The McLean–Harvard First-Episode Project: 6-Month Symptomatic and Functional Outcome in Affective and Nonaffective Psychosis


Background: The McLean–Harvard First-Episode Project recruited affective and nonaffective patients at their first lifetime psychiatric hospitalization.

Methods: Baseline evaluation and 6-month follow-up in 257 cases yielded recovery outcomes defined by syndromal (absence of DSM-IV criteria for a current episode) and functional (vocational and residential status at least at baseline levels) status. Time to recovery was assessed by survival analysis, and risk factors by multivariate logistic regression.

Results: Syndromal recovery was attained by 77% of cases over an average of 84 days. By diagnostic group, syndromal recovery rates ranked (p = .001) major affective disorders (81%) > nonaffective acute psychoses (74%) > schizoaffective disorders (70%) > schizophrenia (36%). Functional recovery was significantly associated to syndromal recovery, diagnosis, shorter hospitalization normalized to year, and older age at onset. Average hospital stay declined across the study period, but recovery did not vary with year of entry.

Conclusions: Syndromal recovery was achieved by nearly one half of patients within 3 months of a first lifetime hospitalization for a psychotic illness, but functional recovery was not achieved by 6 months in nearly two thirds of patients who had attained syndromal recovery.


Key Words: First episode, function, length of stay, outcome, psychotic disorders, recovery

Introduction

Many studies have been conducted to define the course of psychotic disorders and identify predictors of their outcome; however, most outcome studies in psychotic disorders have involved patients considered to have schizophrenia and initiated follow-up at different stages of illness; very few have included patients with affective disorders (Beiser et al 1988, 1989; Bromet et al 1996; Craig et al 1997; Leff et al 1992; Tohen et al 1990a). Findings from such studies have been somewhat variable and are inconclusive, in part, owing to inclusion of newly and chronically ill subjects (Tohen 1991; Zis and Goodwin 1979). This situation has encouraged greater interest in prospective studies of first-episode patients with schizophrenia (Biehl et al 1986; Bromet et al 1996; Craig et al 1997; Gupta et al 1997; Johnstone et al 1990; Kane et al 1982; Lay et al 1997; Leff et al 1992; Lieberman et al et al 1993; Ram et al 1992; Schubart et al 1986; Scottish Schizophrenia Research Group 1989; Tohen 1991; Tohen et al 1990b, 1992a, 1996; Varma et al 1996; Ventura et al 1992) and bipolar disorder (Fennig et al 1996; Strakowski et al 1998; Tohen et al 1990b, 2000), as well as in the prodromal phase of schizophrenia (McGorry et al 2000). Studies begun at the start of the illnesses promise early identification of clinical and biological factors that may help to characterize patients with specific disorders as well as serve to predict their later course and outcome.

Based on this background, The McLean–Harvard First-Episode Project has been observing a large number of first-episode psychotic patients with a range of DSM-IV diagnoses, prospectively, from their first lifetime hospitalization. We recently reported recovery results including only patients with psychotic affective disorders (Tohen et al 2000). This report considers 1) rates and elapsed time to syndromal recovery, 2) occupational and residential measures of functional recovery, and 3) factors associated with recovery in 257 patients with affective and nonaffective...
psychotic disorders at 6 months after their first psychiatric hospital admission.

Methods and Materials

The McLean–Harvard First-Episode Project was initiated in 1989 and has been active continuously since then. In this prospective, naturalistic follow-up study, treatment is not controlled by the investigators, although information about treatment is collected during hospitalization and throughout follow-up. Patients who presented with a psychotic syndrome were diagnosed by DSM-III-R (from 1989 to 1994) or DSM-IV criteria since 1994 (American Psychiatric Association 1994), with all diagnoses adapted to meet DSM-IV criteria for this report. Subjects were recruited from the inpatient units of McLean Hospital, a main psychiatric teaching hospital of Harvard Medical School.

Patients included met the following criteria: 1) age 16 years or older; 2) in a first lifetime episode of a clinically defined psychotic illness (including thought disorder, hallucinations, delusions, or grossly disorganized behavior at the time of first hospitalization) without symptomatic remission since onset; 3) meeting DSM-IV criteria for a principal diagnosis of schizophrenia, schizophreniform disorder, schizoaffective, bipolar, or major depressive disorders with psychotic features, delusional disorder, brief reactive psychosis, or psychosis not otherwise specified (NOS); and 4) providing written informed consent based on McLean Hospital institutional review board approval. Exclusion criteria were 1) presence of acute intoxication or a withdrawal syndrome associated with drug or alcohol abuse, or delirium of any cause; 2) previous psychiatric hospitalizations, unless for alcohol or substance abuse detoxification; 3) presence of mental retardation or other organic mental disorder; 4) duration of illness of >1 year; and 5) prior treatment with an antidepressant agent or mood stabilizer for a total of >3 months. A specially trained research assistant screens potential subjects by daily review of admission notes of all newly admitted patients with psychotic symptoms, as considered in preadmission assessments and verified by daily reviews with treating psychiatrists on each inpatient unit.

Baseline Measures

DSM-IV Axis I diagnoses (American Psychiatric Association 1994) were determined using the Structured Clinical Interview for DSM—patient version (SCID-P; Spitzer et al 1988) carried out by professional raters (masters-level training and more than a year of clinical experience). Final diagnoses were ascertained with a best-estimate diagnostic procedure recommended by Leckman et al 1982). Next, a detailed clinical narrative was prepared using all available information (SCID-P, medical records, and interviews of family members and primary treating clinicians). This narrative was presented to two psychiatrists with expertise in psychotic disorders, and a best-estimate procedure determined primary and comorbid diagnoses. As part of the best-estimate procedure, time of onset, defined as fulfilling DSM criteria for any of the psychotic disorders under study, was determined.

Clinical and demographic variables recorded at baseline included age, gender, race, days of hospital length of stay (LOS), years of education, and employment status. Also, comorbidity factors assessed included 1) other DSM Axis I disorders (current and lifetime), 2) comorbid alcohol or other substance abuse (current and lifetime), and 3) concurrent medical or neurologic illness. This information was obtained from medical records, SCID-P examination, and from the patient, relatives, and responsible clinicians, by research assistants trained to obtain such data reliably. They evaluated patients within 72 hours of admission and weekly thereafter until discharge.

Assessment scales included an expanded version of the Brief Psychiatric Rating Scale (BPRS; Lukoff et al 1986) with 35 items (rated for severity, 1–7) plus an overall sum score (Tohen et al 1992a, 2000), the Clinical Global Impressions (CGI; Guy 1976) and Global Assessment of Functioning (GAF; 0–100 scale; American Psychiatric Association 1994) scales. Occupational status was rated with the Modified Vocational Status Index (MVSI), and residential status rated with a Modified Location Code Index (MLCI; Dion et al 1988; Tohen et al 1990a, 1992a, 1996, 2000). Baseline occupational level and residential status were rated as the highest level achieved within the year before admission, based on information collected from medical records and family members as well as patients.

Outcome Measures

Patients were examined 6 months after hospital admission by an experienced professional rater (PG-M) kept blind to the baseline information. Follow-up information was obtained by telephone or by direct interview, as reported previously (Tohen et al 1990a, 1992a, 2000). If a subject could not be interviewed by telephone or face to face, follow-up information was obtained from a close relative or another member of the patient’s household. Of the reported follow-up assessments, 90% were by telephone, 60% were with the subject only, and 40% with relatives and friends with or without the subject.

In follow-up interviews, information elicited included sociodemographic changes, the course of the primary and comorbid disorders, occupational and residential functional status, diagnostic status to define syndromal recovery, and estimated time of such recovery (days since hospital admission). Follow-up interviews also included the MVSI and MLCI functional level scales and the GAF. A statement of each subject’s general life satisfaction was also rated, as 1, very good; 2, good; 3, fair; 4, poor; and 5, very poor.

Syndromal recovery was defined as no longer meeting criteria for an ongoing episode of illness (Frank et al 1991; Prien et al 1991; Tohen et al 2000). These included a CGI score of 2 and specific operational criteria, as follows:

1. For mania, the DSM mania “A” criteria were 3 in severity, no mania “B” criteria were ≥3, and two B criteria were scored 3.
2. For major depression with psychotic features, no DSM criteria were ≥3, and not more than three were rated 3.
3. For schizophrenia and schizophreniform disorder, no DSM A criteria were rated ≥2, and not more than two criteria were 2.
4. For delusional disorder and psychosis NOS, no affective, delusional, or hallucinatory symptoms were rated >2.

Subjects with schizoaffective disorder had to meet recovery criteria for both schizophrenia and either mania or depression. In addition, syndromal recovery criteria require that these conditions be sustained for at least 8 weeks, and latency to the start of this interval was scored in days from hospital admission.

**Functional recovery** was operationally defined categorically by comparing MVSI (vocational status) and MLCI (living situation) ratings obtained at admission and at 6-month follow-up. Functional recovery by 6-month follow-up requires a return to at least the premorbid level of both vocational and residential functioning, plus attainment of a rating of 1–5 for occupational and 1–4 for residential levels, as defined above.

**Data Analysis**

Interrater reliability was evaluated for the SCID-P for primary (intraclass correlation coefficient [ICC] = .90) and secondary (ICC = .90) diagnoses (Tohen et al 1990a, 1992a, 1996, 2000). High interrater reliability was also obtained for the 35-item BPRS (ICC = .96; Tohen et al 1990a, 1992a, 1996, 2000; Zarate et al 1997b). Good to excellent agreement between telephone and in-person interviews was also obtained (ICC = .90; Revicki et al 1997; Tohen et al 1990a).

By having the same investigator (PG-M) conduct all the follow-up assessments, reliability for the recovery ratings across the different years of recruitment was assured.

Each subject was first designated as recovered or not recovered by 6 months, based on the syndromal and functional criteria just defined. Continuous demographic and clinical variables were dichotomized to yield meaningful contrasts and to facilitate estimates of odds ratios (ORs). Selected categoric variables also were recoded to afford simple, meaningful contrasts. Age at onset was dichotomized at 25, 26–49, and 50 years, and type of onset or prodrome was coded as rapid (1–6 months) or gradual (>6 months). Diagnostic subgroup clusters defined by principal DSM diagnostic codes were 1) major affective disorders with psychotic features (manic, mixed, or NOS bipolar disorders, or major depression), 2) acute nonaffective psychotic disorders (schizophreniform, schizoaffective, delusional, or psychotic NOS), 3) schizoaffective disorders, and 4) schizophrenia.

Admission year (1989–1996) was a categoric variable. Since average LOS diminished yearly, individual LOS (days) was normalized by ranking LOS for each year of admission and forming binary variables to characterize hospitalizations, as shorter, 25th, and longer, 75th percentile for LOS in each year. Individual BPRS scale items were dichotomized as severe (including ratings of 5–7) and nonsevere (0–4). Depressive, manic, and psychotic subtotal ratings of the 35-item BPRS (Lukoff et al 1986; Tohen et al 1990a, 1996) also were dichotomized to indicate presence or absence of severe item scores (5–7), and BPRS total scores were median split to yield high/low scoring subgroups.

Syndromal and functional 6-month recovery rates were compared with contingency tables (\( \chi^2 \)). Both types of recovery were considered within diagnostic and other subgroups of interest defined in Results and compared with 6-month GAF scores with Mann–Whitney rank sum nonparametric methods. Frequencies of categoric variables in recovery groups were compared by cross-tabulations and \( \chi^2 \) tests or Fisher exact \( p \) (if cell size < 10 subjects). Log-rank nonparametric tests were used to compare distributions of continuous variables in subgroups. Variables with suggestive (\( p < .20 \)) bivariate associations with recovery status were considered candidates for multivariate analyses.

Multiple logistic regression models evaluated candidate demographic and clinical variables for independent association with syndromal and functional recovery. Deciles of fitted values and partial residual plot methods were used to check the goodness of fit of multivariate models (Hosmer and Lemeshow 1989). Explanatory variables with adjusted ORs significantly different (\( p < .05 \)) from 1.0 were retained for final multiple logistic regression models. Finally, distributions of days to recovery were compared between demographic and diagnostic groups by Kaplan–Meier survival analysis of times to defined levels of recovery, with SE or 95% confidence intervals (CIs), and Mantel–Cox log-rank \( \chi^2 \) tests of statistical significance (Lee 1992). Averaged continuous data are reported as means \( \pm \) SDs. Statistical analyses were based on commercially available microcomputer programs (Stata, Stata Corp., College Station, TX; Statview-II, Abacus Concepts, Berkeley, CA).

**Results**

**Patient Population**

During the 6-year period of study recruitment from 1989 through 1995, 22,100 patients were hospitalized, of whom 784 (3.6%) were identified as in a first lifetime episode of psychotic illness. Of these, 296 (37.8%) were recruited (174 men [58.8%] and 122 women [41.2%]; mean \( \pm \) SD age at admission = 31.9 \( \pm \) 5.0 years); 257 (86.8% of those recruited) provided 6-month follow-up data for syndromal outcome, and 253 (85.5%) for functional recovery. No significant differences between recruited and nonrecruited patients were found in a large number of demographic and clinical measures.

Diagnostic categories included major affective disorders with psychotic features (\( N = 172, 66.9\% \)), including bipolar disorder (\( N = 128, 49.8\% \)) and major depression (\( N = 44, 17.1\% \)); acute nonaffective psychotic disorders were next most frequent (\( N = 51, 19.8\% \)); schizoaffective disorders (\( N = 20, 7.8\% \)) and schizophrenia (\( N = 14, 5.5\% \)) were least common (Table 1). This distribution of diagnoses was consistent with the recent case mix for all admissions for psychotic disorders at McLean Hospital, but may not generalize to other centers (Carpenter and Kirkpatrick 1988; Craig et al 1997; Lay et al 1997; Tohen et al 1992a; Varma et al 1996; Ventura et al 1992).

**6-Month Recovery Rates**

Syndromal recovery was attained by 77.0% (198/257) of patients, and functional recovery (meeting both vocational
and residential criteria) by 29.2% (74/253) by 6 months after admission for a first lifetime hospitalization for psychotic illness. Of patients achieving syndromal recovery, 64.8% failed to reach functional recovery status within 6 months ($\chi^2(1) = 12.2, p = .0005$). Women tended to gain syndromal recovery more often than men [81.1% vs. 71.5%; $\chi^2(1) = 3.11, p = .078$], but functional recovery rates were similar in women and men [27.4% vs. 31.3%; $\chi^2(1) = 0.46, ns$]. Occupational versus residential functional recovery rates, overall, were 39.1% (99/253) versus 73.1% (185/253). The mean functional recovery rate across the nine diagnoses (28.9 ± 17.2%) was substantially less than syndromal recovery rate (75.0 ± 19.5%) in all nine diagnostic categories encountered (Table 1). Occupational and residential components of functional recovery appear to measure different aspects of recovery and were not correlated across diagnostic groups [$r(1\,b) = .05, ns$].

Syndromal 6-month recovery rates for four clusters of presumably related disorders ranked affective disorders (81.4%), acute nonaffective psychoses (74.5%), schizoaffective disorder (70.0%), and schizophrenia (35.7%), and differed highly significantly ($\chi^2(3) = 16.0, p = .0012$; Table 1). Functional recovery in the same clusters ranked acute nonaffective (74.5%), affective (35.3%), schizophrenia (15.4%), and schizoaffective [0%; $\chi^2(3) = 2.61, ns$].

Table 1. Primary Diagnoses and Recovery in First-Psychosis Patients

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N of all cases (%)</th>
<th>Percent recovery</th>
<th>Computed days to 25% (recovery ± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N = 257)</td>
<td>(N = 253)</td>
<td></td>
</tr>
<tr>
<td>Major affective disorders with psychotic features</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bipolar, manic</td>
<td>98 (38.1)</td>
<td>85.7</td>
<td>32.6</td>
</tr>
<tr>
<td>Major depression</td>
<td>44 (17.1)</td>
<td>75.0</td>
<td>31.8</td>
</tr>
<tr>
<td>Bipolar, mixed</td>
<td>20 (7.8)</td>
<td>65.0</td>
<td>47.4</td>
</tr>
<tr>
<td>Bipolar, NOS</td>
<td>10 (3.9)</td>
<td>100.0</td>
<td>55.6</td>
</tr>
<tr>
<td>Subtotal</td>
<td>172 (66.9)</td>
<td>81.4</td>
<td>35.3</td>
</tr>
<tr>
<td>Nonaffective acute psychotic disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychosis NOS</td>
<td>29 (11.3)</td>
<td>72.4</td>
<td>18.5</td>
</tr>
<tr>
<td>Delusional disorder</td>
<td>14 (5.4)</td>
<td>71.4</td>
<td>38.5</td>
</tr>
<tr>
<td>Schizophreniform</td>
<td>8 (3.1)</td>
<td>100.0</td>
<td>20.0</td>
</tr>
<tr>
<td>Subtotal</td>
<td>51 (19.8)</td>
<td>74.5</td>
<td>24.0</td>
</tr>
<tr>
<td>Schizoaffective disorder</td>
<td>20 (7.8)</td>
<td>70.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>14 (5.4)</td>
<td>35.7</td>
<td>15.4</td>
</tr>
<tr>
<td>Total</td>
<td>257 (100.0)</td>
<td>77.0</td>
<td>29.2</td>
</tr>
</tbody>
</table>

All diagnoses were updated to accord with DSM-IV. Functional recovery required meeting both occupational and residential criteria. Functional recovery rates were less than syndromal rates for all categories (mean ratio of syndromal/functional recovery rates = 2.64). Rates of syndromal recovery differed highly significantly among the four diagnostic clusters ($\chi^2(3) = 16, p = .0012$), but functional recovery did not ($\chi^2(3) = 2.61, ns$). Values of days to 25% chance of syndromal recovery were computed by survival analysis (not all disorders attained 50% rates within 6 months) and differed significantly among the four clusters ($\chi^2(3) = 9.24, p = .026$). NOS, not otherwise specified.

Syndromal recovery was also associated with higher 6-month GAF scores at 6 months after hospitalization: mean GAFs were 70.8 ± 16.0 in syndromally recovered patients, but only 47.0 ± 14.0 in nonrecovered subjects. Mean GAF values for functionally recovered versus nonrecovered patients followed a similar trend (72.7 ± 14.4 vs. 62.7 ± 18.8). Both mean differences are highly significant (rank sum z = 8.40 and 3.70, respectively; both ps < .001). Similarly, subjective measures of patients’ satisfaction with their life situation at 6-month follow-up were also strongly associated with syndromal and functional recovery. The mean patient satisfaction score (1–5 scale) among syndromally recovered patients

---

*Note*: Table and text excerpts are from a research paper, and the full context of the data and analysis is beyond the scope of this extract.
for whom such data were available \((N = 153)\) was 2.36 ± 1.07, versus 3.31 ± 1.05 among nonrecovered patients \((N = 35); \text{rank-sum } z = 2.28, p = .02\). Also, for functionally recovered \((N = 56)\) versus nonrecovered \((N = 132)\) subjects, these satisfaction scores averaged 2.25 ± 1.01 versus 2.66 ± 1.16 \((\text{rank sum } z = 2.28, p = .02)\).

**Time Course of Recovery**

Kaplan–Meier survival analysis was employed to evaluate the time course of recovery in subgroups of interest. The overall computed times to the 25% and 50% levels of syndromal recovery, ± SE, were 29.0 ± 2.3 and 61.0 ± 2.7 days, respectively \((\text{Figure 1})\). Women attained syndromal recovery significantly more rapidly than men, with their computed time to 50% recovery, ± SE, at 43.0 ± 9.0 versus 73.0 ± 4.9 days \((\chi^2 = 6.98, p = .0083; \text{not shown})\). In addition, patients who had attained functional recovery \((\text{meeting both criteria})\) by 6 months, as expected, also reached 50% functional recovery \((42.0 ± 5.8 \text{ days})\) sooner than those who did not \((73.0 ± 14.7 \text{ days}, \text{a 1.74-fold difference}; \chi^2 = 16.8, p < .0001; \text{Figure 1})\).

Time functions were also compared for selected diagnostic groups. Computed times to 25% syndromal recovery for comparison across specific DSM-IV diagnoses and diagnostic groups showed mainly minor variations among disorders and averaged 29.0 ± 2.3 days, overall \((\text{Table 1})\). These recovery time functions were found to be relatively brief among the acute nonaffective psychotic syndromes \((16.0 ± 4.7)\), intermediate among major affective \((30.0 ± 2.9)\) and schizoaffective \((31.0 ± 11.0)\) disorders, and longest in schizophrenia \([65.0 ± 98.9 \text{ days}; \text{Mantel–Cox } \chi^2 (2) = 9.16, p = .01])\).

**Factors Associated with 6-Month Recovery**

Six factors were initially identified in bivariate analyses as having at least suggestive \((p < .20)\) associations with recovery for comparison across specific DSM-IV diagnoses and diagnostic groups showed mainly minor variations among disorders and averaged 29.0 ± 2.3 days, overall \((\text{Table 1})\). These recovery time functions were found to be relatively brief among the acute nonaffective psychotic syndromes \((16.0 ± 4.7)\), intermediate among major affective \((30.0 ± 2.9)\) and schizoaffective \((31.0 ± 11.0)\) disorders, and longest in schizophrenia \([65.0 ± 98.9 \text{ days}; \text{Mantel–Cox } \chi^2 (2) = 9.16, p = .01])\).
syndromal recovery in 198 subjects, versus nonrecovery in 59 subjects, and so were considered candidates for multivariate analysis; these were 1) a major affective diagnosis, 2) relatively acute onset, 3) short hospitalization, 4) relatively high baseline GAF scores, 5) ability to live independently at follow-up (MLCI > 4), and 6) absence of an additional Axis I comorbid condition. These factors and sex were entered into a multivariate logistic regression model; however, only diagnosis emerged as significant in the multivariate analysis (OR = 2.04 [95% CI = 1.20–3.70], z = 2.33, p = .019), with greater recovery frequency among acute nonaffective and major affective groups, as compared with schizoaffective or schizophrenic groups. Surprisingly, various psychiatric, substance abuse, and medical comorbidity factors, as well as measures of illness severity at baseline assessment, had little ability to predict syndromal recovery.

With respect to functional recovery (based on both occupational and residential criteria being at least at baseline levels at 6-month follow-up), five factors were initially identified as having at least suggestive (p < .20) associations with functional recovery in 74 subjects, versus nonrecovery in 179 subjects, and so were determined to be candidates for multivariate analysis, along with sex. Four factors were sustained (p < .05) in multivariate analysis. In descending order of their apparent explanatory power, these ranked 1) having previously attained syndromal recovery, 2) major affective diagnosis, 3) LOS standardized to admission year (shorter time in hospital was associated with favorable outcome, and longer stay with unfavorable), and 4) greater onset age. This four-factor model was highly significant overall [χ²(3) = 31.6, p < .0001], and it accounted for a moderate amount of variance (10.4%; Table 2). A possible confounding was controlled by including in the same model LOS and year of entry into the study.

For both measures of outcome, model fit was evaluated by the area under the receiver operating curve, the ratio of the likelihood functions (similar in interpretation to an r² value, and an indication of explanatory power), and the Hosmer–Lemeshow goodness of fit statistic (Hosmer and Lemeshow 1989); all of these measures indicated acceptable levels of fit of both multivariate models to the data. Despite a sharp decline in the average hospital LOS across the years of entry into the study that might be expected to influence 6-month recovery status, there was no significant relationship between syndromal or functional recovery rates and year of entry into the study (Figure 3).

Discussion
The main findings from this study were that more than three quarters of newly psychotic patients attained syndromal recovery with currently standard, clinically indicated treatments within 6 months of a first lifetime psychiatric hospitalization, but that functional recovery was reached by fewer than a third of such patients. Generalizations from this finding to other settings and patient populations should be made cautiously. This study group was derived from admissions to a private, university-affiliated psychiatric research and teaching center. Patients typically were referred from local hospital emergency rooms or university health services and had acute and severe psychotic symptoms that required treatment in a locked psychiatric unit. This referral pattern may be different from those of other institutions. One finding that particularly suggests cautious generalization is the small proportion of patient...
subjects meeting DSM-IV criteria for schizophrenia (5.4%; Table 1). Instead, our finding pertains largely to the high proportion of patients presenting with affective disorders with psychotic features, or with various acute nonaffective psychoses. Study inclusion criteria of not being ill for more than 1 year and not being on psychotropic medications for more than 3 months limited the number of patients with schizophrenia. Therefore, any generalization of the schizophrenic cohort should be limited to similar patients. Another limitation of this study was the lack of systematic information on admissions to other facilities in the area where patients with first-episode schizophrenia could have been admitted.

Important impressions arising from the present findings include the following:

1. A large proportion of first-episode psychotic patients (77.0%) achieved syndromal or symptomatic recovery within 6 months of hospitalization.

2. The time course of syndromal recovery was such that 25% of all patients recovered within 6 weeks, and 50% within 12 weeks for most disorders (Figure 1); only those diagnosed initially with schizophrenia failed to reach the 50% level of recovery within 6 months.

3. Many subjects (79.8%) failed to achieve functional recovery within 6 months (Table 1), even to the level of moderate independence, and nearly two thirds (64.8%) of those reaching syndromal recovery failed to attain functional recovery. Functional recovery based on occupational level was less often achieved than functional recovery based on residential status. Those who reached functional recovery achieved syndromal recovery earlier than those who did not (Figure 1).

Few predictive factors were significantly related to syndromal recovery in multivariate analysis, other than the diagnosis of a bipolar or major depressive syndrome with psychotic features or a nonaffective acute psychotic disorder, although a relatively acute onset tended to be associated (Tables 2 and 3). Several factors were significantly associated with functional recovery, however. They included 1) having attained syndromal recovery, 2) diagnosis of a major affective disorder or a nonaffective acute psychotic disorder, 3) relatively brief hospitalization, and 4) a relatively later age at onset (Table 2). Various medical, psychiatric, or substance abuse comorbidity factors had little effect at this early stage of new psychotic illness, in contrast to expectations based on studies of populations with chronic psychotic illness (Drake et al 1996; however, a relatively small number of patients (N = 21) with a history of epileptic seizures were less likely to recovery syndromally (p = .001) or functionally (p = .04), based on multivariate modeling.

Another striking and unexpected finding was an evident lack of relationship of 6-month outcomes to the year of enrollment in this study between 1989 and 1996. We had previously observed a progressive diminution in percent improvement on standard rating scales (BPRS and CGI) between initial hospitalization and discharge, along with a largely economically driven shortening average length of hospitalization during the same years at the study site (Figure 3; Zarate et al 1997a). Both syndromal and functional recovery rates were similar across the years of entry into the study (Figure 3). These findings indicate that outcome at 6 months after hospitalization was largely unaffected by the marked recent decreases in average LOS. Apparently, many first-psychosis patients sustained the recovery process initiated during increasingly time-limited hospitalization (Figures 1 and 2). The fact that decreased LOS did not worsen functional recovery suggests that the improvement in functional outcomes may take place during the posthospitalization period.

Studies conducted at the University of Cincinnati have
focused on similar outcomes. Keck and collaborators (1998), in a 1-year follow-up study of 134 multiple-episode bipolar patients, found that symptomatic recovery occurred in 26% of patients and functional recovery in 24%. The relatively higher recovery rates in our bipolar subgroup may be explained by the inclusion of first-episode patients only. A similar study from the same group in the University of Cincinnati focused on first-episode affective psychosis (Strakowski et al. 1998). In that study 56% of the patients achieved syndromic recovery and 35% achieved functional recovery. In our study the 32.6% rate of functional recovery is remarkably similar to the Cincinnati rate; however, the 85.7% of syndromic recovery in our study is clearly higher than the 56% figure reported by Strakowski and collaborators. In the Cincinnati study higher socioeconomic status (SES) was a predictor of both symptomatic and functional recovery. It is possible that the higher SES of the McLean patients may explain the higher rates of symptomatic recovery.

Our findings have clear implications for the long-term aftercare of patients with psychotic disorders. It is encouraging that a majority of patients achieved a substantial level of symptomatic recovery within even 3 months of aftercare; however, this was not the case with patients initially diagnosed with schizophrenia. Moreover, it is especially disturbing that nearly two thirds of patients considered syndromally recovered had not recovered functionally by 6 months after hospitalization, in that they failed to return even to their baseline levels of residential and, particularly, occupational functioning, or to minimal levels of functional independence. For many patients, even baseline functioning may already have been compromised due to prodromal illness or comorbidity for some months before the index hospitalization. It remains to be determined how many subjects, in which diagnostic groups, will go on to further improvements or relapses with longer follow-up, and that aspect of the investigation is ongoing. An issue that has been addressed by our group and other authors (Fennig et al. 1994; Tohen et al. 1992b) is the shift of diagnosis. In this study, reassessment of diagnosis was conducted at the 2-year follow-up; thus, this information is not available for the 6-month follow-up period.

The inconsistency between syndromal and functional recovery reported here parallels clinical experience, in which substantial symptomatic recovery in acute phases of psychotic illnesses may occur before, or without, return to a baseline level or to a substantially improved functional status. Even with major resolution of acute symptoms, independent living, interactions with other persons, and, particularly, ability to work productively may continue to be compromised for prolonged periods or may result in sustained disability, with its associated high indirect costs to society (Greenberg et al. 1993; Wyatt et al. 1997; Wyatt and Henter 1995). There may be particular difficulties associated with first episodes and the new experience of psychotic illness, resulting in denial or demoralization that can complicate efforts at treatment and rehabilitation. We suggest that future research on treatment and outcomes in new psychotic illness should emphasize functional outcome as well as symptomatic improvement.

These findings highlight a growing appreciation that symptom-based assessments are insufficient to assure long-term functional recovery and an improved quality of life in psychotic patients. Recent improvements in diagnostic and clinical assessment methods in psychiatry have supported advances in the scientific understanding of psychotic disorders. Nevertheless, in our opinion even modern psychiatry—including its outcomes research—remains excessively preoccupied with medically oriented, symptomatic assessments. These measures are important, but represent an incomplete evaluation of clinical status and level of recovery. Accordingly, we strongly encourage further attempts to improve and to include various functional assessments in studies of treatment effects and outcomes, particularly early in the course of the potentially chronic and disabling psychotic disorders. The assessment of functional recovery needs to be considered in clinical trials. New treatments need to be compared to older treatments in terms of their ability to improve functional outcomes. In addition, the role of rehabilitation treatments at the onset of major psychiatric disorders needs to be evaluated to determine if new treatments provide long-term benefits. Challenges include the need to assess baseline functional levels in light of relevant premorbid disability and to understand differences between ability to live more or less independently and ability to work productively and gainfully.

In conclusion, although 77% of patients with psychotic disorders were judged to have achieved substantial symptomatic recovery within 6 months of a first hospitalization, 65% of these patients did not regain their premorbid functional status as defined by occupational activities and living situations indicative of at least minimal independence, and those diagnosed with schizophrenia did especially poorly by both syndromal and functional criteria for recovery. The findings support further efforts to improve functional as well as symptomatic assessments of psychotic patients.


Aspects of this work were presented at the conference “Bipolar Disorder: From Preclinical to Clinical, Facing the New Millennium,” January 19–21, 2000, Scottsdale, Arizona. The conference was sponsored by the Society of Biological Psychiatry through an unrestricted educational grant provided by Eli Lilly and Company.
References


