# The Long-Term Course of Remission and Recovery in Psychotic Disorders

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**Data availability:** Raw data from the Suffolk County Mental Health Project are available through dbGap (accession number phs001020.v2.p1). Additional phenotypic data that support the findings of this study are available from the corresponding author upon request.

**Abstract**

*Objective*

Understanding prognosis is critical to anticipating public health needs and providing care to individuals with psychotic disorders. However, the long-term course of remission and recovery remains unclear. In this cohort of individuals followed for 25 years since first admission for psychosis, we describe the most common trajectories of illness course.

*Methods*

Participants are from the Suffolk County Mental Health Project, an epidemiological study of first-admission psychosis. Data for the present study was gathered from six follow-ups. 311 individuals were assessed at the 25-year follow-up. Common patterns of remission and recovery were assessed in the baseline cohort of 591 individuals and the subsample observed at the 25-year follow up.

*Results*

In the baseline cohort and 25-year subsample the most common trajectory for those with schizophrenia spectrum disorders was no remission and no recovery. Among those with other psychotic disorders, in both the baseline and 25-year cohorts, the modal pattern was one of intermittent remission and recovery. Those with other psychotic disorders were more likely to experience stable remission (15.1%) and stable recovery (21.1%), outcomes that were rare in schizophrenia spectrum disorders (0% and 0.6%, respectively).

*Conclusions*

The modal longitudinal pattern for those with other psychoses is one multiple transitions into and out of symptomatic and functional recovery. Engagement in a long-term health care plan may help individuals detect and respond to these changes. Sustained remission and recovery are rare among people with schizophrenia spectrum disorders. Efforts should be put towards developing more effective treatments for this population.

## Introduction

Psychotic disorders, in which individuals experience hallucinations and delusions, negatively impact quality of life (1), relationships (1), physical health (2), and occupational function (3). However, remarkably little is known about the long-term course of remission and recovery in psychotic disorders. Understanding the likelihood of remission—the presence of only mild symptoms—and recovery—remission of symptoms plus good psychosocial function—is critical to understanding these disorders, providing accurate prognoses for patients and families, and for providing appropriate levels of care throughout the illness course.

Cross-sectional estimates of remission and recovery vary widely. A recent meta-analysis of longitudinal first-episode psychosis cohorts estimated 38% of individuals recover (range 14.9%-49.2%), and 58% of individuals remit (range 26.7%-93.9%, 4). Among those with schizophrenia, rates are lower. A systematic review found that 1 in 7 individuals with schizophrenia recovers (5). The wide range of these estimates may be attributable to different definitions of remission and recovery, although neither analysis identified this as a significant source of variance (4,5). However, some general trends explain variation in these rates. Both remission and recovery are more common among individuals with affective psychosis, relative to individuals with non-affective psychosis (4). Length of follow-up does not does not predict rates of recovery or remission (4), but there are relatively few studies with a follow-up greater than 10 years. Among studies that have followed individuals for at least 10 years, rates of remission have ranged from 50.5% in non-affective psychoses (6), to 60.2% in affective and non-affective psychoses combined (7). In two 20-year first-episode psychosis cohorts, rates of remission were 40% (8) and 65% (9), respectively. Rates of recovery have generally been lower. A small 17-year follow-up of individuals with schizophrenia in Bali observed only a 23.7% recovery rate (10), while the 20-year follow-ups described above estimated rates of 18% (8) and 35.2% (9), and a 21-year follow-up of

first-admission psychosis found 32.5% of individuals met criteria for symptomatic, functional, and personal recovery (11).

Knowing cross-sectional probabilities of remission and recovery is useful for understanding population averages, but can obscure meaningful patterns within individuals. To understand trajectories of remission and recovery, longitudinal analyses are needed. In 1980, Ciompi reported the first such analysis, dividing a sample of individuals with schizophrenia into 8 discrete symptom trajectories (12). The four groups accounting for a plurality of individuals were a course of recovery (24%), an undulating course, in which psychotic episodes grew less frequent and periods of remission more frequent (49%), an undulating course with fewer periods of remission over time (9%), and a chronic course (12%). An epidemiologically-ascertained first-episode sample sorted participants into similar trajectories, and found 13% experienced a course of stable recovery, 65% had an undulating course with good outcome, 11% an undulating course with poor outcome, and 23% had a chronic course (13). A 15-year follow-up from the DOSMeD study (14) found a somewhat higher proportion of individuals in trajectories with good outcomes than Ciompi (60% with periodic episodes and a good outcome, 14% with a gradual recovery), likely due to ascertainment from individuals in the developing world.

Two other first-episode cohorts, following individuals for 10 (15) and 20 years post-onset (16), have also reported data on individual trajectories of recovery in psychotic disorders. In the OPUS cohort, 22-25% of individuals were remitted and 14-17% recovered at any given time point across 2-, 5- and 10-year follow-ups (15). However, while most individuals experienced remission at least once in the follow up and 30% experienced recovery, only a minority of individuals stayed remitted or recovered in consecutive time points. Similar rates of recovery, ranging from 10-22% in schizophrenia and 20-43% in other psychotic disorders, were observed across 2-, 4.5-, 7.5-, 10-, and 15-year assessments in the Chicago Follow-Up Study cohort (16). As in the OPUS cohort, periods of recovery were less common in schizophrenia (41%) than other psychosis (67%), as was stable recovery.

While each of these studies inform our understanding of long-term remission and recovery in psychotic disorders, they have some limitations. Some are relatively short (15), given that psychotic disorders onset in early adulthood and individuals may live with symptoms for decades. The OPUS cohort has been followed for 20 years, but trajectories of remission and recovery were last studied at the 10-year follow-up (8). Others are not epidemiological samples (16), or defined outcomes qualitatively rather than quantitatively (12,14).

This present study addresses these limitations in an analysis of remission and recovery, operationalized using Andreasen's (17) and Liberman's (18) definitions, respectively, from an epidemiologically ascertained cohort assessed six times over the 25 years following first admission. Out of 628 participants at baseline, 311 (61% of survivors) were successfully assessed at the 25-year follow-up. We compare patterns or remission and recovery between schizophrenia spectrum and other psychotic disorders, in order to describe the most common trajectories of illness course.

## Method

### Sample

Participants are members of the Suffolk County Mental Health Project, a longitudinal study of first-admission psychosis. Participants were recruited from the 12 inpatient facilities in Suffolk County, New York from 1989-1995. Response rate for the baseline assessment was 72%. Eligibility criteria included first admission within the past 6 months, ages 15-60, current psychosis, no medical cause for psychosis, ability to understand English, a baseline IQ of 70+, and capacity to consent. The Stony Brook University Committee on Research Involving Human Subjects approved the study annually. Written informed consent was obtained from adult study participants, and from parents of participants age 15-17. A total of 628 study participants met inclusion criteria. In-person follow-up interviews were conducted at 6-month, 24-month, 48-month, 10-year, 20-year, and 25-year follow-ups (19). Clinical

interviews were conducted by master-level mental health professionals who did not have access to the consensus study diagnosis.

Figure S1 reports details of participation, death, and attrition across follow-ups. Table 1 reports the demographic characteristics the cohort of 591 participants for whom remission or recovery was known at one or more follow-ups—referred to as the baseline cohort—and the 25-year follow-up of 311 participants—referred to as the 25-year cohort.

**Measures**

Age, race/ethnicity and gender were assessed by self-report, as were marital status, employment status, and lifetime history of homelessness as of first admission. Individuals were classified as having experienced homelessness if, at any time before baseline, they considered themselves homeless and had, for at least one night, slept in a shelter, park, or abandoned building, in the street, or in a bus or train station because they had nowhere else to stay (20). Socioeconomic status was operationalized using the Hollingshead index, based on the occupation of the primary earner of the participant's family. Ratings are made on a scale from 1 to 8, where 1 indicates "large business owner/major professional/executive", 4 indicates "clerical/sales/technician", 5 indicates "skilled manual labor" and 8 indicates "not working". Scores were reversed to ease interpretation.

Age at onset was defined as the age at which the first clear psychotic symptom occurred. The age of onset was determined from symptom timelines obtained during the baseline and 6-month follow-ups, including the SCID, informant interviews, school records, and medical records. Symptoms at baseline were assessed using the Schedule for the Assessment of Positive Symptoms and Schedule for the Assessment of Negative Symptoms (21,22). Ratings were made by interviewers using all available information, including the clinical interview, review of medical records, and collateral interview. Ratings were scored into four factor-analytically derived subscales (23): Avolition-Apathy, Inexpressivity, Reality Distortion, and Disorganization.

Lifetime history of alcohol, cannabis, and other drug use disorders at first admission was derived from the Structured Interview for DSM-III-R (24) administered at baseline and supplemented by items from the National Household Survey on Drug Abuse (25). Research diagnoses for psychotic disorders were made by a consensus of study psychiatrists at the baseline, 6-month, 24-month, 10-year, and 20-year follow-up assessments. Diagnoses were made based on all available information, including the structured clinical interview, medical records, and collateral interviews.

The type of facility to which individuals were first admitted was operationalized dichotomously, in which community units and academic hospitals were contrasted with public hospitals (26). Medications at discharge were derived from discharge summaries and self-report. At subsequent follow-ups medication data were documented based on self-report, pill bottles and medication lists, and medical records. Individuals who reported attending a psychotherapy appointment lasting at least 20 minutes in the 6 months preceding follow-up were considered in psychotherapy.

Symptom remission was operationalized according to Andreasen's (17) definition, using the Scale for the Assessment of Positive Symptoms and the Scale for the Assessment of Negative Symptoms (21,22). Notably, symptoms were rated based on their severity over the past month, rather than the past 6 months as Andreasen's definition stipulates. Both scales range from 0 to 5, where 0=no symptom, 2=mild, and 5=severe. A rating of 2 or less on all of the following symptoms was required for remission: hallucinations, delusions, bizarre behavior, formal thought disorder, affective flattening, alogia, avolition-apathy, and anhedonia-asociality.

Recovery was defined according to criteria from Liberman (18), using eight variables on the Brief Psychiatric Rating Scale (BPRS, 29) and two variables on the Quality of Life Scale (QLS, 30). Symptoms were rated based on their severity over the past month, deviating from Liberman's definition, which spans 2 years. For a participant to be recovered, they had to have scores of 4 or less (moderate or better) on BPRS ratings of conceptual disorganization, mannerisms and posturing, grandiosity,

suspiciousness, hallucinatory behavior, unusual thought content, blunted affect, and emotional withdrawal. Participants also had to have a score of 3 or higher on the QLS rating of social activity (0=virtually absent, 2= occasional social activity, and 6=adequate social activity), and 3 or higher on the QLS rating of accomplishment (0=attempted no role function, 3=generally adequate functioning, and 6=very good functioning). If there was not enough information to complete this rating but the individual was employed or a student, they were considered occupationally recovered.

**Analyses**

Analyses were performed in the baseline cohort of 591 individuals, in order to understand prospective trajectories from first-admission, as well as the 25-year follow up cohort of 311 individuals, to evaluate long-term patterns among those observed into late adulthood. The exception to this was prediction analyses, as prediction of outcomes is most relevant at first admission. Analyses of the baseline cohort were stratified by diagnoses made at first admission. Analyses in the 25-year cohort were stratified on the last available consensus diagnosis. Diagnoses were grouped into schizophrenia-spectrum disorders (schizophrenia, schizoaffective, and schizophreniform disorders) and other psychotic disorders (bipolar disorder with psychosis, major depression with psychosis, drug-induced and other psychotic disorders).

In order to evaluate systematic attrition, the 25-year cohort was compared to the 196 living non-participants. T-tests and chi-square tests were used for comparison of continuous and categorical variables, respectively. P-values $< 0.05$ were considered significant. Those in the 25-year cohort were younger at both age of onset and baseline assessment by 2.5 years, and were of higher socioeconomic status, although this effect was small. The two groups did not differ in terms of race/ethnicity or gender.

The primary aim of this study was to describe longitudinal patterns of remission and recovery. As missing data would prevent the grouping people into longitudinal patterns, missing data were imputed. The distribution of missing ratings within individuals across study timepoints is reported in Table S1.

Imputation was conducted in SPSS using Multivariate Imputation by Chained Equations (MICE, 31). In the MICE algorithm, a chain of regression equations is used to impute ratings one by one, using information from all other variables in the model. The ratings on which remission and recovery are based (see above) were imputed using the same ratings from other time points, as well as ethnicity, gender, age at assessment, age at first psychotic symptom, and socioeconomic status. Twenty imputated datasets were generated. Data were not imputed for timepoints following death. Table S2 reports the descriptive statistics of raw and imputed data. Analyses were repeated in each imputed dataset, and the $50^{th}$, $2.5^{th}$ and $97.5^{th}$ quantiles were used to generate parameter estimates and 95% confidence intervals, respectively, for cross-sectional rates of remission and recovery and rates of patterns of remission and recovery.

Tetrachoric correlations were used to assess stability of remission and recovery across follow-ups. Patterns of remission and recovery were identified using upset plots made using the R package `ComplexHeatmap` (32). Upset plots are reported in Figure S2. Upset plots were used to depict observed patterns of recovery and remission, and the frequency with which each pattern was observed. These plots identified four common patterns of remission and recovery:

1. Stable remission/recovery: participants who were remitted or recovered across all time points.
2. No remission/recovery: participants who were not remitted or recovered at any time.
3. Early remission/recovery: participants who had a period of remission or recovery in the four years following first admission, but not thereafter.
4. Intermittent remission/recovery: participants not falling into groups 1-3.

Multinomial regression was used to identify predictors of patterns of remission and recovery. The likelihood ratio test was used to assess statistical significance. Predictors with a median p-value $< 0.05$ were considered significant. Post-hoc logistic regression was used for pairwise comparisons of significant predictors. Analyses were repeated in each imputed dataset, and pooled parameter estimates were

estimated using Rubin's Rules (33). Penalized logistic regression was used for contrasts of stable remission by diagnosis, as few individuals with schizophrenia had a trajectory of stable recovery, causing estimation of standard errors to fail. Due to a small amount of missing predictor data, the sample size for regressions was 584.

## Results

Cross-sectional rates of remission and recovery in baseline cohort of 591 individuals are reported in the left side of Table 2. Data missing for reasons other than death are imputed. Among those ascertained at first admission, 41.9% of those with other psychotic disorders and 27.2% of those with schizophrenia spectrum disorders were recovered 6 months after first admission. However, rates declined over time, and at the end of the 25-year follow-up only 28.1% of those with other psychoses and 14.2% of those with schizophrenia spectrum disorders were in recovery. Remission rates followed a similar trajectory, beginning at 46.2% in other psychotic disorders and 24.9% in schizophrenia spectrum disorders, and falling to 20.0 and 7.4%, respectively.

Cross-sectional rates of remission and recovery in the 25-year cohort are reported in the right half of Table 2. Data missing for reasons other than death are imputed. Among those with schizophrenia spectrum disorders, cross-sectional rates of remission and recovery were higher, but generally similar to those observed in the baseline cohort. In the first four years of illness, approximately one quarter of those with schizophrenia spectrum disorders were remitted. Notably, among those with other psychotic disorders, individuals in the 25-year cohort were more likely to be remitted or recovered at any given time point compared to the baseline cohort. However, these differences are attributable to diagnostic shifts between baseline and the 25-year follow-up, as 74 of the 159 individuals with schizophrenia spectrum disorders at the 25-year follow-up transitioned into that group from other psychotic disorders. These individuals were less likely to be remitted or recovered, so their transition increases the rate of remission and recovery in other psychoses, and reduces it in schizophrenia spectrum disorders.

Table 3 reports the stability of remission and recovery between time points. Stability between consecutive time points was high and increased over time. The highest stability estimates for both remission (r=0.69-0.79) and recovery (r=0.64-0.73) were observed between the 20- and 25-year follow-ups.

Table 4 summarizes patterns of remission and recovery in schizophrenia spectrum disorders and other psychoses. Among those with schizophrenia spectrum disorders, the most common pattern in both the baseline and 25-year cohort was a trajectory of no remission and no recovery. Among those with other psychotic disorders, the modal pattern in both the baseline and the 25-year cohort was one of intermittent remission and recovery. Those with other psychotic disorders were more likely to experience stable remission (15.1%) and stable recovery (21.1%), than those with schizophrenia spectrum disorders, where these outcomes were rare (0% and 0.6%, respectively).

Table 5 reports demographic and clinical factors associated with patterns of remission and recovery. Gender, diagnosis, and avolition predicted patterns of both remission and recovery. Race and treatment with mood stabilizers at discharge predicted recovery, while socioeconomic predicted remission.

## Discussion

Among those with schizophrenia spectrum disorders followed for 25 years after first admission, approximately one in four was in recovery or remission through the first four years of illness. As of the 25-year follow-up, those rates decreased to 13% and 5%, respectively. Among those with other psychotic disorders followed for 25 years, rates of both remission and recovery exceeded 50% through the first two decades of illness, only falling below this threshold at the 25-year follow-up. Mortality was also high, reaching 20% over the course of the study. Even though remission requires the absence of symptoms, while recovery requires moderate symptoms and good functioning, rates of recovery were

higher than rates of remission at almost every follow-up, indicating many individuals achieve a state of recovery despite a moderate burden of symptoms.

The most common trajectory for individuals with schizophrenia spectrum disorders is one of no remission and no recovery. The increasing stability of symptoms across the follow-up period indicates more effective treatments are needed to impact the course of remission and recovery in schizophrenia spectrum disorders, and illuminates the need for sustained intervention and support for this population. Individuals with other psychotic disorders were more likely to be in a period of remission or recovery at any given follow-up, but also more likely to transition out of these states. In this population, continued symptom monitoring—even during periods of remission and recovery—may help detect and potentially prevent the return of symptoms.

Our results emphasize a need for continued research and treatment for individuals with psychotic disorders in midlife and beyond. Substantial resources have been directed to the study of at-risk and first-episode cohorts. The value of prevention and early intervention cannot be overstated, given the burden of psychotic disorders to individuals and society. However, our findings highlight the often chronic or recurring course of psychosis, and highlight outstanding questions beyond the peri-onset period. Treatment disengagement is common among those with psychotic disorders (34). Over the course of illness, social function declines, weakening ties that facilitate continued treatment engagement (35). Research moderators of treatment engagement could provide valuable targets for improving long-term physical and mental health.

Other long-term studies have found higher remission and recovery rates (7,9,11,16). Unlike most prior research, this sample was epidemiologically-sampled in a defined catchment area. Poorer outcomes in this study are consistent with evidence that worse outcomes are observed in population-representative samples (36). Differences in health care systems may also play a role, as health care available in received by the cohort was inconsistent and largely limited to pharmacotherapy (37).

Our findings most closely mirror those from OPUS, another epidemiological study which identified low cross-sectional rates of remission and recovery and high transition rates between states (15). Our findings also align with a meta-analysis of first-episode psychosis finding favorable outcomes in 34.5% of individuals (38), as well as the systematic review of long-term outcomes in schizophrenia, in which 1 out of 7 individuals recovered (5). These results are also consistent with two prior analyses of this cohort. In a 24-month follow-up of participants with bipolar disorder, non-white participants were less likely to experience complete remission (39). At the 48-month follow-up, the majority of participants with schizophrenia had experienced both recovery and relapse (40).

**Limitations**

These analyses do not include individuals with psychosis who were never hospitalized. While more than 90% of individuals with schizophrenia are hospitalized at some point (41), this rate is lower in bipolar disorder (42) and other psychosis, suggesting this cohort may represent a more severe subsample of individuals with other psychoses. Women were less likely to enroll in the study (19), which may bias the cohort towards worse outcomes. These analyses are limited by cross-sectional assessments, which miss episodes occurring entirely between follow-up intervals. However, symptoms are relatively stable over time (23) so the influence of symptom fluctuations may be minimal. The length of follow-up intervals varied substantially, from 6-months to 10 years. However, the first three intervals were the shortest, capturing changes when remission and recovery are least stable. This analysis is also influenced by attrition. Younger and higher socioeconomic status individuals were more likely to participate in follow-ups. These variables were included in multiple imputation models to address the bias. Retention was relatively high and imputed data allowed for the comparison of complete and incomplete cases.

## Conclusion

Sustained, long-term care is critical for individuals with psychotic disorders. Though people with other psychoses often have periods of remission and recovery, the modal longitudinal pattern is one of recurrence. In this population, continued symptom monitoring—even during periods of remission and recovery—may help detect and potentially prevent the return of symptoms. In this cohort, individuals with schizophrenia spectrum disorders rarely experienced stable remission or recovery, highlighting the need for more effective treatments and continual access to care.

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**Table 1**

*Demographics*

| | Baseline Cohort (N=591) | | | | 25-Year Cohort (N=311) | | | | Attritted (N=196) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | SZ (N=173) | | OP (N=418) | | SZ (N=159) | | OP (N=152) | | | | |
| | Mean | SD | Mean | SD | Mean | SD | Mean | SD | Mean | SD | p |
| Age | | | | | | | | | | | |
| At psychosis onset | 25.4 | 8.1 | 29.3 | 9.7 | 25.7 | 7.5 | 27.0 | 9.2 | 29.0 | 9.3 | <.001 |
| At baseline assessment | 28.0 | 8.9 | 30.2 | 9.8 | 27.2 | 7.7 | 27.8 | 9.4 | 30.0 | 9.6 | <.001 |
| Occupational status (SES) | 4.2 | 2.0 | 4.8 | 1.9 | 4.3 | 2.0 | 4.8 | 1.8 | 4.9 | 1.9 | 0.02 |
| | N | % | N | % | N | % | N | % | N | % | |
| Gender (M) | 107 | 61.8 | 236 | 56.5 | 99 | 62.3 | 80 | 52.6 | 112 | 57.1 | 1.00 |
| Race/Ethnicity | | | | | | | | | | | 0.15 |
| Native American | 0 | 0.0 | 2 | 0.5 | 0 | 0 | 0 | 0 | 2 | 1.0 | |
| Asian | 4 | 2.3 | 9 | 2.2 | 7 | 4.4 | 0 | 0 | 7 | 3.6 | |
| Black | 47 | 27.2 | 46 | 11.0 | 24 | 15.1 | 16 | 10.5 | 34 | 17.3 | |
| Hispanic | 12 | 6.9 | 29 | 6.9 | 16 | 10.0 | 7 | 4.6 | 16 | 8.2 | |
| White | 110 | 63.6 | 332 | 79.4 | 112 | 70.4 | 129 | 84.9 | 137 | 69.9 | |
| Never married at baseline | 139 | 80.3 | 247 | 59.1 | 124 | 78.0 | 98 | 64.5 | | | |
| Employed at baseline | 70 | 40.7 | 256 | 61.7 | 78 | 49.1 | 103 | 67.8 | | | |
| Prior homelessness at baseline | 34 | 25.8 | 71 | 22.8 | 24 | 19.0 | 33 | 25.6 | | | |
| Antipsychotic treatment | | | | | | | | | | | |
| 6-month | 157 | 93.5 | 327 | 81.5 | 149 | 95.5 | 116 | 77.3 | | | |
| 24-month | 127 | 81.9 | 228 | 59.5 | 132 | 86.8 | 67 | 46.2 | | | |
| 48-month | 112 | 75.2 | 178 | 51.0 | 118 | 80.3 | 45 | 33.3 | | | |
| 10-year | 99 | 77.3 | 148 | 47.9 | 127 | 85.8 | 40 | 29.6 | | | |
| 20-year | 66 | 75.0 | 105 | 44.3 | 107 | 83.6 | 39 | 30.0 | | | |
| 25-year | 63 | 70.8 | 104 | 46.0 | 109 | 73.6 | 53 | 35.3 | | | |
| Psychotherapy | | | | | | | | | | | |
| 48-month | 57 | 32.9 | 103 | 24.6 | 53 | 33.3 | 41 | 27.0 | | | |
| 10-year | 53 | 30.6 | 100 | 23.9 | 60 | 37.7 | 39 | 25.7 | | | |
| 20-year | 39 | 22.5 | 67 | 16.0 | 55 | 34.6 | 36 | 23.7 | | | |
| 25-year | 31 | 17.9 | 55 | 13.2 | 54 | 34.0 | 32 | 21.1 | | | |

*Note.* SZ=schizophrenia spectrum disorders; OP=other psychoses. The baseline cohort is stratified by the baseline diagnosis, while the 25-year subsample is stratified by last consensus diagnosis. Socioeconomic status is operationalized using the Hollingshead index of occupational status, which is rated on a scale from 1 ("large business owner/major professional/executive") to 8 ("not working"). P-values reflect the result of t-tests (for continuous variables) and chi-square tests (for categorical variables) contrasting individuals with

known remission or recovery status at the 25-year follow-up, and individuals who were alive as of the 25-year follow-up but for whom remission and recovery status are unknown.

**Table 2**

*Cross-sectional rates of remission and recovery*

| | Baseline Cohort | | | | | | | | 25-Year Cohort | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Recovery (N=591) | | | | | | | | Recovery (N=311) | | | | | | | |
| | SZ (N=173) | | | | OP (N=418) | | | | SZ (N=159) | | | | OP (N= 152) | | | |
| | N | Total N | % | 95% CI | N | Total N | % | 95% CI | N | Total N | % | 95% CI | N | Total N | % | 95% CI |
| 6 month | 47 | 173 | 27.2 | 25.4-30.1 | 175 | 418 | 41.9 | 40.5-43.1 | 41 | 159 | 25.8 | 23.9-27.7 | 82 | 152 | 53.6 | 50.7-55.6 |
| 24 month | 46 | 172 | 26.7 | 24.4-30.5 | 210 | 415 | 49.6 | 47.3-52.4 | 47 | 159 | 29.6 | 27.0-32.7 | 104 | 152 | 65.5 | 61.8-68.8 |
| 48 month | 46 | 171 | 26.3 | 23.7-28.1 | 188 | 411 | 47.8 | 45.7-50.9 | 37 | 159 | 23.3 | 21.1-26.1 | 97 | 152 | 63.8 | 61.2-69.7 |
| 10 year | 33 | 168 | 19.6 | 18.5-23.0 | 172 | 395 | 43.0 | 41.0-44.5 | 25 | 159 | 15.7 | 14.5-18.3 | 98 | 152 | 63.8 | 61.5-66.5 |
| 20 year | 36 | 158 | 24.1 | 21.2-26.6 | 154 | 365 | 43.2 | 41.2-47.0 | 35 | 159 | 22.3 | 21.1-25.2 | 93 | 152 | 61.2 | 58.6-65.2 |
| 25 year | 23 | 148 | 14.2 | 11.5-15.9 | 94 | 335 | 28.1 | 25.5-30.3 | 21 | 159 | 13.2 | 12.6-13.8 | 68 | 152 | 44.7 | 43.4-46.1 |
| | Remission (N=591) | | | | | | | | Remission (N=311) | | | | | | | |
| | SZ (N=173) | | | | OP (N=418) | | | | SZ (N=159) | | | | OP (N= 152) | | | |
| | N | Total N | % | 95% CI | N | Total N | % | 95% CI | N | Total N | % | 95% CI | N | Total N | % | 95% CI |
| 6 month | 41 | 173 | 24.9 | 23.1-28.9 | 195 | 418 | 46.2 | 44.4-47.6 | 39 | 159 | 24.5 | 23.3-26.4 | 91 | 152 | 59.9 | 56.2-62.2 |
| 24 month | 37 | 172 | 21.2 | 18.9-24.5 | 193 | 415 | 46.5 | 44.6-48.6 | 37 | 159 | 23.6 | 21.7-26.4 | 95 | 152 | 62.5 | 59.9-65.1 |
| 48 month | 42 | 171 | 24.6 | 20.8-26.9 | 214 | 411 | 52.2 | 49.6-55.1 | 41 | 159 | 24.8 | 21.4-26.8 | 98 | 152 | 64.5 | 61.4-69.8 |
| 10 year | 35 | 168 | 20.8 | 17.5-22.9 | 205 | 395 | 51.9 | 50.2-54.1 | 28 | 159 | 17.6 | 16.7-19.2 | 114 | 152 | 75.0 | 72.7-77.3 |
| 20 year | 16 | 158 | 10.1 | 9.2-13.7 | 122 | 365 | 34.1 | 32.9-36.0 | 15 | 159 | 9.1 | 8.8-9.4 | 84 | 152 | 55.3 | 52.6-58.0 |
| 25 year | 11 | 148 | 7.4 | 5.7-9.5 | 66 | 335 | 20.0 | 18.8-22.4 | 9 | 159 | 5.7 | 5.0-6.3 | 55 | 152 | 36.2 | 34.9-37.9 |

*Note.* SZ=schizophrenia spectrum disorders; OP=other psychoses. The baseline cohort is stratified by the baseline diagnosis, while the 25-year cohort is stratified by last consensus diagnosis. Remission and recovery are imputed for individuals who were lost to follow-up for reasons other than death. Confidence intervals derived through multiple imputation.

**Table 3**

*Stability of remission and recovery between time points*

Panel A: Correlations

| | Baseline Cohort (N=591) | | | | | | 25-Year Cohort (N=311) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 6-month | 24-month | 48-month | 10-year | 20-year | 25-year | 6-month | 24-month | 48-month | 10-year | 20-year | 25-year |
| 6-month | 1.00 | 0.58 | 0.54 | 0.55 | 0.51 | 0.38 | 1.00 | 0.65 | 0.57 | 0.66 | 0.62 | 0.48 |
| 24-month | 0.49 | 1.00 | 0.58 | 0.52 | 0.40 | 0.32 | 0.45 | 1.00 | 0.62 | 0.64 | 0.53 | 0.45 |
| 48-month | 0.50 | 0.64 | 1.00 | 0.54 | 0.49 | 0.35 | 0.40 | 0.67 | 1.00 | 0.54 | 0.56 | 0.49 |
| 10-year | 0.46 | 0.53 | 0.50 | 1.00 | 0.67 | 0.57 | 0.53 | 0.59 | 0.56 | 1.00 | 0.68 | 0.60 |
| 20-year | 0.44 | 0.35 | 0.41 | 0.57 | 1.00 | 0.69 | 0.48 | 0.42 | 0.51 | 0.64 | 1.00 | 0.79 |
| 25-year | 0.30 | 0.27 | 0.41 | 0.57 | 0.64 | 1.00 | 0.41 | 0.34 | 0.52 | 0.69 | 0.73 | 1.00 |

Panel B: Ns at each time point

| | 6-month | 24-month | 48-month | 10-year | 20-year | 25-year | 6-month | 24-month | 48-month | 10-year | 20-year | 25-year |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6-month | 591 | 586 | 581 | 563 | 523 | 483 | 311 | 311 | 311 | 311 | 311 | 311 |
| 24-month | 586 | 586 | 581 | 563 | 523 | 483 | 311 | 311 | 311 | 311 | 311 | 311 |
| 48-month | 581 | 581 | 581 | 563 | 523 | 483 | 311 | 311 | 311 | 311 | 311 | 311 |
| 10-year | 563 | 563 | 563 | 563 | 523 | 483 | 311 | 311 | 311 | 311 | 311 | 311 |
| 20-year | 523 | 523 | 523 | 523 | 523 | 483 | 311 | 311 | 311 | 311 | 311 | 311 |
| 25-year | 483 | 483 | 483 | 483 | 483 | 483 | 311 | 311 | 311 | 311 | 311 | 311 |

*Note*: Correlations are tetrachoric correlations. Remission and recovery are imputed for individuals who were lost to follow-up for reasons other than

Recovery
Remission

**Table 4**

*Patterns of remission and recovery*

| | Baseline Cohort | | | | | | 25-Year Cohort | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Recovery (N=591) | | | | | | Recovery (N=311) | | | | | |
| | SZ (N=173) | | | OP (N=418) | | | SZ (N=159) | | | OP (N=152) | | |
| | N | % | 95% CI | N | % | 95% CI | N | % | 95% CI | N | % | 95% CI |
| Stable recovery | 2 | 1.2 | 0.6-2.3 | 45 | 10.8 | 9.3-12.1 | 1 | 0.6 | 0.6-0.6 | 32 | 21.1 | 17.8-22.7 |
| Intermittent recovery | 59 | 34.1 | 31.5-36.7 | 197 | 47.2 | 45.1-49.3 | 53 | 33.3 | 31.4-36.8 | 89 | 58.6 | 56.6-60.9 |
| Early recovery | 43 | 24.9 | 21.9-26.9 | 90 | 21.5 | 19.7-25.0 | 48 | 30.2 | 27.3-32.1 | 22 | 14.5 | 13.2-15.8 |
| No recovery | 69 | 39.9 | 36.4-42.5 | 86 | 20.6 | 18.2-22.4 | 57 | 35.8 | 33.0-37.4 | 9 | 5.9 | 5.3-7.6 |
| | Remission (N=591) | | | | | | Remission (N=311) | | | | | |
| | SZ (N=173) | | | OP (N=418) | | | SZ (N=159) | | | OP (N=152) | | |
| | N | % | 95% CI | N | % | 95% CI | N | % | 95% CI | N | % | 95% CI |
| Stable remission | 2 | 1.2 | 0.0-1.7 | 36 | 8.6 | 7.7-9.6 | 0 | 0.0 | 0.0-0.0 | 23 | 15.1 | 13.5-16.1 |
| Intermittent remission | 42 | 24.3 | 20.8-28.3 | 213 | 51.0 | 49.0-52.1 | 36 | 22.6 | 21.7-23.9 | 106 | 69.7 | 68.1-72.1 |
| Early remission | 48 | 27.7 | 22.2-31.5 | 84 | 20.1 | 17.7-22.2 | 48 | 30.2 | 27.6-31.4 | 14 | 9.2 | 7.2-11.8 |
| No remission | 81 | 46.8 | 44.5-51.2 | 85 | 20.3 | 18.6-22.4 | 75 | 47.2 | 45.0-49.4 | 9 | 5.9 | 3.9-6.9 |

*Note.* SZ=schizophrenia spectrum disorders; OP=other psychoses. The baseline cohort is stratified by the baseline diagnosis, while the 25-year cohort is stratified by last consensus diagnosis. Data missing for reasons other than death are imputed. Confidence intervals derived through multiple imputation.

**Table 5**

*Predictors of patterns of remission and recovery (N=584)*

Recovery

| | | | Stable v Intermittent | | Stable v Early | | Stable v None | | Intermittent v Early | | Intermittent v None | | Early v None | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | LR | p-value | OR | 95% CI | OR | 95% CI | OR | 95% CI | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Race/Ethnicity (white) | **8.46** | **0.04** | **5.77** | **1.12-29.65** | **5.37** | **1.15-24.99** | **8.42** | **1.81-39.11** | 0.93 | 0.76-1.13 | **1.46** | **1.28-1.66** | **1.57** | **1.27-1.94** |
| Gender (male) | **8.78** | **0.03** | **0.54** | **0.42-0.69** | **0.49** | **0.36-0.67** | **0.26** | **0.19-0.36** | 0.91 | 0.81-1.03 | **0.49** | **0.44-0.55** | **0.54** | **0.45-0.64** |
| Socioeconomic status | 7.28 | 0.06 | | | | | | | | | | | | |
| Diagnosis (SZ) | **10.54** | **0.02** | **0.15** | **0.03-0.81** | **0.10** | **0.02-0.53** | **0.05** | **0.01-0.29** | **0.64** | **0.56-0.73** | **0.37** | **0.32-0.42** | **0.57** | **0.48-0.68** |
| Facility type (public) | 7.05 | 0.07 | | | | | | | | | | | | |
| Lifetime alcohol use disorder | 2.63 | 0.45 | | | | | | | | | | | | |
| Lifetime drug use disorder | 3.47 | 0.33 | | | | | | | | | | | | |
| Lifetime cannabis use disorder | 2.00 | 0.57 | | | | | | | | | | | | |
| Mood stabilizer treatment | **11.42** | **0.01** | **3.61** | **2.76-4.72** | **4.99** | **3.55-7.00** | **5.40** | **3.84-7.59** | **1.38** | **1.11-1.71** | **1.49** | **1.23-1.81** | 1.08 | 0.81-1.45 |
| Antidepressant treatment | 4.12 | 0.25 | | | | | | | | | | | | |
| Antipsychotic treatment | 0.95 | 0.81 | | | | | | | | | | | | |
| Inexpressiveness | 4.91 | 0.18 | | | | | | | | | | | | |
| Avolition/Apathy | **15.44** | **0.00** | **0.48** | **0.43-0.55** | **0.37** | **0.32-0.43** | **0.29** | **0.25-0.33** | **0.76** | **0.74-0.79** | **0.55** | **0.53-0.56** | **0.70** | **0.67-0.73** |
| Reality Distortion | 1.20 | 0.75 | | | | | | | | | | | | |
| Disorganization | 1.07 | 0.78 | | | | | | | | | | | | |

Remission

| | | | Stable v Intermittent | | Stable v Early | | Stable v None | | Intermittent v Early | | Intermittent v None | | Early v None | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | LR | p-value | OR | 95% CI | OR | 95% CI | OR | 95% CI | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Race/Ethnicity (white) | 7.79 | 0.05 | | | | | | | | | | | | |
| Gender (male) | **12.64** | **0.01** | 0.99 | 0.75-1.32 | **0.63** | **0.45-0.89** | **0.39** | **0.28-0.53** | **0.64** | **0.57-0.72** | **0.39** | **0.35-0.43** | **0.61** | **0.52-0.71** |
| Socioeconomic status | **12.13** | **0.01** | **1.19** | **1.09-1.31** | **1.48** | **1.33-1.65** | **1.90** | **1.74-2.07** | **1.24** | **1.20-1.28** | **1.69** | **1.65-1.74** | **1.38** | **1.33-1.43** |
| Diagnosis (SZ)[†] | **22.15** | **0.00** | 0.24 | 0.02-3.79 | 0.09 | 0.01-1.38 | **0.05** | **0.01-0.70** | **0.36** | **0.30-0.44** | **0.21** | **0.18-0.24** | **0.57** | **0.47-0.7** |
| Facility type (public) | 5.62 | 0.13 | | | | | | | | | | | | |
| Lifetime alcohol use disorder | 3.93 | 0.27 | | | | | | | | | | | | |
| Lifetime drug use disorder | 7.39 | 0.06 | | | | | | | | | | | | |
| Lifetime cannabis use disorder | 4.76 | 0.19 | | | | | | | | | | | | |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mood stabilizer treatment | 3.71 | 0.30 | | | | | | | | | | | | |
| Antidepressant treatment | 3.75 | 0.29 | | | | | | | | | | | | |
| Antipsychotic treatment | 2.32 | 0.51 | | | | | | | | | | | | |
| Inexpressiveness | 6.80 | 0.08 | | | | | | | | | | | | |
| Avolition/Apathy | **25.98** | **0.00** | **0.45** | **0.37-0.55** | **0.27** | **0.20-0.36** | **0.18** | **0.14-0.23** | **0.68** | **0.66-0.7** | **0.44** | **0.42-0.45** | **0.62** | **0.59-0.64** |
| Reality Distortion | 1.06 | 0.79 | | | | | | | | | | | | |
| Disorganization | 2.88 | 0.41 | | | | | | | | | | | | |

*Note.* All predictors assessed at baseline. Data missing for reasons other than death are imputed. P-values reflect the median likelihood ratio test statistic observed across imputations. For multinomial tests, a p-value < 0.05 was considered significant. For logistic regressions, a 95% CI which did not include 1 was considered significant. † Penalized logistic regression was used for contrasts of stable remission by diagnosis, as few individuals with schizophrenia had a trajectory of stable recovery, causing estimation of standard errors to fail. Bold indicates statistically significant predictors. LR=likelihood ratio test statistic; OR=odds ratio; SZ=schizophrenia spectrum disorder.