Boundaries of Schizoaffective Disorder
Revisiting Kraepelin

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IMPORTANCE Established nosology identifies schizoaffective disorder as a distinct category with boundaries separating it from mood disorders with psychosis and from schizophrenia. Alternative models argue for a single boundary distinguishing mood disorders with psychosis from schizophrenia (kraepelinian dichotomy) or a continuous spectrum from affective to nonaffective psychosis.

OBJECTIVE To identify natural boundaries within psychotic disorders by evaluating associations between symptom course and long-term outcome.

DESIGN, SETTING, AND PARTICIPANTS The Suffolk County Mental Health Project cohort consists of first-admission patients with psychosis recruited from all inpatient units of Suffolk County, New York (72% response rate). In an inception cohort design, participants were monitored closely for 4 years after admission, and their symptom course was charted for 526 individuals; 10-year outcome was obtained for 413.

MAIN OUTCOMES AND MEASURES Global Assessment of Functioning (GAF) and other consensus ratings of study psychiatrists.

RESULTS We used nonlinear modeling (locally weighted scatterplot smoothing and spline regression) to examine links between 4-year symptom variables (ratio of nonaffective psychosis to mood disturbance, duration of mania/hypomania, depression, and psychosis) and 10-year outcomes. Nonaffective psychosis ratio exhibited a sharp discontinuity—10 days or more of psychosis outside mood episodes predicted an 11-point decrement in GAF—consistent with the kraepelinian dichotomy. Duration of mania/hypomania showed 2 discontinuities demarcating 3 groups: mania absent, episodic mania, and chronic mania (manic/hypomanic >1 year). The episodic group had a better outcome compared with the mania absent and chronic mania groups (12-point and 8-point difference on GAF). Duration of depression and psychosis had linear associations with worse outcome.

CONCLUSIONS AND RELEVANCE Our data support the kraepelinian dichotomy, although the study requires replication. A boundary between schizoaffective disorder and schizophrenia was not observed, which casts further doubt on schizoaffective diagnosis. Co-occurring schizophrenia and mood disorder may be better coded as separate diagnoses, an approach that could simplify diagnosis, improve its reliability, and align it with the natural taxonomy.

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The delineation of schizophrenia (dementia praecox) and psychotic mood disorders (manic-depressive insanity) as 2 distinct entities was one of Emil Kraepelin's seminal contributions to nosology. More than 100 years later, this kraepelinian dichotomy remains highly influential. However, some patients exhibit features of both schizophrenia and psychotic mood disorders, which led Kasanin to propose a new category labeled schizoaffective disorder. Conceptualization of this condition evolved across editions of the DSM from a subtype of schizophrenia to a distinct disorder. DSM-IV defines it as (A) co-occurrence of schizophrenia symptoms and mood episodes, (B) psychosis present for at least 2 weeks in the absence of mood symptoms, and (C) mood episodes present for a substantial portion of illness duration. Thus, DSM-IV elaborates on the kraepelinian dichotomy by adding an intermediate condition, with criterion B defining its boundary with psychotic mood disorder and criterion C with schizophrenia. The key to classifying these disorders is the ratio of nonaffective psychosis to mood disturbance: in psychotic mood disorder, nonaffective psychosis is absent; in schizoaffective disorder, both nonaffective psychosis and mood episodes are prominent; and in schizophrenia, nonaffective psychosis predominates. However, some have argued that these boundaries are artificial and that psychotic disorders fall along a continuous spectrum that ranges from psychotic mood disorder to schizophrenia.

Among diagnostic validators, illness course is of particular interest. Indeed, it was most central to Kraepelin's work because he sought to develop diagnoses that would be diagnostic of future symptoms and functioning (ie, global outcome). Unfortunately, existing longitudinal studies were not designed to answer questions about the natural organization of psychotic disorders. They typically compared outcomes among diagnostic groups: schizophrenia, schizoaffective disorder, and psychotic mood disorder, but such analyses cannot distinguish gradual differences (ie, a continuum) from qualitative changes (ie, natural boundaries). Indeed, in many studies outcome of schizoaffective disorder fell between that of schizophrenia and psychotic mood disorder, which is consistent with both the continuum and 3-disorders models.

Kendell and Brockington proposed a solution to this problem. They examined associations between the spectrum ranging from typical psychotic mood disorder to typical schizophrenia and continuous outcome measures. Their hypothesis was that a natural boundary would manifest as a significant drop in the outcome at some point along the spectrum, whereas a continuum would result in a linear decline. Kendell and Brockington found no evidence of a boundary, but their study was underpowered and analyses were limited to visual inspection of graphs. The latter shortcoming might explain why this technique has not been widely adopted. More recent developments in statistical methods make it possible to test such data for nonlinearity rigorously.

The aim of the present study was to test for the existence of natural boundaries in psychotic disorders using modern statistical methods. We analyzed detailed symptom course data from an epidemiologic cohort of inpatients with psychosis monitored prospectively for 10 years after their first hospitalization. In particular, we examined links between nonaffective psychosis ratio during the first 4 years of the study and outcomes at year 10. The continuum model predicts a linear association, the kraepelinian model predicts a single boundary between psychotic mood disorder and the schizophrenia spectrum, and the DSM-IV model predicts 2 boundaries, one between psychotic mood disorder and schizoaffective disorder and another between schizoaffective disorder and schizophrenia (Supplement [eFigure 1]). In the latter 2 models, differences are expected between groups (eg, low nonaffective psychosis and high nonaffective psychosis), but no association is predicted between nonaffective psychosis and outcome within groups. We constructed statistical models to test these hypotheses. We also used this method to explore natural boundaries within depression and mania.

**Methods**

**Participants**

Data for this study came from the Suffolk County Mental Health Project, an epidemiologic study of first-admission psychosis. Patients were recruited from the 12 psychiatric inpatient units of Suffolk County, New York, between October 1989 and December 1995. Inclusion criteria were first admission, either current or within 6 months; clinical evidence of psychosis; age 15 to 60 years; IQ higher than 70; proficiency with English; and no apparent general medical etiology. The study was approved annually by the institutional review boards of Stony Brook University and the participating hospitals. Treating physicians determined participants’ capacity to provide consent. Written consent was obtained from adults and from parents of patients younger than 18 years.

We initially interviewed 675 participants (72% of referrals); 628 of them met the eligibility criteria. By the 4-year point, 10 participants had died, 29 were untraceable, 41 refused further participation, and 22 provided insufficient information about symptom course; the remaining 526 participants (83.8%) constituted the course sample. Of them, by the 10-year assessment, 27 had died, 28 were untraceable, 41 refused further participation, and 17 provided insufficient outcome information; the remaining 413 participants (78.5%) composed the outcome sample. These samples were very similar to each other and to the total cohort on the study variables (Table 1). The only
significant differences between the course sample and the rest of the cohort (n = 102) were slightly younger age (P = .008) and lower prevalence of other psychoses in the sample (P = .044). The only significant difference between the outcome sample and the rest of the course sample (n = 113) was the slight over-representation of patients with low parental socioeconomic status in the former (P = .008).

### Measures

Face-to-face assessments were conducted by master’s level mental health professionals at baseline, 6-month, 2-year, 4-year, and 10-year follow-up; telephone interviews were performed every 3 months until the 2-year wave and every 6 months until the 4-year wave. Interviewers were blinded to study diagnoses. Medical records and interviews with significant others were also obtained at each major assessment. These detailed data allowed raters to chart symptom course between baseline and year 4. At least half of the interval was documented for everyone in the course sample; 91.7% of them had at least 3.5 years of follow-up data.

Symptom documentation included start and end dates of psychotic, depressive, and manic episodes, each rated separately and defined according to DSM-IV criteria except for duration, which we did not require. Episodes were scored as (1) percentage of the observed interval psychotic, (2) percentage of patients depressed, and (3) percentage of patients manic (including hypomania). Of particular interest was the nonaffective psychosis ratio, scored as percentage of illness psychotic and not in mood episode (illness was defined as mood or psychotic episode), because this ratio defines the diagnostic boundaries of schizoaffective disorder in DSM-IV (especially criterion C).

Overall outcome is particularly relevant to validation of psychotic disorders.1,15,17,18 We examined 3 measures targeting its different aspects: Global Assessment of Symptoms (GAS) indicated overall symptom severity in the best month between the 4-year and 10-year interviews, Global Assessment of Functional Performance (GAF-F) indicated overall social and occupational functioning in the best month between 4-year and 10-year interviews, and Global Assessment of Functioning (GAF) was rated for the best month of the year before the 10-year interview considering both symptoms and functioning. Each measure was rated on a 0 to 90 scale (with 10 anchors specific to that rating) according to the DSM-III-R version of GAF, which was standard at the start of this study. To ensure that results were not influenced by format, we also evaluated the overall rating of psychosocial functioning from the Schedule for Affective Disorders and Schizophrenia (SADS),27 scored as 1, marked chronic condition; 2, moderate chronic condition; 3, mild chronic condition; and 4, complete return to highest functioning. These ratings were made by consensus of study psychiatrists (including L.J.F., E.C., and G.A.C.). Interrater reliability of consensus scores could not be assessed, but reliability of the individual raters was excellent, ranging intra-class r = 0.90-0.94 across outcomes.

Primary DSM-IV diagnosis was formulated at the 2-year point by consensus of 4 or more psychiatrists (including L.J.F. and G.A.C.) using all available information, including Struc-

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### Table 1. Demographic and Clinical Characteristics of the Sample

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total Cohort (N = 628)</th>
<th>Course Sample (n = 526)</th>
<th>Outcomes Sample (n = 413)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at baseline, mean (SD), y</td>
<td>29.7 (9.7)</td>
<td>29.2 (9.5)</td>
<td>29.1 (9.5)</td>
</tr>
<tr>
<td>Male sex</td>
<td>365 (58.1)</td>
<td>299 (56.8)</td>
<td>231 (55.9)</td>
</tr>
<tr>
<td>White race</td>
<td>470 (74.8)</td>
<td>400 (76.0)</td>
<td>313 (75.8)</td>
</tr>
<tr>
<td>SES of family of origin: blue collar</td>
<td>284 (45.2)</td>
<td>236 (44.9)</td>
<td>199 (48.2)</td>
</tr>
<tr>
<td>DSM-IV diagnosis at year 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia/schizophreniform</td>
<td>199 (33.8)</td>
<td>184 (35.1)</td>
<td>145 (35.1)</td>
</tr>
<tr>
<td>Schizoaffective</td>
<td>30 (5.1)</td>
<td>26 (5.0)</td>
<td>21 (5.1)</td>
</tr>
<tr>
<td>Bipolar with psychosis</td>
<td>148 (25.1)</td>
<td>135 (25.8)</td>
<td>112 (27.1)</td>
</tr>
<tr>
<td>MDD with psychosis</td>
<td>104 (17.7)</td>
<td>91 (17.4)</td>
<td>68 (16.5)</td>
</tr>
<tr>
<td>Other psychoses</td>
<td>108 (18.3)</td>
<td>88 (16.8)</td>
<td>67 (16.2)</td>
</tr>
<tr>
<td>Symptom course, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Psychosisb</td>
<td>NA</td>
<td>36.4 (38.4)</td>
<td>37.4 (38.7)</td>
</tr>
<tr>
<td>% Maniab</td>
<td>NA</td>
<td>7.5 (18.6)</td>
<td>8.3 (19.9)</td>
</tr>
<tr>
<td>% Depressionb</td>
<td>NA</td>
<td>24.0 (32.6)</td>
<td>24.5 (32.8)</td>
</tr>
<tr>
<td>% Nonaffective psychosis ratioa</td>
<td>NA</td>
<td>35.7 (43.4)</td>
<td>34.9 (43.0)</td>
</tr>
<tr>
<td>Outcome, mean (SD)d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAF</td>
<td>NA</td>
<td>NA</td>
<td>54.8 (16.2)</td>
</tr>
<tr>
<td>GAF-F</td>
<td>NA</td>
<td>NA</td>
<td>57.5 (15.9)</td>
</tr>
<tr>
<td>GAS</td>
<td>NA</td>
<td>NA</td>
<td>57.4 (16.5)</td>
</tr>
<tr>
<td>Psychosocial functioning (SADS)</td>
<td>NA</td>
<td>NA</td>
<td>2.4 (1.2)</td>
</tr>
</tbody>
</table>

Abbreviations: GAF, Global Assessment of Functioning; GAF-F, Global Assessment of Functional Performance; GAS, Global Assessment of Symptoms; MDD, major depressive disorder; NA, not applicable; SADS, Schedule for Affective Disorders and Schizophrenia; SES, socioeconomic status.

* Percentages may vary because of missing data.

† Percentage of observed interval from baseline to 4-year point.

‡ Percentage of illness during interval from baseline to 4-year point.

§ Outcome at 10-year point.
We used LOESS to examine nonlinearity of associations. LOESS was significantly superior across all outcomes, and the improvement in fit ranged from Akaike Information Criterion Corrected 1 of 6.69 (substantial) to 51.57 (very substantial). Consistent with the fit indices, LOESS curves for psychosis and depression were essentially linear (Figure 1). Mania curves had an initial rise that plateaued and then gradually returned to the starting level. Nonaffective psychosis curves showed an initial drop that soon leveled. An apparent discontinuity in nonaffective psychosis contradicted the continuum model and was most consistent with the Kraepelinian model. However, more rigorous modeling was needed to understand the exact form of the nonlinearity.

Spline Models
We used spline regression to more precisely evaluate nonlinearity detected by LOESS for nonaffective psychosis and mania. Psychosis and depression were not considered further be-
cause their associations with outcomes were purely linear. Spline regression allowed us to specify basic shapes of the curves to test target models and likely alternatives (Supplement[eMethods]).

For nonaffective psychosis, the fit indices consistently supported the kraepelinian model across the outcomes (Table 3). The only exception was GAS, for which 3 indices favored the DSM-IV model, but the fit of the kraepelinian model was nearly identical and superior on the Bayesian Information Criterion—the most parsimonious index. We named the identified groups nonaffective psychosis absent and nonaffective psychosis present. The boundary between them was at 1.5% of nonaffective psychosis ratio, that is, 10 days of psychosis outside of mood episodes (Figure 2).

For mania, the fit indices consistently supported the 3-group model over all alternatives (Table 3). The only exception was SADS, for which 3 indices favored the 4-group model, but fit of the 3-group model was nearly identical and the Bayesian Information Criterion favored 3 groups. We named the 3 groups mania absent, episodic mania, and chronic mania. The boundaries between them were 0.8% (11 days) and 27.0% (394 days) manic (Figure 2). In the episodic group, elevated mood consisted primarily of mania (mean, 65.4% of time in episodes), with the rest being mixed state (23.5%) or hypomania (11.1%). In the chronic group, mania (35.0%), mixed state (37.3%), and hypomania (27.7%) were evenly represented. The selected spline models fit the data much better than LOESS, indicating further support for these specific types of nonlinearity.

Diagnostic Comparisons

Next, we examined concordance between empirical groups identified by spline regression and DSM-IV diagnoses. Because diagnoses were assigned at the 2-year point, we scored empirical groups from the first 2 years of course data using the aforementioned cutoffs (1.5% on nonaffective psychosis, and 0.8% and 27.0% on mania).

Overall, concordance between the empirical groups and DSM-IV diagnoses was high. Nearly all (88.6) participants with schizophrenia or schizoaffective disorder diagnosis were in the nonaffective psychosis present group (Table 4); those who were assigned to nonaffective psychosis absent either had nonaffective psychosis before the first hospitalization—including the 5 schizoaffective cases—or had prominent negative symptoms outside mood episodes. Almost all (97.3%) cases of psychotic mood disorders were in the nonaffective psychosis absent group; the remaining 2.7% had only brief periods of nonaffective psychosis and their mood symptoms were much more severe than psychotic symptoms, resulting in psychotic mood disorder diagnosis.

Of participants with bipolar disorder, 20.7% were in the chronic mania group. Others were in the episodic mania group, except for 4 patients who had mania only before the first hospitalization and thus were classified in the absent group. Ap-
Discussion

Using modern statistical techniques—LOESS and spline regression—we detected strong nonlinearity in the relationship between ratio of nonaffective psychosis to mood disturbance and later outcome in our first-admission cohort with psychotic disorders. Specifically, we observed a qualitative difference in outcome between cases in which psychosis is limited to mood episodes and cases in which at least some psychosis is nonaffective. No other discontinuities emerged in analyses of nonaffective psychosis. These findings clearly support the Kraepelinian dichotomy over the DSM-IV and continuum accounts. We found no evidence of a distinct schizoaffective disorder. Judged by outcome, this diagnosis appears to be a part of the schizophrenia spectrum. Other definitions of schizoaffective disorder that do not rely on nonaffective psychosis are possible and were not evaluated here. The analyses also revealed 2 distinct types of mania: episodic and chronic. In contrast, duration of psychosis and depression both had linear associations with outcomes and did not demarcate natural boundaries within psychotic disorders.

If replicated in other samples and with other validators, our results would have several implications for future editions of the DSM. Given the lack of validity of schizoaffective disorder diagnosis observed in this study and questionable

Table 3. Comparison of Spline Regression Models

<table>
<thead>
<tr>
<th>Predictor/Outcome</th>
<th>Global Assessment</th>
<th>Functioning (Overall)</th>
<th>Functional Performance</th>
<th>Symptoms</th>
<th>Psychosocial Functioning</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>GCV</td>
<td>AICC1</td>
<td>AIC</td>
<td>BIC</td>
<td>GCV</td>
</tr>
<tr>
<td>Nonaffective psychosis</td>
<td>LOESSa</td>
<td>0.588</td>
<td>2684</td>
<td>2268</td>
<td>2282</td>
</tr>
<tr>
<td></td>
<td>2 Flat (Kraepelinian)a</td>
<td>0.581</td>
<td>2678</td>
<td>2261</td>
<td>2265</td>
</tr>
<tr>
<td></td>
<td>3 Flat (DSM-IV)</td>
<td>0.585</td>
<td>2680</td>
<td>2263</td>
<td>2271</td>
</tr>
<tr>
<td></td>
<td>2 Linear</td>
<td>0.584</td>
<td>2680</td>
<td>2263</td>
<td>2271</td>
</tr>
<tr>
<td></td>
<td>3 Linear</td>
<td>0.590</td>
<td>2685</td>
<td>2268</td>
<td>2284</td>
</tr>
<tr>
<td></td>
<td>1 Quadratic + 1 linear</td>
<td>0.588</td>
<td>2684</td>
<td>2268</td>
<td>2278</td>
</tr>
<tr>
<td></td>
<td>2 Quadratic + 1 linear</td>
<td>0.593</td>
<td>2687</td>
<td>2270</td>
<td>2290</td>
</tr>
<tr>
<td></td>
<td>1 Cubic + 1 linear</td>
<td>0.585</td>
<td>2681</td>
<td>2270</td>
<td>2290</td>
</tr>
<tr>
<td>Mania</td>
<td>LOESS</td>
<td>0.577</td>
<td>2676</td>
<td>2258</td>
<td>2282</td>
</tr>
<tr>
<td></td>
<td>2 Flat</td>
<td>0.596</td>
<td>2689</td>
<td>2272</td>
<td>2276</td>
</tr>
<tr>
<td></td>
<td>3 Flat</td>
<td>0.561</td>
<td>2664</td>
<td>2247</td>
<td>2255</td>
</tr>
<tr>
<td></td>
<td>4 Flat</td>
<td>0.566</td>
<td>2668</td>
<td>2251</td>
<td>2263</td>
</tr>
<tr>
<td></td>
<td>2 Linear</td>
<td>0.576</td>
<td>2675</td>
<td>2262</td>
<td>2270</td>
</tr>
<tr>
<td></td>
<td>3 Linear</td>
<td>0.569</td>
<td>2670</td>
<td>2259</td>
<td>2279</td>
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<td></td>
<td>4 Linear</td>
<td>0.580</td>
<td>2678</td>
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<td></td>
<td>1 Cubic + 1 linear</td>
<td>0.591</td>
<td>2686</td>
<td>2271</td>
<td>2287</td>
</tr>
</tbody>
</table>

Abbreviations: AIC, Akaike information criterion; AICC1, Akaike information criterion corrected 1; BIC, Bayesian information criterion; GCV, generalized cross validation criterion; LOESS, locally weighted scatterplot smoothing.

* Bold indicates best fit of the series. These indices are derived from different statistical theories and are scaled differently. However, all 4 can be decomposed into 2 components: a measure of fit between the model and data and a penalty for model complexity. Based on the latter, the indices can be ordered from least to most parsimonious: AIC, GCV, AICC1, and BIC. There are no absolute cutoffs on these indices, but they can be used to compare models, with lower values representing better fit.38,39 Conventional guidelines suggest that on AIC, AICC1, and BIC, a difference less than 6 is small, 6 to 10 is substantial, and greater than 10 is very substantial.39

a LOESS uses weighted least squares to fit linear functions within a fixed neighborhood of each data point, as determined by the smoothing parameter (percentage of the sample included). We examined a range of smoothing parameters and selected 60%, as greater inclusion did not increase fit of the curve.

b Polynomials of degree 0, 1, 2, or 3 (flat, linear, quadratic, or cubic function) were fit onto each segment. Other than the flat function regressions, all regressions were restricted to be continuous. The locations of break points and the slope of each segment were freely estimated.

approximately half (53.8%) of participants with schizoaffective disorder diagnosis were in the episodic or chronic group. Mania was rare in other disorders.

With regard to outcomes, nonaffective psychosis present had notably worse scores than nonaffective psychosis absent (Table 4). The differences were more than 10 points on GAF, GAF-F, and GAS, and one level on SADS (ie, between moderate and mild condition). Similar differences were observed between mania absent and episodic mania. In contrast, the chronic mania group was similar to mania absent on all outcomes. Outcomes for DSM-IV schizoaffective disorder were similar to those of nonaffective psychosis present, whereas outcomes for schizophrenia were slightly worse (4–5 points on GAF metric). Participants with bipolar disorder did about as well as the episodic mania group.
Outcome expected at each level of symptom is shown. GAF indicates Global Assessment of Functioning; GAF-F, Global Assessment of Functional Performance; GAS, Global Assessment of Symptoms; and SADS, Schedule for Affective Disorders and Schizophrenia.
Our findings suggest that patients who currently are assigned a diagnosis of schizoaffective disorder would be better described as having schizophrenia (or schizophreniform disorder) with co-morbid mood disorder. This nosologic change would reflect a diagnosis of psychotic illnesses without invoking an arbitrary diagnostic category. Continuous ratings of severity for mood disorders and schizophrenia could further increase informational value of such a classification. Indeed, such ratings have been proposed for the DSM-5. With regard to schizoaffective diagnosis, the only significant revision considered for the DSM-5 is to make it explicitly a lifetime diagnosis.

In contrast, we found a clear discontinuity between schizophrenia spectrum disorders and psychotic mood disorder. In our data, even 10 days of nonaffective psychosis resulted in a qualitatively worse outcome. This is consistent with DSM-IV criteria for demarcating schizoaffective disorder and psychotic mood disorder (ie, 2 weeks of nonaffective psychosis).

Bipolar disorder with psychosis also was clearly distinguished from other psychotic disorders, even with several days of manic symptoms forecasting qualitatively better outcomes. This finding is consistent with research indicating favorable outcomes for this disorder relative to other psychoses. In addition, we observed a discontinuity within the bipolar spectrum, suggesting existence of a chronic mania subtype defined by being manic for at least a year. This subtype has prognostic significance because it was associated with a distinctly worse outcome. Of note, all of these findings were consistent across several outcome measures, strengthening conclusions of the study. These measures reflect a single validator—global outcome—and are not independent replications, but they helped to ensure that the present results are not due to characteristics of a particular rating scale.

We did not hypothesize the chronic mania group a priori, and it requires confirmation, but this finding aligns well with the extant literature. Chronic mania was recognized as a distinct category in the 19th century. More recently, it has been operationalized as a manic episode lasting at least 2 years, and 6% to 13% of patients with bipolar I disorder fit this subtype.

The observed empirical groups were defined by symptoms only. Nevertheless, both nonaffective psychosis and mania categories showed the anticipated convergence with DSM-IV diagnoses. There was only a handful of inconsistencies resulting from symptoms present before the first hospitalization or to highly prominent symptoms that received special weight in diagnostic decision making. In addition, mania groups included some patients with schizophrenia and other psychoses, which reflects the presence of comorbid mood disorders in these cases.

These empirical groupings had substantial predictive validity, forecasting more than 10-point differences in GAF among both nonaffective psychosis and mania groups years later. The DSM-IV diagnosis was somewhat more predictive, with schizoaffective disorder being a distinct condition. Our findings argue for reconsideration of DSM-5.
phrenia outcome being 5 GAF points lower than the nonaffective psychosis present group. Schizophrenia diagnosis explicitly requires marked deterioration of functioning (criterion B), which likely explains why this group fared worse than the nonaffective psychosis present group. Altogether, it is remarkable that simple classification rules based solely on symptomatology were almost as predictive as full DSM-IV diagnosis.

The observed sharp distinction between nonaffective psychosis and any nonaffective psychosis and the large effect it had on outcome suggests differences in etiologies of these groups. For instance, psychotic symptoms in schizophrenia spectrum disorders may result from neurodevelopmental pathologic factors, whereas psychosis in psychotic mood disorder may be induced by stress. These findings contradict the continuum view of psychotic disorders, but psychotic mood disorder and nonaffective psychosis may share some risk factors and pathophysiologic processes. Many such commonalities have been documented and may explain their substantial comorbidity. In our sample, 57% of the nonaffective psychosis group experienced at least one mood episode. The degree of overlap versus distinction among these conditions can be further explicated by applying nonlinear modeling to other validators.

Our rejection of the 3-disorder model in favor of the kraepelinian dichotomy seems to be at odds with studies reporting better outcomes in schizoaffective disorder compared with schizophrenia. Importantly, schizoaffective disorder is defined only by symptom pattern and, unlike schizophrenia, does not require marked functional impairment or 6-month duration, which likely explains differences in outcome. Indeed, in our cohort, outcome of schizoaffective disorder was no different from the outcome of the rest of the nonaffective psychosis group. Quantitative distinctions among patients with psychotic disorders also must be recognized. We found that of all variables considered, duration of psychosis was the most important predictor of outcome. Clinicians need to remain vigilant to long-term disability associated with chronic psychosis.

Strengths of this investigation include a first-admission epidemiologic cohort that was followed long-term and a painstaking tracking of symptoms and functioning using interviews, informant reports, and medical records. Nevertheless, the present findings need to be considered against the study’s limitations. First, detailed documentation of symptoms was limited to 4 years and sometimes did not include illness onset. This investigation targeted a crucially important period of illness course, but close tracking of symptoms over a long term would provide a more definitive test of diagnostic boundaries. Second, validation of diagnostic distinctions was limited to long-term outcome. Kraepelin considered illness course the key consideration for diagnostic validity, but a comprehensive evaluation has to include other characteristics, such as genetic risk factors, neural substrates, and treatment response. This effort requires integration of findings from different research paradigms, and the present study is a step toward this goal. Third, the present report focused on global outcomes, as these have been the primary benchmarks for other longitudinal studies of schizoaffective disorder. We also collected fine-grained information and will investigate specific outcomes in subsequent studies. Fourth, each outcome was a single rating, and such variables tend to have low reliability. To ensure strong psychometric properties, the present ratings were made by consensus of research psychiatrists based on all available information. Fifth, consensus diagnosis was available at the 2-year rather than 4-year point, so we had to limit analyses comparing diagnoses and empirical groups to 2 years of symptom course. Sixth, we could not investigate treatment effects in this naturalistic study, and it is important to confirm present findings in randomized trials, controlling for treatment experiences. Finally, generalizability of the present results was limited by attrition. Fortunately, attrition during the 10-year study was modest and had little effect on study variables.

In conclusion, if replicated, our findings would provide clear support for the kraepelinian dichotomy, and this sharp boundary presents a significant challenge for the continuum view of psychotic disorders. Also, absence of the boundary between schizophrenia and schizoaffective disorder calls validity of the latter into question. Schizoaffective disorder was an early advance that recognized the co-occurrence of schizophrenia and mood disorders. It was an imperfect solution, however, and the present findings suggest that coding of comorbid schizophrenia (or schizophreniform disorder) and mood disorder as 2 separate diagnoses may serve the field better than the schizoaffective category. In fact, the DSM-IV already permits such coding, and this proposal would extend it to cases currently diagnosed as schizoaffective disorder. This change would also streamline differential diagnosis for psychotic disorders. Indeed, the reliability of schizoaffective disorder diagnosis is remarkably poor. Much of this difficulty stems from criterion C, which separates schizoaffective disorder from schizophrenia with comorbid mood disorder. Our results suggest that this distinction is superfluous, which may explain the associated unreliability. Thus, abolishing the schizoaffective disorder category while maintaining the qualitative distinction between psychotic mood disorder and schizophrenia spectrum disorders, it may be possible to align the nosology with the natural taxonomy of psychoses, simplify diagnosis, and improve its reliability. This contention requires verification in other samples and with a variety of validators.
boundaries of schizoaffective disorder

original investigation research

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