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Review Paper

Long-Term Outcome of Patients with Schizophrenia: A Review

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ABSTRACT

Objective: To review empirical studies that assess outcome of patients with schizophrenia and evaluate the degree to which reported outcome is affected by research methodology, treatment variables, prognostic factors, epidemiologic factors, and patient resilience. **Method:** We reviewed studies that used control subjects and lasted for a decade or more, comparing them with respect to research methodology and choice of outcome variables. **Results:** Like other mental illnesses and medical illness in general, the natural course of schizophrenia showed itself to have a threefold division of mild, moderate, and severe. Although a great deal of variance in outcome occurred across the studies reviewed, schizophrenia is nevertheless a disorder with relatively poor outcome. Patients with schizophrenia consistently showed poorer courses and outcomes than patients with other psychotic and nonpsychotic psychiatric disorders. On the positive side, subgroups of schizophrenia patients had extended periods of recovery—some without the benefit of extensive mental health aftercare treatment—and patients with schizophrenia did not show a progressive downhill course. **Conclusion:** While documenting the heterogeneity in outcome and the generally poorer outcomes of patients with schizophrenia, the studies reviewed also alert us to the danger of suicide and early death in schizophrenia. In addition, they expose problems in clinical management and treatment and also help us anticipate the possibility of intervals or periods of recovery, some of which appear spontaneously and may be tied to individual patient factors such as resilience. **Clinical Implications 1.** While schizophrenia is generally a poor-outcome disorder, a moderate-to-large subgroup of patients potentially experience periods of recovery (including both the absence of major symptoms and adequate psychosocial functioning) lasting several years or longer. **2.** Mental health professionals should be alerted to the high risk of completed suicide among schizophrenia patients, especially in the first 10 to 12 years of this disorder. **3.** Long-term outcome is influenced by current treatments, but the personal strengths, the developmental achievements, and the resiliency of individual patients are equal or more important influences. **Limitations 1.** This review focuses primarily on long-term North American studies of schizophrenia and also on the WHO study. There is less focus on European studies. **2.**This review only focuses somewhat on prognostic factors that may be involved in outcome and recovery. **3.**The lack of uniform methods among long-term outcome studies limits generalizations regarding the difference between current outcomes in schizophrenia and outcomes prior to the advent of current treatments.

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Among the major psychiatric disorders, schizophrenia's longitudinal course and outcome has been studied the most extensively (1). In part, this is because fundamental concepts about the nature of schizophrenia were formerly based on views about its longitudinal course. The disorder was originally viewed as having a progressive downhill course (2). Considerable longitudinal research has changed this outlook to one that is less negative. These long-term follow-up studies have provided more detailed information on course and outcome in schizophrenia; on diagnostic issues, specific symptoms, and problems in functioning; on treatment; and on important prognostic factors.

Overview of Major North American Follow-Up Studies of Schizophrenia Lasting 10 or More Years

The Iowa 500 study is one of the landmark follow-up studies. It addressed important methodological issues, such as use of control groups (both medical and psychiatric), rigorous diagnostic criteria, and a sample of patients exhibiting a natural course without modern medication, ECT, or specific psychosocial treatments, at least during the initial course of their disorder. As a result, this study more completely documented the negative course of schizophrenia than did any other long-term study. This retrospective study of 500 psychiatric patients admitted to Iowa State Psychiatric Hospital between 1934 and 1944 used the restrictive Feighner criteria to diagnose both schizophrenia and affective disorders. Over 60% of the original patients with a chart diagnosis of schizophrenia were rejected as not meeting the Feighner criteria. Follow-up data were acquired between 1972 and 1976, averaging roughly 35 years after the index hospitalization; 95% of the original schizophrenia cohort were characterized. Each of the 4 outcome dimensions (symptom severity, work history, marital status, and residential status) were scored on a 3-point scale indicating poor, fair, and good outcome. The 200 patients with schizophrenia had a substantially poorer outcome on all outcome dimensions, com- pared with other psychiatric patients and nonpsychiatric surgical patients. Despite the overall poor outcome, 30% of the schizophrenia cohort were married, and 20% emerged from the study symptom-free.

Vermont State Hospital Follow-Up Study

Almost at the opposite end of the recovery spectrum, the Vermont study exhibited far different results. Harding and others conducted a retrospective study of 268 psychiatric patients diagnosed according to DSM-I criteria, 168 of whom received a diagnosis of schizophrenia. Patients were recruited from the hospital if they met criteria to enter a new rehabilitation pro- gram between 1955 and 1960 (13,14). The average age at follow-up in 1982 was 61 years for the 82 patients who further qualified by meeting the DSM-II and DSM-III criteria for schizophrenia. The criteria for referral to the outpatient rehabilitation program provided a selection bias for higher- functioning patients. Also, the DSM-I diagnosis did not require 6 months of active symptoms or dysfunction. Even so, there was no difference in outcome among the groups diagnosed according to the DSM-I, the DSM-II, and the DSM-III. After 20 years, 60% of the schizophrenia cohort scored over 61 on the GAF. In contrast to the Iowa study, there was no difference in outcome between schizophrenia patients and other psychiatric patients. This was a most unusual result that has not been replicated in any of the many other comparable follow-up studies. Equally surprising, the schizophrenia cohort scored very well on the Strauss and Carpenter outcome dimensions (15), with 68% showing minimal or no symptoms and 61% employed in the last year of the study, although the criteria for employment status were not reported (15). This

study of patients with schizophrenia in their 60s opens up the possibility of some gradual improvement as patients with schizophrenia get older. The differences in outcome between this study and the Iowa 500 are attributable not only to diagnostic criteria and a positive selection bias but also to the fact that the Vermont cohort of schizophrenia patients benefited both from medication and from intensive outpatient rehabilitation.

Columbia Psychiatric Institute Follow-Up Study

This retrospective study shared some similarities with the Chestnut Lodge Study: chronic patients were selected and treated with inpatient, psychoanalytically oriented psycho- therapy. Stone and others retrospectively examined 552 patients with a DSM-III diagnosis who had at least a 3-month hospitalization at New York State Psychiatric Insti- tute (21). Of the total number of patients, 99 met criteria for schizophrenia. Interestingly, this was the only study to control for IQ (it used a cut-off score of 90). Patients were followed up for between 10 and 23 years, and 92% of the total sample com- pleted the follow-up. The results again showed that other psy- chiatric patients did substantially better than the schizophrenia patients, who, on average, had a GAF score of 39 (range 6 to 81). The cut-off for "good" or "recovered" was a GAF score of 61, achieved by only 8% of the schizophrenia patients.

Phipps Clinic Follow-Up Study

Another attempt to find predictors of outcome, or prognostic factors, was the follow-up study conducted by Stephens and others (3). Stephens used the Phipps Clinic in Baltimore, Maryland, to test the predictive power of the process–reactive distinction. This large retrospective study included 472 patients discharged with a diagnosis of schizophrenia after their first hospital admission of at least 3 weeks' duration. Their charts were classified as process or no process and were scored for presence or absence of 43 prognostic variables. Follow-up averaged 10 years, and 3 outcome categories were defined. Patients considered recovered (24%) had com plete recovery without evidence of further relapses and remissions. The second category, improved (46%), included patients who showed repeated relapses and remissions as well as those who showed continuous residual symptoms. The third category, unimproved (30%), included patients who remained hospitalized or who had continuous psychotic symptoms. Stephens proved that those who were lost to follow-up did not bias the outcome. With conclusions differing slightly from Vaillant's, Stephens, who also contributed to

WHO Study

In addition to the North American long-term studies discussed above, there are other important studies from North America, Europe, and Asia. The WHO Study, known as the ISoS, included an American component and is important enough that we briefly summarize a few of its results. In the ISoS, a total of 1633 subjects were followed up at 15 and 25 years; this sample comprised 14 culturally diverse treated incidence cohorts and 4 prevalence cohorts. The ICD-10 was used to subcategorize diagnostically the surviving participants in the study. Important findings that emerged from the ISoS study were data indicating that outcome in schizophrenia in developed industrialized countries is poorer than in developing countries. Possibly, greater tolerance and a more benevolent attitude exists in developing countries toward some of the symptomatic and poorer-functioning patients; this may contribute to the view that these patients are functioning moderately well, with some of their problematic features being downplayed. However, more recent epidemiologic analysis suggests that this cannot account for all the difference in outcome between developed and developing countries.

Assessed only according to the Bleuler Scale for outcome, the living ISoS subjects did well, with 56% of the incidence cohort and 60% of the prevalence cohort scoring a 4 (recovered). However, assessed with both a Bleuler Scale score of 4 and a GAF-D score of greater than 60, only 37.8% of subjects with schizophrenia and 54.8% of subjects with other psychoses within the incidence cohort would be rated as recovered. Again, if treatment received within the past 2 years was con- trolled for, only 16.3% of subjects with schizophrenia and 35.8% of subjects with other psychoses in the incidence groups qualified as recovered. Even using the strictest criteria for recovery, there remained some level of symptoms and dis- ability among some recovered patients.

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Excluded, since they are associated with better outcome when present during the acute phase. Also, some of these studies measured negative symptoms, which seem to be associated with cognitive impairments, poor outcome, and work and social impairment. Some of the studies from the Carpenter– Kirkpatrick research group have led to a reframing of the concept of negative symptoms, with a focus on an important subgroup of schizophrenia patients who have a more enduring type of negative symptoms, labelled "deficit syndrome," and who have poorer outcomes, as well as other important differences.

Overall Outlook

When one surveys the research on long-term course and out- come in schizophrenia, one can find several flaws in the studies outlined above. These include, among others, a lack of uniform criteria used to diagnose schizophrenia, a lack of uniform assessment methods, different statistical approaches, a lack of clarity regarding the stages of the disorder at which patients were being studied, and the study of patients under different treatment regimes. At the same time, while each of the studies is imperfect, each has produced some unique advances in the field. In addition, when considered as a group, they have substantially increased our knowledge of schizophrenia and provided many new leads concerning issues about schizophrenia that need further study. In regard to our current knowledge of course and outcome in schizophrenia, the studies have provided data showing both negative and positive aspects of outcome. On the negative side, the long-term studies that compare schizophrenia patients with other types of patients have produced data indicating that, even with current treatments, schizophrenia patients as a group show poorer outcome than patients with other types of psychiatric disorders; in this sense, schizophrenia is a poor-outcome disorder. On the positive side, these studies have provided important data on prognostic factors, as well as overwhelming evidence that very few patients with schizophrenia show a progressive downhill course and that a sub- group of schizophrenia patients shows intervals or periods of recovery. However, still open to question is the percentage of patients with schizophrenia who have this potential for recovery as well as all the factors involved in facilitating recovery.

Overall, we now have a much better understanding of how the course of schizophrenia differs from that of other disorders, and we have been alerted to the danger of suicide and early death among schizophrenia patients. We have also been alerted to potential problems in the management and treatment of schizophrenia as well as the possibility of intervals or periods of recovery. Even the heterogeneity that has been found should alert us to explore in greater detail the internal characteristics of our schizophrenia patients that lead to this heterogeneity.

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Conflict of Interest

The author(s) declared no conflict of interest.

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