The Natural Histories of Schizophrenic Processes

by Lyman C. Wynne

Abstract

The natural history of schizophrenia cannot be studied directly, but nevertheless can be inferred and conceptualized as a frame of reference for examining the heterogeneity of the syndrome and for evaluating the impact of treatment, environment, and other factors influencing its course. Alternative diagnostic systems, including DSM-III, imply differing, largely unscrutinized concepts of the natural history and have generated skewed samples and noncomparable longitudinal data. The suggestion is made that sounder future research on the course of schizophrenia will focus upon component processes clustered, for example, in the enduring deficit syndrome.

The reviews of the literature on the long-term course of schizophrenia in this issue of the Schizophrenia Bulletin are impressive in the great diversity of the reported data and conclusions. Although much of this diversity can be attributed to methodological inadequacies and difficulties, enough of a pattern emerges to raise the question: Can a "core" natural history for schizophrenia, or a range of natural histories, be identified as a conceptual frame of reference for clarifying the clinical heterogeneity of the schizophrenic syndrome?

A decade ago, in a panel discussion on the course of schizophrenia, Joseph Zubin (1978) stated: "There is no consensus" on "acceptance of the concept of a 'natural history' of schizophrenia" (p. 641). A major reason then and now for this lack of consensus has been the considerable variability in the course of schizophrenia even when narrowly defined. It is obvious that diseases that are etiologically much better defined, such as syphilis, may have multiple manifestations and highly variable courses (pleiotropism). But perhaps a range of natural histories, rather than a single pattern, can be linked to components of the schizophrenic syndrome. First, it seems necessary to consider how data on the course of schizophrenia have been shaped by treatment and environmental factors.

Treatment Modifications of Natural History

The natural history of an illness can be conceptualized as the untreated course of that illness—that is, as the trajectory that may be altered by treatment. If we lack knowledge, or at least reasonable deductions, about the untreated "natural" course, we have no clear frame of reference for assessing the effects of treatment and other interventions. To be sure, alternative treatments can be compared with one another, but the question will then remain whether either treatment has significantly modified the long-term natural history. For schizophrenia, neuroleptic medication appears to be well-documented as altering the short-term (up to 5 years) course. However, the evidence for treatment benefits for longer-term outcome is much less clear-cut.

More fundamentally, there is a real question about whether meaningful empirical data actually exist about the course of unmodified schizophrenia. In contrast to the symptoms of many physical illnesses, schizophrenic psychotic

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symptoms necessarily provoke interventions to contain, channel, or otherwise modify their expression and their impact upon others. Whether or not these reactions are called treatment, social control, or shamanism, manifestations of psychosis are curbed or altered, or at least strenuous efforts usually are made to do so. The deficit symptoms of schizophrenia, in contrast, may evoke intense involvement by caring persons, especially family members, in efforts to stimulate the patient to become more active. Later, the environmental reaction may be ostracism or indifference that aggravates the patient’s self-neglect. My point is that schizophrenia is seldom allowed to follow a “natural history,” with partial exceptions for those patients who have only mild deficit symptoms and/or have unobtrusive psychotic symptoms.

In comparison to present-day programs that emphasize deinstitutionalization and routine usage of neuroleptics, the era of “moral treatment” more than a century ago is usually regarded as having helped patients function optimally with “natural” supports; the evidence is suggestive that discharge and improvement rates were as high then as they are now (Bockoven 1956). McGlashan (1988) states: “Long-term followup studies have yet to demonstrate clearly the effects of treatment on the natural history of schizophrenia” (p. 531). However, he also concludes that the Iowa-500 study “comes the closest of all the North American followup studies to approximating the natural history of schizophrenia unperturbed by modern treatments” (p. 521). Yet, the Iowa patients were in fact “treated” for years with custodial hospital care, which surely should be regarded as profoundly shaping whatever the quality and course of their functioning would otherwise have been.

It seems to me that, in recent times, a more “natural” course of illness has been observed in the nonstigmatizing community care of traditional “Third World” cultures such as Nigeria, as noted by Lin and Kleinman (1988); it also can be argued that the rehabilitation programs and community supports for the patients in the Vermont study, as reported by Harding (1988), may have allowed a reasonable approximation of a natural history. “Untreated” or placebo-treated schizophrenia was described in some of the initial psychopharmacological research, but these studies were short-term compared to the Vermont study, and also were lacking in descriptive reports of how the placebo-treated cases were actually being managed in the hospital or community.

These considerations about treatment pertain to a closely related, more general point: the tendency toward a particular clinical course and outcome that is known as the natural history assumes a “constant environment” (Wing 1978) within which the illness unfolds. However, the environments of schizophrenic patients are obviously not constant. Family and community settings vary widely, not only from time to time for the same patient, but also across patients. The interactive, reciprocal impact of the illness and environmental factors has been extensively documented (e.g., Day 1981; Liberman 1982; Leff and Vaughn 1985). Strauss and Carpenter (1981) have incorporated these variables into an interactive developmental systems model that rightly gives explicit attention to multiple factors beyond the illness itself.

The methodological and conceptual difficulties in delineating a natural history for schizophrenia have led many investigators to abandon the effort. Manfred Bleuler (1978), in a penetrating discussion of the problems of investigating the long-term course of schizophrenia, wisely concluded:

All these problems impose narrow limits on the meaning of statistical studies of the course of illness. The point is to keep them in mind; ... it is not necessary to capitulate before them. We need to have statistics on disease courses. We need them for prognoses, for the evaluation of our prophylactic and therapeutic methods, and we need them for research on the nature and origin of schizophrenias. [p. 188]

Our efforts will not yield a directly observed natural history, but they may produce more crisply formulated research designs that can relate more adequately to the diversity of patients and the multiplicity of factors that shape the course of schizophrenia and that define its boundaries and components.

Present-Day Conclusions

Aware of but undaunted by the methodological limitations of existing studies, McGlashan (1988b) summarizes his conclusions about the natural history of schizophrenia with the following points: (1) “Schizophrenia is a chronic disease, frequently disabling for a lifetime” (p. 527). (4) “The schizophrenic process, while disabling and chronic, does not get progressively worse over the long-term... At some point... loss of functioning appears to ‘bottom out’ or plateau... roughly 5 to 10 years after the manifest illness becomes...
unequivocally established” (p. 528).

(5) “Among patients with schizophrenia, however defined, outcome is heterogeneous…. For many patients, the disease never [becomes manifestly chronic]…. Among this larger group, all of whom lay legitimate claim to the diagnosis of schizophrenia, heterogeneity of outcome is the rule” (p. 528, original emphases omitted).

Although McGlashan’s summary seems to me to be a fair assessment of the North American literature, my own reading of the worldwide literature leads me to somewhat different conclusions. First, the view that “schizophrenia is a chronic disease” is prematurely wedded to DSM-III (American Psychiatric Association 1980) criteria, which make chronicity a requirement for diagnosis and do not permit acute or chronic variations in course of illness to emerge and be studied naturalistically. Reasonably defined full recovery, as described by Manfred Bleuler (1978), occurs sufficiently frequently, as one of the heterogeneous outcomes, to make the characterization of schizophrenia as a “chronic” disease an overstatement.

Second, I do not find the evidence highly persuasive for the timing of 5–10 years as the plateau period when the early deterioration bottoms out. The variability seems too great to warrant this generalization, especially across cultural groups worldwide.

Third, with a few noteworthy exceptions, the literature is silent about the qualitative, later-life changes that continue to occur well after 10 years (Bridge et al. 1978). Should these changes be regarded as part of the natural history? I believe we can learn much more than we have thus far about the nature of schizophrenia if we examine in more detail the quality and circumstances of what is regained, sustained, or lost after the florid symptoms have long since passed.

Fourth, sample selection and consequent inferences about the natural history of schizophrenia are undermined, more than has been recognized, by inconsistent conceptualizations and definitions of the prodromal phase and onset that set an essential boundary. Often the administratively defined date of first hospitalization or first psychiatric contact, rather than the onset of illness, is used as the starting point. In many current studies using DSM-III, nonpsychotic, prodromal symptoms vaguely and unreliably mark the onset. In other studies, a more clear-cut definition has been used—for example, by M. Bleuler (1978):

"[P]ersonality changes that are not unequivocally psychotic are disregarded. An onset of illness is considered, rather, when the patient first expresses delusions or hallucinations, when he begins to talk in such confusion that he is regarded as mentally ill by people around him, when he begins to neglect his customary duties for no apparent reason, when he ceases to talk, refuses to eat, when he rants, etc. [p. 190]"

**DSM-III and the Natural History of Schizophrenia**

Current researchers often write as if most of the methodological shortcomings of past studies have been surmounted so long as they have diagnosed their subjects with DSM-III or, now, DSM-III-R (American Psychiatric Association 1987). Despite the many gains that accrued with the wide acceptance of DSM-III, there is a serious danger that certain problems have been buried by DSM-III and may now be overlooked altogether. This is particularly likely in research on the onset, course, and natural history of schizophrenia.

**DSM-III-R contains a model for the natural history of schizophrenia that powerfully skews subject and data sampling. The DSM-III-R natural history is defined as having three phases: prodromal; active, with “presence of characteristic psychotic symptoms”; and residual. The active phase may be as brief as 1 week (or less, if the symptoms are successfully treated before 1 week elapses). For all the rest of the minimum total duration of 6 months, any two of nine prodromal or residual symptoms are indiscriminately described as equivalent. This rudimentary “natural history” may appear to allow many conceptual and research options. Actually, certain aspects of the course of schizophrenia are emphasized strongly while other aspects are excluded or easily neglected.**

First, and most obviously, the minimum total duration of 6 months skews toward chronicity. Patients with precisely the same symptoms but less than 6 months’ duration are counted as schizophreniform, not as schizophrenic. If a schizophreniform disorder recurs after 6 months, it is all too easy to find two “residual,” interim symptoms to justify moving the case into the ranks of subchronic or chronic schizophrenia. Furthermore, when the symptoms continue for more than 6 months, no diagnostic distinction is made between those patients whose natural history has begun with an insidious onset versus an abrupt or acute onset, even though type of onset has long been a pivotal reference point for many hypotheses about schizophrenia.

Second, E. Bleuler’s formulation of a “simple” form of schizo-
schizophrenia, in which the “fundamental” symptoms were manifest without the “accessory” psychotic symptoms, is excluded from study as an alternative form of natural history for schizophrenia. A present-day “solution” for classifying such patients with enduring “prodromal” (?latent, simple) features is to assume that they will meet criteria for schizotypal personality disorder and hence be included in the schizophrenia spectrum. However, the criteria for prodromal/residual features and for a schizotypal diagnosis are not the same. Descriptively, patients who meet the prodromal/residual criteria for schizophrenia often will not satisfy the criteria for schizotypal personality disorder. There are no clear guidelines for distinguishing between the prodromal phase of schizophrenia, “poor” premorbid adjustment, and those personality disorders—especially schizotypal, schizoid, and paranoid personality disorders—which may be precursors of or comorbid with schizophrenia.

Although genetic studies have most commonly linked schizotypal personality disorder and schizophrenia, an interesting study by Pfohl and Winokur (1983) provides life-history data that suggest a stronger relationship to schizoid personality disorder. They found that the most frequent DSM-III premorbid personality disorder in 52 chronic hebephrenic/catatonic schizophrenics was schizoid personality disorder (22 percent), not schizotypal personality disorder (0 percent). Because schizophrenia often has an insidious onset, only behavior 2 or more years before “the apparent onset of schizophrenia” was used in these premorbid personality assessments. (This implies the onset was dated from the start of psychotic symptoms, not from the DSM-III beginning of “insidious” prodromal symptoms.)

The DSM-III criteria used in the study explicitly exclude such schizotypal eccentricities of speech and behavior and emphasize, for schizoid personality disorder, indifference to praise or criticism, emotional coldness and aloofness, absence of warm, tender feelings for others, and few close friendships. Surprisingly, the Pfohl/Winokur data suggest that these schizoid, relational problems may be more relevant to the early stages of the natural history of chronic schizophrenia than the cognitive and speech schizotypal features that often are regarded as more central to typical schizophrenia. This study involved a selected sample of chronic, institutionalized patients and obviously needs to be replicated with other samples. However, the work clearly suggests that the nonschizophrenic impairments in functioning need to be studied in more detail over the course of the life history of schizophrenic patients.

A third and less noticed point about the DSM-III criteria is that although changes in the course of schizophrenia are recognized from 6 months to 2 years, the disorder is defined as “chronic” and no further variations in longer-term course are differentiated when the duration of illness has exceeded 2 years. With schizophrenic patients, 2 years is often only the beginning of relapses or continuous illness. Followup that is limited to 2 years or less is convenient for researchers who have difficulty carrying out studies for longer time periods, but this does not have much to do with the “natural history” of schizophrenia as documented in studies that have extended for 25 years or longer. At present, it appears unclear whether late-life improvements represent (1) part of the evolution or natural history of schizophrenia in which an intrinsic disease process burns out, (2) late-life mellowing of personality that results in nonspecific improvements, or (3) the subsiding of environmental challenges that in earlier years may have triggered or aggravated decompensation.

These comments about DSM-III and DSM-III-R illuminate a broader dilemma for researchers who study the long-term course of schizophrenia. Present-day investigators start with diagnostically homogeneous groups and therefore use structured interviews and standardized diagnostic criteria such as DSM-III. At the same time, however, they wish to understand schizophrenic processes more comprehensively than is possible when one looks at a cross-sectional slice of the life history. Even when conscientious efforts are made to assemble diagnostically relevant data over the life span, as in the Iowa-500 study, the diagnostic system used for sample selection will already have excluded some subjects on demographic grounds (as with the Feighner criteria) or have skewed the sample in other ways—for example, toward institutionalized chronicity. Thus, the sample is nonrepresentative of schizophrenic patients more generally, even though a given, selected sample may be quite well described. As on other aspects of the study of long-term schizophrenia, Manfred Bleuler (1978) has taken a sensible attitude that is neither romantic nor nihilistic:

One must recognize the impossibility of assembling an ideal group of probands. It is an unattainable goal to gain control of a group of patients whose schizo-
Classification of Courses of Illness

After samples have been selected, the remaining problem in longitudinal research is how to describe and classify the varieties of course of illness. Harding’s article (1988) exemplifies how the eight course patterns of Ciompi (1980) can be applied to the long-term investigations in Vermont, Lausanne, and Zürich. Clearly, Harding is able to document the conclusion that schizophrenia has a highly variable, long-term course. The data also support her view that because “many patients eventually do move in the direction of improvement, early closure of assessment needs to be avoided.”

These important but global conclusions are difficult to pursue in greater detail because of questions about how the patterns of course of illness were classified. For example, the two course types that begin with an insidious (“chronic”) onset and follow an undulating course of psychotic episodes constitute 65 percent of the Vermont sample but none of the Burghölzli, Zürich sample. Such a gross discrepancy presumably results in part from sample differences, but it also suggests that different criteria were used in making the classifications.

Even if such methodological problems are resolved by improved operational definitions, I am concerned that the eightfold classification system does not readily facilitate the formulation and testing of hypotheses about the meaning of the differences between the eight subgroups of subjects. The alternative approach to reducing heterogeneity when studying the long-term course, as suggested by Carpenter and Kirkpatrick (1988), has substantial advantages. Instead of trying to classify the whole lifespan into multiple, distinctive patterns, Carpenter and Kirkpatrick start more manageably with patients selected at a particular “epoch” during the course of illness, and in successive studies would then divide the study cohort into two groups that are selected on the basis of specific hypotheses about differences associated with aspects of the course of illness, such as acute versus insidious onset of psychotic symptoms. Such cohorts can be more readily identified for both retrospective and prospective studies than when multiple variables must fit together. Also, in this approach, multivariate statistics can now be used to consider the effects of covariates, without having to select subjects to fit a complete control-group design.

More work needs to be done in defining operationally the distinction between the epochs of middle course and late course. It also is not clear how the patient’s chronological age and stage in the life cycle relates to the epoch of the illness. A recurrent problem in research on the natural history of schizophrenia has been the difficulty of taking into account differences related to the age and life-cycle stage at which the illness disrupted social and work functioning. Presumably, the “onset epoch” for a person who becomes psychotic at age 15 differs from that which follows when a person first becomes ill at age 45.

An important question is whether the concept of epochs can be integrated with these issues concerning development across the life cycle.

The study of the life history of schizophrenic patients, beginning with cohorts selected at certain epochs in the course of the illness, is an approach that definitely deserves to be evaluated empirically. I believe that this hypothesis-based strategy is likely to be more illuminating than to continue to compare the life courses of patients across traditional diagnostic groups or subtypes, such as schizophrenic patients versus “typical” schizophrenic patients. Even when these investigations have produced group differences, they have not clarified much about the underlying processes that contribute to the differences in the subtypes.

Study of Schizophrenic Processes or Dimensions

Clearly, fresh approaches to the study of the natural history of schizophrenia need to be tried and compared in actual research. My hunch is that the most promising approach will begin with a refinement of the concept of epochs, combined with attention to the life cycle, and incorporate a focus on indices of hypothesized underlying processes. A central problem will then be how to select and assess these “processes” meaningfully. Important progress has been made in doing so in the distinction between the Type I and Type II “dimensions of pathology” proposed by Crow (1985), and in the threefold classification of Strauss et al. (1974) describing antecedents to positive symptoms, negative symp-
toms, and disorders in relating.

Recently, Carpenter et al. (1988) have focused upon what they call the deficit syndrome as a way of describing negative symptoms longitudinally. They conceptualize the deficit syndrome as enduring features of schizophrenic illness, consisting of negative symptoms that have been present during periods of clinical stability and during recovery from psychotic exacerbations, and which are not fully accounted for by depression or anxiety, drug effects, or environmental deprivation. The deficit syndrome is highly relevant to the concept of natural history if it can be confirmed that the identified features in fact do “hang together” over time and especially if they can then be studied with the hypothesis that this clustering reflects an underlying pathophysiological, psychological, or psychosocial process.

The concept of a deficit syndrome suggests a modified model for studying natural history—that is, to study the natural history of component processes or dimensions of schizophrenic functioning rather than to continue to expect that a single, unified natural history can be identified for the overall schizophrenic syndrome or even for any of the traditional diagnostic subtypes. This approach would first conceptualize features that hypothetically have functional and longitudinal coherence. Developing and applying the methods for studying them is the subsequent empirical task. Work that constitutes the initial stages of this approach has already been carried out in the burgeoning studies of negative symptoms.

The so-called positive symptoms do not appear to be so coherent, and probably will need to be subdivided into groups such as hallucinations, delusions, and formal thought disorder, each of which seems to have its own “natural history.” This approach also could be applied in longitudinal studies of traits that are presently studied with laboratory methods, such as attentional dysfunctions (Nuechterlein et al. 1986) and smooth pursuit eye tracking (Matthysse et al. 1986).

The process-oriented approach recommended here would take seriously the multifactorial complexity of the schizophrenic syndrome. Two or three component sets of processes may well emerge as primary, with other processes potentiating or modifying the central processes. My expectation would be that the various processes have different longitudinal patterns, a formulation that is supported by the analyses of symptom patterns carried out for patients with hebephrenic/catatonic schizophrenia by Pfohl and Winokur (1983). They have charted similarities in the year-by-year course of avolition and flat affect, in striking contrast to that for auditory hallucinations and persecutory delusions. If obtained for other samples of patients, such longitudinal data would help clarify what components belong together. The data also would facilitate examination of other correlates of these clustered features—for example, their relationship to various biological, genetic, and psychosocial variables. Something of this sort has been attempted in the effort to show that different kinds of central nervous system changes are associated with the Type-II (deficit) syndrome compared to the Type-I syndrome (Crow 1985). Additionally, the delineation of the “natural history” of distinctive schizophrenic processes should be facilitated by small-sample studies such as those proposed by Breier (1988) and Strauss et al. (1985). Such studies should focus upon points of change. If two or more processes are studied in relation to one another, the sequences may suggest how one process triggers/inhibits or augments/counteracts the other.

I trust that these proposals are understood as requiring empirical research before the details can be described with any assurance. Such empirical work will need to build upon careful conceptualizations and operational definitions so that the underlying processes of the schizophrenic syndrome can be delineated with the help of longitudinal “natural history” data.

References


Bridge, T.P.; Cannon, E.; and Wyatt, R.J. Burned-out schizophrenia: Evidence for age effects on...
schizophrenic symptomatology. 


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