Published in final edited form as:
Bipolar Disord. 2012 February ; 14(1): 19–30. doi:10.1111/j.1399-5618.2012.00982.x.

Early determinants of four-year clinical outcomes in bipolar disorder with psychosis

Gabrielle A Carlson[a], **Roman Kotov**[a], **Su-Wei Chang**[b], **Camilo Ruggero**[c], and **Evelyn J Bromet**[a]

[a]Department of Psychiatry and Behavioral Sciences, Stony Brook University School of Medicine, Stony Brook, NY, USA

[b]Institute of Biomedical Sciences, Academia Sinica, Nankang, Taipei, Taiwan

[c]Department of Psychology, University of North Texas, Denton, TX, USA

Abstract

Objectives—Bipolar disorder with psychosis is common in inpatient settings and is associated with diverse outcomes after hospital discharge, which can range from a return to premorbid functioning with no recurrence to a chronic or recurring illness. Less is known, however, about factors that can predict a better or worse clinical outcome. The present report sought to assess four-year clinical outcomes and their predictors in patients hospitalized for bipolar I disorder with psychosis.

Methods—Participants from the Suffolk County Mental Health Project (SCMHP) with a baseline diagnosis of bipolar I disorder with psychotic features (N = 126) were reassessed using face-to-face interviews at six months, two years, and four years following their first hospitalization. At each time point, clinical status, role functioning, and treatment were assessed by highly trained interviewers using standardized instruments.

Results—The majority of participants (73.2%) returned to their premorbid level of role functioning by the four-year follow-up and the median percent time ill during the interval was less than 20%. Nevertheless, almost half the sample (46.9%) was rehospitalized at least once. Psychotic symptoms at baseline (particularly Schneiderian symptoms), depressive phenomenology, childhood psychopathology, and younger age at first hospitalization predicted worse outcome; whereas mood incongruent psychotic features and age of mood disorder onset did not.

Conclusions—The four-year outcomes of a first-admission cohort with bipolar I disorder with psychosis were generally favorable. Poorer premorbid functioning, Schneiderian delusions, greater depressive symptoms, and a younger age of first hospitalization portend a worse course.

Keywords

bipolar disorder; childhood; depression; longitudinal; mania; psychopathology; psychosis

Corresponding author: Gabrielle A. Carlson, M.D., Department of Psychiatry and Behavioral Sciences, Stony Brook University School of Medicine, Putnam Hall-South Campus, Stony Brook, NY 11794-8790, USA, Fax: (631) 632-8953, gabrielle.carlson@sbumed.org.

Disclosures

GAC has received research support from the National Institute of Mental Health (NIMH), Bristol-Myers Squibb, GlaxoSmithKline, and Eli Lilly & Co. RK and EJB have received research support from NIMH. S-WC and CR have no conflicts of interest to report.

Bipolar I disorder can cause substantial disability and suffering, however, this is not always the case. Longitudinal studies over the past 60 years indicate considerable variability in clinical outcomes, with 30% to 75% of patients being able to function reasonably well over time (e.g., maintain jobs, marriages, periods of good function) (1–7). Psychotic features have been associated with poorer outcomes, including more frequent relapses, greater chronicity, and less adequate intermorbid functioning (8–14), although not all studies have found psychosis to have prognostic significance (15–18).

Apart from the question of whether psychosis predicts a worse course, few studies have examined other predictors of better or worse outcomes among bipolar disorder patients presenting with psychosis (BP-Psy), even though BP-Psy is the second most common diagnosis among inpatients admitted with prominent psychotic symptoms (19). Prior studies of predictors of outcome in this population suggest that older age of onset (4, 9, 20), good functioning prior to hospitalization (21), absence of childhood psychopathology or its risk factors (22, 23), mood congruent psychotic symptoms (10, 24, 25), fewer depressive symptoms (26), longer time in treatment during follow-up (21), and less drug use (4) are associated with better outcomes in BP-Psy. In this report, we examine the specificity of predictors for different aspects of clinical outcome four years after discharge from an initial hospitalization. We also extend the scope of prognostic factors by investigating such factors as specific types of psychotic features, family history of mood disorders, and the medications prescribed at hospital discharge.

The data comes from the Suffolk County Mental Health Project (SCMHP), a naturalistic prospective follow-up of a county-wide sample of patients hospitalized with a first episode of psychosis. One-fifth (21%) of the cohort was diagnosed at baseline with BP-Psy. The current report focuses on the four-year clinical outcomes of these participants, measured in terms of overall functioning: percent time ill; number of subsequent depressive, manic, and psychotic episodes; percent time in treatment; and rehospitalizations. The objective of this study is to describe the distributions of these outcomes and identify their most salient predictors.

Methods

Sample and procedure

The study cohort consisted of the 126 SCMHP participants given a baseline research diagnosis of BP-Psy and reassessed up to three times during the four years following their first hospitalization. The sample was recruited between 1989 and 1995 from the 12 existing inpatient psychiatric facilities in Suffolk County, New York (19, 27). Inclusion criteria were: first admission to a psychiatric hospital currently or within the prior six months, ages 15–60, residency in Suffolk County, IQ > 70, ability to communicate in English, and clinical evidence of psychosis. Potentially eligible patients were referred to the project by the head nurse or social worker, and 72% of referrals participated.

The procedures for obtaining informed consent were approved annually by the Institutional Review Board at Stony Brook University and the hospitals from which participants were recruited. For subjects aged 15–17 years old, written parental consent was required. Verbal consent was also obtained from young participants.

At baseline, the cohort was interviewed with the lifetime version of the Structured Clinical Interview for DSM-III-R (SCID) (28). Consensus diagnoses by experienced psychiatrists were based on the SCID, information in the medical records, and informant and clinician interviews (29). We initially diagnosed 133 participants (21.2% of the eligible cohort) with BP-Psy. Three died and four refused to participate or were lost to follow-up. Of the 126

patients comprising the analysis sample, 106 were assessed at all three successive follow-ups. The number of re-interviews was not associated with the study variables in this report.

Follow-up assessments and measures

The sample was re-interviewed face-to-face and consensus rediagnoses were done at six-month, two-year, and four-year follow-ups. Baseline diagnosis was used in this study to be compatible with other outcome studies. Inter-rater reliability was maintained by having the project director randomly observe and rate 5–10% of the interviews. The inter-rater reliability on the SCID was good, with average kappas of 0.73 for mood symptoms and 0.75 for psychotic symptoms (27, 30).

Background characteristics included gender, age at baseline, household socioeconomic status (blue collar versus other), age at onset of mood disorder (from SCID), childhood psychopathology (present/absent) (22), and the Global Assessment of Function (GAF) for the best month during the year prior to admission (31). Also, family history of mania and depression was compiled from medical records and a structured interview module modeled on the Family History-Research Diagnostic Criteria (32) administered to participants and relatives at the six-month and two-year follow-ups.

Baseline clinical risk factors included whether the psychotic symptoms were mood incongruent [SCID rating based on DSM-IV criteria (i.e., persecutory delusions without self-derogatory or grandiose content, thought insertion, thought broadcasting, and delusions of being controlled)], severity of negative and positive symptoms, and severity of mood symptoms. Negative symptoms were assessed with the Schedule for the Assessment of Negative Symptoms (SANS), and based on the total score across 18 items rated 0 = none to 5 = severe (33–34). Psychotic symptoms were assessed with the Scale for the Assessment of Positive Symptoms (SAPS) (35). We included five factor-analytically derived subscales: disorganization (13 items tapping formal thought disorder and bizarre behavior), Schneiderian symptoms (delusions of being controlled, mind reading, thought broadcasting, thought insertion, and thought withdrawal), hallucinations (auditory, somatic/tactile, olfactory, and visual), paranoid delusions (persecutory and delusions of reference), and manic delusions (grandiose and religious delusions). Severity of manic symptoms was assessed with the excitement item from the Brief Psychiatric Rating Scale (BPRS) (36) rated 1 = absent to 7 = very severe. Severity of depressive symptoms was based on the total score of the 21-item version of the Hamilton Depression Rating Scale (HAM-D) (37).

The type of medication prescribed at discharge from the index hospital was abstracted from the medical record. Four non-mutually exclusive variables were included: antipsychotic medication, antidepressants, mood stabilizers (lithium, valproate, carbamazpine), and the combination of antipsychotic medication and mood stabilizers.

This paper focused on seven clinically relevant outcomes. Four of these outcomes were ascertained from a chronological record of changes in psychiatric status developed for the SCMHP. Specifically, we recorded changes in psychiatric status, including onset and offset dates of manic symptoms (rated as none, hypomania, mixed, or mania), depressive symptoms (none, dysthymia, and major depression), and positive psychotic symptoms (rated as none, subthreshold, definite). A period of eight weeks of remission was used to define the interval between discrete mood episodes. We thus calculated the number of threshold depressive episodes, manic episodes, and psychotic episodes. We also calculated the percent time in each mood state and combined them into overall percent time ill to be used in the analysis.

Chronological records were maintained for all hospitalizations and for medication changes (dates of initiation and cessation of each medication was based on participant report and medical records). We then calculated the number of rehospitalizations and the percent of follow-up time that participants received medication treatment.

The GAF for the best month of the year prior to final follow-up was determined by consensus by the project psychiatrists at the diagnosis meetings.

Four additional variables were explored to expand the clinical picture: percent time spent in subthreshold depressive symptoms (defined as three or four depressive symptoms, at least one of which was depressed mood *or* loss of interest), switch from depression to mania in initial episode, converting to schizophrenia by 24 months, and the interviewer rating of whether participants returned to their premorbid level of role functioning (versus some downward drift, marked deterioration, or never functioned well at a job) (27).

Statistical analysis

In addition to exploring the distributions of all outcome variables, bivariate associations between the predictors and the seven main clinical outcomes were computed as Pearson's *r* (for continuous predictors) and Cohen's *d* (for dichotomous predictors). We used multiple regression with stepwise selection to identify independent predictors of each outcome. A p-value of < 0.05 was used to select regression predictors. Both standardized and unstandardized regression weights are reported. To provide a meaningful metric for the estimates, unstandardized *B*'s were presented as the difference in expected outcome between those without a risk factor (for pre-baseline GAF and age the reference was mean sample score) and those with its highest level observed in this sample. The regression analyses adjusted for length of follow-up.

Results

Sample characteristics

At baseline, the sample had a mean age of 29.3 (SD = 9.8), about half were male, and 40% came from blue collar homes (Table 1). In addition, most were Caucasian (85%) and never married (59.5%).

The mean age of onset of mood disorder was 25.4 (SD = 8.8) years; one fifth had a family history of bipolar disorder and close to half (44.8%) had a family history of depression (Table 1). A history of childhood psychopathology was common (72.6%) with behavior disorders present in 24.5% of the sample, and a further 44.9% having other non-behavioral childhood psychiatric disorders.

Clinically, the majority (79.5%) was first hospitalized with a manic episode, 13.4% had a mixed episode, and 6.3% were depressed. Almost half had mood incongruent psychotic symptoms (45.7%), one-quarter had Schneiderian symptoms (28.6%), and many had paranoid features (46.8%). Of those with persecutory delusions, 76% were deemed mood incongruent. Hallucinations were present in 50.8%, while 74.6% had manic delusions. At discharge, two-thirds were prescribed antipsychotics, half were prescribed mood stabilizers, and a handful were prescribed antidepressants; one-third was discharged on antipsychotics plus mood stabilizers (Table 1).

Clinical course and treatment over the four years

Respondents had a reasonably positive outcome at four years. Of those seen at all time points, most (73.2%) returned to their premorbid level of role functioning, and more than

half (57.3%) had a GAF ≥ 70. Nonetheless, participants spent on average almost a third of the interval ill and almost half of them were rehospitalized at least once (Table 1).

Across the four-year follow-up period, the 126 participants had a total of 353 mood episodes (average episodes per person = 2.9 ± 1.8), with 40.5% of these being depressive in nature. Among participants, 35% had no depression, 36.6% had one episode, and the remaining 28.5% had two or more episodes of depression. In addition, 15.5% of the entire sample experienced periods of subthreshold depression or dysthymic symptoms. Across the whole sample, participants spent 19.5% (SD 30%; median 6.3%) of the follow-up depressed, with another 4.4% (SD 15.0%; median 0%) of the time spent with subthreshold depressive symptoms. Participants who experienced at least one episode of depression spent 28.7% (SD 31.2%; median 14%) of the time clinically depressed.

The remaining 59.5% of the episodes were manic/mixed or hypomanic in nature. Only 11.4% of respondents had no such recurrences, and 41.5% had two or more episodes. Time spent in mania/hypomania/mixed states was 16.4% of the follow-up period on average (SD 24.8%; median 6.4%). Sixteen respondents (12.7%) had at least one switch from depression to mania/hypomania.

With regard to psychotic episodes, 89.4% had at least one episode during the follow-up. Overall, patients experienced psychosis during 17.5% (SD 28%; median 5.3%) of the follow-up time. At the 24-month consensus diagnosis meeting, 17 participants (13.5%) were given a non-bipolar disorder diagnosis, eight of which included a diagnosis of schizophrenia spectrum disorders.

Three participants died within the four-year time frame (i.e., one from homicide, one from a motor vehicle accident, and one from AIDS). There were no completed suicides.

As seen in Table 2, the correlations among the four-year clinical outcome variables (percent time ill after discharge; number of discrete depressive, manic, and psychotic episodes; and GAF) were moderate for the most part. Specifically, the median absolute value of the correlations was $r = 0.24$, with coefficients ranging from $r = |0.04|$ (GAF and manic episodes) to $r = |0.51|$ (manic and psychotic episodes; $p < 0.001$) (Table 2). The correlation between percent time in medication treatment and the number of rehospitalizations was 0.19 ($p < 0.05$).

Predicting four-year outcomes from baseline characteristics

Bivariate analyses revealed several baseline prognostic factors for each outcome (Table 3). Not surprisingly, different risk factors were associated with different outcome variables. Good prognostic factors for four-year GAF were absence of childhood psychopathology, absence of Schneiderian symptoms, and better GAF prior to baseline. Longer percent time ill was predicted by being discharged from index hospitalization on an antidepressant, childhood psychopathology, higher HAM-D scores, and presence of Schneiderian symptoms. Number of subsequent depressive episodes was associated with being discharged on antidepressant medication, higher HAM-D scores, lower BPRS excitement scores, family history of mania, and discharge on a combination of an antipsychotic plus a mood stabilizer medication. There were relatively few prognostic factors for manic episodes (more severe hallucinations, higher GAF), and psychotic episodes (more severe paranoid and Schneiderian symptoms, and younger age).

The percent time in treatment was predicted by medication at discharge (antidepressant, antipsychotic, and antipsychotic plus mood stabilizer) as well as more severe negative

symptoms and lower BPRS excitement score. Finally, rehospitalization was associated with more severe hallucinations and younger age at baseline.

Next, we used multiple regression analyses to identify independent prognostic factors for each clinical outcome at the four-year follow-up. Table 4 shows the significant risk factors for each outcome. The percent of variance explained by the models was greatest for the GAF (25%), depression (22%), and percent time in treatment (18%). Rehospitalization, psychotic and manic episodes proved to be the most difficult outcomes to predict (8%, 9%, 12% of variance, respectively).

Independent predictors of the four-year GAF were absence of childhood psychopathology and absence of Schneiderian symptoms. Participants with both of these characteristics were estimated to have a four-year GAF (best month of past year) of 75.3 (intercept). We also estimated an independent effect of each prognostic factor (unstandardized *B*) and by adding it to the value of the intercept, obtained the expected outcome for patients with that particular risk factor. Schneiderian symptoms of maximal severity observed at baseline independently predicted the GAF of 60.1. A history of childhood psychopathology was associated with a GAF of 66.4, and this effect was primarily due to the history of behavioral disorders.

Percent time ill over the four-year interval was linked to similar prognostic factors, namely Schneiderian symptoms and childhood psychopathology. Discharge from index hospitalization on antidepressants was a novel contributor. Subjects who lacked all of these risk factors were ill only for 13.2% of the follow-up (Table 3). Very severe Schneiderian symptoms were estimated to result in much longer illness (51.5% of the interval), and childhood psychopathology increased illness length to 30.7%; each reflects an independent effect of the corresponding variable. Antidepressants were rarely prescribed, but discharge on these medications was associated with longer illness duration (42.9% of the interval), largely due to ongoing depression.

The number of depressive episodes over the follow-up was associated with family history of depression, discharge on antidepressant medication, and baseline depression severity (HAM-D total score). Individuals without any of these risk factors experienced very few depressive episodes (0.1 on average). Positive family history of depression independently increased this to 0.7 episodes, while antidepressants predicted 1.2 episodes. Individuals with the greatest depression severity at admission were estimated to suffer 1.6 episodes, usually protracted ones.

The number of manic episodes was forecasted by good functioning prior to admission and severity of hallucinations at the index hospitalization. Patients with average functioning (GAF of 70 in this sample) who were not suffering from hallucinations experienced 1.4 episodes during the follow-up. Excellent functioning was estimated to increase this to 1.9 episodes and very severe hallucinations to 3.0 episodes.

The number of subsequent psychotic episodes was associated with younger age and paranoid symptoms. A 30-year-old, nonparanoid participant was estimated to experience 1.1 episodes. First admission by subjects in their late 50’s decreased this to 0.6 episodes, whereas, severe paranoid symptoms increased to 1.9 episodes.

Percent time in medication treatment was associated with the absence of manic symptomatology at baseline (BPRS excitement) and the type of medication prescribed at discharge. Those who were not prescribed these medications and were not manic spent 53.9% of the follow-up in treatment. Severe mania at admission was associated with much shorter treatment duration (18.8% of the interval). Longer treatment duration was forecasted

by discharge on antidepressants (85.4% of the follow-up in treatment) or on a combination of antipsychotic and mood stabilizing drugs (73.7%).

Rehospitalization was also associated with younger age and severity of hallucinations at baseline. A 30-year-old participant who was free from hallucinations was estimated to be rehospitalized once over the four years. According to the model, participants in their late 50's were almost never rehospitalized (0.1 times), and very severe hallucinations predicted 2.8 rehospitalizations.

Discussion

In this report of a county-wide sample of people hospitalized with a first episode of psychosis and given a research diagnosis of bipolar disorder (mania/mixed mania in 93% of cases) at initial assessment, we found that more than half returned to their previous levels of function and had a level of function on the GAF of 70 or more at four-year follow-up.

Different baseline factors predicted different outcomes, but four of the originally hypothesized factors emerged as particularly important: psychotic symptoms (Schneiderian symptoms, hallucinations and paranoia), depressive phenomenology, childhood psychopathology, and age at baseline.

Schneiderian symptoms were associated with lower global functioning and more time ill. Hallucinations were associated with manic recurrence, rehospitalization, and percent time in treatment. Paranoia was associated with number of psychotic episodes but not function per se.

Depressive phenomenology (either the HAM-D score at baseline interview or being discharged from index hospitalization on an antidepressant) anticipated depressive episode recurrence, percent time ill, and percent time in treatment. Finally, childhood psychopathology and lower GAF score the year prior to index hospitalization were associated with poorer overall functioning at follow-up and greater time ill (childhood psychopathology), but it was also associated with less mania recurrence. Younger age at baseline was associated with number of psychotic episodes and rehospitalizations.

Mood incongruent psychotic symptoms contributed little to the outcome variables we examined. Although the presence of mood incongruent symptoms during the initial psychosis appears to bode ill for outcome in some studies (9, 17, 38, 39), not all follow-up studies have confirmed the finding (11, 40–42), including the current one. There are two possible explanations for the seeming paradox that mood incongruent symptoms generally did not predict a poor outcome, while a subset of them (Schneiderian symptoms) did. The first is that the mood incongruence of psychosis is less meaningful than the features of psychosis that compose it. In this sample, paranoia (persecutory delusions) was the most common *mood incongruent* symptom and as these data reveal, paranoia has little to contribute to outcome other than the number of future psychotic episodes. Although persecutory delusions are commonly associated with mania, according to DSM-IV, they are considered mood incongruent. By contrast, Schneiderian symptoms (basically bizarre delusions), which are not frequent in bipolar disorder but still occur (43), suggest a more protracted course. Indeed, just as they portend a poorer outcome in schizophrenia (44) their presence independently lowered the four-year GAF by 15 points.

A second possible explanation is that mood incongruent psychotic symptoms contribute to specific aspects of outcome. Thus, residential (10) and occupational status (26) were specifically affected in those studies, whereas global functioning was considered in the present report.

Unlike samples from the collaborative depression study (18) and the hospitalized, early episode sample reported by Baldassarini and colleagues (45), the SCMHP sample was mostly comprised of patients with a predominantly psychotic manic presentation and a subsequent manic course. This remained true even if *mixed episodes* were counted into the depressive rather than mania spectrum. Consistent with studies that report high rates of depressive morbidity, however, we found greater number of depressive episodes to be associated with both longer time ill and in medication treatment during follow-up. Additionally, subjects who switched directly from depression to mania at least once also spent more time over follow-up with symptoms (59). Greater depression severity at admission, antidepressant treatment at index hospital discharge, and family history of depression predicted a depressive course. In terms of percent time ill, the major difference between the Suffolk County sample and others is that 71% had no (or only one) depressive episode over the ensuing four years and subthreshold depressive symptoms were also rare.

Mania was more difficult to predict in a sample of people who were already psychotic at admission. Frequent mania recurrence was associated only with good premorbid function (as indicated by a high GAF score for the year prior to baseline) and hallucinations at index episode. Other studies, too, have found mania to be difficult to predict from the phenomenologic variables studied (47, 48). The fact that mania (unlike depression or psychosis) recurrence was also associated with better premorbid functioning suggests again that bipolar I disorder with prominent mania, rather than depression, while severely disruptive during illness, may carry less long term disability than depression-oriented bipolar disorder.

Angst et al. (49) examined the heterogeneity of bipolar disorder and hypothesized that patients hospitalized for both mania and depression might represent a different group from those hospitalized for mania only. He and others have concluded that there were enough differences to keep these putative subtypes separate (49–54). For instance, psychosis was associated with a predominant manic course (18, 50, 55–57) while percent time ill was associated with a predominantly depressive course (18, 45, 46, 48, 50, 58, 60).

Insofar as childhood psychopathology is likely a proxy for premorbid adjustment, we found comparatively poorer function prior to onset of bipolar disorder to be an important predictor of outcomes. Poor premorbid function has been studied much more extensively in schizophrenia than bipolar disorder (61–63). The former condition is considered to be neurodevelopmental and impaired cognitive processing and its effect on function has been demonstrated frequently (64–66). The neurodevelopmental status of bipolar disorder is more controversial, although there are data to suggest neuropsychological changes occur as a result of having episodes of mania and depression (57, 68–71). Although cormorbid externalizing disorders in early onset bipolar disorder have been found repeatedly in child psychiatry studies (see 72 for a review), and neuropsychological problems resulting from those conditions are well recognized (73, 74), the question of pre-existing childhood psychopathology as at least a contributor to outcome in adult bipolar studies has been addressed only occasionally (22, 75, 76). Comorbid childhood psychopathology contributed substantially to the GAF at both the 24-month follow-up (22), and now at the 48-month follow-up. Whether childhood psychopathology contributes independently to outcome, or indirectly via executive function problems with which it presents, needs further study. More specifically, childhood externalizing disorders are strongly associated with adult antisocial and other personality disorders which themselves have a negative impact on outcome (77–79).

Younger age of onset has traditionally been associated with a worse outcome in bipolar disorder (80–84). These data often address time to admission and relapse. Data from our

sample also support longer time to remission and shorter time to relapse (22, 85) for young onset respondents. For variables examined in this study, however, age at baseline per se (which correlated 0.73 with age of onset) was associated only with increased number of rehospitalizations and more psychotic episodes. Consistent with previous reports at 24-month follow-up (22), the presence of child psychopathology prior to onset of mood disorder was more predictive of functioning and time ill than age of onset. We speculate, therefore, younger age of onset and worse outcome found in other studies may have been associated with childhood psychopathology, rather than the age of onset of bipolar disorder itself.

The Suffolk County study and its design have several limitations. Although the Suffolk County study is as close to a representative sample as has been studied, not every bipolar disorder respondent consented to be in the study, and not every bipolar disorder respondent was followed at each time-point, face-to-face, through the four-year period. Nevertheless, we were able to follow-up 126 of 133 respondents. Our sample differs from those of other studies in that respondents were relatively early in their course of illness. Their mean age at four-year follow-up was about 33 years, a decade younger than most samples of individuals with bipolar disorder. The presence of psychotic symptoms at the index admission also makes respondents in our sample different from outpatient and some inpatient bipolar samples in which psychosis is less prevalent.

We did not complete weekly ratings of mood and, thus, probably missed some subthreshold symptoms. Our extensive collection of records and data from informants make it unlikely that we missed major episodes, however, and if subthreshold symptoms were occurring, they did not appear to interfere with function. In addition, our measure of mania severity was based on a single item on the BPRS. A mania rating scale was added only at the two-year point, because initially we did not expect bipolar disorder to be prevalent in a cohort with psychosis and thus did not include a more rigorous assessment of mania severity at baseline. We also chose to consider schizoaffective mania as separate from bipolar I disorder mania and those respondents received that diagnosis because of their clinical presentation at baseline. Although we assessed substance abuse, it has not proven to be a significant predictor of outcome in our population and was not included in this report. Moreover, the only anxiety disorders captured by the baseline SCID were obsessive compulsive disorder and panic disorder, and their rates were less than 20% in the bipolar sample (86). Hence we could not adequately address comorbidity as a predictor of outcome.

This paper defined the sample based on the initial research diagnosis rather than longitudinal diagnosis, which would be more accurate. For instance, at the two-year follow-up consensus diagnosis meeting, 123 of the 126 participants were rediagnosed, and 99 (78.6%) kept their original diagnosis of definite bipolar disorder, another eight (6.3%) had probable bipolar disorder, eight (6.3%) had schizophrenia spectrum disorders, and the remainder had other psychoses. We chose baseline diagnosis to ensure that analyses were comparable to other studies of outcome in bipolar disorder and were relevant to clinical care. Lastly, the sample size was moderate, which allowed us to detect only substantial effects and perhaps miss more subtle associations.

In conclusion, the findings from this four-year follow-up of early episode bipolar I disorder patients supports the distinction of a predominantly manic versus depressive subtype of bipolar I disorder. Within the realm of psychotic symptoms, Schneiderian delusions portend a worse outcome. Childhood psychopathology has greater prognostic value than age of onset. At the 10-year follow-up of this sample, we may be better able to discern how informative the identified risk factors were over the longer term of the study.

Acknowledgments

This study was funded by NIMH Grant 44801. The creation of the medications chronology dataset was funded in part by a grant from Eli Lilly & Co.

References

1. Carlson GA, Kotin J, Davenport YB, Adland M. Follow-up of 53 bipolar manic-depressive patients. Br J Psychiatry. 1974; 124:134–139. [PubMed: 4825659]
2. Carlson GA, Davenport YB, Jamison K. A comparison of outcome in adolescent- and later-onset bipolar manic-depressive illness. Am J Psychiatry. 1977; 134:919–922. [PubMed: 879359]
3. Brown AS, Varma VK, Malhotra S, Jiloha RC, Conover SA, Susser ES. Course of acute affective disorders in a developing country setting. J Nerv Ment Dis. 1998; 186:207–213. [PubMed: 9569888]
4. Conus P, Cotton S, Abdel-Baki A, Lambert M, Berk M, McGorry PD. Symptomatic and functional outcome 12 months after a first episode of psychotic mania: barriers to recovery in a catchment area sample. Bipolar Disord. 2006; 8:221–231. [PubMed: 16696823]
5. Montoya A, Tohen M, Vieta E, Casillas M, Chacón F, Polavieja P, Gilaberte I. Functioning and symptomatic outcomes in patients with bipolar I disorder in syndromal remission: a 1-year, prospective, observational cohort study. J Affect Disord. 2010; 127:50–57. [PubMed: 20557947]
6. Tohen M, Hennen J, Zarate CM Jr, et al. Two-year syndromal and functional recovery in 219 cases of first-episode major affective disorder with psychoticfeatures. Am J Psychiatry. 2000; 157:220–228. [PubMed: 10671390]
7. Tsuang MT, Woolson RF, Fleming JA. Long-term outcome of major psychoses. I. Schizophrenia and affective disorders compared with psychiatrically symptom-free surgical conditions. Arch Gen Psychiatry. 1979; 36:1295–1301. [PubMed: 496548]
8. Rosen LN, Rosenthal NE, Van Dusen PH, Dunner DL, Fieve RR. Age at onset and number of psychotic symptoms in bipolar I and schizo-affective disorder. Am J Psychiatry. 1983; 140:1523–1524. [PubMed: 6625008]
9. Tohen M, Waternaux CM, Tsuang MT. A 4 year prospective follow up of 75 patients utilizing survival analysis. Arch Gen Psychiatry. 1990; 47:1106–1111. [PubMed: 2244795]
10. Tohen M, Tsuang MT, Goodwin DC. Prediction of outcome in mania by mood-congruent or mood-incongruent psychotic features. Am J Psychiatry. 1992; 149:1580–1584. [PubMed: 1415828]
11. Strakowski SM, Williams JR, Sax KW, Fleck DE, DelBello MP, Bourne ML. Is impaired outcome following a first manic episode due to mood-incongruent psychosis? J Affect Disord. 2000; 61:87–94. [PubMed: 11099745]
12. Coryell W, Leon AC, Turvey C, Akiskal HS, Mueller T, Endicott J. The significance of psychotic features in manic episodes: a report from the NIMH collaborative study. J Affect Disord. 2001; 67:79–88. [PubMed: 11869754]
13. Van Riel WG, Vieta E, Martinez-Aran A, Haro JM, Bertsch J, Reed C, Van Os J. Chronic mania revisited: factors associated with treatment non-response during prospective follow-up of a large European cohort (EMBLEM). World J Biol Psychiatry. 2008; 9:313–320. [PubMed: 18949649]
14. González-Pinto A, van Os J, Peralta V, et al. The role of age in the development of Schneiderian symptoms in patients with a first psychotic episode. Acta Psychiatr Scand. 2004; 109:264–268. [PubMed: 15008799]
15. Goldberg JE, Harrow M, Grossman JS. Course and outcome in bipolar affective disorder: a longitudinal follow-up study. Am J Psychiatry. 1995; 152:379–384. [PubMed: 7864263]
16. Keck PE Jr, McElroy SL, Strakowski SM, et al. 12-month outcome of patients with bipolar disorder following hospitalization for a manic or mixed episode. Am J Psychiatry. 1998; 155:646–652. [PubMed: 9585716]
17. Harrow M, Goldberg JF, Grossman LS, Meltzer HY. Outcome in manic disorders. A naturalistic follow-up study. Arch Gen Psychiatry. 1990; 47:665–671. [PubMed: 2113802]

18. Judd LL, Akiskal HS, Schettler PJ, et al. The long-term natural history of the weekly symptomatic status of bipolar I disorder. Arch Gen Psychiatry. 2002; 59:530–537. [PubMed: 12044195]
19. 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. [PubMed: 10839338]
20. Carlson GA, Bromet EJ, Sievers S. Phenomenology and outcome of subjects with early-and adult-onset psychotic mania. Am J Psychiatry. 2000; 157:213–219. [PubMed: 10671389]
21. Coryell W, Turvey C, Endicott J, et al. Bipolar I affective disorder: predictors of outcome after 15 years. J Affect Disord. 1998; 50:109–116. [PubMed: 9858070]
22. Carlson GA, Bromet EJ, Driessens C, Mojtabai R, Schwartz JE. Age at onset, childhood psychopathology, and 2-year outcome in psychotic bipolar disorder. Am J Psychiatry. 2002; 159:307–309. [PubMed: 11823277]
23. Neria Y, Bromet EJ, Carlson GA, Naz B. Assaultive trauma and illness course in psychotic bipolar disorder: findings from the Suffolk county mental health project. Acta Psychiatr Scand. 2005; 111:380–383. [PubMed: 15819732]
24. Fennig S, Bromet EJ, Karant MT, Ram R, Jandorf L. Mood-congruent versus mood-incongruent psychotic symptoms in first-admission patients with affective disorder. J Affect Disord. 1996; 37:23–29. [PubMed: 8682975]
25. Harrow M, Grossman LS, Herbener ES, Davies EW. Ten-year outcome: patients with schizoaffective disorders, schizophrenia, affective disorders and mood-incongruent psychotic symptoms. Br J Psychiatry. 2000; 177:421–426. [PubMed: 11059995]
26. Judd LL, Akiskal HS, Schettler PJ, et al. Psychosocial disability in the course of bipolar I and II disorders: a prospective, comparative, longitudinal study. Arch Gen Psychiatry. 2005; 62:1322–1330. [PubMed: 16330720]
27. Bromet EJ, Schwartz JE, Fennig S, et al. The epidemiology of psychosis: the Suffolk County Mental Health Project. Schizophr Bull. 1992; 18:243–255. [PubMed: 1621071]
28. Spitzer R, Williams J, Gibbon M, First M. The Structured Clinical Interview for DSM III-R (SCID). I: History, rationale, and description. Arch Gen Psychiatry. 1992; 49:624–629. [PubMed: 1637252]
29. Fennig S, Craig T, Lavelle J, Kovasznay B, Bromet EJ. Best-estimate versus structured interview-based diagnosis in first-admission psychosis. Compr Psychiatry. 1994; 35:341–348. [PubMed: 7995025]
30. Brown AS, Susser ES, Jandorf L, Bromet EJ. Social class of origin and cardinal symptoms of schizophrenic disorders over the early illness course. Soc Psychiatry Psychiatr Epidemiol. 2000; 35:53–60. [PubMed: 10784367]
31. American Psychiatry Association. DSM IV: Diagnostic and Statistical Manual of Mental Disorders. Washington, DC: 1994.
32. Andreasen NC, Endicott J, Spitzer RL, Winokur G. The family history method using diagnostic criteria. Reliability and validity. Arch Gen Psychiatry. 1977; 34:1229–1235. [PubMed: 911222]
33. Andreasen, NC. The Scale for the Assessment of Negative Symptoms (SANS). Iowa City: The University of Iowa; 1983.
34. Kotov R, Guey LT, Bromet EJ, Schwartz JE. Smoking in schizophrenia: diagnostic specificity, symptom correlates, and illness severity. Schizophr Bull. 2010; 36:173–181. [PubMed: 18562340]
35. Andreasen, NC. The Scale for the Assessment of Positive Symptoms (SAPS). Iowa City: The University of Iowa; 1984.
36. Woerner M, Manuzza S, Kane J. Anchoring the BPRS: an aid to improved reliability. Psychopharmacol Bull. 1988; 24:112–124. [PubMed: 3387514]
37. Hamilton M. A rating scale for depression. J Neuro Neurosurg Psychiatry. 1960; 23:56–62.
38. Coryell W, Tsuang MT. Major depression with mood-congruent or mood-incongruent psychotic features: outcome after 40 years. Am J Psychiatry. 1985; 142:479–482. [PubMed: 3976922]
39. Grossman LS, Harrow M, Sands JR. Features associated with thought disorder in manic patients at 2–4-year follow-up. Am J Psychiatry. 1986; 143:306–311. [PubMed: 3953863]

40. Conus P, Abdel-Baki A, Harrigan S, Lambert M, McGorry PD. Schneiderian first rank symptoms predict poor outcome within first episode manic psychosis. J Affect Disord. 2004; 81:259–268. [PubMed: 15337330]
41. Gaudiano BA, Uebelacker LA, Miller IW. Course of illness in psychotic mania: is mood incongruence important? J Nerv Ment Dis. 2007; 195:226–232. [PubMed: 17468682]
42. Keck PE Jr, McElroy SL, Havens JR, et al. Psychosis in bipolar disorder: phenomenology and impact on morbidity and course of illness. Compr Psychiatry. 2003; 44:263–269. [PubMed: 12923703]
43. Ihara K, Morgan C, Fearon P, et al. The prevalence, diagnostic significance and demographic characteristics of Schneiderian first-rank symptoms in an epidemiological sample of first-episode psychoses. Psychopathology. 2009; 42:81–91. [PubMed: 19225242]
44. Rosen C, Grossman LS, Harrow M, Bonner-Jackson A, Faull R. Diagnostic and prognostic significance of Schneiderian first-rank symptoms: a 20-year longitudinal study of schizophrenia and bipolar disorder. Compr Psychiatry. 2011; 52:126–131. [PubMed: 21295217]
45. Baldessarini RJ, Salvatore P, Khalsa H-MK, et al. Morbidity in 303 first-episode bipolar I disorder patients. Bipolar Disord. 2010; 12:264–270. [PubMed: 20565433]
46. Judd LL, Akiskal HS, Schettler PJ, et al. A prospective investigation of the natural history of the long-term weekly symptomatic status of bipolar II disorder. Arch Gen Psychiatry. 2003; 60:261–269. [PubMed: 12622659]
47. Coryell W, Keller M, Lavori P, Endicott J. Affective syndromes, psychotic features, and prognosis. II. Mania. Arch Gen Psychiatry. 1990; 47:658–662. [PubMed: 2360859]
48. Tohen M, Zarate CA Jr, Hennen J, et al. The McLean-Harvard First-Episode Mania Study: prediction of recovery and first recurrence. Am J Psychiatry. 2003; 160:2099–2107. [PubMed: 14638578]
49. Angst J, Gerber-Werder R, Zuberbühler HU, Gamma A. Is bipolar I disorder heterogeneous? Eur Arch Psychiatry Clin Neurosci. 2004; 254:82–91. [PubMed: 15146337]
50. Colom F, Vieta E, Daban C, Pacchiarotti I, Sánchez-Moreno J. Clinical and therapeutic implications of predominant polarity in bipolar disorder. J Affect Disord. 2006; 93:13–17. [PubMed: 16650901]
51. Calabrese JR, Vieta E, El-Mallakh R, et al. Mood state at study entry as predictor of the polarity of relapse in bipolar disorder. Biol Psychiatry. 2004; 56:957–963. [PubMed: 15601606]
52. Quitkin FM, Rabkin JG, Prien RF. Bipolar disorder: are there manic-prone and depressive-prone forms? J Clin Psychopharmacol. 1986; 6:167–172. [PubMed: 3711367]
53. Perlis RH, Ostacher MJ, Patel JK, et al. Predictors of recurrence in bipolar disorder: primary outcomes from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). Am J Psychiatry. 2006; 163:217–224. [PubMed: 16449474]
54. Rosa AR, Andreazza AC, Kunz M, et al. Predominant polarity in bipolar disorder: diagnostic implications. J Affect Disord. 2008; 107:45–51. [PubMed: 17804081]
55. Post RM, Denicoff KD, Leverich GS, et al. Morbidity in 258 bipolar outpatients followed for 1 year with daily prospective ratings on the NIMH life chart method. J Clin Psychiatry. 2003; 64:680–690. [PubMed: 12823083]
56. Daban C, Colom F, Sánchez-Moreno J, García-Amador M, Vieta E. Clinical correlates of first-episode polarity in bipolar disorder. Compr Psychiatry. 2006; 47:433–437. [PubMed: 17067865]
57. Martínez-Arán A, Vieta E, Torrent C, et al. Functional outcome in bipolar disorder: the role of clinical and cognitive factors. Bipolar Disord. 2007; 9:103–113. [PubMed: 17391354]
58. Solomon DA, Leon AC, Coryell WH, et al. Longitudinal course of bipolar I disorder: duration of mood episodes. Arch Gen Psychiatry. 2010; 67:339–347. [PubMed: 20368510]
59. Carlson GA, Finch SJ, Fochtmann LJ, et al. Antidepressant-associated switches from depression to mania in severe bipolar disorder. Bipolar Disord. 2007; 9:851–859. [PubMed: 18076534]
60. Joffe RT, MacQueen GM, Marriott M, Young LT. A prospective, longitudinal study of percentage of time spent ill in patients with bipolar I or bipolar II disorders. Bipolar Disord. 2004; 6:62–66. [PubMed: 14996142]
61. Forty L, Jones L, Jones I, et al. Polarity at illness onset in bipolar I disorder and clinical course of illness. Bipolar Disord. 2009; 11:82–88. [PubMed: 19133970]

62. Cannon-Spoor HE, Potkin SG, Wyatt RJ. Measurement of premorbid adjustment in chronic schizophrenia. Schizophr Bull. 1982; 8:470–484. [PubMed: 7134891]
63. Isohanni M, Isohanni I, Koponen H, et al. Developmental precursors of psychosis. Curr Psychiatry Rep. 2004; 6:168–175. [PubMed: 15142469]
64. Shapiro DI, Marenco S, Spoor EH, Egan MF, Weinberger DR, Gold JM. The Premorbid Adjustment Scale as a measure of developmental compromise in patients with schizophrenia and their healthy siblings. Schizophr Res. 2009; 112:136–142. [PubMed: 19410430]
65. Keshavan MS, Diwadkar VA, Montrose DM, Rajarethinam R, Sweeney JA. Premorbid indicators and risk for schizophrenia: a selective review and update. Schizophr Res. 2005; 79:45–57. [PubMed: 16139479]
66. Leeson VC, Barnes TR, Hutton SB, Ron MA, Joyce EM. IQ as a predictor of functional outcome in schizophrenia: a longitudinal, four-year study of first-episode psychosis. Schizophr Res. 2009; 107:55–60. [PubMed: 18793828]
67. van Winkel R, Myin-Germeys I, Delespaul P, Peuskens J, De Hert M, van Os J. Premorbid IQ as a predictor for the course of IQ in first onset patients with schizophrenia: a 10-year follow-up study. Schizophr Res. 2006; 88:47–54. [PubMed: 16904292]
68. Mann-Wrobel MC, Carreno JT, Dickinson D. Meta-analysis of neuropsychological functioning in euthymic bipolar disorder: an update and investigation of moderator variables. Bipolar Disord. 2011; 13:334–342. [PubMed: 21843273]
69. Goodwin GM, Martínez-Arán A, Glahn DC, Vieta E. Cognitive impairment in bipolar disorder: neurodevelopment or neurodegeneration? An ECNP expert meeting report. Eur Neuropsychopharmacol. 2008; 18:787–793. [PubMed: 18725178]
70. Rabinowitz J, Haim R, Reichenberg A, Weiser M, Kaplan Z, Davidson M, Hafner H. Association between functioning in adolescence prior to first admission for schizophrenia and affective disorders and patterns of hospitalizations thereafter. Schizophr Res. 2005; 73:185–191. [PubMed: 15653261]
71. Robinson LJ, Ferrier IN. Evolution of cognitive impairment in bipolar disorder: a systematic review of cross-sectional evidence. Bipolar Disord. 2006; 8:103–116. [PubMed: 16542180]
72. Toulopoulou T, Quraishi S, McDonald C, Murray RM. The Maudsley Family Study: premorbid and current general intellectual function levels in familial bipolar I disorder and schizophrenia. J Clin Exp Neuropsychol. 2006; 28:243–259. [PubMed: 16484096]
73. Carlson GA, Meyer SE. Phenomenology and diagnosis of bipolar disorder in children, adolescents, and adults: complexities and developmental issues. Dev Psychopathol. 2006; 18:939–969. [PubMed: 17064424]
74. Doyle AE. Executive functions in attention-deficit/hyperactivity disorder. J Clin Psychiatry. 2006; 67:21–26. [PubMed: 16961426]
75. Kyte ZA, Carlson GA, Goodyer IM. Clinical and neuropsychological characteristics of child and adolescent bipolar disorder. Psychol Med. 2006; 36:1197–1211. [PubMed: 16566850]
76. Klassen LJ, Katzman MA, Chokka P. Adult ADHD and its comorbidities, with a focus on bipolar disorder. J Affect Disord. 2010; 124:1–8. [PubMed: 19683348]
77. Rydén E, Thase ME, Stråht D, Aberg-Wistedt A, Bejerot S, Landén M. A history of childhood attention-deficit hyperactivity disorder (ADHD) impacts clinical outcome in adult bipolar patients regardless of current ADHD. Acta Psychiatr Scand. 2009; 120:239–246. [PubMed: 19426162]
78. Goldberg JF, Garno JL. Age at onset of bipolar disorder and risk for comorbid borderline personality disorder. Bipolar Disord. 2009; 11:205–208. [PubMed: 19267703]
79. Goldstein BI, Levitt AJ. A gender-focused perspective on health service utilization in comorbid bipolar I disorder and alcohol use disorders: results from the national epidemiologic survey on alcohol and related conditions. J Clin Psychiatry. 2006; 67:925–932. [PubMed: 16848652]
80. Perlis RH, Miyahara S, Marangel I, et al. Long-term implications of early onset in bipolar disorder: data from the first 1000 participants in the systematic treatment enhancement program for bipolar disorder (STEP-BD). Biol Psychiatry. 2004; 55:875–881. [PubMed: 15110730]
81. Ernst CI, Goldberg JF. Clinical features related to age at onset in bipolar disorder. J Affect Disord. 2004; 82:21–27. [PubMed: 15465573]

82. Lin PI, McInnis MC, Potash JR, et al. Clinical correlates and familial aggregation of age of onset in bipolar disorder. Am J Psychiatry. 2006; 163:240–246. [PubMed: 16449477]

83. Leverich GS, Post RM, Keck PE Jr, et al. The poor prognosis of childhood-onset bipolar disorder. J Pediatr. 2007; 150:485–490. [PubMed: 17452221]

84. Lopez P, Mosquera F, de León J, et al. Suicide attempts in bipolar patients. J Clin Psychiatry. 2001; 62:963–966. [PubMed: 11780877]

85. Bromet EJ, Finch SJ, Carlson GA, et al. Time to remission and relapse after the first hospital admission in severe bipolar disorder. Soc Psychiatry Psychiatr Epidemiol. 2005; 40:106–113. [PubMed: 15685401]

86. Craig T, Hwang MY, Bromet EJ. Obsessive-compulsive and panic symptoms in patients with first-admission psychosis. Am J Psychiatry. 2002; 159:592–598. [PubMed: 11925297]

Table 1

Study characteristics of cohort hospitalized with bipolar disorder with psychotic features (N=126)

Variable	Statistic
Baseline characteristics: dichotomous, n (%)	
Gender: male	65 (51.2)
Caucasian	107 (85.0)
SES of head of house: blue collar	36 (40.9)
Marital status: never married	75 (59.1)
Childhood psychopathology	90 (72.6)
Baseline substance abuse	41 (32.3)
Manic episode	101 (79.5)
Mixed/rapid cycling episode	17 (13.4)
Bipolar depression	8 (6.3)
Family history of mania	22 (19.0)
Family history of depression	52 (44.8)
Mood incongruent psychosis	58 (45.7)
Discharged on AP	98 (77.2)
Discharged on AD	8 (6.3)
Discharged on MS	64 (50.4)
Discharged on AP and MS	47 (37.3)
Baseline characteristics: continuous, mean (SD)	
Age at baseline, years	29.3 (9.8)
Age of onset of mood disorder, years	25.4 (8.8)
Length of follow up, weeks	201.2 (22.2)
GAF best in 12 months preceding hospitalization	68.5 (9.5)
HAM-D total score	11.8 (6.4)
BPRS excitement	2.5 (1.5)
SANS	8.6 (9.2)
SAPS-D[a]	9.9 (6.4)
SAPS-P[b]	10.0 (7.4)
SAPS Schneiderian	1.1 (2.4)
SAPS hallucinations	1.7 (2.4)
SAPS paranoid	3.6 (2.6)
SAPS manic delusions	2.8 (2.6)
Four-year outcomes, mean (SD)	
GAF for best month of past year	67.3 (13.1)
Percent time ill	31.1 (34.1)
Percent time in medication treatment	54.6 (37.2)
No. depressive episodes, n (%)	

Variable	Statistic
0	43 (35.0)
1	45 (36.6)
2+	35 (28.5)
No. manic episodes, n (%)	
0	14 (11.4)
1	58 (47.2)
2+	51 (41.5)
No. psychotic episodes, n (%)	
0	13 (10.6)
1	70 (56.9)
2+	40 (32.5)
No. rehospitalizations after baseline interview, n (%)	
0	67 (52.8)
1	20 (15.7)
2+	40 (31.5)

SES = socioeconomic status; AP = antipsychotic; AD = antidepressant; MS = mood stabilizer; GAF = Global Assessment of Functioning; HAM-D = Hamilton Depression Rating Scale; BPRS = Brief Psychiatric Rating Scale; SANS = Scale for the Assessment of Negative Symptoms; SAPS = Scale for the Assessment of Positive Symptoms.

[a] Average of 13 individuals ratings of disorganization (e.g., thought disorder, bizarre behavior).

[b] Average of 16 individual ratings of psychosis (e.g., delusions, hallucinations).

Table 2

Correlations among outcomes measures

GAF outcomes	Four-year GAF	Percent time ill	No. depressive episodes	No. manic episodes	No. psychotic episodes	Percent time in treatment
Percent time ill	−0.49					
No. depressive episodes	−0.06	0.24				
No. manic episodes	−0.04	0.11	0.39			
No. psychotic episodes	−0.20	0.20	0.31	0.51		
Percent time in treatment	−0.06	0.14	0.40	0.39	0.30	
No. rehospitalizations	−0.26	0.18	0.23	0.26	0.36	0.19

$|r| > 0.15$ are significant at $p < 0.05$. GAF = Global Assessment of Functioning.

Table 3

Bivariate associations between predictors and outcomes[a]

	48-month GAF[b]	Percent time ill[c]	No. depressive episodes[c]	No. manic episodes[c]	No. psychotic episodes[c]	Percent time in treatment[d]	No. rehospitalizations[d]
Continuous predictors, *r*							
Age at baseline	0.02	−0.05	−0.06	−0.14	−0.21[e]	−0.13	−0.21[e]
Age of onset of mood disorder	0.05	−0.06	−0.06	−0.14	−0.13	−0.10	−0.19[e]
GAF best in preceding 12 monthss	0.21[e]	−0.11	0.07	0.22[e]	0.09	0.02	0.07
SANS	−0.18	0.08	0.10	−0.04	0.14	0.28[f]	−0.04
SAPS disorganization	−0.13	0.09	−0.11	−0.02	−0.01	−0.07	−0.12
SAPS Schneiderian	−0.28[g]	0.21[e]	0.02	0.16	0.20[e]	0.04	0.14
SAPS hallucinations	−0.06	0.08	0.04	0.24[f]	0.17	0.06	0.22[e]
SAPS paranoid	−0.11	−0.01	0.07	0.16	0.23[f]	0.17	0.05
SAPS manic delusions	−0.17	0.10	−0.02	0.06	0.17	−0.04	0.11
BPRS excitement	0.01	0.04	−0.20[e]	−0.05	−0.07	−0.28[f]	−0.09
HAM-D	−0.10	0.21[e]	0.28[f]	0.11	0.13	0.15	0.06
Length of follow up, weeks	0.19	−0.12	−0.04	0.15	0.13	−0.02	0.06
Dichotomous predictors, Cohen's *d*							
Gender: male	−0.21	−0.04	−0.34	−0.18	−0.02	−0.18	0.06
SES head of house: blue collar	−0.45	0.11	0.11	−0.09	0.04	−0.09	0.26
Childhood psychopathology: present	−0.68[f]	0.53[e]	0.22	−0.15	−0.02	0.08	0.27
Family history of mania	0.16	−0.06	0.58[e]	0.16	−0.08	0.14	0.10
Family history of depression	0.22	−0.05	0.54[f]	0.03	0.21	0.09	0.01
Mood incongruent psychosis	−0.21	0.34	0.10	0.02	0.16	0.09	0.18
Discharged on AP	−0.16	−0.22	0.41	0.15	0.31	0.48[e]	0.02
Discharged on AD	−0.16	0.64[e]	1.05[e]	0.07	0.24	0.97[f]	0.01
Discharged on MS	0.20	0.14	0.05	−0.13	0.07	0.29	−0.26

	48-month GAF[b]	Percent time ill[c]	No. depressive episodes[c]	No. manic episodes[c]	No. psychotic episodes[c]	Percent time in treatment[d]	No. rehospitalizations[d]
Discharged on AP and MS	0.11	0.17	0.40[e]	0.07	0.19	0.54[f]	−0.09

GAF = Global Assessment of Functioning; SANS = Scale for the Assessment of Negative Symptoms; SAPS = Scale for the Assessment of Positive Symptoms; BPRS = Brief Psychiatric Rating Scale; HAM-D = Hamilton Depression Rating Scale; SES = socioeconomic status; AP = antipsychotic; AD = antidepressant; MS = mood stabilizer.

[a] For continuous variables the measure of association is Pearson's *r*; for dichotomous variables it is Cohen's *d*.

[b] n = 115.

[c] n = 123.

[d] n = 126.

[e] $p < 0.05$.

[f] $p < 0.01$.

[g] $p < 0.001$.

Table 4

Significant baseline predictors from multiple regression analyses[a,b]

Variables	Intercept	Unstandardized *B*	Standardized *B*	*t*	p-value
48-month GAF[c]	75.30				
SAPS Schneiderian		−15.24	−0.24	−2.81	0.006
Childhood psychopathology: present versus none		−8.89	−0.30	−3.47	0.001
Percent time ill[d]	13.18				
SAPS Schneiderian		38.35	0.22	2.49	0.014
Child psychopathology: present versus none		17.50	0.23	2.63	0.010
On AD at first discharge		29.74	0.20	2.20	0.030
No. depressive episodes[e]	0.14				
HAM-D total score		1.50	0.32	3.76	< 0.001
Family history of depression		0.61	0.28	3.30	0.001
On AD at first discharge		1.01	0.21	2.48	0.015
No. manic episodes[f]	1.40				
GAF best in preceding 12 months		0.45	0.22	2.58	0.011
SAPS hallucinations		1.56	0.27	3.08	0.003
No. psychotic episodes[g]	1.12				
Age at baseline, years		−0.54	−0.19	−2.20	0.030
SAPS paranoid		0.80	0.22	2.50	0.014
Percent time in treatment[h]	53.92				
BPRS excitement		−35.10	−0.24	−2.84	0.005
On AD at first discharge		31.46	0.21	2.49	0.014
On AP and MS at first discharge		19.76	0.26	3.14	0.002
No. rehospitalizations[i]	0.95				
Age at baseline, years		−0.81	−0.18	−2.07	0.040
SAPS hallucinations		1.80	0.19	2.22	0.028

GAF = Global Assessment of Functioning; SAPS = Scale for the Assessment of Positive Symptoms; AD = antidepressants; HAM-D = Hamilton Depression Rating Scale; BPRS = Brief Psychiatric Rating Scale; AP = antipsychotics; MS = mood stabilizers.

[a] All analyses controlled for the length of follow-up. Intercepts were computed so that they corresponded to the best scores on all relevant predictors, except for age and GAF (centered at sample averages: 30 years and GAF of 70).

[b] *B* reflects the difference between the highest and lowest scores observed, except for age and GAF as sample averages were used for those variable instead of lowest scores.

[c] $R^2 = 0.25$, $p < 0.001$.

[d] $R^2 = 0.13$, $p = 0.002$.

[e] $R^2 = 0.22$, $p < 0.001$.

[f] $R^2 = 0.12$, $p = 0.001$.

[g] $R^2 = 0.09$, $p = 0.003$.

[h] $R^2 = 0.18$, $p < 0.001$.

[i] $R^2 = 0.08$, $p = 0.006$.