Data supplement for Kotov et al., Declining Clinical Course of Psychotic Disorders Over the Two Decades Following First Hospitalization: Evidence From the Suffolk County Mental Health Project. Am J Psychiatry (doi: 10.1176/appi.ajp.2017.16101191)

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.

References

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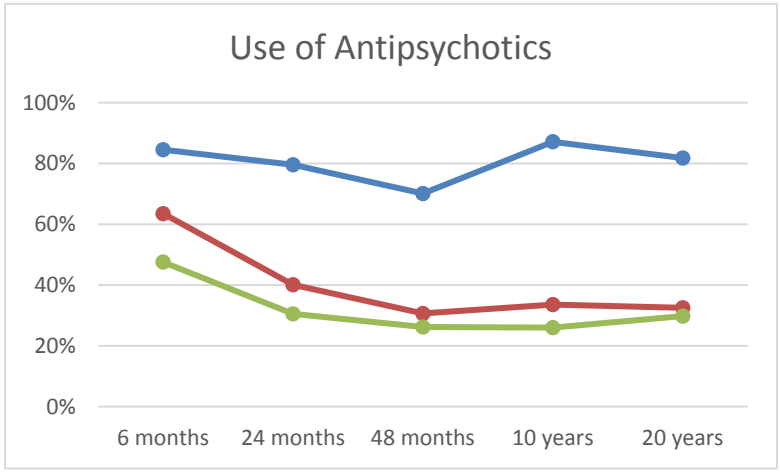
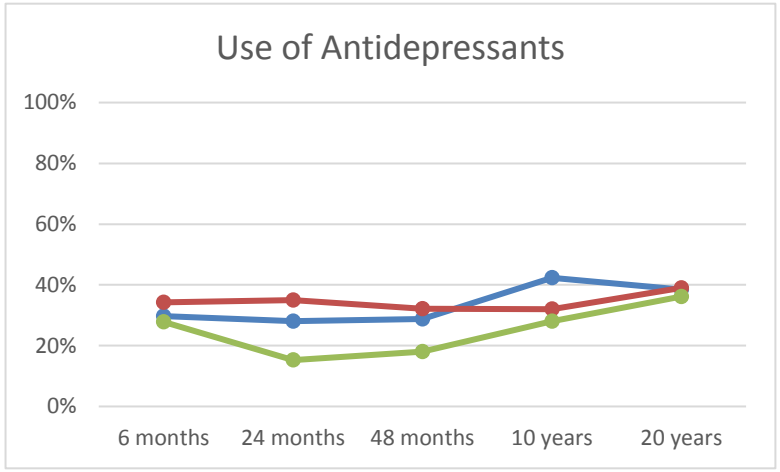
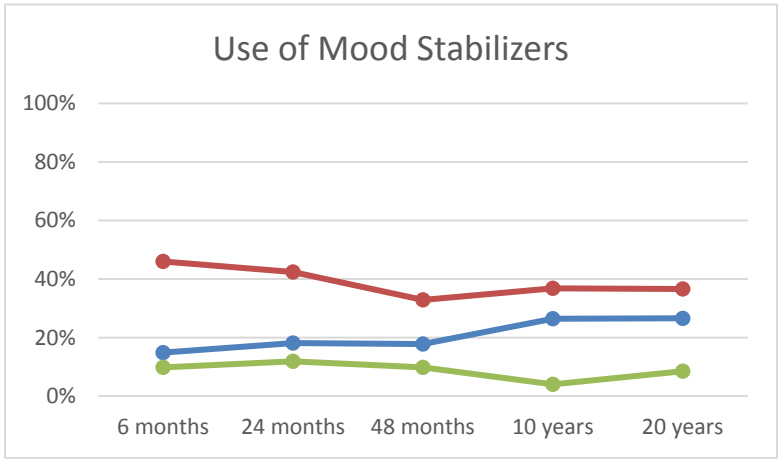
FIGURE S1. Antipsychotics, antidepressants, and mood stabilizers in major diagnostic groups: prevalence at each follow-up and comparison to month 6

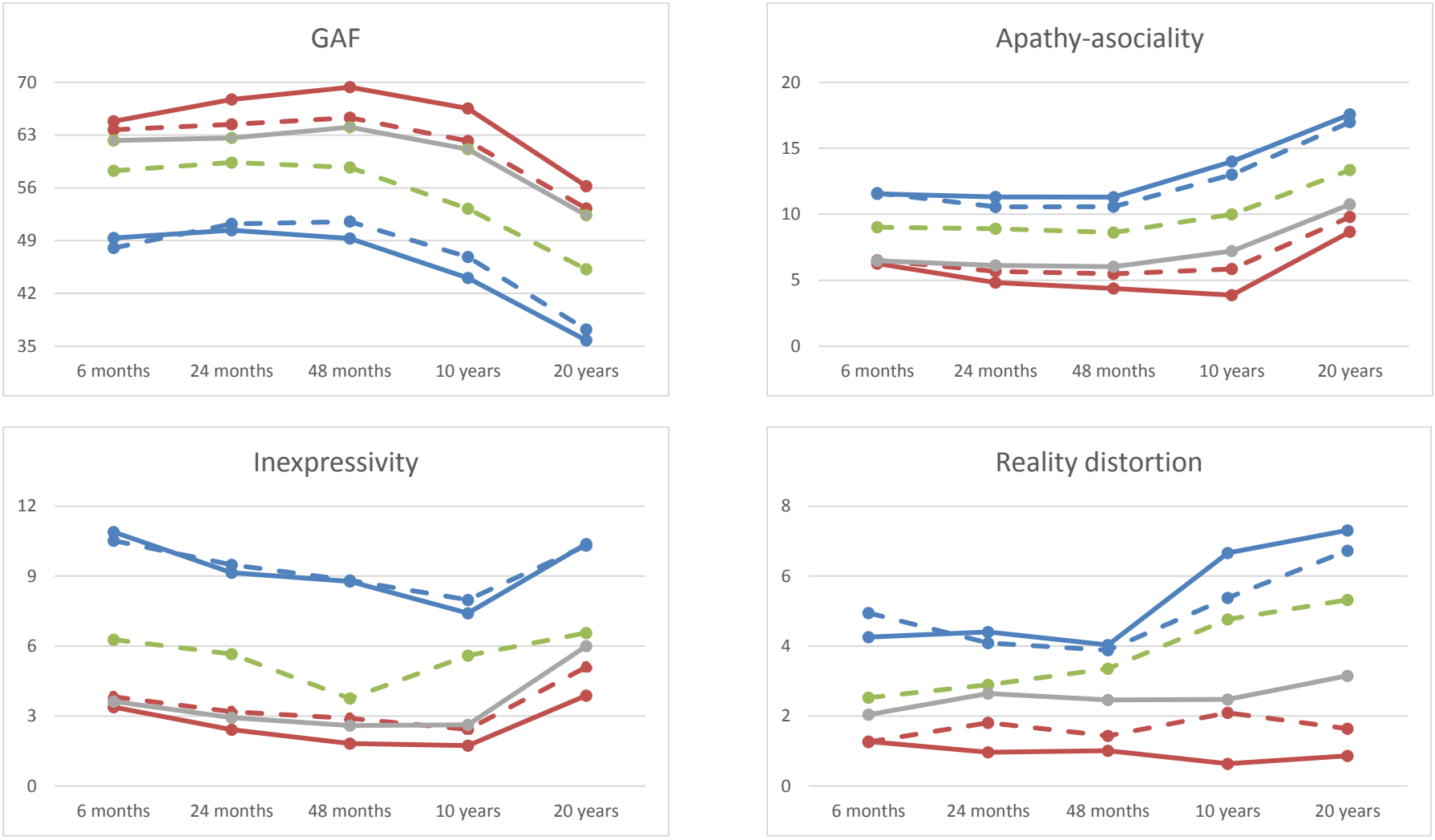


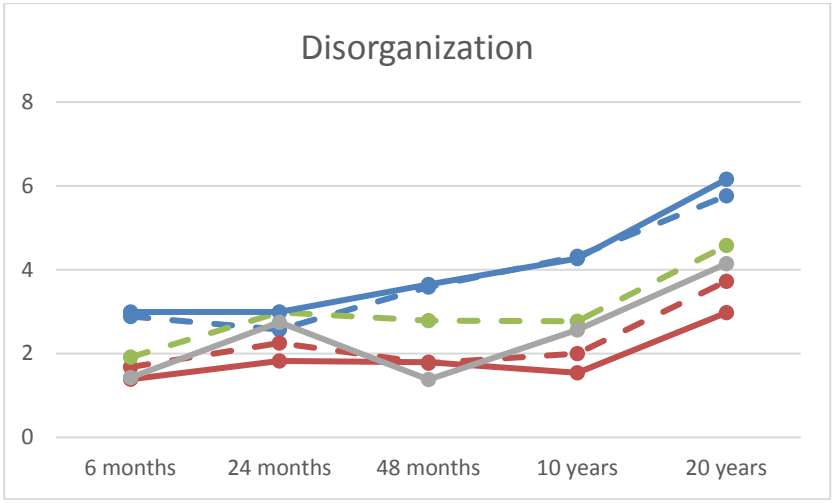


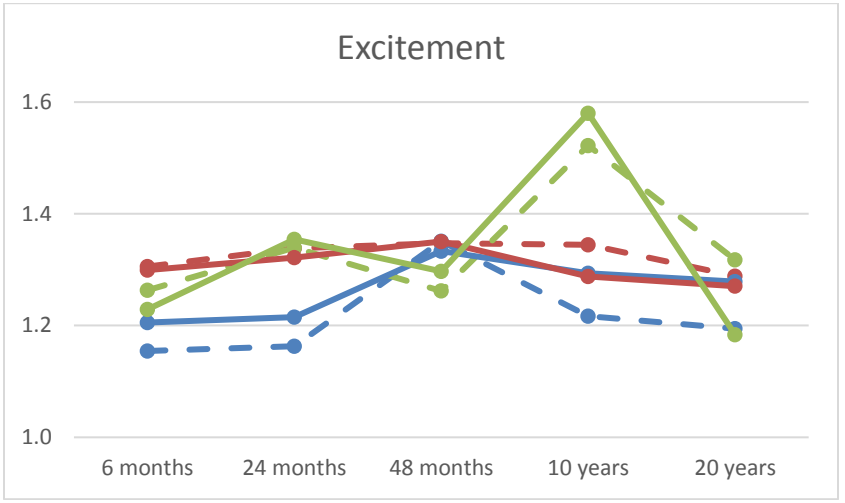


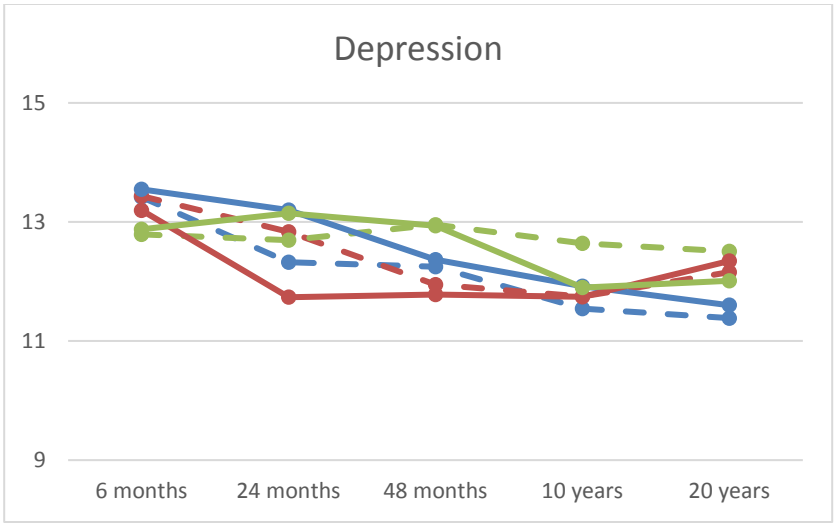
[a] Blue=schizophrenia, orange=mood disorders with psychosis, gray=other psychoses. Sample size is N=175, 171, 174, 163, and 143 for schizophrenia (6-month to 20-year wave, respectively), 137, 137, 137, 125, and 123 for mood disorders with psychosis, and 61, 59, 61, 50, and 47 for other psychoses. *p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



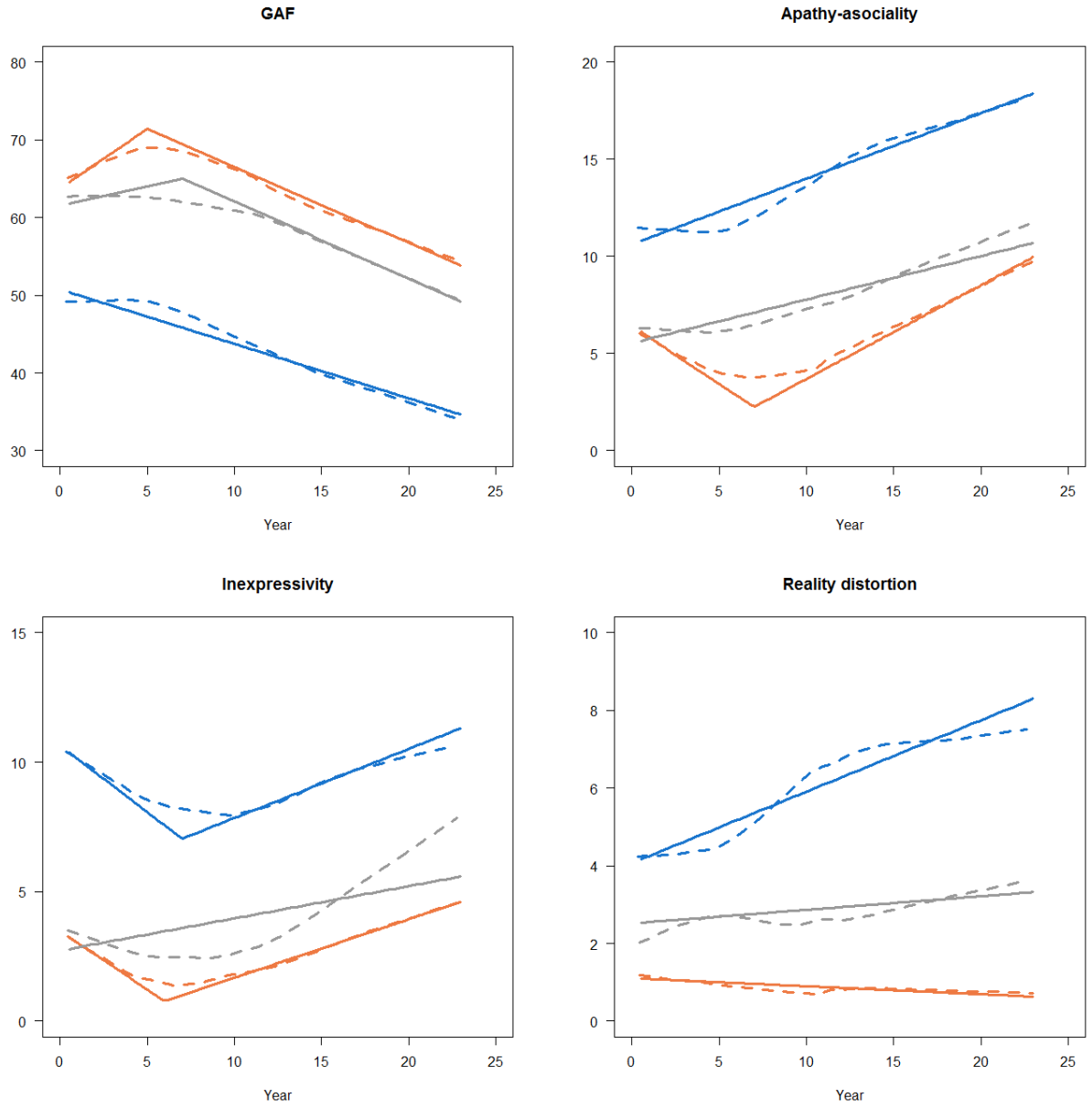


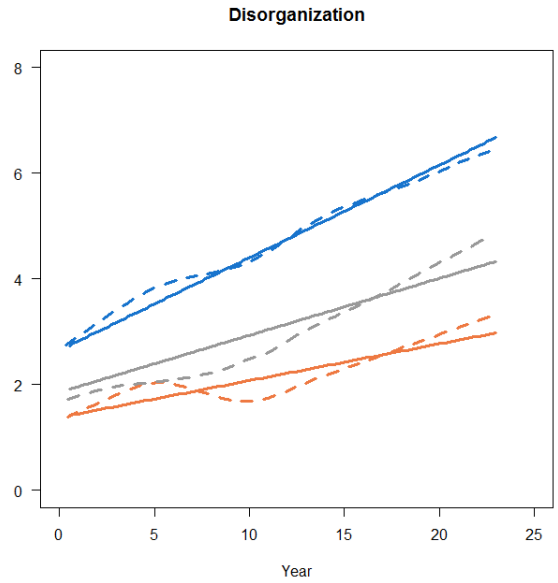


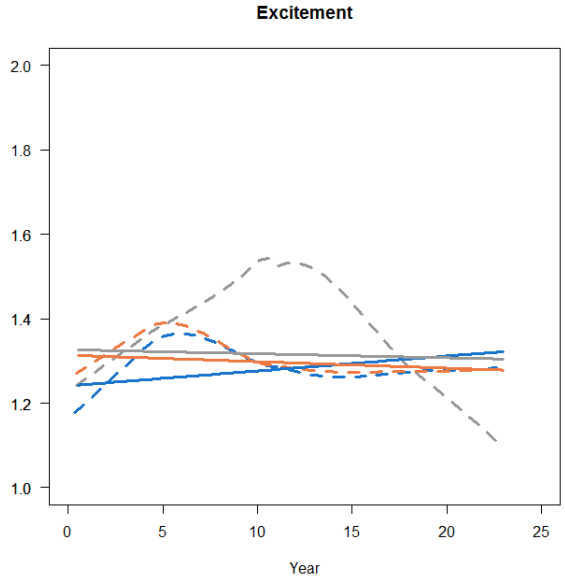


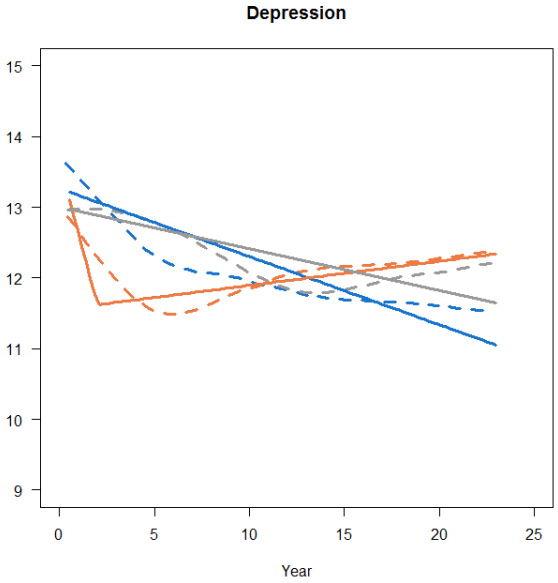
Note: To evaluate confounding of 10-year diagnosis with illness course, we compared trajectories for the three disorder groups defined according to 10-year diagnosis (solid lines) to groups defined by 6-month diagnosis (dashed lines). Blue = schizophrenia, orange = mood disorders with psychosis, grey = 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.