stable schizophreniform disorder group had a higher remission rate, a lower prevalence of depression at follow-up, and a lower number of noncompliant subjects during treatment; were less likely to be unemployed; and were more likely to show full insight into illness (Table 3). At follow-up, the stable SZ/SA group was undistinguishable from the group shifting from schizophreniform disorder to SZ/SA with the exception of a significantly higher mean CGI-S score.

DISCUSSION

To the authors' knowledge, the present investigation is the largest naturalistic study on diagnostic stability in FEP patients treated within a specialized first-episode program with long-standing early detection. The strength of this study is that it used an epidemiologically based cohort from a geographically circumscribed area and a "first contact with treatment" rather than a "first hospital admission" sample. Accordingly, the duration of untreated psychosis is rather short in many patients, leading to a high prevalence of patients diagnosed with schizophreniform disorder. These important advantages limit comparability to other studies.

Key Findings

The overall consistency of diagnoses between baseline and 18-month follow-up was 69.9%; 344 of 492 patients received the same diagnosis at both evaluations. Excluding schizophreniform disorder, the overall consistency increased to 88.7%.

With regard to stability of diagnostic categories, there were few shifts from schizophrenia spectrum disorders to psychotic mood disorders over the 18-month period (prospective consistency of 97.9%), while more patients shifted from psychotic mood disorders toward schizophrenia spectrum disorders. The majority shifted toward schizoaffective disorder (prospective consistency of 84.9%). This finding is consistent with the more restrictive and descriptive definition of schizophrenia since the introduction of DSM-III in 1980. Since then, a significant decline in the rate of schizophrenia and a relative increase in the frequency of psychotic mood disorders has been observed. Expectedly, more shifts from psychotic mood disorders to schizophrenia spectrum disorders may be observed over the course of illness.[17] Additionally,

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Table 3. Endpoint (18-month) Characteristics of First-Episode Psychosis Subjects by Diagnostic Shift Groups (N = 330)

Characteristic	Stable SZ/SA (N = 147)	Stable Schizophreniform Disorder (N = 76)	Shift From Schizophreniform Disorder to SZ/SA (N = 107)
GAF score, mean (SD)	57.0 (14.2)	71.5^{+++} (10.4)	58.9 (13.6)
CGI-S score, mean (SD)	3.5* (1.2)	2.1^{+++} (0.9)	3.2 (1.2)
Remission, N (%)	58 (39.5)	73^{+++} (96.1)	45 (42.1)
Comorbid depression, N (%)	23 (15.6)	3^{+} (3.9)	12 (11.2)
Unemployed, N (%)	87 (59.2)	16^{+++} (21.1)	59 (55.1)
Living with family, N (%)	118 (80.3)	52 (68.4)	81 (75.7)
At least 1 antipsychotic trial, N (%)	143 (97.3)	75 (98.7)	107 (100)
Full insight, N (%)	51 (34.7)	53^{+++} (69.7)	45 (42.1)
Noncompliant during treatment, N (%)[a,b]	87 (60.8)	26^{++} (34.7)	62 (58.5)
Attempted suicide during treatment, N (%)[c]	25 (17.0)	8 (10.5)	13 (12.1)

[a]At least 1 full week of medication refusal.
[b]Eight patients missing information.
[c]Two completed suicides were reported: 1 in the stable SZ/SA group and 1 in the shift from schizophreniform to SZ/SA group.
*$p < .05$ for stable SZ/SA vs. shift from schizophreniform to SZ/SA (t test, df = 252).
$^{+}p < .01$ for stable schizophreniform disorder vs. shift from schizophreniform to SZ/SA (χ^2 test, df = 1, N = 183).
$^{++}p < .01$ for stable schizophreniform disorder vs. shift from schizophreniform disorder to SZ/SA (χ^2 test, df = 1, N = 181; t test, df = 181).
$^{+++}p < .001$ for stable schizophreniform disorder vs. shift from schizophreniform disorder to SZ/SA (χ^2 test, df = 1, N = 181, 183; t test, df = 181, 183).
Abbreviations: CGI-S = Clinical Global Impressions-Severity of Illness scale, GAF = Global Assessment of Functioning scale, SZ/SA = schizophrenia or schizoaffective disorder.

there is a known tendency to fail to identify affective elements in psychotic disorders, and the clinical notes on which this study is based may reflect this tendency. Consequently, there is a possible underestimation of shifts toward psychotic mood disorders. However, investigators of this study were conscious of this problem and therefore were cautious to identify any element suggestive of psychotic mood disorders.

Consistent with results of recent prospective studies,[1,2] schizophrenia was found to have the highest prospective consistency (97.3%) compared to schizoaffective disorder (94.1%) and bipolar disorder (83.2%), while schizophreniform disorder was less stable (40.0%), with shifts mainly toward schizophrenia (52.6%) and less often to schizoaffective or bipolar disorder (3.7% and 3.2%, respectively).

In accordance with results by Fennig et al.[2] and Schwartz et al.,[1] all other psychoses were less stable (prospective consistency of 76.2%). The categories receiving the largest influx of cases at follow-up were schizophrenia (109 cases, retrospective stability of 50.2%) and schizoaffective disorder (24 cases, retrospective stability of 57.1%).

There are 3 major differences between this study and earlier studies. (1) Some authors reported the problem of early misdiagnosis of bipolar disorder as schizophrenia.[18] This study, however, did not reveal many shifts from schizophrenia spectrum disorders to bipolar disorder. While this finding might be attributed to the good quality of initial assessment, it is impossible to exclude that some patients with bipolar disorder were wrongly diagnosed with schizophrenia early on as well as after 18 months of treatment in this study. (2) Notably, the stability of schizoaffective disorder is higher than in the study by Schwartz et al.[1] The authors reported 42% shifts toward schizophrenia compared to only 6% in this study. While misdiagnoses cannot be fully excluded, the continuous and highly frequent assessments conducted by 1 team over the complete treatment period in this sample may allow the detection of even subtle psychotic symptoms in the absence of affective symptoms. Additionally, Schwartz et al.[1] reported shifts toward psychotic mood disorders in 21% of cases (mainly toward major depressive episodes) compared to none in this sample. This difference may be caused by the underlying definition of schizoaffective disorder used in this study. In accordance with Marneros,[19] patients were diagnosed with stable schizoaffective disorder if they fulfilled longitudinal criteria of either "concurrent type" (coincidence of schizophrenic and affective episodes) or "sequential type" (longitudinal change from schizophrenic to affective episodes and vice versa). Subsequently, only shifts from schizoaffective disorder to schizophrenia were possible. (3) Subjects with major depressive disorder with psychotic symptoms were stable in all cases in this study, while other studies[2,3,5] reported lower prospective stability (below 80%). Notably, the prevalence of major depressive disorder with psychotic features was much lower than that reported by Schwartz et al.[1] (2.4% vs. 18.8%). This difference is possibly due to the much broader age range in the latter sample (15–58 years, median = 28 years).

Subjects who shifted from schizophreniform disorder to SZ/SA were similar to subjects with stable SZ/SA with respect to outcomes. Following the results of Schwartz et al.,[1] it seems that those whose diagnoses changed from schizophreniform disorder to SZ/SA were admitted at an earlier stage of illness. With regard to the comparison between those with stable schizophreniform disorder and those who shifted to SZ/SA, the multivariate analysis revealed inconclusive results. Despite the large variety

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of baseline predictors assessed, the overall variance accounted for was only 7%.

Methodological Considerations

The variability of diagnostic stability across different studies may be affected by the following methodological differences. (1) The diagnostic system used.[4] Studies using diagnostic systems including the 6-month duration criterion report higher specificity and lower sensitivity of the diagnosis of schizophrenia. (2) Cross-sectional versus longitudinal diagnostic assessments.[2] Studies relying on 2 assessment time points (e.g., SCID-I/P interviews at baseline and follow-up) may miss information on temporary changes between assessment time points, thereby possibly misjudging diagnostic stability. Therefore, longitudinal "best-estimate diagnosis" based on personal interview, information from family, and medical records is considered the most valid method for diagnosing psychiatric disorders.[20] (3) Sample selection (patients with first-episode vs. chronic psychosis and duration of untreated psychosis). Data derived from patients with chronic psychosis may overestimate diagnostic stability due to the longitudinal nature of schizophrenia and bipolar disorder.[21] Within studies of first-episode samples, a shorter mean duration of untreated psychosis may result in higher rates of schizophreniform disorder and brief psychotic disorder at baseline. These diagnoses—by definition—may shift to other psychotic disorders over the course of illness, leading to lower diagnostic stability.

Limitations

The current study reports comparatively high diagnostic stability in the major diagnostic categories despite a first-episode sample and rather short duration of untreated psychosis. This high stability may be a result of a high-quality baseline assessment. In EPPIC, a specialized assessment team administers a well-rounded assessment of patients' symptom evolution through questioning both patients and their families. It may be assumed that, after this thorough initial assessment, the incidence of missed relevant information on type and duration of psychotic symptoms before admission is low. However, retrospective chart reviews may be biased by the varying degrees of chart quality and by the qualifications of clinicians originally responsible for the MRs. Furthermore, the raters were not blind to the initial diagnosis. Therefore, it is still possible that some diagnostic categories are less stable than reported in this study. In conclusion, the stability may be a mix of several components: genuine stability, artifact deriving from the operational definition, and stability introduced by methodology of the study.

Clinical Implications

Diagnosing patients with FEP is complicated by the broad symptomatic overlap of various psychotic disorders, the overlap with other nonpsychotic psychiatric disorders, and the frequently overlooked psychiatric comorbidities. Furthermore, diagnosis of these patients is complicated by the evolution of the illness, the emergence of new information on patients' symptomatic history, and the unreliability of measurement. However, subjecting a patient to an appropriate evidence-based psychosocial and pharmacologic treatment as well as planning mid- and long-term treatment is partially related to diagnostic categories rather than to psychiatric syndromes. Therefore, both a thorough initial assessment of FEP patient and family by a specialized team regarding the kind and duration of patient symptoms and a repeated reevaluation of diagnosis over the course of illness including standardized assessments, especially in the first year of treatment, are recommended.[22]

The second recommendation of repeated diagnostic assessments in the early course of treatment is especially important in FEP patients initially diagnosed with schizophreniform disorder with a short duration of untreated psychosis as well as in patients with bipolar disorder. In the current study, no relevant predictors of shifts from schizophreniform disorder toward the more severe disorders of schizophrenia or schizoaffective disorder were detected. Therefore, any patient initially diagnosed with schizophreniform disorder must be considered at risk for persistent symptoms including affective symptoms. The latter underlines the need for a routinely early identification within the first 3 months as already implemented in EPPIC (Treatment Resistance Early Assessment Team [TREAT][23]) of people with enduring symptoms. Despite the special awareness of bipolar disorder in EPPIC, there still is a significant diagnostic shift of approximately 20% toward schizophrenia spectrum disorders, especially toward schizoaffective disorder. The latter shift has implications not only for pharmacotherapy, but also for psychosocial interventions and prognosis.[19]

Especially in young people, information and education about diagnosis have implications beyond treatment as they involve the risk for patients and their families of therapeutic nihilism within the context of stigmatizing attitudes conveyed by the media. While it is important to take this risk seriously, studies of patients' and families' opinions of good quality treatment have shown that information on diagnosis and treatment is one of the most important elements.[24] Accordingly, psychoeducation programs that include education on both psychotic syndromes and diagnostic categories have been shown to improve adherence to treatment and lead to better outcomes, better management of subsequent relapse, lower readmission rates, and a greater sense of well-being.[22]

Clinicians should present the spectrum of psychotic syndromes to each patient during recovery and describe what these syndromes consist of, that they overlap, that several elements may be present (e.g., positive, negative,

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or affective syndromes; substance abuse; anxiety), and that all may need specific attention. Patients should be informed that there are descriptions of subtypes of psychosis such as schizophrenia and bipolar disorder that may be relatively stable and clear but that can change or overlap with each other.

Drug name: olanzapine (Zyprexa).

REFERENCES

1. Schwartz JE, Fennig S, Tanenberg-Karant M, et al. Congruence of diagnoses 2 years after a first-admission diagnosis of psychosis. Arch Gen Psychiatry 2000;57:593–600
2. Fennig S, Kovasznay B, Rich C, et al. Six-month stability of psychiatric diagnoses in first-admitted patients with psychosis. Am J Psychiatry 1994;151:1200–1208
3. Marneros A, Deister A, Rohde A. Stability of diagnoses in affective, schizoaffective and schizophrenic disorders: cross-sectional versus longitudinal diagnosis. Eur Arch Psychiatry Clin Neursci 1991;241:187–192
4. Mason P, Harrison G, Croudace T, et al. The predictive validity of a diagnosis of schizophrenia. Br J Psychiatry 1997;170:321–327
5. Tsuang MT, Woolson RF, Winokur G, et al. Stability of psychiatric diagnosis. Arch Gen Psychiatry 1981;38:535–539
6. McGorry PD, Copolov DL, Singh BS. Royal Park Multidiagnostic Instrument for Psychosis, pt 1: rationale and review. Schizophr Bull 1990;16:501–515
7. McGorry PD, Singh BS, Copolov DL, et al. Royal Park Multidiagnostic Instrument for Psychosis, pt 2: development, reliability, and validity. Schizophr Bull 1990;16:517–536
8. Edwards J, McGorry PD. Implementing Early Intervention in Psychosis. London, England: Martin Dunitz Publisher; 2002
9. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Press; 1994
10. Ventura J, Liberman RP, Green MF, et al. Training and quality assurance with the Structured Clinical Interview for DSM-IV (SCID-I/P). Psychiatry Res 1998;79:163–173.
11. Cannon-Spoor HE, Potkin SG, Wyatt RJ. Measurement of premorbid adjustment in chronic schizophrenia. Schizophr Bull 1982;8:470–484
12. Yung AR, Phillips LJ, McGorry PD, et al. Prediction of psychosis: a step towards indicated prevention of schizophrenia. Br J Psychiatry Suppl 1998;172:14–20
13. Guy W. ECDEU Assessment Manual for Psychopharmacology, revised. US Dept Health, Education, and Welfare publication (ADM) 76-338. Rockville Md: National Institute of Mental Health; 1976:218–222
14. Strakowski SM, Tohen M, Flaum M, et al. Substance abuse in psychotic disorders: associations with affective syndromes. DSM-IV Field Trial Work Group. Schizophr Res 1994;14:73–81
15. Kay SR, Fiszbein A, Opler LA. The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. Schizophr Bull 1987;13:261–276
16. McGorry PD, Killackey E, Lambert M, et al. Summary Australian and New Zealand Clinical Practice Guidelines for the treatment of schizophrenia. Australas Psychiatry 2003;11:1–13
17. Hegarty JD, Baldessarini RJ, Tohen M, et al. One hundred years of schizophrenia: a meta-analysis of the outcome literature. Am J Psychiatry 1994;151:1409–1416
18. Joyce PR. Age of onset in bipolar affective disorder and misdiagnosis as schizophrenia. Psychol Med 1984;14:145–149
19. Marneros A. Schizoaffective disorder: clinical aspects, differential diagnosis, and treatment. Curr Psychiatry Rep 2003;5:202–205
20. Leckman JF, Sholomskas D, Thompson WD, et al. Best estimate of lifetime psychiatric diagnosis: a methodological study. Arch Gen Psychiatry 1982;39:879–883
21. McGlashan TH. Testing four diagnostic systems for schizophrenia. Arch Gen Psychiatry 1984;41:141–144
22. Royal Australian and New Zealand College of Psychiatrists Clinical Practice Guidelines Team for the Treatment of Schizophrenia and Related Disorders. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of schizophrenia and related disorders. Aust N Z J Psychiatry 2005;39:1–30
23. Edwards J, Maude D, McGorry PD, et al. Prolonged recovery in first-episode psychosis. Br J Psychiatry Suppl 1998;172:107–116
24. De Haan L, van Raaij B, van den Berg R, et al. Preferences for treatment during a first psychotic episode. Eur Psychiatry 2001;16:83–89

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