Long-Term Followup Studies of Schizophrenia: Editors’ Introduction

by Thomas H. McGlashan and William T. Carpenter, Jr.

Abstract

What are the major long-term followup studies of schizophrenia from around the world? What have we learned about schizophrenia and its vicissitudes over a lifetime? Does the lifelong vantage point help us to identify the primary psychopathologic components of schizophrenia and to distinguish it from other forms of mental illness? What are the implications of the longitudinal perspective for reducing heterogeneity, for transcultural comparisons, and for updating nosology? Is it time to emphasize hypothesis testing in longitudinal studies? These and other questions about schizophrenia are addressed in the Bulletin issue which focuses upon the long-term followup study, its productivity, and its promise.

The metamorphosis of schizophrenia, captured in chilling metaphor by Franz Kafka (1971), introduces a horror that all too often lingers lifelong among its victims and their families. For Gregor Samsa, the protagonist-changeling of the novel, this alien process was brief—its denouement a numbed excommunication from human endeavors. For millions similarly afflicted, the anguish frequently lasts much longer, and the primary issue becomes how to live with the disorder, not how to succumb. While we do not yet know what causes this transformation, or group of transformations, we can track its effects over time. Often this only deepens our horror, as the accumulated data outline the disease’s magnitude in bolder relief. Ultimately, however, it helps us measure more clearly what we are up against. The truth may be stultifying at times, but it guides our coping strategies—as victims, treaters, and investigators.

The long-term followup study provides a macroscopic perspective of schizophrenia, a description of its grosser vicissitudes over human natural history. What can we discern from such a laborious endeavor? Robins and Guze (1970) regard followup as essential to the nosologic exercise of discriminating and validating psychopathological entities, including schizophrenia. Processes with widely divergent long-term outcomes are assumed to be different until proved otherwise. Kraepelin’s original two-psychoses hypothesis rests upon this rationale. Without knowing etiologies, we must follow course to reduce manifest heterogeneity, to construct subtypes, to study comorbidity, and to prognosticate. Long-term followup enlightens issues that cannot be seen at the level of the individual, like interactions between gender and psychopathology, or between socioeconomic status and psychopathology. While short-term course studies are informative on treatment efficacy, long-term followups are more likely to reflect natural history and define the limitations of current treatments.

Above all, followup provides validation for many endeavors. Diagnoses that are based on both cross-sectional and long-term outcome data are far superior to diagnoses based on cross-sectional data alone. Such diagnoses are more valid and can upgrade investigations, including those not directly related to followup, like family studies (Kendler et al. 1986).

Reprint requests should be sent to Dr. T.H. McGlashan, Chestnut Lodge Research Institute, 500 W. Montgomery Ave., Rockville, MD 20850.
By tracking longitudinal course of illness, followup can provide observations about many processes of interest, like the process of recovery (McGlashan 1980), the process of therapy (Keats and McGlashan 1985), or the interaction between symptoms and work (Strauss et al. 1985).

The original question, “Why followups?”, however, can best be answered by close scrutiny of what such endeavors have already provided, that is, by careful review and critique of existing long-term followup studies of schizophrenia. What are the major long-term followup studies, what have we learned from them, and what are the implications for nosology? These are the principal questions addressed here.

The collection begins with a review by Angst of the major pioneering European long-term followup studies of schizophrenia, with a special emphasis on the impact that diagnostic criteria have upon results. McGlashan follows with a review of selected North American long-term followup studies of schizophrenia which demonstrate the powerful link between sample characteristics and outcome. A review of studies on course of schizoaffective disorders by Samson, Simpson, and Tsuang comes next and demonstrates the importance of long-term followup for classification. The data suggest that schizoaffective disorder is intermediate to schizophrenia and affective disorder, and belongs to neither. Lin and Kleinman complete the review of existing large n long-term followup studies with a careful consideration of non-Western investigations. Some of these are not only new to most Western readers, but their results are striking in demonstrating persistently superior outcomes for schizophrenia.

The large n studies covered by the above reviews have progressed in their methodological sophistication over the years. This constitutes the subject of the next two reports. McGlashan, Carpenter, and Bartko summarize key advances of design that have emerged. In the next article they focus more exclusively on statistical issues, tests, and techniques (especially multivariate) that have become crucial to the analysis of data and to the interpretation of results.

The focus then shifts to smaller n studies where testing power may diminish, but where the true complexity of the long-term interplay between individual and environment receives proper consideration. Breier discusses the small sample study from a conceptual perspective, and Mirsky and Quinn exemplify this genre of investigation with their fascinating followup studies of the Genain Quadruplets.

Most of the reviews in this issue are “followup,” that is, concerned with the long-term trajectory of people who have already developed and been diagnosed schizophrenic. A complete longitudinal perspective, however, should also include descriptions of identified patients before their “official” onset of illness. The paper by Asarnow, which reviews the at-risk studies in schizophrenia to date, serves as a preliminary approximation of this frontier.

The final two articles build upon the long-term followup literature in a more speculative fashion and point to new directions that are potentially fruitful. Harding highlights the European concept of long-term course type and relates it to her own study of the Vermont State Hospital cohort. Carpenter and Kirkpatrick take this concept of course pattern or type and propose a way to operationalize it into “epochs” for future investigations.

As you sample these reviews, we think you will agree that the long-term followup has been central to the study of schizophrenia. What are the key issues to be addressed in future followup studies? We consider the following to be important opportunities:

1. What aspects of course and long-term outcome distinguish the schizophrenia syndrome from other forms of serious mental illness? Such questions require a movement to the qualitative. To date, comparisons across diagnostic lines have generally validated classification by revealing quantitative differences in functional outcome measures such as employment or time spent in hospital. From the vantage of psychopathology, it is also important to ascertain whether there are any relatively unique manifestations of illness as it unfolds over time. For example, when comparing schizophrenia with psychotic forms of affective disorder, it is not clear whether the difference between diagnostic classes is simply quantitative. Perhaps 10–20 percent of affective disorder cases run a chronic course. How is this chronicity similar, and how is it different from chronicity observed in a much greater proportion of schizophrenic patients? Where similarities exist, followup could help to determine whether, for example, affective disorder patients with chronic deterioration in personality functioning can be distinguished from similarly dysfunctional schizophrenic patients.

2. Schizophrenia Bulletin
no reports to date of pedigree-based studies comparing illness in biological relatives of chronic psychotic forms of affective disorder with chronic psychotic forms of schizophrenia (Carpenter and Stephens 1982).

2. There is now considerable interest in the heuristic proposition that multiple psychopathological disorders exist in various combinations in patients with schizophrenia. Kraepelin clearly described two such processes, personality deterioration (the deficit syndrome) and the positive symptom syndromes (including cognitive impairment). In 1974, Strauss, Carpenter, and Bartko proposed positive symptoms, negative symptoms, and interpersonal symptoms as three key components—a point of continued emphasis in Wing's discussion in this issue. We now call attention to five domains of psychopathology: hallucinations and delusions, cognitive impairment, dissociative affective processes, deficit processes, and neurological processes (Carpenter and Buchanan, in press). These categories are distinguished from secondary manifestations and confounded categories such as negative symptoms and social impairment which may be due to a number of causes including drug effects and consequences of psychosis. Focus on domains may help define the phenotypic “target” in genetic studies, open new approaches to developing animal models, serve as a subject for treatment development, and enhance the study of nosology. Attention to the course of psychopathology within each domain may provide a better basis for judging the relationship between domains. These domains may also be helpful in defining the qualitative similarities and differences between patients with schizophrenia and other mental disorders, as described in point (1) above.

3. It is also clear that “course of disorder” is not a unitary phenomenon, especially over the long term. A variety of temporal vicissitudes can be discerned. It may be heuristic to emphasize course epochs in future followup studies. This may clarify long-term course typology, thereby sharpening the utility of outcome as a validating criterion.

4. The interest in using followup studies to validate between-class differences in a previous generation of studies can be applied for within-class distinctions. This may help to resolve the heterogeneity of the schizophrenia syndrome, especially if the studies integrate some of the newer validating criteria. For example, the field needs more data regarding course distinctions associated with different patterns of psychopathology in biological relatives. We need to know whether patients with and without altered brain structure at onset of illness have a different course. If deviations from the norm in smooth pursuit eye movement identify a form of the illness with a particular genetic liability, it is important to ascertain in what way the illness differs over time from forms not associated with such abnormalities. Do patients with a history of pregnancy and birth complications, or exposure of their mothers to a flu epidemic during the second trimester, have a different pattern of illness than patients not exposed to these risk factors?

5. It is important to ascertain the extent to which the more favorable course observed in developing countries is actually caused by culturally based social and environmental factors. The material reviewed by Lin and Kleinman encourages further attention to this phenomenon. It is imperative that valid cross-cultural prognostic measures be developed to ascertain the extent to which differences in course derive from differences in the prognostic potential of the selected cases. It is clear that samples generated from clinical settings will represent different patient types in different cultures.

6. The long-term followup studies now convincingly describe a substantial proportion of patients showing remarkable improvement in symptom intensity and social competence after many years of illness. Detailed study of this aspect of course is needed to inform the field about the nature of late-course change and its treatment implications. The question of how one copes with increasing health after years of illness has received precious little attention.

We look forward to the next generation of course and outcome studies. If these studies are pursued intelligently, the limitations presently associated with design, sampling, and methodology issues can be reduced. New questions arise from observations already made that provide a strong basis for hypothesis-testing followup studies likely to be more theoretically informative than the present generation. Finally, considerable skepticism about present classification approaches and more careful attention to psychopathology may enable the next generation of followup studies to have more direct implications for innovations in nosology.

References
Carpenter, W.T., Jr., and Buchanan, R.W. Domains of psy-


The Authors

Thomas H. McGlashan, M.D., is Director of Research, Chestnut Lodge Research Institute, Rockville, MD. William T. Carpenter, Jr., M.D., is Professor of Psychiatry and Director of the Maryland Psychiatric Research Center, Baltimore, MD.

---

**Announcement**

The 7th World Congress of the World Association for Dynamic Psychiatry will be held in Berlin, Federal Republic of Germany, March 17-21, 1989. The theme of the Congress is “The Borderline Syndrome From a Holistic View of Man, Science, and Society.” The Congress will be held at the same time as the XX International Symposium of the German Academy for Psychoanalysis. The post clinical day will take place on March 23, 1989 at the Dynamic Psychiatry Hospital Menterschwaige in Munich.

For further information and registration write to:

Deutsche Akademie für Psychoanalyse (DAP) e. V.
Wielandstrasse 27-28
Berlin 15, Federal Republic of Germany
Telephone: 030/3318059