Declining Clinical Course of Psychotic Disorders Over the Two Decades Following First Hospitalization: Evidence From the Suffolk County Mental Health Project

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Objective: Kraepelin considered declining course a hallmark of schizophrenia, but others have suggested that outcomes usually stabilize or improve after treatment initiation. The authors investigated this question in an epidemiologically defined cohort with psychotic disorders followed for 20 years after first hospitalization.

Method: The Suffolk County Mental Health Project recruited first-admission patients with psychosis from all inpatient units of Suffolk County, New York (response rate, 72%). Participants were assessed in person six times over two decades; 373 completed the 20-year follow-up (68% of survivors); 175 had schizophrenia/schizoaffective disorder. Global Assessment of Functioning (GAF), psychotic symptoms, and mood symptoms were rated at each assessment. Month 6, when nearly all participants were discharged from the index hospitalization, was used as a reference.

Results: In the schizophrenia group, mean GAF scores declined from 49 at month 6 to 36 at year 20. Negative and positive symptoms also worsened (Cohen's d values, 0.45–0.73). Among participants without schizophrenia, GAF scores were higher initially (a mean of approximately 64) but declined by 9 points over the follow-up period. Worsening began between years 5 and 8. Neither aging nor changes in antipsychotic treatment accounted for the declines. In all disorders, depression improved and manic symptoms remained low across the 20 years.

Conclusions: The authors found substantial symptom burden across disorders that increased with time and ultimately may undo initial treatment gains. Previous studies have suggested that better health care delivery models may preempt this decline. In the United States, these care needs are often not met, and addressing them is an urgent priority.

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Emil Kraepelin (1) considered declining course a distinguishing feature of schizophrenia (dementia praecox) in contrast to the nondeclining, episodic course of mood disorders with psychosis. Others have challenged this view, suggesting that a downward trajectory is not typical of schizophrenia and that outcomes tend to improve over time (2, 3). Prospective investigations of clinical course—evolution of symptom burden over time—in first-episode or first-admission psychosis can provide key evidence for answering this question, as they employ a well-defined early starting point.

Numerous studies have followed first-episode psychosis cohorts in the short and medium terms. A systematic review (4) found global outcome to be fairly stable across the first decade of illness. Recent 10-year follow-up studies of two seminal first-episode cohorts found that positive symptoms initially improve and then stabilize, while negative symptoms remain largely unchanged (5) and only a minority of participants are continuously ill (6). Overall, this research did not suggest a decline in the first decade of illness, but the second decade may be different.

The international Determinants of Outcome of Severe Mental Disorders (DOSMeD) project is, to date, the only prospective study to have followed first-episode patients for two decades (7, 8). More than half of participants with schizophrenia had good outcome (defined as a Global Assessment of Functioning [GAF] score >60), and 50% improved over the interval, whereas only 23% declined (8). However, limited interim information precluded charting of illness trajectories. Also, these analyses included only one small sample (N=56) from the United States, and large cross-national differences in outcomes were observed (8). The most similar U.S. project, the Chicago Follow-Up Study, assessed an early-course sample six times over two decades after admission with psychosis. In participants with schizophrenia, global outcome improved through year 7.5 and then

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stabilized, with about 20% having good outcomes (9). Repeated assessments provided a detailed picture of illness course, but conclusions are limited by a sample drawn primarily from a private hospital.

Less is known about the long-term course of mood disorders with psychosis. The DOSMeD study did not analyze this group separately but presented all participants with nonschizophrenia psychoses together and found better outcomes (two-thirds had GAF scores >60) and course (69% improving and only 12% declining) than in the schizophrenia group (8). In the Chicago Follow-Up Study, nonschizophrenia psychoses also had a better course, with global outcomes improving through year 4.5 and then stabilizing, with about 40% of participants having good outcomes (9). Another investigation (6) found that only 8% of patients with psychotic mood disorders were continuously ill during the decade after first admission. To our knowledge, no study has charted the illness trajectories of this group over 20 years.

TABLE 1. Baseline Characteristics of the Follow-Up Cohort and Surviving Nonparticipants in a Study of Psychotic Disorders Over the Two Decades Following First Hospitalization[a]

Measure	Follow-Up Cohort (N=373)		Nonparticipants (N=176)	
Demographic characteristics	N	%	N	%
Male	222	59.5	97	55.1
Age <28 years	195	52.3	87	49.4
Blue-collar household	165	44.2	75	42.6
Caucasian[b]	290	77.7	119	67.6
Research diagnosis (last available)				
Schizophrenia spectrum disorder	175	46.9	73	41.5
Bipolar I disorder with psychosis	94	25.2	41	23.3
Major depressive disorder with psychosis	43	11.5	25	14.2
Substance-induced psychosis	25	6.7	16	9.1
Other/undetermined psychosis	36	9.7	21	11.9
Baseline ratings	Mean	SD	Mean	SD
GAF (best month in year before hospitalization)	58.17	14.25	59.98	14.87
Apathy-asociality	9.38	7.61	8.90	6.21
Inexpressivity	7.32	8.08	6.28	6.98
Reality distortion[b]	10.73	8.71	12.78	10.39
Disorganization	6.89	6.52	6.32	5.89
Depression	17.52	5.38	17.22	4.93
Mania/excitement	1.66	1.16	1.53	1.07

[a] Surviving nonparticipants were patients who completed the baseline assessment but did not participate in the 20-year follow-up and were not known to be deceased: 78 declined, 70 were lost to follow-up, 15 were impossible to interview (abroad or institutionalized), and 13 provided brief updates that were insufficient for target ratings. There were no significant differences between groups except as otherwise noted. GAF=Global Assessment of Functioning.
[b] Significant difference between the follow-up cohort and the surviving nonparticipants ($p<0.05$).

Previous long-term studies have focused largely on global outcome and overall pattern of course. Consequently, trajectories of specific symptoms are less understood. At least four clearly distinct dimensions of psychotic symptoms have been identified: reality distortion (i.e., hallucinations, delusions), disorganization, inexpressivity, and apathy-asociality (10, 11). This scheme is an elaboration of the classic three-dimensional model (12) through division of negative symptoms into apathy-asociality and inexpressivity. Mood symptoms—depression and mania—also play a prominent role in psychotic disorders (13, 14). These six dimensions follow distinct trajectories (15), yet long-term data on changes in many of these symptoms over time are lacking.

We sought to address the aforementioned limitations of long-term follow-up studies of clinical course by 1) examining an epidemiologically defined first-admission psychosis cohort, 2) tracing trajectories of the six symptom dimensions as well as global outcome (GAF) across two decades, 3) following a sufficiently large group of patients with psychotic mood disorders to chart their course precisely and compare it with the course of schizophrenia, and 4) using longitudinal consensus diagnoses to define study groups with high accuracy. To our knowledge, this is the first study to put the four techniques together, offering an unprecedented opportunity to clarify the disagreement between modern views of illness course and Kraepelin's descriptions. Moreover, this also is the first study to attempt direct replication of DOSMeD's long-term findings in the United States.

METHOD

Participants

The cohort was assembled by the Suffolk County Mental Health Project, an epidemiologic study of first-admission psychosis (11, 16, 17). Participants were recruited from the 12 psychiatric inpatient units of Suffolk County, New York, between 1990 and 1995. Inclusion criteria were first admission either current or within 6 months, clinical evidence of psychosis, ages 15–60, IQ >70, proficiency with English, residency in Suffolk County, and no apparent medical etiology for the psychosis. The study was approved annually by the institutional review boards of Stony Brook University and the participating hospitals.

We initially interviewed 675 participants (72% of referrals); 628 of them met the eligibility criteria. Follow-ups were conducted at 6 months, 24 months, 48 months, 10 years, and 20 years. Seventy-nine participants died during the 20 years. Of the 549 survivors, 373 were successfully contacted at year 20 and constitute the analysis sample. Of these, 68.9% lived in Suffolk County, 6.4% moved to another county in New York, and 24.7% moved to another state. Surviving nonparticipants—patients who completed baseline assessment but did not participate in the 20-year follow-up assessments and were not known to be deceased (N=176)—were similar to the analysis sample on baseline study variables (demographic characteristics, diagnosis, and symptoms) (Table 1), but they were less likely to be Caucasian (67.6% compared with 77.7%) and on

TABLE 2. Characteristics of Diagnostic Groups Over Time in a Study of Psychotic Disorders Over the Two Decades Following First Hospitalization[a]

Outcome Measure and Assessment Point	Schizophrenia		Bipolar Disorder With Psychosis		Psychotic Depression		Substance-Induced Psychosis		Other/Undetermined	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
GAF										
Baseline	52.65	14.17	67.83	9.44	60.30	12.99	57.68	11.92	57.53	14.64
6 months	49.34	13.18	66.37	11.90	61.45	13.94	61.74	11.45	62.73	12.67
24 months	50.39	12.90	69.14	10.83	64.98	12.31	64.65	11.45	60.96	14.39
48 months	49.27	12.21	70.05	11.81	67.93	12.03	65.05	13.06	63.13	15.10
10 years	44.06	10.67	66.95	13.14	65.61	11.72	61.39	13.99	60.93	15.49
20 years	35.79	10.57	57.79	16.78	52.81	16.06	53.88	16.82	51.33	19.03
Apathy-asociality										
Baseline	12.11	7.36	4.95	5.74	10.67	7.60	8.40	5.61	6.86	8.26
6 months	11.55	7.92	5.23	6.05	8.51	7.87	7.35	4.98	5.69	7.11
24 months	11.31	6.64	3.76	5.20	6.97	7.32	5.87	5.74	6.36	6.90
48 months	11.30	6.70	3.70	4.67	5.67	6.88	4.47	4.90	7.67	7.12
10 years	13.99	8.14	3.53	4.75	4.60	5.77	7.87	7.96	6.62	8.13
20 years	17.56	8.84	8.00	7.70	10.11	8.52	9.74	9.05	11.51	10.23
Inexpressivity										
Baseline	10.22	8.39	3.86	6.10	6.60	8.43	4.28	5.70	5.28	7.23
6 months	10.52	8.92	2.64	4.79	5.00	7.09	3.30	4.20	3.92	6.58
24 months	9.48	8.19	1.80	2.63	3.68	5.62	3.22	5.14	2.68	4.64
48 months	8.82	8.82	1.61	3.15	2.24	3.66	1.53	3.22	3.72	5.30
10 years	7.99	7.67	1.68	3.98	1.87	4.15	2.40	4.57	2.83	6.49
20 years	10.32	10.37	3.69	5.45	4.26	7.13	4.00	6.17	7.90	11.34
Reality distortion										
Baseline	12.54	9.36	10.77	8.87	6.23	6.00	8.40	6.89	8.83	6.05
6 months	4.26	7.44	0.56	1.29	2.81	4.56	1.52	3.19	2.50	4.67
24 months	4.41	6.36	0.99	3.19	0.92	2.74	1.83	3.66	3.40	6.30
48 months	4.03	6.67	1.05	2.78	0.94	2.52	1.53	3.01	3.44	7.96
10 years	6.66	8.24	0.46	1.86	1.03	2.29	1.78	3.25	3.07	5.69
20 years	7.31	9.34	0.84	2.16	0.93	2.32	2.73	4.79	3.47	5.92
Disorganization										
Baseline	7.19	7.00	8.97	6.05	1.86	2.96	5.68	5.37	6.89	6.07
6 months	2.99	5.14	1.61	3.00	0.89	1.37	0.70	1.15	2.08	2.64
24 months	2.99	4.35	2.19	3.93	1.08	2.13	2.09	3.63	3.36	5.22
48 months	3.65	4.87	2.34	4.22	0.73	1.86	0.47	1.02	2.33	3.07
10 years	4.27	6.00	1.79	3.74	0.94	2.45	1.29	2.24	3.64	6.20
20 years	6.16	7.28	3.21	5.22	2.45	4.33	2.07	3.76	5.71	6.32
Depression										
Baseline	17.04	5.02	16.85	5.13	22.21	5.23	16.96	5.83	16.42	5.10
6 months	13.55	4.03	12.13	3.35	15.51	5.51	12.70	3.97	13.04	5.08
24 months	13.20	4.46	11.16	3.47	12.86	5.27	12.52	4.67	13.72	5.00
48 months	10.69	3.79	9.94	3.07	12.00	5.72	10.53	3.42	11.72	5.38
10 years	11.92	3.76	10.99	3.47	13.35	5.10	12.55	4.27	11.37	3.25
20 years	11.60	3.28	11.87	3.93	13.35	4.57	11.43	3.51	12.45	3.85
Mania/excitement										
Baseline	1.49	1.00	2.13	1.39	1.07	0.34	1.96	1.34	1.78	1.22
6 months	1.21	0.66	1.44	0.90	1.00	0.00	1.26	0.75	1.20	0.71
24 months	1.22	0.65	1.41	0.92	1.14	0.48	1.22	0.60	1.48	1.08
48 months	1.33	0.68	1.47	0.96	1.12	0.42	1.21	0.54	1.39	0.78
10 years	1.29	0.80	1.35	0.90	1.15	0.48	1.57	1.20	1.59	1.37
20 years	1.28	0.83	1.34	0.87	1.13	0.47	1.14	0.48	1.21	0.63
	N	%	N	%	N	%	N	%	N	%
Use of antipsychotics										
Baseline	152	86.9	82	87.2	31	72.1	15	60.0	31	86.1
6 months	148	84.6	63	67.0	24	55.8	9	36.0	20	55.6
24 months	136	79.5	37	39.4	18	41.9	4	16.7	14	40.0
48 months	122	70.1	32	34.0	10	23.3	4	16.0	12	33.3
10 years	142	87.1	34	40.0	8	20.0	6	26.1	7	25.9
20 years	117	81.8	30	36.1	10	25.0	4	20.0	10	37.0

continued

TABLE 2, *continued*

Outcome Measure and Assessment Point	Schizophrenia		Bipolar Disorder With Psychosis		Psychotic Depression		Substance-Induced Psychosis		Other/Undetermined	
Illness pattern over 20 years										
Single episode	1	0.6	10	11.4	8	19.0	4	17.4	10	38.5
Multiple episodes	43	25.3	70	79.5	28	66.7	13	56.5	8	30.8
Continuous illness	126	74.1	8	9.1	6	14.3	6	26.1	8	30.8

[a] For the apathy-asociality, inexpressivity, reality distortion, and disorganization scales, zero indicates no symptoms; the depression scale ranges from 9 (no symptoms) to 27; the mania/excitement scale ranges from 1 (none) to 7 (very severe). Ns were 153, 148, 145, 166, and 175 for the schizophrenia group for 6-month to 20-year waves, respectively, 83, 81, 82, 86, and 94 for the bipolar disorder with psychosis group, 38, 41, 40, 41, and 43 for the psychotic depression group, 26, 28, 23, 29, and 36 for the substance-induced psychosis group, and 23, 23, 21, 23, and 25 for the other/undetermined psychoses group. GAF=Global Assessment of Functioning.

average had more severe reality distortion symptoms (Cohen's d=0.23). For the analysis sample (N=373), we had 2,046 observations across six waves (i.e., the data were 91.4% complete). Follow-ups that were done over the telephone (277 across the six waves) did not allow the behavioral ratings necessary for scoring inexpressivity, resulting in 1,769 observations available for inexpressivity. The primary analyses employed maximum likelihood estimation and thus used all available data.

Measures

Interviews were conducted by master's-level mental health professionals. Medical records and interviews with significant others were solicited at every assessment. This multisource information was used to complete the following rating scales about past-month symptoms: the Scale for the Assessment of Negative Symptoms (SANS) (18), the Scale for the Assessment of Positive Symptoms (SAPS) (19), the Brief Psychiatric Rating Scale (BPRS) (20), and the Structured Clinical Interview for DSM-III-R (SCID) (21). For the present sample, we scored four reliable factor-analytically derived subscales from the SANS and SAPS: inexpressivity (Cronbach's alpha≥0.88, nine items), apathy-asociality (alpha≥0.81, six items), reality distortion (alpha≥0.80, 14 items), and disorganization (alpha≥0.72, 11 items) (11). Mania was operationalized with the excitement rating of the BPRS. Depressive symptoms were assessed with the current depression module of the SCID, administered without skip-outs. We constructed a nine-symptom depression composite (score range, 9–27) that has excellent reliability (alpha≥0.81) and validity (11, 17). All ratings were highly reliable (see the Supplemental Methods section in the data supplement that accompanies the online edition of this article).

Primary DSM-IV diagnoses were formulated at the 10-year point by consensus of study psychiatrists using all available information (17). The same process was performed in previous waves, including the 6-month assessment. Diagnoses were grouped into five categories: schizophrenia/schizophreniform/schizoaffective disorder, bipolar disorder with psychosis, depression with psychosis, substance-induced psychosis, and other/undetermined psychosis (e.g., psychotic disorder not otherwise specified). Psychiatrists made consensus ratings of the Global Assessment of Functioning (GAF) for the best month of the year before interview, an index that captures both symptom burden and functional impairment. At year 20, psychiatrists also rated the overall pattern of clinical course, using the DOSMeD criteria (see the Supplemental Methods section in the data supplement) (22). For interpretability, we grouped eight course categories into three: single episode (i.e., baseline episode resolved, no recurrence), multiple episodes, and continuous illness (i.e., no remission).

Data Analysis

We investigated trajectories of each disorder on seven outcome measures: the GAF (primary measure) and the six symptom dimensions. At baseline all participants were highly symptomatic and hospitalized; therefore, baseline could not be included in the model, and we started charting trajectories from month 6. We focus here on mean disorder trajectories. Within-group heterogeneity was reported previously (11).

First, we examined clinical course in bivariate analyses, using paired t tests to compare outcomes at follow-ups subsequent to month 6. We used independent-samples t tests to compare outcomes between disorders. Next, we charted trajectories of disorders across all waves by fitting multilevel spline regression models with a random intercept (see the Supplemental Methods section in the data supplement) (23–25). Models were fitted for each disorder separately; they estimated trajectories of individual participants and then calculated the mean trajectory for the group. These analyses took advantage of variation in follow-ups around target dates (i.e., some were done late and others early), which allowed us to chart trajectories through year 23. However, data were limited for years 5–8 and 13–16 (< 20 observations/year), and these portions of the trajectories were estimated less precisely. Spline regression is a piecewise regression that allows different slopes in different segments of the predictor variable. We considered up to three segments (the largest number suggested by descriptive analyses). Transition points between segments were determined empirically by testing the full range of possible transition points and selecting the model with the best Bayesian information criterion (26). The number of segments was determined similarly. Finally, we added age and antipsychotic medication as time-varying covariates to the resulting models to determine whether the observed changes were independent from variation in these covariates.

RESULTS

Description of Clinical Course

Table 2 summarizes the outcomes and antipsychotic medication use of the five diagnostic groups across the two

decades. The pattern is notable for worse outcomes in schizophrenia. Differences among the other groups were less pronounced, although the bipolar disorder with psychosis group and the psychotic depression group often had better outcomes than the substance-induced and other/undetermined psychoses groups. Notably, within-group variability was substantial and often dwarfed between-group differences. The overall pattern of clinical course over 20 years indicated that schizophrenia typically followed a chronic course (74.1% of patients continuously ill), whereas an episodic course was common in bipolar disorder with psychosis (79.5%) and psychotic depression (66.7%), and the other two groups fell between them. The psychotic depression, substance-induced psychosis, and other/undetermined groups were too small (Ns <50) for planned analyses; therefore, we combined groups based on similarity of course, resulting in three larger categories: schizophrenia (N=175), mood disorders with psychosis (N=137), and other psychoses (N=61).

Next, we tested the significance of changes within the three groups from month 6 to each follow-up wave (Figure 1). GAF scores remained stable or improved from month 6 through month 48 for each group, but thereafter they declined by 13 points in the schizophrenia group and 9 points in the other groups. With regard to specific symptom dimensions, apathy-asociality also remained stable or improved through month 48 but then worsened (Cohen's d values, 0.35–0.73, comparing year 20 to month 6). Inexpressivity improved through year 10, but by year 20 it returned to initial levels. Reality distortion symptoms were at stable low levels throughout the follow-up period in the psychotic mood disorders and other psychoses groups. In the schizophrenia group, reality distortion ratings were stable through month 48 but then increased substantially (d=0.45), whereas disorganization worsened even more (d=0.61). These increases are particularly notable given that rates of antipsychotic medication use remained largely stable in the schizophrenia group, while they declined dramatically in the other groups (see Figure S1 in the data supplement). In contrast, depression ratings decreased and mania/excitement ratings remained stable across the interval.

We also compared clinical course among disorders, focusing on the initial outcome (month 6), the long-term outcome (year 20), and the change between these waves (see Table S1 in the data supplement). Compared with the mood disorders with psychosis group, the schizophrenia group had consistently worse outcomes on the GAF and in ratings for apathy-asociality, inexpressivity, reality distortion, and disorganization. Moreover, worsening was greater in the schizophrenia group than in the psychotic mood disorders group on these outcomes, except for inexpressivity. No differences were observed between disorder groups on depression and mania/excitement. The only difference between the other psychoses group and the psychotic mood disorders group was higher ratings in the former on reality distortion symptoms at year 20.

Although highly accurate, 10-year diagnosis may be confounded by illness course during the first decade. To consider the impact of this potential confounding, we repeated the analyses using 6-month diagnosis (see Figure S2 in the data supplement). Schizophrenia trajectories were virtually unchanged on the GAF and on ratings for apathy-asociality, inexpressivity, reality distortion, and disorganization. Trajectories of the psychotic mood disorders and other psychoses groups were more severe using 6-month diagnoses compared with 10-year diagnoses. This pattern is consistent with misclassification, that is, that some patients who followed a schizophrenia trajectory were assigned other diagnoses at month 6. Indeed, we previously found that many 6-month nonschizophrenia cases in this cohort were later reclassified as schizophrenia, whereas few patients were reclassified from schizophrenia to other diagnoses (17). The reanalysis with 6-month diagnosis had little impact on trajectories of mood symptoms.

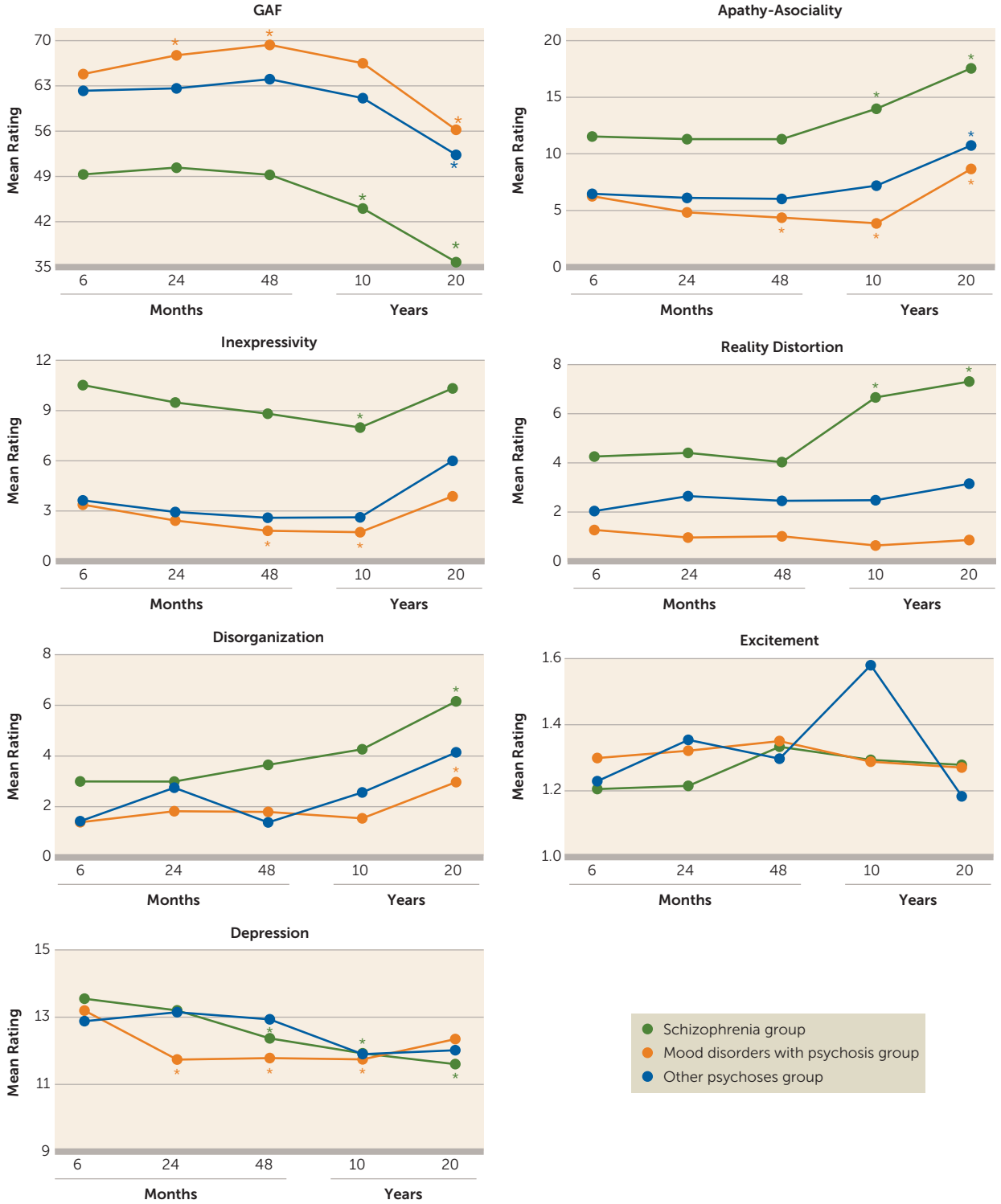
Trajectories of Diagnostic Groups

Next, we used multilevel spline regression to estimate trajectories for the three groups across the entire follow-up period for each outcome. The number of segments was determined empirically (see Table S2 in the data supplement). Selected models either were linear (i.e., had only one segment) or were allowed one change in the trajectory's slope (i.e., had two segments). Estimated trajectories (Figure 2) closely resembled longitudinal patterns obtained by smoothing raw data (see Figure S3 in the data supplement), which suggests that the models represented the data well. Table 3 lists magnitude of change in symptom scores per year (unadjusted columns).

GAF score declined significantly in the schizophrenia group; it improved initially in the psychotic mood disorders group and the other psychoses group but declined significantly after approximately year 7 (Figure 2). Apathy-asociality ratings worsened in all groups, although in the psychotic mood disorders group it improved through about year 7 and then deteriorated well beyond the initial level. Inexpressivity lessened until approximately year 7 but increased thereafter, except in the other psychoses group, where the trajectory was flat throughout. Reality distortion ratings increased in the schizophrenia group but remained stable in the other groups. Disorganization ratings worsened in all groups. Depression ratings improved in all groups, but in the psychotic mood disorders group, improvement plateaued at year 2. Mania/excitement ratings did not change significantly across the interval. Changes in GAF score were primarily driven by changes in apathy-asociality and reality distortion ratings (see Table S3 in the data supplement).

To test whether the observed patterns reflect effects of aging or changes in treatment rather than illness evolution, we repeated the analyses controlling for age and antipsychotic use at each assessment point (Table 3). Age had no

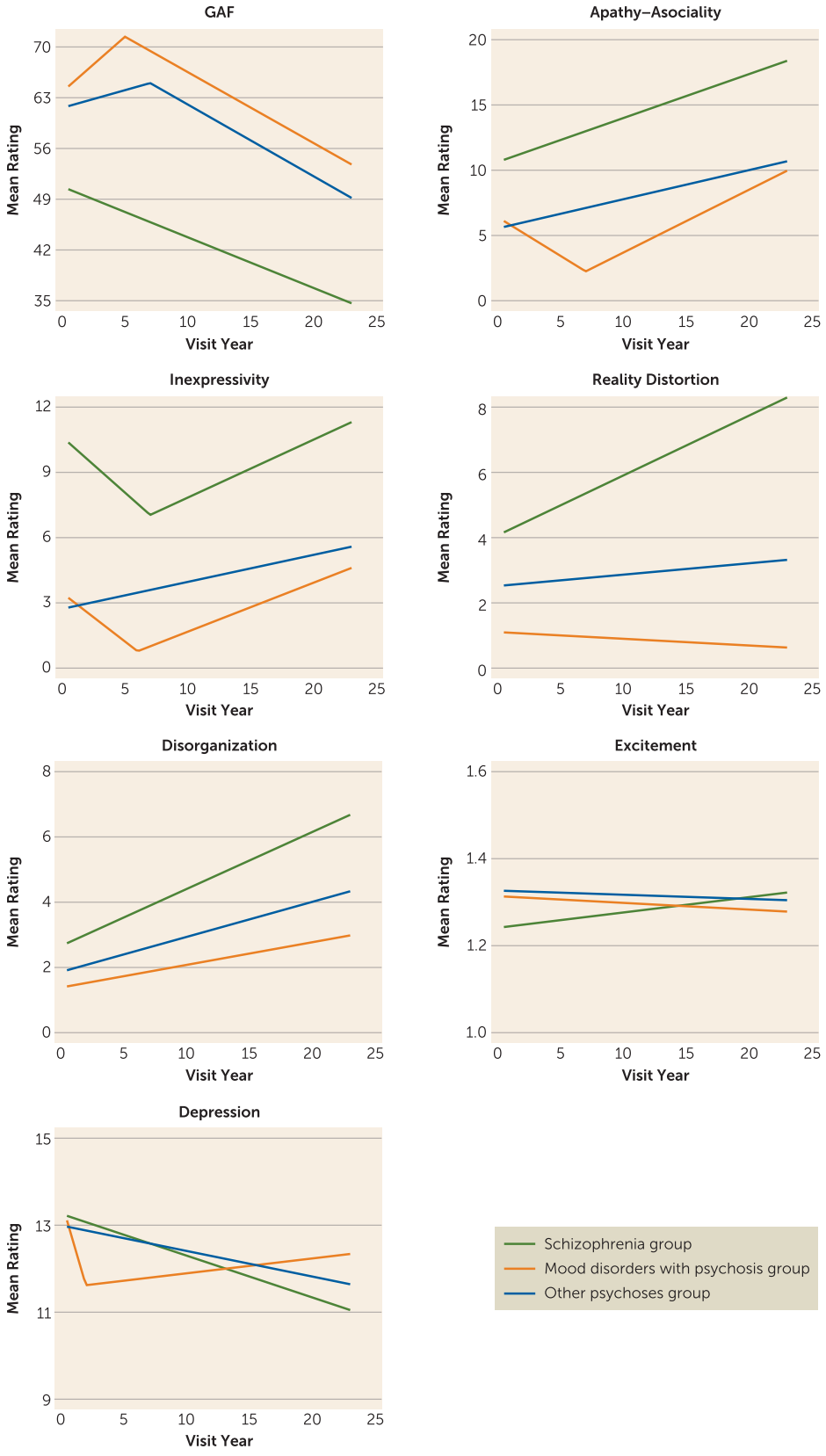
FIGURE 1. Outcomes in Major Diagnostic Groups in a Study of Psychotic Disorders Over the Two Decades Following First Hospitalization: Mean Ratings at Each Follow-Up and Comparison With Month 6[a]



[a] Ns were 153, 148, 145, 166, and 175 for the schizophrenia group at the 6-month to 20-year waves, respectively, 121, 122, 122, 127, and 137 for the mood disorders with psychosis group, and 49, 51, 44, 52, and 61 for the other psychoses group. Significant findings are indicated for the comparison with month 6.
*p<0.01.

effect on psychopathology after accounting for time since baseline. Antipsychotic use was associated with worse GAF scores, inexpressivity ratings, and apathy-asociality ratings overall, but with lower disorganization and mania/excitement ratings in the schizophrenia group. Also, antipsychotic use was associated with lower reality distortion ratings in the

FIGURE 2. Trajectories of Diagnostic Groups Over the Two Decades Following First Hospitalization, Modeled Using Spline Regression[a]



[a] Ns are 175 for the schizophrenia group, 137 for the mood disorders with psychosis group, and 61 for the other psychoses group.

schizophrenia group, but greater symptom ratings in the other psychoses group. This pattern may indicate medication side effects or selection effects (for example, sicker participants are more likely to receive long-term treatment with antipsychotics). Adjustment for these two variables did not change the findings for illness trajectories except that three slopes became nonsignificant in the other psychoses group and two became nonsignificant in the psychotic mood disorders group. Adjustments for various other potential confounders had little impact on the pattern of results (see the Supplementary Results section and Table S4 in the data supplement).

DISCUSSION

We found that schizophrenia exhibits substantial and consistent decline over the two decades following first hospitalization. The mean GAF score for this group decreased from 49 at the 6-month assessment to 36 at the 20-year assessment, and the latter score indicates impairment in reality testing, communication, or pervasive disability. With regard to specific symptom dimensions, worsening was observed in ratings for apathy-asociality, reality distortion, and disorganization. Initially, the psychotic mood disorders group was less severely ill than the schizophrenia group (a mean GAF score of 65 at 6 months), but the psychotic mood disorders group also showed worsening in GAF score and ratings for apathy-asociality and disorganization. This decline was smaller (9 points on the GAF)

TABLE 3. Changes in Symptoms Over Time in a Study of Psychotic Disorders Over the Two Decades Following First Hospitalization: Unadjusted and Adjusted for Age and Antipsychotic Medications[a]

Measure and Variable	Schizophrenia Group (N=175)				Mood Disorders With Psychosis Group (N=137)				Other Psychoses Group (N=61)			
	Unadjusted		Adjusted		Unadjusted		Adjusted		Unadjusted		Adjusted	
	B	p	B	p	B	p	B	p	B	p	B	p
GAF												
Time (S1)	−0.70	<0.001	−0.59	<0.001	1.52	<0.001	1.26	<0.001	0.49	0.119	0.60	0.097
Time (S2)	—	—	—	—	−0.98	<0.001	−0.94	<0.001	−0.99	<0.001	−0.60	0.011
Age	—	—	−0.10	0.231	—	—	−0.07	0.415	—	—	−0.31	0.055
Antipsychotics	—	—	−0.84	0.480	—	—	−4.78	<0.001	—	—	−5.19	0.004
Apathy-asociality												
Time (S1)	0.34	<0.001	0.26	<0.001	−0.59	<0.001	−0.58	<0.001	0.22	<0.001	0.05	0.571
Time (S2)	—	—			0.48	<0.001	0.40	<0.001	—	—	—	—
Age	—	—	0.09	0.133	—	—	0.09	0.014	—	—	0.16	0.045
Antipsychotics	—	—	2.59	0.001	—	—	2.33	<0.001	—	—	1.90	0.058
Inexpressivity												
Time (S1)	−0.51	<0.001	−0.55	<0.001	−0.45	<0.001	−0.29	0.019	0.12	0.035	0.11	0.245
Time (S2)	0.27	<0.001	0.32	0.002	0.23	<0.001	0.21	<0.001	—	—	—	—
Age	—	—	0.00	0.957	—	—	−0.02	0.453	—	—	0.01	0.912
Antipsychotics	—	—	2.59	0.003	—	—	2.04	<0.001	—	—	1.98	0.035
Reality distortion												
Time	0.18	<0.001	0.20	0.003	−0.02	0.102	−0.04	0.056	0.03	0.299	−0.04	0.553
Age	—	—	−0.02	0.679	—	—	0.02	0.124	—	—	0.07	0.208
Antipsychotics	—	—	−1.82	0.027	—	—	0.54	0.020	—	—	2.24	0.001
Disorganization												
Time	0.18	<0.001	0.18	0.001	0.07	<0.001	0.05	0.064	0.11	0.001	0.03	0.602
Age	—	—	−0.01	0.875	—	—	0.02	0.393	—	—	0.07	0.146
Antipsychotics	—	—	−1.65	0.005	—	—	0.00	0.990	—	—	−0.05	0.939
Depression												
Time (S1)	−0.10	<0.001	−0.08	0.016	−0.99	0.001	−0.89	0.002	−0.06	0.065	−0.15	0.007
Time (S2)	—	—	—	—	0.03	0.166	0.00	0.969	—	—	—	—
Age	—	—	−0.02	0.466	—	—	0.04	0.130	—	—	0.08	0.056
Antipsychotics	—	—	0.72	0.088	—	—	0.83	0.033	—	—	1.49	0.019
Mania/excitement												
Time	0.00	0.313	0.01	0.149	0.00	0.696	0.00	0.887	0.00	0.889	−0.01	0.368
Age	—	—	−0.01	0.291	—	—	0.00	0.549	—	—	0.01	0.332
Antipsychotics	—	—	−0.20	0.009	—	—	0.09	0.229	—	—	0.02	0.896

[a] B=change in symptom score per year; GAF=Global Assessment of Functioning; dashes indicate nonapplicable (i.e., effects not included in the model). S1 is first segment of the 20-year interval or the entire interval if the model has only one segment, and S2 is the second segment. The transition point between segments for the GAF was at year 5 for the mood disorders with psychosis group and at year 7 for the other psychoses group; for apathy-asociality, it was at year 7 for the mood disorders with psychosis group; for inexpressivity, it was at year 6 for the mood disorders with psychosis group and at year 7 for the schizophrenia group; for depression, it was at year 2 for the mood disorders with psychosis group. Effects with p values <0.01 were considered significant.

than that in schizophrenia. The decline began 5 to 8 years after the first hospitalization. Depression and mania ratings showed no signs of worsening in any of the disorder groups.

Overall, 74% of participants in the schizophrenia group were continuously ill, compared with 14% in the psychotic mood disorders group, and the majority of other patients in the two groups experienced multiple episodes during the 20-year interval.

Our results align with the Kraepelinian view of schizophrenia as following a downward trajectory. The illness worsened gradually, but in the second decade the decline become noticeable. Treatment initiation improved reality distortion and disorganization substantially, as indicated by change from baseline to month 6, but symptoms gradually returned, undoing many treatment gains by year 20. Contrary to Kraepelin's observations, participants in the mood disorders with psychosis group also experienced significant worsening, although it was less pronounced than worsening in the schizophrenia group, and it was limited to negative symptoms (reality distortion and disorganization ratings remained low). Of note, mood symptoms showed a different pattern, either improving or remaining consistently low.

Heterogeneity within diagnostic groups was substantial, and many participants achieved good outcomes (i.e., GAF score >60 at year 20): 42% in the mood disorders with psychosis group, 31% in the other psychoses group, and 4% in the schizophrenia group. We previously reported (11) that rank-order stability over 20 years is modest for negative symptoms (test-retest r values, ~0.40) and low for reality distortion and disorganization (r values, ~0.20). Thus,

trajectories of individual participants varied around the mean trend for their group, with some increasing and others decreasing.

To minimize misclassification, which is a common problem early in the course of psychosis (17), we used consensus diagnoses based on 10 years of observation. Such diagnoses are very accurate but are influenced by illness course. To examine this potential confounding, we repeated the analyses using 6-month diagnoses. This had little impact on trajectories for schizophrenia, other than moderating the increase in psychotic symptom severity somewhat. In contrast, other disorders looked consistently worse when 6-month diagnoses were used. This pattern can be explained by initial misclassification of schizophrenia cases as nonschizophrenia psychoses. Nevertheless, illness course is integral to diagnostic criteria (e.g., 6 months of symptoms are required for schizophrenia diagnosis), and some circularity is inherent in comparing course of diagnostic groups.

Trajectories of reality distortion were notable in that symptoms worsened in schizophrenia, despite consistently high rates of antipsychotic medication use across the two decades (~80% at each wave). This pattern is consistent with suggestions that antipsychotics may lose some of their effectiveness in the long term and may even lead to paradoxical effects (27, 28), perhaps as a result of nonadherence and relapses (29). Also, changes in the medications prescribed or their dosages may contribute to this finding. Our study cannot directly test these possibilities, as they require an experimental design.

The present findings paint a bleaker picture than the DOSMeD study did; in that study, only 29% of participants with schizophrenia were continuously ill and more than half had GAF scores >60 after two decades (7). A variety of factors distinguish the United States from the other countries included in the DOSMeD study (India, Russia, Japan, England, Ireland, and the Czech Republic). Availability of family support and community integration may contribute to differences in outcomes (8), but a particularly salient issue is access to treatment. The Suffolk County, New York, cohort received community services typical of the United States and experienced a substantial unmet need for care (30), which may account for poor outcomes, especially compared with countries that have universal health care.

On the other hand, our results are consistent with meta-analyses that found outcome in schizophrenia to be almost universally poor (31, 32). Moreover, a systematic review of first-episode psychosis studies found that during the first decade of illness, outcomes in treatment studies (which had a mean GAF score of 66) were much better than in observational studies (a mean GAF score of 50), and the latter outcomes are consistent with initial outcomes in the present cohort. The present study extends these reviews by documenting the timing and pace of decline across multiple symptom dimensions.

Our findings are also consistent with evidence of accelerated neurodegeneration in schizophrenia (33) that may underpin worsening negative symptoms. Poor physical health also may contribute to worse clinical course, as it limits daily functioning, impairs cognitive performance, and is common in psychotic disorders (34). We observed significant effects of poor health in the psychotic mood disorders group but not in the other groups (see Table S4 in the data supplement). Furthermore, our results for the psychotic mood disorders group are consistent with studies that reported functional impairment and residual symptoms to be common in psychotic bipolar disorder years after first admission (35).

These results should not be interpreted as an indication that good outcomes are out of reach. There is extensive evidence that aggressive treatment, especially psychotherapy and vocational rehabilitation, can substantially improve outcomes (36–38). Moreover, 10-year follow-up studies of first-episode psychosis in Denmark and the United Kingdom, countries with universal access to psychiatric services, found relatively good outcomes with no evidence of decline and few continuously ill participants both in schizophrenia and nonschizophrenia groups (5, 6). It is possible that with better care, outcomes in the United States would mirror those of Denmark and the United Kingdom.

This study has several limitations. First, it is limited to one geographic location and does not necessarily reflect illness course in other regions or health care systems. Nevertheless, the findings call attention to a glaring public health problem in the United States. Second, attrition was nonnegligible; 32% of survivors could not be contacted or declined participation. However, our attrition analyses suggest that the nonparticipants were largely similar to the participants, except for a slightly higher likelihood of being in a minority group and of having severe psychotic symptoms at baseline, both of which are risk factors for worse outcomes (29, 39). Thus, our results may underestimate severity of clinical course. Third, assessments began at first admission rather than first onset of symptoms. Fortunately, duration of preadmission illness was short relative to the follow-up, with a median duration of untreated psychosis of 40 days (only 27% were ill for more than a year). Fourth, we did not measure mania symptoms dimensionally and had to rely on a proxy measure, the excitement rating of the BPRS. Fifth, the study focused on symptoms and global outcome and did not consider dimensions of functioning. Functioning was beyond the scope of the present study, but we are reporting several functional outcomes in another article (40).

Our results suggest an alarming public health problem, namely, a high symptom burden in psychotic disorders that increases with time and ultimately may undo initial treatment gains. Previous studies have suggested that better care may preempt this decline. In the United States, psychotic disorders are associated with a large unmet need for care, and the present study highlights this shortcoming as an urgent priority. Reasons for the decline are unclear, and numerous explanations are possible. Greater research attention to the

middle and late course of psychotic disorders is needed to identify factors that drive this decline, as it unfolds, and to inform the field on how to preempt it.

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Supplemental Methods

DOSMeD rating of overall pattern of clinical course considers both psychotic and mood symptoms. The rating consists of eight mutually exclusive categories (1):

1. Single psychotic episode followed by full symptom remission
2. Single psychotic episode followed by incomplete remission
3. Single psychotic episode followed by one or more nonpsychotic episodes, with full symptom remissions between all or most of the episodes.
4. Single psychotic episode followed by one or more nonpsychotic episodes, with incomplete remissions between all or most of the episodes.
5. Two or more psychotic episodes, with full symptom remissions between all or most of the episodes.
6. Two or more psychotic episodes, with incomplete remissions between all or most of the episodes.
7. Continuous psychotic illness (no remission):
8. Continuous nonpsychotic illness (no remission); psychotic symptoms may have been present for some time but nonpsychotic symptoms predominate throughout.

Due to small number of cases in some of the categories, we aggregated eight categories into three common patterns: single episode (categories 1 and 2), multiple episodes (categories 3, 4, 5 and 6), and continuous illness (categories 7 and 8).

The BPRS Excitement rating reflects affective core of mania, but does not capture associated symptoms. Interviewers are instructed to rate "heightened emotional tone, including irritability and expansiveness (hypomanic affect)." Rating scale ranges from 0 (not observed) to 7 (very severe).

As reported previously, reliability of ratings from baseline to year 10 was excellent with intraclass correlations ≥0.75 (2, 3, 4). At year 20, interviewers rated 30 randomly selected audio recordings of 10-year interviews to evaluate consistency between waves. Intraclass correlations were 0.94 for Apathy-Asociality, 0.97 for Reality Distortion, and 0.93 for Disorganization, 0.96 for BPRS Excitement, and 0.87 for SCID Depression. Inexpressivity could not be rated from audio recordings.

Multilevel spline regression was used to estimate outcome trajectories of the diagnostic groups from month 6 to year 20. This model describes individual trajectory of each participant in terms of starting level (intercept) and subsequent progression (captured by slope in each segment). Intercept was modeled as a random effect (parameter that varies between people). Since change may be nonlinear, we compared two-segment spline models (i.e., trajectory is continuous but has one slope in the first segment and a different slope in the second segment) to single-segment models (consistent change throughout the entire follow-up). In the two-segment

model, transition between segments was determined empirically by selecting time point for transition that maximized model fit. Model selection was done in each diagnostic group independently. After a spline model was selected, we estimated mean trajectory for the group and calculated significance of slopes to test for change in the outcome over time. Next, we added time-varying covariates to the model (e.g., age, medication) to determine whether changes in these variables explain changes in an outcome over time. Analyses were performed in in SAS version 9.2 with PROC GLIMMIX.

Supplemental Results

Although focus of the study is on trajectories of symptoms, we thought it informative to also describe patterns of medication use over time (Figure S1). Antipsychotics were used at a consistently high rate (~80%) in schizophrenia group, other than a small reduction at year 10; while use of antipsychotics declined substantially in mood disorders with psychosis (from 63% at month 6%–32% at year 20), and other psychoses showed a similar decline but it did not reach statistical significance. In contrast, use of antidepressants and mood stabilizers remained unchanged in all groups from month 6 to year 20, except for a small increase in mood stabilizer use in schizophrenia (from 15% to 25%).

We examined six additional time-varying covariate that might explain slopes of trajectories: 1) hospitalizations (annual rate in the interval preceding the assessment), 2) number of medical conditions the participant reported being treated for or diagnosed with during the interval (assessed with the chronic conditions module of the Composite International Diagnostic Interview (5), which includes diabetes, hypertension, other heart problems, gastrointestinal problems, asthma, arthritis, cancer, liver problems, thyroid problems, headaches, seizures, eye problems, hearing problems, and HIV), 3) major depressive episode in the interval (assessed with the SCID), 4) manic episode in the interval (assessed with the SCID), 5) number of medication visits to a mental health provider (monthly rate averaged across six months prior to the assessment), and 6) number of psychotherapy visits (monthly rate averaged across six months prior to the assessment). Data were obtained by interviews with participants, interviews with significant others, and review of medical records when available.

These variables were added to spline regression models that controlled for age and antipsychotic use, resulting in eight time-varying covariates altogether. Simultaneous adjustment for these covariates generally did not alter the course of the seven outcomes in the three diagnostic groups, except that increase in apathy-asociality became nonsignificant in other psychoses after controlling for psychotherapy visits, initial decrease in inexpressivity became nonsignificant in mood disorders with psychosis after controlling for antipsychotics, increase in disorganization was fully explained in mood disorders with psychosis by occurrence of manic episodes and hospitalizations in the interval, and decrease in depression became nonsignificant in schizophrenia and mood disorders with psychosis after controlling for occurrence of major depressive episodes in the interval (Table S4). Thus, even controlling for a range of covariates, we observed a global decline (indicated by the GAF) in all groups and an increase in psychosis specific to schizophrenia. This suggests that the declining clinical course observed in this cohort is not due to aging, mood episodes, physical comorbidities, or changes in treatment, although our ability to test treatment effects is limited by the observational nature of the study.

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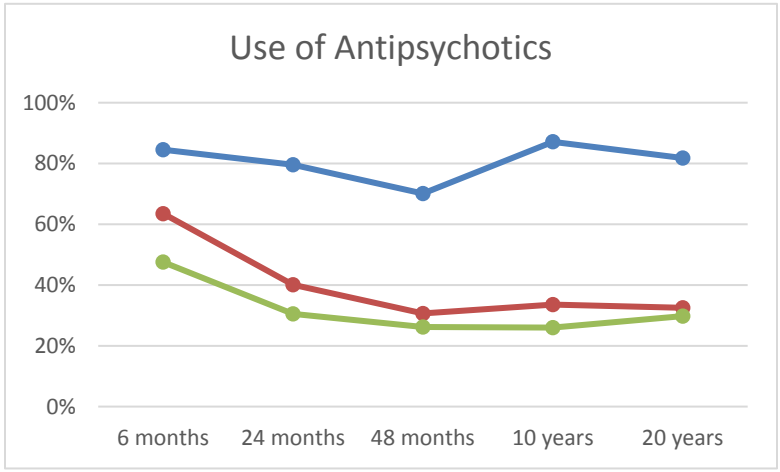
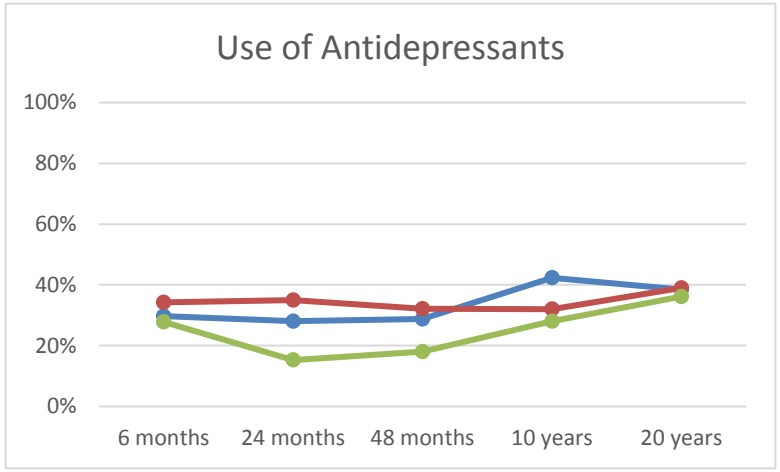
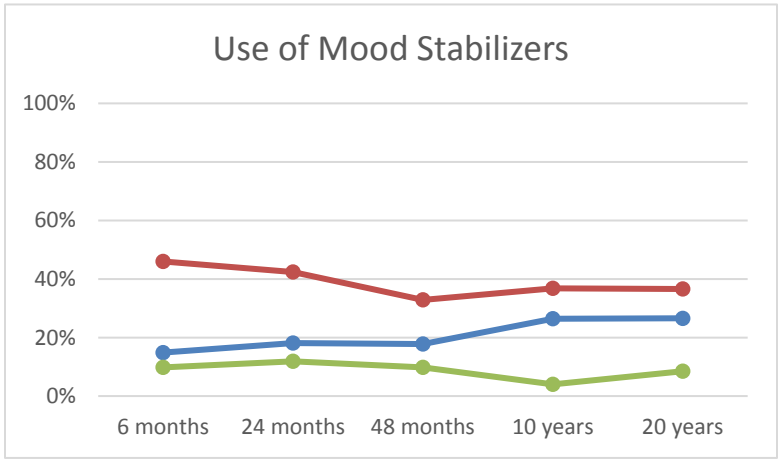
FIGURE S1. Antipsychotics, antidepressants, and mood stabilizers in major diagnostic groups: prevalence at each follow-up and comparison to month 6

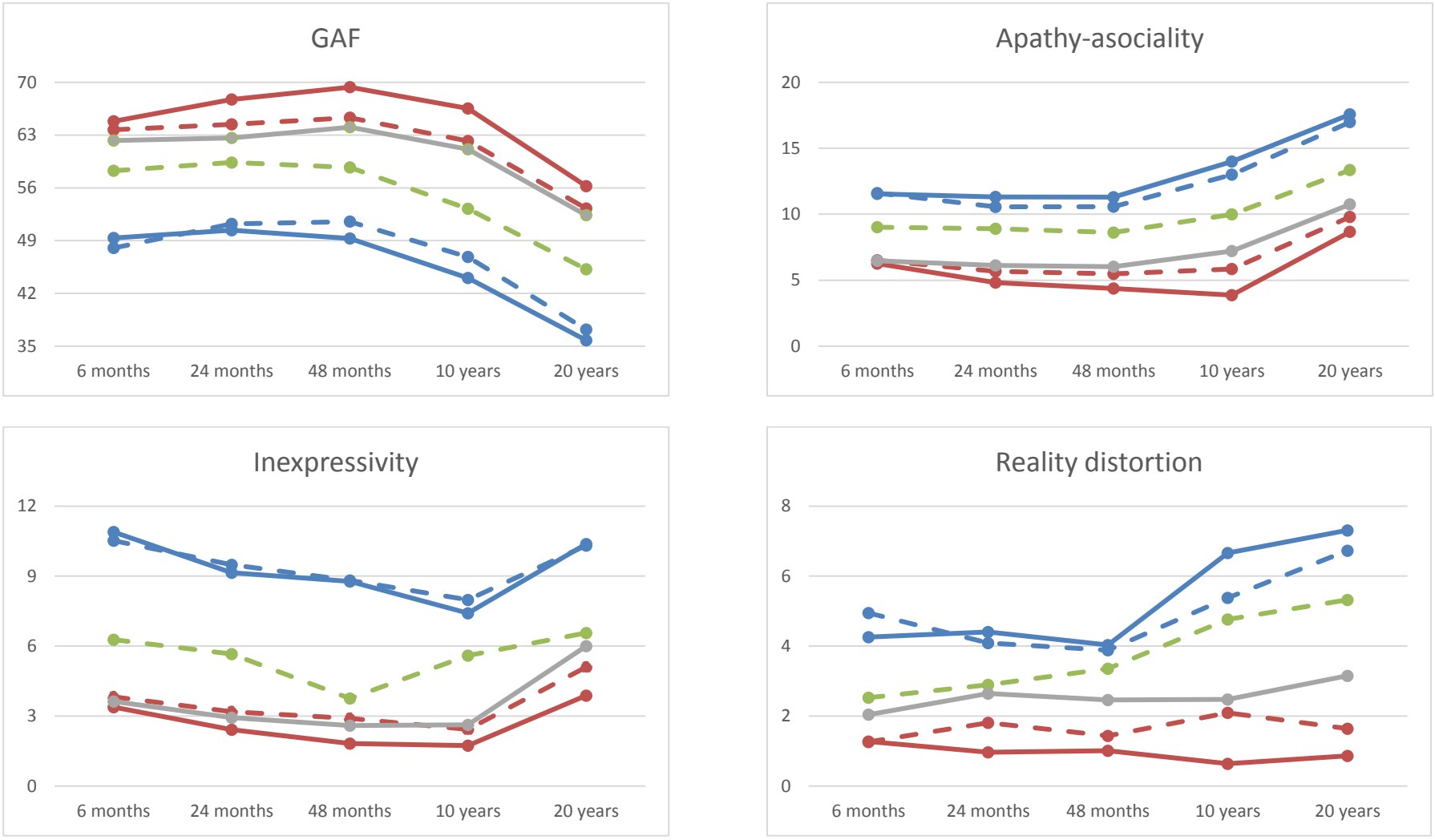


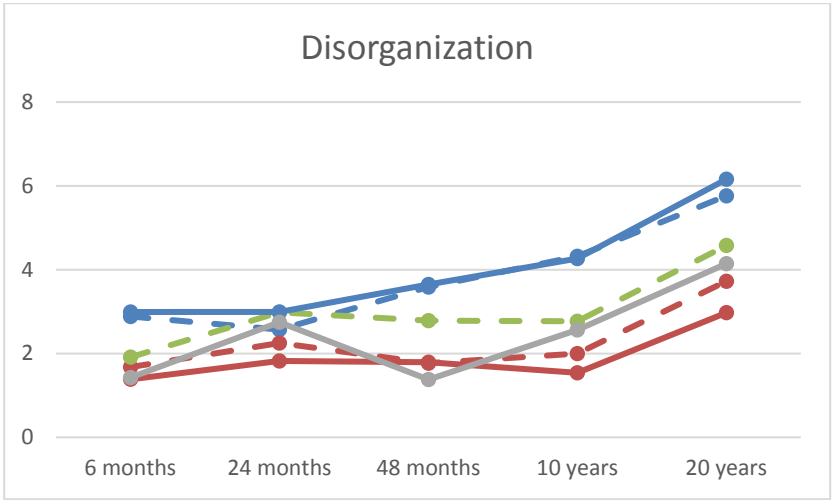


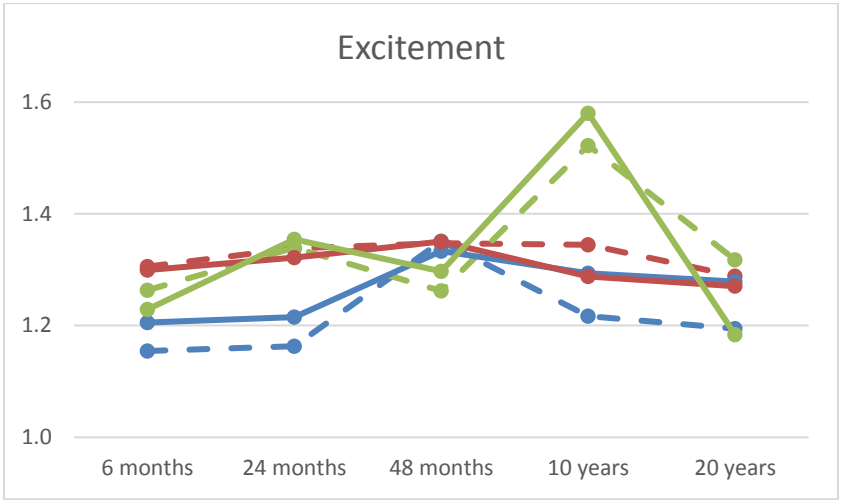


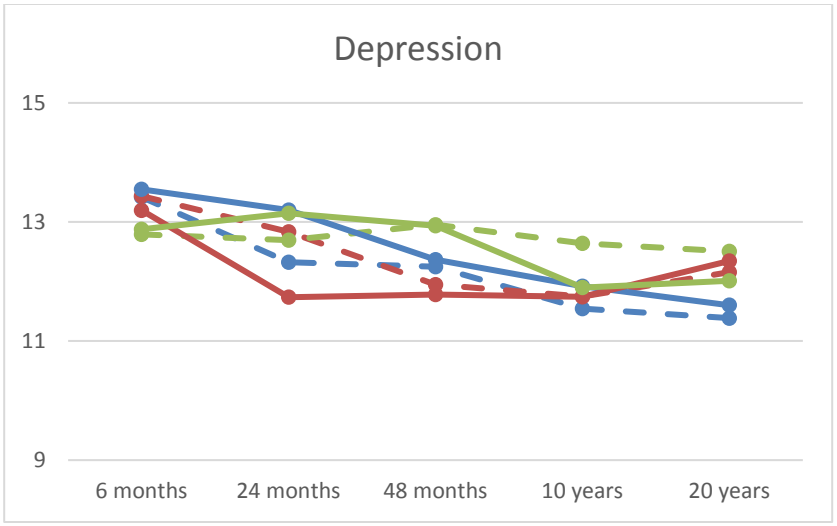
[a] Blue=schizophrenia, orange=mood disorders with psychosis, gray=other psychoses. Sample size is N=175, 171, 174, 163, and 143 for schizophrenia (6-month to 20-year wave, respectively), 137, 137, 137, 125, and 123 for mood disorders with psychosis, and 61, 59, 61, 50, and 47 for other psychoses. *p<0.01 for difference between 6-month and a later follow-up.

FIGURE S2. Mean outcomes in major groups for 6-month and 10-year diagnoses



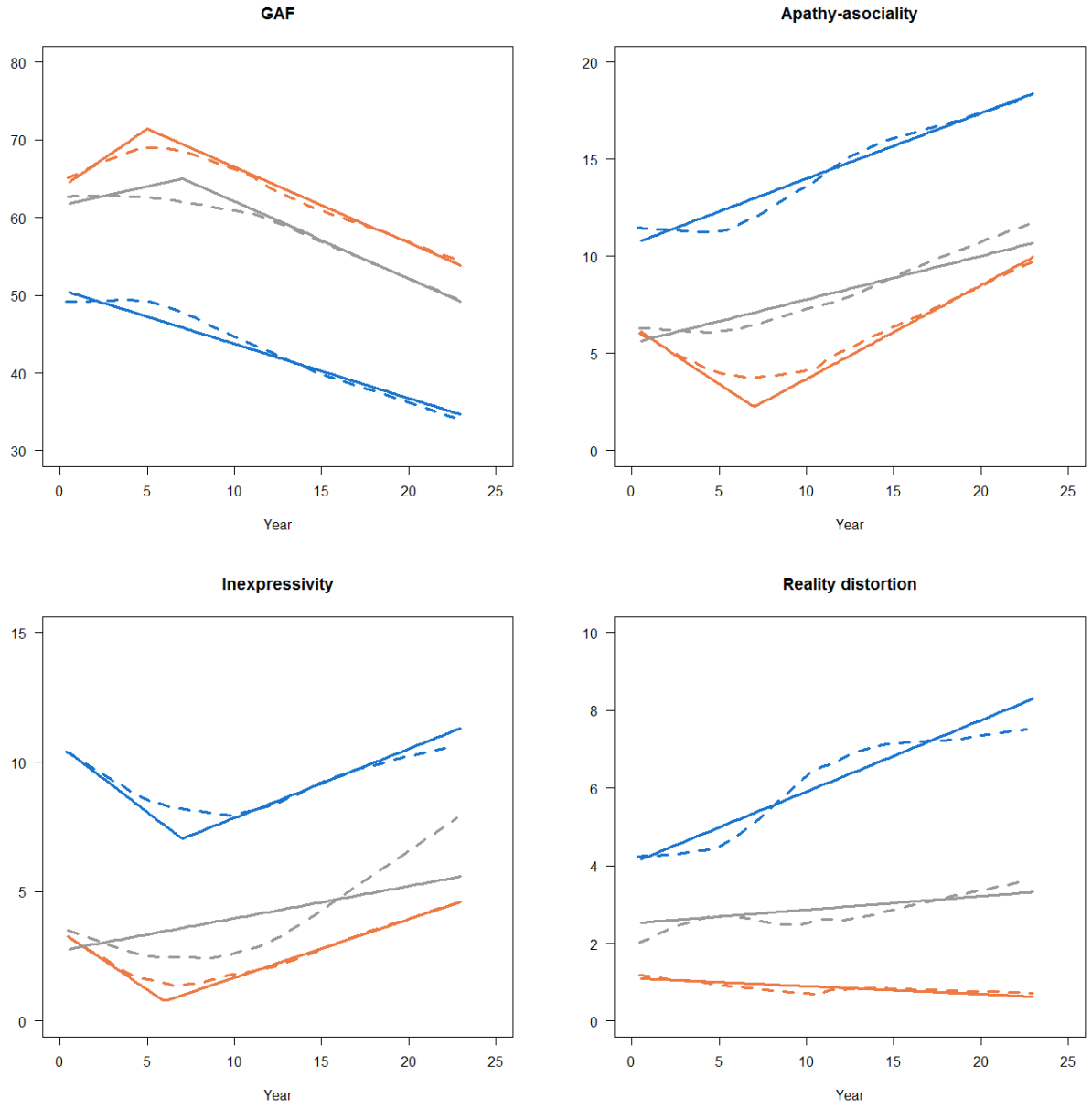


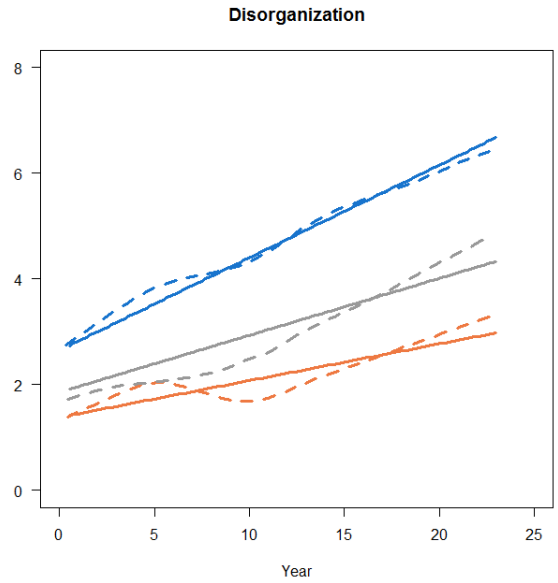


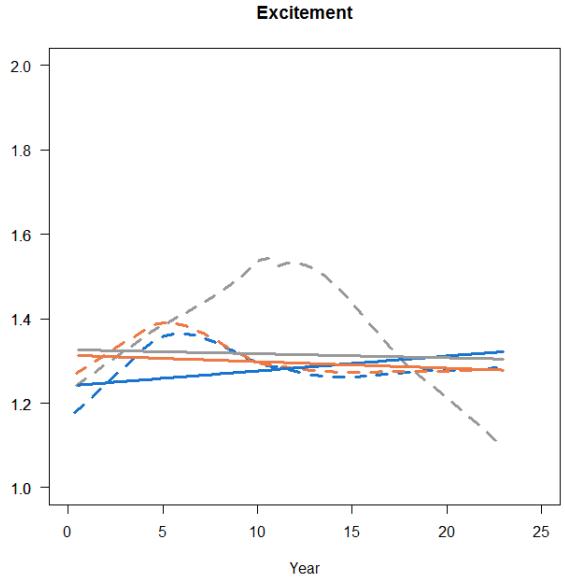


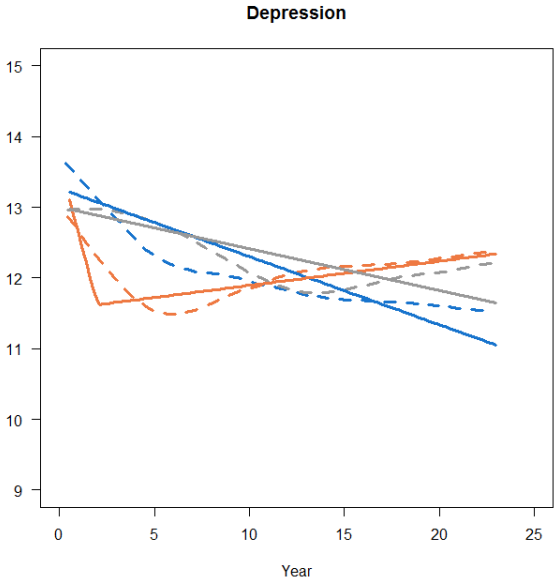
Note: To evaluate confounding of 10-year diagnosis with illness course, we compared trajectories for the three disorder groups defined according to 10-year diagnosis (solid lines) to groups defined by 6-month diagnosis (dashed lines). Blue = schizophrenia, orange = mood disorders with psychosis, grey = other psychoses. Sample size is *N* = 115, 110, 111, 124, and 129 for 6-month schizophrenia (6-month to 20-year wave, respectively), 147, 149, 146, 152, and 165 for 6-month MoDWP, and 61, 62, 54, 69, and 79 for 6-month other psychoses. Sample size is *N* = 153, 148, 145, 166, and 175 for 10-year schizophrenia (6-month to 20-year wave respectively), 121, 122, 122, 127, and 137 for 10-year MoDWP, and 49, 51, 44, 52, and 61 for 10-year other psychoses.

FIGURE S3. Comparison of trajectories from spline regression to smoothing of raw data









[a] To evaluate accuracy of the multilevel spline regression models, we compared these models to smoothing data with locally weighted scatterplot smoothing (LOESS). LOESS uses weighted least squares to fit linear functions within a fixed neighborhood of each data

point. It was applied for each diagnostic group separately. Solid lines are modeled curves from Figure 2. Dashed lines are LOESS curves. Blue=schizophrenia, orange=mood disorders with psychosis, gray=other psychoses. Sample size is N=175 for schizophrenia, 137 for mood disorders with psychosis, and 61 for other psychoses.

TABLE S1. Differences between disorders at month 6, year 20, and in change from month 6 to year 20[a]

	Mood Disorders With Psychosis			Other Psychoses				Schizophrenia			
	N	M	SD	N	M	SD	p	N	M	SD	p
GAF											
6mo	121	64.83	12.73	49	62.27	12.00	0.229	153	**49.34**	13.18	0.000
20yr	137	56.23	16.66	61	52.37	18.05	0.144	175	**35.79**	10.57	0.000
20yr–6mo	121	–8.86	15.72	49	–8.64	17.16	0.933	153	**–13.19**	14.08	0.017
Inexpressivity											
6mo	117	3.38	5.70	49	3.63	5.55	0.797	146	**10.52**	8.92	0.000
20yr	93	3.88	6.03	39	6.00	9.29	0.195	129	**10.32**	10.37	0.000
20yr–6mo	84	0.33	7.15	31	3.39	10.10	0.073	111	0.44	10.84	0.933
Apathy-asociality											
6mo	117	6.26	6.82	49	6.47	6.20	0.857	146	**11.55**	7.92	0.000
20yr	128	8.67	8.00	51	10.75	9.68	0.178	149	**17.56**	8.84	0.000
20yr–6mo	110	2.58	7.97	41	4.19	8.58	0.280	126	**6.13**	8.86	0.001
Reality distortion											
6mo	117	1.27	2.95	49	2.04	4.03	0.233	146	**4.26**	7.44	0.000
20yr	128	0.87	2.20	52	**3.15**	5.44	0.005	151	**7.31**	9.34	0.000
20yr–6mo	110	–0.40	3.42	42	1.00	4.80	0.089	126	**3.77**	11.47	0.000
Disorganization											
6mo	117	1.38	2.61	49	1.43	2.17	0.917	146	**2.99**	5.14	0.001
20yr	126	2.97	4.96	51	4.14	5.62	0.173	148	**6.16**	7.28	0.000
20yr–6mo	110	1.76	5.51	41	1.87	4.61	0.910	124	**3.79**	7.20	0.016
Depression											
6mo	117	13.20	4.42	49	12.88	4.55	0.675	146	13.55	4.03	0.502
20yr	124	12.35	4.18	49	12.01	3.70	0.625	141	11.60	3.28	0.111
20yr–6mo	106	–0.96	5.30	40	–0.97	4.21	0.991	118	–1.90	4.54	0.154
Excitement											
6mo	117	1.30	0.77	48	1.23	0.72	0.590	146	1.21	0.66	0.290
20yr	122	1.27	0.77	49	1.18	0.57	0.476	147	1.28	0.83	0.932
20yr–6mo	105	0.00	1.03	39	–0.05	0.89	0.783	126	0.13	0.87	0.281

[a] p values reflect t tests comparing schizophrenia and other psychoses to mood disorders with psychosis. Bold indicates statistically significant differences ($p<0.05$).

TABLE S2. Fit of spline models[a]

	segments	Schizophrenia			**Mood Disorders With Psychosis**			Other	
Symptom		BIC	ΔBIC		BIC	ΔBIC		BIC	ΔBIC
GAF									
	1	**5603**	–		4533	–		1912	–
	2	5596	7		**4483**	50		**1901**	11
	3	5589	7		4479	3		1896	4
Apathy-asociality									
	1	**4772**	–		3745	–		**1537**	–
	2	4767	6		**3710**	35		1534	3
	3	4760	6		3706	3		1533	1
Inexpressivity									
	1	4600	–		3057	–		**1377**	–
	2	**4586**	14		**3040**	16		1373	5
	3	4579	7		3039	2		1369	4
Reality distortion									
	1	**4870**	–		**2701**	–		**1373**	–
	2	4869	1		2701	0		1372	1
	3	4866	2		2702	–2		1372	0
Disorganization									
	1	**4226**	–		**3023**	–		**1300**	–
	2	4226	0		3022	1		1301	0
	3	4224	1		3020	2		1300	1
Depression									
	1	**3749**	–		3205	–		**1309**	–
	2	3744	4		**3191**	14		1308	1
	3	3743	1		3191	–1		1307	1
Mania/Excitement									
	1	**1502**	–		**1326**	–		**589**	–
	2	1504	–2		1329	–3		585	4
	3	1507	–3		1332	–3		584	2

[a] BIC=Bayesian Information Criterion. Bold indicates selected model (less parsimonious model was selected if it improved BIC by at least 10 points). Analyses were stratified by primary diagnosis. Sample size is N=175 for schizophrenia, 137 for mood disorders with psychosis, and 61 for other psychoses.

TABLE S3. Changes in symptoms explain contemporaneous changes in GAF[a]

	Schizophrenia		Mood Disorders With Psychosis		Other Psychoses	
	β	p	β	p	β	p
Inexpressivity	**–0.11**	0.0005	**–0.11**	0.0005	0.00	0.9965
Apathy-asociality	**–0.45**	<0.0001	**–0.49**	<0.0001	**–0.53**	<0.0001
Reality distortion	**–0.25**	<0.0001	**–0.05**	0.0414	**–0.29**	<0.0001
Disorganization	**–0.18**	<0.0001	**–0.08**	0.0195	–0.07	0.1521
Depression	**0.07**	0.0167	–0.02	0.5919	–0.02	0.6760
Excitement	**0.09**	0.0081	**–0.06**	0.0441	–0.03	0.5355

[a] To evaluate contributions of individual symptoms to global outcome, we constructed a multilevel model (with random intercept and slopes) for GAF regressed on the six symptom dimensions treated as time-varying predictors. The predictors entered the model simultaneously. All predictors were converted to z-scores prior to analysis to ensure comparability of effect sizes. Sample size is N=175 for schizophrenia, 137 for mood disorders with psychosis, and 61 for other psychoses.
p<0.05 effects are bolded.

TABLE S4. Changes in symptoms over time: unadjusted and adjusting for eight time-varying covariates[a]

	Schizophrenia				Mood Disorders With Psychosis				Other Psychoses			
	Unadjusted		Adjusted		Unadjusted		Adjusted		Unadjusted		Adjusted	
	B	p	B	p	B	p	B	p	B	p	B	p
GAF												
Time(S1)	–0.7	<0.001	–0.56	<0.001	1.52	<0.001	0.89	0.006	0.49	0.119	0.59	0.145
Time(S2)	—	—	—	—	–0.98	<0.001	–0.93	<0.001	–0.99	<0.001	–0.70	0.007
Age	—	—	–0.11	0.215	—	—	0.01	0.938	—	—	–0.27	0.113
Antipsychotics	—	—	–0.93	0.485	—	—	–4.00	<0.001	—	—	–4.99	0.016
Hospitalizations	—	—	–0.64	0.346	—	—	–1.41	0.006	—	—	–0.34	0.764
Physical conditions	—	—	–0.48	0.275	—	—	–1.82	<0.001	—	—	0.04	0.954
MDE	—	—	0.03	0.978	—	—	–0.63	0.500	—	—	0.91	0.627
Manic episode	—	—	4.40	0.013	—	—	1.16	0.334	—	—	3.32	0.372
Medication visits	—	—	0.45	0.456	—	—	–0.55	0.438	—	—	–0.89	0.515
Psychotherapy visits	—	—	0.16	0.516	—	—	0.02	0.952	—	—	–0.01	0.987
Apathy-asociality												
Time(S1)	0.34	<0.001	0.24	0.001	–0.59	<0.001	–0.43	0.002	0.22	<0.001	0.09	0.342
Time(S2)	—	—	—	—	0.48	<0.001	0.40	<0.001	—	—	—	—
Age	—	—	0.10	0.105	—	—	0.06	0.109	—	—	0.12	0.116
Antipsychotics	—	—	2.43	0.003	—	—	2.16	<0.001	—	—	1.06	0.323
Hospitalizations	—	—	0.22	0.584	—	—	0.65	0.041	—	—	0.62	0.318
Physical conditions	—	—	0.28	0.322	—	—	0.98	<0.001	—	—	0.60	0.142
MDE	—	—	–0.58	0.430	—	—	0.25	0.664	—	—	1.25	0.218
Manic episode	—	—	0.73	0.500	—	—	–0.66	0.348	—	—	–1.77	0.382
Medication visits	—	—	0.40	0.278	—	—	0.21	0.611	—	—	0.22	0.777
Psychotherapy visits	—	—	–0.13	0.394	—	—	0.11	0.525	—	—	0.64	0.006
Inexpressivity												
Time(S1)	–0.51	<0.001	–0.56	<0.001	–0.45	<0.001	–0.24	0.072	0.12	0.035	0.15	0.095
Time(S2)	0.27	<0.001	0.35	0.002	0.23	<0.001	0.24	<0.001	—	—	—	—
Age	—	—	0.02	0.767	—	—	–0.03	0.345	—	—	–0.01	0.847
Antipsychotics	—	—	2.80	0.003	—	—	2.04	<0.001	—	—	1.54	0.153
Hospitalizations	—	—	0.56	0.238	—	—	0.48	0.056	—	—	1.39	0.031
Physical conditions	—	—	–0.25	0.434	—	—	0.13	0.473	—	—	0.46	0.264
MDE	—	—	–1.25	0.147	—	—	0.17	0.710	—	—	–0.61	0.575
Manic episode	—	—	–2.04	0.111	—	—	–0.74	0.196	—	—	–0.91	0.666
Medication visits	—	—	0.27	0.509	—	—	–0.06	0.858	—	—	0.48	0.544
Psychotherapy visits	—	—	–0.05	0.774	—	—	–0.07	0.606	—	—	0.11	0.646

Psychosis												
Time	0.18	<0.001	0.20	0.005	–0.02	0.102	–0.05	0.019	0.03	0.299	–0.02	0.759
Age	—	—	–0.03	0.609	—	—	0.01	0.381	—	—	0.05	0.363
Antipsychotics	—	—	–1.42	0.116	—	—	0.26	0.315	—	—	2.01	0.006
Hospitalizations	—	—	0.44	0.341	—	—	0.28	0.046	—	—	0.86	0.039
Physical conditions	—	—	0.46	0.125	—	—	0.36	<0.001	—	—	0.35	0.185
MDE	—	—	–0.17	0.837	—	—	0.62	0.012	—	—	–0.40	0.550
Manic episode	—	—	1.84	0.129	—	—	0.48	0.111	—	—	2.94	0.030
Medication visits	—	—	–1.14	0.006	—	—	–0.14	0.451	—	—	–0.51	0.303
Psychotherapy visits	—	—	0.03	0.866	—	—	0.01	0.941	—	—	–0.17	0.278
Disorganization												
Time	0.18	<0.001	0.16	0.004	0.07	<0.001	0.00	0.978	0.11	0.001	0.05	0.290
Age	—	—	–0.01	0.814	—	—	0.03	0.151	—	—	0.03	0.488
Antipsychotics	—	—	–1.23	0.021	—	—	–0.51	0.167	—	—	–0.02	0.972
Hospitalizations	—	—	0.16	0.541	—	—	0.60	0.001	—	—	0.81	0.027
Physical conditions	—	—	0.18	0.363	—	—	0.10	0.468	—	—	0.14	0.539
MDE	—	—	–0.57	0.222	—	—	–0.14	0.689	—	—	–0.02	0.969
Manic episode	—	—	1.00	0.150	—	—	1.65	<0.001	—	—	4.13	<0.001
Medication visits	—	—	–0.50	0.036	—	—	–0.34	0.185	—	—	–0.87	0.049
Psychotherapy visits	—	—	–0.01	0.946	—	—	0.11	0.311	—	—	0.11	0.428
Depression												
Time(S1)	–0.1	<0.001	–0.07	0.027	–0.99	0.001	–0.45	0.145	–0.06	0.065	–0.12	0.030
Time(S2)	—	—	—	—	0.03	0.166	–0.05	0.177	—	—	—	—
Age	—	—	–0.01	0.655	—	—	0.02	0.277	—	—	0.03	0.408
Antipsychotics	—	—	0.87	0.044	—	—	0.19	0.629	—	—	1.20	0.070
Hospitalizations	—	—	0.14	0.552	—	—	0.11	0.614	—	—	–0.16	0.696
Physical conditions	—	—	0.19	0.175	—	—	0.65	<0.001	—	—	0.74	0.003
MDE	—	—	3.11	<0.001	—	—	2.25	<0.001	—	—	4.08	<0.001
Manic episode	—	—	1.47	0.013	—	—	1.21	0.010	—	—	–0.47	0.726
Medication visits	—	—	–0.29	0.147	—	—	0.23	0.424	—	—	–0.22	0.657
Psychotherapy visits	—	—	0.12	0.137	—	—	0.21	0.071	—	—	–0.06	0.701
Mania/Excitement												
Time	0.00	0.313	0.00	0.427	0.00	0.696	–0.01	0.111	0.00	0.889	–0.01	0.561
Age	—	—	–0.01	0.277	—	—	0.00	0.822	—	—	0.00	0.703
Antipsychotics	—	—	–0.15	0.054	—	—	0.02	0.755	—	—	–0.04	0.785
Hospitalizations	—	—	0.02	0.592	—	—	0.06	0.144	—	—	0.01	0.918
Physical conditions	—	—	0.02	0.529	—	—	0.02	0.413	—	—	–0.02	0.725

MDE	—	—	–0.09	0.221	—	—	–0.09	0.227	—	—	0.02	0.869
Manic episode	—	—	0.12	0.247	—	—	0.35	<0.001	—	—	0.59	0.026
Medication visits	—	—	–0.08	0.023	—	—	–0.01	0.855	—	—	–0.16	0.103
Psychotherapy visits	—	—	0.00	0.826	—	—	–0.01	0.688	—	—	0.00	0.932

[a] B=change in symptom score per year. Dashes indicate nonapplicable (i.e., effects not included in the model). S1 is first segment of the 20-year interval or the entire interval, if we model has only one segment; S2 is the second segment. Transition point between segments for GAF was at year 5 in mood disorders with psychosis and year 7 in other psychoses; for apathy-asociality it was at year 7 in mood disorders with psychosis; for inexpressivity it was at year 6 in mood disorders with psychosis and year 7 in schizophrenia; for depression it was at year 2 in mood disorders with psychosis. Unadjusted results are the same as in Table 3 and are included for reference to help interpret impact of covariates on trajectories. Sample size is N=175 for schizophrenia, 137 for mood disorders with psychosis, and 61 for other psychoses.