. . . the diagnosis and understanding of schizophrenia

part I. use of signs and symptoms for the identification of schizophrenic patients

William T. Carpenter, Jr., John S. Strauss, and John J. Bartko

Since its introduction by Bleuler, the term schizophrenia has found widespread acceptance in world psychiatry. Because the diagnosis is so widely used, it is particularly important that clear diagnostic criteria be established to permit comparison of findings and advances in our knowledge. Important refinements in the definition of the "schizophrenia" concept have been made by European psychiatrists, who have identified highly discriminating characteristics of schizophrenic patients (Jaspers 1963, Kleist 1960, Langfeldt 1969, Leonhard 1966, Mayer-Gross, Slater, and Roth 1969, and Schneider 1959). Despite these improvements, diagnostic unreliability continues to be a problem (Babigian et al. 1965, Beck et al. 1962, Cooper et al. 1972, Katz, Cole, and Lowery 1969, Kendell 1968, Kramer 1969, Kreitman 1961, and Sandifer et al. 1969), and it is evident that even clearer diagnostic markers must be developed if the improved classification necessary for meaningful investigative work and clinical advances with schizophrenic patients is to be achieved. One such effort has been the recent development of computerized classification programs such as CATEGO (World Health Organization 1973) and DIAGNO (Spitzer and Endicott 1968 and 1969), which specify the sequence of the decisions to be made and the criteria to be followed in assigning patients to diagnostic categories. Although the validity of the diagnostic concepts used must still be established, these computerized classification systems are highly reliable and will certainly facilitate the teaching of future diagnosticians by clarifying the clinical rules to be followed in assigning patients to psychopathologic categories.

Attempts to expand our knowledge of the connotations of a schizophrenic label beyond simple description have had mixed results. They have encouraged the humanization of our concepts through intensive psychological investigation of patients but have also led to unwarranted assumptions about the people who are labeled schizophrenic. For example, a characteristic symptom should denote a diagnostic class, but often has been taken connotatively to mean a deteriorating clinical course. The societal-reaction theorists have presented a convincing case regarding the connotative misuse of the word schizophrenia (Becker 1963, Erikson 1964, Goffman 1961, Gruenberg and Zussman 1974, Scheff 1966, and Wing and Brown 1970).

Psychiatric classification is complex and controversial. Practically everyone is dissatisfied with the diagnostic systems of others, and many are unhappy with their own approaches. Manifest human behavior remains the critical evidence used in diagnosis. This fact, along with the failure of psychiatry to develop simple validating criteria (e.g., laboratory tests), limits the clarity and certainty with which we can approach psychiatric classification.

Despite these shortcomings and problems, most taxonomic approaches in psychiatry have a unifying theme—the use of signs and symptoms as prime variables. The

focus on signs and symptoms is characteristic of both clinically established systems of classification (American Psychiatric Association 1968, Bleuler 1950, Great Britain General Registrar's Office 1968, Kraepelin 1919, Langfeldt 1937 and 1969, Mayer-Gross, Slater, and Roth 1969, and Schneider 1959) and innovative systems (Astrachan et al. 1972, Carpenter, Strauss, and Bartko 1973, Feighner et al. 1972, Grinker and Holzman 1973, Kendell 1968, Kendell and Gourlay 1970, Lorr 1966, Lorr, Klett, and McNair 1963, Snezhnevsky 1968, Spitzer and Endicott 1968 and 1969, Strauss 1973, Strauss, Bartko, and Carpenter 1973, and World Health Organization 1973).

There are compelling reasons for choosing sign and symptom data when making diagnostic assignments. First, in so doing, one uses the fundamental method of scientific medicine—clinical observation. Second, the immediate manifestations of mental disorders (i.e., disordered cognition, affect, and behavior) have been cataloged and defined as signs and symptoms. It is important to note, however, that the symptoms and signs used to establish clear diagnostic criteria may not necessarily indicate a specific disease with a single cause, treatment course, and outcome. Although the discovery of a disease is difficult indeed without a clear diagnostic concept, the description of the concept may be only an intermediate step to defining underlying pathological processes. Symptoms are manifestations of disease, not disease itself. Signs and symptoms do not describe a person or his experience—they merely mark it. Also, there is as yet no established relationship between discriminating symptoms and specific etiologic factors. It is apparent that various causative factors can give rise to the same symptom, and perhaps to the same behavioral syndrome. Concepts of final common pathways through which illness is manifest in descriptively similar behavior, despite disparate etiology, are parsimonious in organizing our current knowledge. For example, the phenomenology of severe depression has major sign and symptom comparability whether the apparent critical etiologic factor is reserpine (catecholamine depletion), Cushing's disease (cortisol excess), reactive depression (object loss), or unknown (endogenous depression). It would be foolhardy to regard any single factor as the etiology of a functional psychosis, for as one can readily see in the examples above, even very similar behavioral manifestations do not necessarily indicate a uniform etiology or treatment. Akiskal and

McKinney (1973) recently presented an interesting conceptualization of depression as a final common pathway, drawn in part from their work with primates, in which causative events can be experimentally separated more satisfactorily than is possible in studies of man.

The problems associated with a diagnosis of depression are compounded in schizophrenia because 1) little is known about etiology, 2) the presenting clinical picture varies greatly between patients and over time in the same patient, and 3) outcome is extremely divergent. Thus, psychiatry's emphasis on signs and symptoms of schizophrenia is not based on a belief that a group of patients with a relatively homogeneous etiology or clinical course can be presently identified. Rather, in the midst of tremendous confusion and variable use of the schizophrenia diagnosis, it is incumbent upon psychiatry to develop methods for classifying patients with psychotic manifestations into categories in which criteria are clear and can be reliably communicated.

Other types of data besides symptoms and signs compete for the clinician's attention and may be of considerable importance in his decision regarding diagnosis, treatment, and disposition. However, these other types of data take time to ascertain and are less reliable. For example, accurate classification of biological relatives afflicted with mental disorders may yield diagnostic information, but it is extremely difficult to make reliable diagnostic judgments of relatives without extensive, time-consuming efforts. Response to treatment, especially differential pharmacotherapy, is another attractive variable to use in classification (Katz 1968), but it provides information after treatment, rather than guides the initial decisions. In psychiatric communities deeply interested in individual psychology, an ontogenetic and dynamic formulation may be regarded as important for diagnosis; reliable methods for applying this formulation have not yet been established, however, and there is no consensus as to the validity or specificity of such a formulation to psychopathologic classification. Therefore, at the present time, the arguments for using signs and symptoms in differential classification are persuasive. Because signs and symptoms have traditionally been emphasized in psychiatry, their use provides a basis for communication. A quick glance at the DSM II (American Psychiatric Association 1968) will adequately illustrate this point, since the vast majority

of the diagnostic criteria stated are signs and symptoms.

In this report, attention is focused on the use of a cross-cultural research strategy 1) to evaluate established diagnostic systems and 2) to derive clear and more commonly acceptable diagnostic criteria.

Review of Some Approaches to Diagnosis

To describe the context into which the proposed system fits, we will review briefly some of the major types of approaches to the diagnosis of schizophrenia currently in use.

The innovations of Kraepelin (1919) and Bleuler (1950) have already been alluded to, and their contributions are so well known and widely used that no further review of them will be attempted here.

Another major diagnostic school is represented by the phenomenological approach of Jaspers (1963), which laid the foundation for the signal contributions to psychodiagnosis made by Schneider (1959), Mayer-Gross, Slater, and Roth (1969), Leonhard (1966), and Kleist (1960). Jaspers asserted that it is natural for human beings to establish contact and empathy with one another. Psychiatrists, he noted, can readily empathize with a neurotic patient, but they meet with frustration in attempts to relate to the schizophrenic. Therefore, Jaspers reasoned that the psychiatrist's failure to empathize, when confronted with a patient's psychopathologic cognition, might be of central importance in identifying the schizophrenic process. One example of such an inability to empathize is the following: A patient reports that the passing of a salt shaker at dinner is a sign that he should visit the Pope; the psychiatrist, having no sense of the origins or meaning of the delusional percept, experiences a failure of empathy vis-à-vis this symptom. While difficult to describe, this phenomenon is of fundamental importance to the influential German psychodiagnostic schools (Schneider 1959 and Mayer-Gross, Slater, and Roth 1969).

In America, reflecting the influence of Meyer (1951) and Sullivan (1953 and 1956), a different approach to schizophrenia has been taken. Unlike Jaspers and the German school, Meyer, Sullivan, and their followers focused considerable attention on the schizophrenic patient's psychology and social interactions. They were less inclined than the German school to dwell on the

qualitative differences between schizophrenic and normal behavior; rather, they attempted to see similarities. Recognizing that the schizophrenic patient's symptoms represented an extreme on the continuum of human behavior, they nonetheless believed that these symptoms were potentially understandable and communicative. This heritage, along with the widespread psychoanalytic influence in this country, has enabled many psychiatrists to develop a sense of empathy with the bizarre symptomatic manifestations of the schizophrenic patient. The American psychiatrist's interest in the patient's unconscious and his own tendency to introspection have permitted an empathic bond to develop between psychiatrist and patient. Thus, when poor rapport is discussed as a distinguishing feature of schizophrenia in American psychiatry, the term is used, not in Jaspers' sense, but in reference to subtle aspects of social function—for example, the psychiatrist's perception that the patient feels anxiety in relating and thus tends to distance himself from intimacy. In this setting, it is natural that Bleuler's interest in psychological mechanisms of schizophrenia has excited interest in the United States, while attempts at more clearly defining and objectifying manifestations of schizophrenia have taken greater hold in Europe. Thus, more recent investigators, such as Artiss (1962), Bateson et al. (1956), Burnham, Gladstone, and Gibson (1969), Fromm-Reichmann (1950), Kasanin (1964), Lidz, Fleck, and Cornelison (1965), Searles (1965), Stierlin (1961 and 1969), Wynne (1961 and 1970) and Wynne et al. (1958), have influenced American psychiatrists to become interested in unconscious mechanisms and subtle aspects of relating in a dynamically oriented diagnostic or therapeutic interview. Other psychiatrists, especially in Europe, have been relatively more receptive to the work of men like Kleist (1960), Langfeldt (1937), Leonhard (1966), Mayer-Gross, Slater, and Roth (1969), and Schneider (1959), who attempted to clearly distinguish psychiatric syndromes. Much of this work has been summarized by Fish (1957, 1958, and 1962) and also by Basit (1971) and Hirsch and Shepherd (1974).

It is often asserted (Kendell and Gourlay 1970, Kuriansky, Deming, and Gurland 1974, and Sandifer et al. 1969) that American psychiatrists, perhaps as a result of the influences described above, have less well-defined and broader limits for a schizophrenia diagnosis than their European colleagues. If so, an important exception to this rule is the systematic approach to psychiatric

diagnosis developed by a research team at Washington University. Their system cannot be easily summarized in this report, but it is readily available elsewhere (Feighner et al. 1972). Attempts at validation of their system, in which family history and followup data are used, are encouraging. On the other hand, in this system, early diagnosis of acute psychotic episodes is inadequate, since schizophrenia cannot be diagnosed until a more established illness pattern evolves.

The most interesting data relevant to whether the definition of schizophrenia used in the United States is, as generally supposed, an exceptionally broad one are based on comparisons between New York and London (Babigian et al. 1965, Beck et al. 1962, Katz, Cole, and Lowery 1969, Kendell 1968, Kramer 1969, Kreitman 1961, and Sandifer et al. 1969); but Sandifer (1972) has pointed out that diagnostic practices in New York City deviate significantly from diagnostic practices in the rest of the country. If systematic differences do indeed exist between the diagnostic practices of American psychiatrists in general (i.e., not merely those located in New York City) and those of their European counterparts, then investigators must determine whether there is greater validity to the narrowly or broadly defined entity called schizophrenia.

Many have assumed that the more narrowly defined entity represents true schizophrenia. This assumption has received support from investigators who are finding a more homogeneous outcome when a narrow definition is used (Achté 1967, Astrup and Noreik 1966, Eitinger, Laane, and Langfeldt 1958, Faergeman 1963, and Langfeldt 1969). Many of these studies, however, appear to have unwittingly included poor prognostic variables other than symptoms as diagnostic criteria (Strauss and Carpenter 1974). Nonetheless, an important concept of "true schizophrenia" and "pseudoschizophrenia" has arisen, creating an illusion in some psychodiagnostic schools that a properly made diagnosis necessarily carries dire consequences for the schizophrenic patient. This concept is questionable, since there is a tendency to invalidate the diagnosis if the case does not fulfill the prediction of bad outcome. Recently, there has also been some evidence supporting a broader concept. Investigators have observed that the monozygotic twin of a diagnosed schizophrenic patient often has observable psychopathology, but instead of being a replica of the index case, the twin may be considerably divergent in his psychiatric manifestations (Hoffer and Pollin 1970

and Shields and Gottesman 1972). Also, in the adoptive studies of Kety et al. (1968), a concept of schizophrenia spectrum disorder was developed indicative of a poorly defined entity with broad limits in the biological relatives of schizophrenic patients. Furthermore, the biological relatives of borderline cases, who might have been diagnosed as schizophrenic by broader criteria, were similar to relatives of schizophrenic patients (Kety et al. 1968).

Some workers have attended less to specific psychiatric signs and symptoms but rather have attempted to assess ego functioning in the hope of finding discriminating features of schizophrenia that will serve as a basis for both classifying and understanding the patient. Two groups of Americans have made noteworthy attempts at systematizing discriminating features of schizophrenia. Over the past decade, Bellak and his co-workers (1970) have developed measures of ego function which they have assessed in schizophrenic patients. Comparisons of the schizophrenic ego profile with those of other psychiatric patients and normal controls have revealed significant differences. Although this work is extremely interesting, the complexities involved in assessing a variety of ego mechanisms have prevented widespread use of the system of Bellak et al. Their studies have increased and will continue to increase our understanding of ego function in schizophrenia, but they have yet to develop highly discriminating and readily assessible features of the schizophrenic patient that could lead to reliable identification of patients by a variety of clinicians.

A second effort at a more holistic assessment is found in the work of Grinker and Holzman (1973), where they attempt to determine discriminating features of patients with early schizophrenic symptoms and to develop validating criteria for diagnostic assignments. An initial report of their work was recently made and the following five distinguishing features were described:

- Presence of a thought disorder.
- *Reduced capacity for pleasure.*
- Characterological dependency.
- Significant impairment of social competence.
- Exquisitely vulnerable sense of self-regard.

Definition of these terms and case illustrations are detailed by the authors. Although these are critical features, several of them may not be highly discriminat-

ing. Similar findings have been reported by Grinker, Werble, and Bryce (1968) in their work on the border-line syndrome.

Despite the innovative work reviewed above, the need remains for clearly defined diagnostic rules for identifying schizophrenic patients—rules that can be used reliably in various settings. An example of an approach that satisfies the need for reliable diagnosis based on specified rules can be seen in the computer-derived diagnostic systems developed by Wing, Cooper, and Sartorius (1974) and Spitzer and Endicott (1968 and 1969). These programs have the capacity to make psychiatric diagnoses that are 100 percent reliable. The diagnostic rules are clearly specified and followed in every instance. Regardless of when or how often any case is entered into the diagnostic program, it will always be assigned the same diagnosis, since the programs apply the same diagnostic principles to each case regardless of the origin of the patient data. Although these programs avoid the perennial problem of individual diagnostic habits, it must be remembered that each program is itself based on a particular diagnostic assumption. Spitzer and Endicott, for example, have attempted to replicate the diagnostic rules described in DSM II, whereas Wing's CATEGO program is based on European concepts of schizophrenia. The advantages of such an approach are considerable, but are limited by the necessity to have standardized data collection and computer access. At the moment, these programs can be used mainly by research groups and are not readily applicable to clinical diagnosticians.

Another approach to reliable diagnosis is the derivation of highly discriminating signs and symptoms that can be used as guides or checklists for the interviewing psychiatrists. Schneider's (1959) work (to be described below) lends itself to such an approach, as does that of Astrachan et al. (1972). Astrachan et al. provided a symptom checklist and scoring system that correctly identified a high percentage of patients who had been clinically diagnosed as schizophrenic, and that included in the schizophrenic category a relatively small number of patients who had not been so diagnosed. This checklist system is heavily weighted with items of thought disorder, hallucinations, and delusions; but it also includes ratings of inappropriate affect, paranoid ideas, catatonic behavior, and depersonalization. Astrachan and his colleagues, drawing on findings of earlier investigators, constructed a list of symptoms that were

expected to be discriminating and that were consistent with major theoretical work in the field. This procedure resulted in six symptom categories made up of 21 illustrative symptoms, with a variable system for scoring each symptom and category. When this system was applied to several patient cohorts, Astrachan et al. had considerable success in correlating high scores on the checklist with a schizophrenic diagnosis and low scores with a nonschizophrenic diagnosis. This work has received less application that it merits, perhaps because the complexity of the system discourages general use.

A Report From the International Pilot Study of Schizophrenia

Having briefly outlined the development and current status of diagnostic approaches to schizophrenia, we now turn to an exhaustive study that has attempted to answer some of the unanswered questions referred to above. The International Pilot Study of Schizophrenia (IPSS) is a transcultural psychiatric investigation of 1,202 patients in nine countries: Republic of China, Columbia, Czechoslovakia, Denmark, India, Nigeria, the Union of Soviet Socialist Republics, the United Kingdom, and the United States. It was designed to lay scientific groundwork for future international epidemiological studies of schizophrenia and other psychiatric disorders. Details of the methodology employed in this investigation are provided elsewhere (World Health Organization 1973). The basic research instrument used was a standardized interview schedule, the Present State Examination (PSE), which was initially developed by Wing, Cooper, and Sartorius (1974) and later modified for use in the IPSS. The schedule is made up of the following three sections: 1) The PSE begins with an open-ended introduction (5-20 minutes) in which the psychiatrist inquires about problems and experiences that have troubled the patient in the past month. 2) Following these general inquiries, the psychiatrist uses the interview questions to make a series of specific inquiries, section by section, on various psychopathologic dimensions such as depression, anxiety, auditory hallucinations, and delusions of grandeur. 3) When the interview has been completed, generally after 45-90 minutes, the psychiatrist rates the behavior that he has observed during the interview for presence or absence of psychopathologic signs.

The major tasks presented to a psychiatrist using the PSE are to establish a relationship with the patient, learn about his experiences and problems, and make judgments regarding the presence or absence of a number of psychopathologic variables. The advantage of the structured interview schedule is that it provides a format in which all patients are asked the same questions in a comparable fashion, and the interviewing psychiatrist can indicate his judgments on the presence, absence, and, if present, the severity of a multitude of behavioral variables in the course of an interview. The questions on symptoms cover the 1-month period immediately preceding the interview, and the questions on signs cover the behavior observed during the interview itself. The applicability and reliability of the PSE have been established in the course of the IPSS and have been reported by the World Health Organization (1973). In brief, the interviewing psychiatrists in each of the nine centers used the PSE to make 360 ratings, which provide the basic data base on which to test diagnostic systems and from which highly discriminating signs and symptoms for the identification of schizophrenia can be derived. Since these data are collected separately from psychiatric history data, they can be rated, coded, and analyzed so that discriminating signs and symptoms can be determined independently of other variables such as chronicity. Furthermore, and most critically, since reliability among investigators has been established for ratings of individual signs and symptoms regardless of diagnostic agreement (or, quite often, in spite of diagnostic disagreement), there is evidence that these data are not significantly weakened by the interviewer's diagnostic biases.

Evaluation of Established Diagnostic Systems

There are three fundamental principles to be respected in using signs and symptoms to establish diagnostic criteria. The signs and symptoms that define a clinical entity should be highly discriminating, they should occur frequently so as to have general applicability, and they should be easily understood and readily agreed upon by various observing clinicians (reliable).

Schneider's First-Rank Symptoms

Perhaps the foremost diagnostic school adhering to these principles for the identification of schizophrenia is that of Schneider (1959). Taking an atheoretical and purely pragmatic approach, he identified 11 symptoms

of first-rank importance for the positive identification of a schizophrenic patient. These first-rank symptoms (FRS's) were chosen because of their discriminating ability and were designated as pathognomonic—that is, as only occurring in schizophrenia (with the occasional exception of organic psychosyndrome). Schneider also believed that the FRS's occurred frequently enough to be generally applicable—although a diagnosis of schizophrenia could be made in the absence of FRS's, the presence of any of these 11 symptoms meant schizophrenia. Schneider's system has been widely used in German-speaking countries, Scandinavia, the United Kingdom, and other parts of the world for almost half a century. While the widespread acceptance of this system suggests its general usefulness, scientific evaluation of the frequency distribution of FRS's in schizophrenia, the reliability with which they can be judged present or absent, and the degree to which they actually discriminate has only recently been undertaken (Abrams and Taylor 1973, Mellor 1970, Skoda 1973, and Taylor 1972). In our own studies using data from the IPSS (Carpenter, Strauss, and Muleh 1973 and Carpenter and Strauss 1974), we were able to determine the frequency distribution of nine FRS's in schizophrenia (see table 1). Fifty-eight percent of the diagnosed schizophrenic patients had at least one FRS. The frequency distribution is comparable to that found by Mellor (1970), who used unstructured interviews of unknown reliability. Thus, we conclude that Schneider's system is applicable and reliable; it therefore satisfies two of the three fundamental requirements for using signs and symptoms as diagnostic criteria.

What remains in evaluating Schneider's diagnostic system is to test the degree to which FRS's discriminate between schizophrenia and nonschizophrenia. In advocating that all nonorganic patients who had an FRS be diagnosed as schizophrenic, Schneider (1959) wrote that FRS's "must take primacy in the assignment of the individual case [p. 135]." A diagnostic system so defined and operationalized functions well, but questions of its validity cannot be evaluated simply by examining the results of its application by its proponents.

Because the IPSS includes psychiatric investigators from many cultures schooled in various diagnostic approaches, an examination of their collective efforts will diminish any incidental diagnostic biases held by some investigators. Table 2 shows the percentage of patients in each major diagnostic category across the nine countries who had one or more FRS. Schneider's

Table 1. Frequency distribution of first-rank symptoms in Schneider's positive schizophrenic patients ($N = 466$).[1]

First-rank symptom	Percentage positive	Intraclass r
Audible thoughts	28	.83
Voices argue or discuss patient	22[2]	.76
Voices comment on patients' activity	10[2]	.76
Thought insertion	24	.77
Thought withdrawal	25	.91
Thought broadcast	26	.95
Made feelings and/or made impulses	15	.76
Made volition	29	.87

[1] Schizophrenic patients without an FRS are not included in this analysis.
[2] U.S. patients not included (incomplete data).

Table 2. Prevalence of first-rank symptoms by diagnosis for all nine centers.

Diagnostic groups	N	Percentage with one or more FRS
Schizophrenia	817	58
Manic psychosis	72	22
Depressive psychosis	142	14
Neurotic and personality disorders	126	4

rule—that the presence of an FRS always means schizophrenia—is at variance with the clinical judgments made in a significant number of cases receiving a diagnosis of affective psychoses and a small proportion of cases assigned a diagnosis of a neurosis or personality disorder.[1]

We have no way of controlling for the influence of Schneider's teachings on the diagnosing psychiatrists; thus the discriminating power of these symptoms may be inflated in our results. On the other hand, there is no method for determining if diagnostic error has biased our results for or against Schneider's postulates. A multination design lets the chips fall where they may, with some reason to hope that biases are diluted rather than unidirectional. We conclude, therefore, that these data support FRS's as highly discriminating and frequently occurring in schizophrenia, but fail to support

an automatic assignment of any nonorganic patient with an FRS to schizophrenia. To do so would lead to significant diagnostic error, although not necessarily greater error than usual in clinical diagnosis.

Next, we altered Schneider's diagnostic rules to see if a modified approach using cumulative tallies of FRS's could produce a greater split between schizophrenic and nonschizophrenic patients and provide an estimate of the degree of diagnostic error that one might anticipate when using his system. Table 3 shows the proportion of diagnosed schizophrenic patients who would be assigned a schizophrenic diagnosis based on the presence of any one, any two, or any three FRS's, and the proportion of patients receiving a nonschizophrenic diagnosis who would be judged to be schizophrenic "erroneously" based on one, two, or three FRS's.[2] One can again see that FRS's are highly discriminating, but not exclusive to

[1] This is a particularly severe neurotic and personality disorder cohort, and most patients were thought to have at least one psychotic symptom on admission.

[2] We also devised a system wherein weights were assigned to each FRS based on its discriminating power. This more complex scoring system did not function significantly better than the cumulative tally, and thus is not reported.

Table 3. Comparative diagnostic discrimination of nine first-rank symptoms.

Diagnostic rules	Percentage schizophrenic	Percentage nonschizophrenic
Any one FRS	61	14
Any two FRS's	45	7
Any three FRS's	31	3

schizophrenia. Confidence in the schizophrenic diagnosis is quite high when a patient has multiple FRS's, but only a minority of acute and subacute schizophrenic patients are included. Thus, the system loses its general applicability.

Langfeldt's Diagnostic System

Another important European diagnostic school was established by Langfeldt (1937 and 1969), who believed that true schizophrenics could be separated from atypical psychotic patients whom he labeled schizophreniform psychotics. He identified six characteristic symptoms of schizophrenia that distinguished between these two groups and which predicted poor outcome in the schizophrenic group and good prognosis in the schizophreniform group.

Other investigators have supported these findings (Achte' 1967, Astrup and Noreik 1966, and Eitinger, Laane, and Langfeldt 1958). Since signs and symptoms information can be analyzed separately from other information, the IPSS presents a unique opportunity to evaluate Langfeldt's diagnostic criteria and their prognostic power.[3] Consequently, we have analyzed the 2-year outcome data in the American patients, dividing our diagnosed schizophrenics (DSM II criteria) into those who have, questionably have, or do not have signs and symptoms regarded as characteristic by Langfeldt. A 2-year followup can only provide tentative conclusions, but in our measures of outcome, we did not find a significant difference in our schizophrenic patients when they were divided according to the above criteria (Strauss and Carpenter 1974a).

The same type of outcome investigation could be made by dividing our American patients who were

diagnosed as schizophrenic into those who did and did not have one of Schneider's FRS's. This analysis has been of less interest, since there is almost no literature on outcome of patients diagnosed with the aid of Schneider's criteria. Many investigators believe, however, that a schizophrenic population, defined by characteristic symptoms such as Schneider's, would have a worse outcome than a cohort diagnosed by broader criteria such as DSM II (American Psychiatric Association 1968). We divided our American patients who were diagnosed as schizophrenic into those who did and those who did not have an FRS. Outcome at 2-year followup was comparable for these two groups.

Our tentative conclusion, from investigating Langfeldt's and Schneider's postulates, is that the use of characteristic signs and symptoms of schizophrenia facilitates the generation of diagnostic groups that can be more easily defined and replicated; but their use neither ensures diagnostic accuracy nor generates a schizophrenic category that can be validated by 2-year outcome.[4]

## Application of a Cross-Cultural Design to the Derivation of Highly Discriminating Signs and Symptoms

A large multination study such as the IPSS has distinct methodologic advantages. First, it generates large numbers of patients on which hypotheses can be tested. Second, it provides a systematic data base on patients from diverse cultures who have come through varied pathways to be included in the study. This broad base weakens the possibility of locally determined artifacts appearing as critical variables. For example, an epidemiologic study of schizophrenia in a culture in which mental illness is a stigma for men but not for women would certainly find the prevalence of schizophrenia higher among women. If the study design included patients from several cultures, only one of which had that particular bias, then the high female-to-male ratio for schizophrenia would be seriously weakened, and erroneous conclusions about sex distribution would be less likely. A third advantage of the IPSS is similar to the first two. When a number of psychiatrists with divergent backgrounds and biases are able to generate comparable and reliable signs and symptoms

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[3] Langfeldt assessed a number of variables other than symptoms for their prognostic value. The details of his comprehensive studies and supportive case records are of considerable interest.

[4] Since preparation of this manuscript, these findings have been replicated using 5-year followup data (Hawk, Carpenter, and Strauss, in press).

data regardless of their diagnostic assumptions, then one can anticipate that the study design will permit the identification of attributes of schizophrenia that are considered important across diagnostic schools and cause a weakening of variables regarded as powerful discriminators in one school and trivial in another. A Venn diagram (figure 1) can be used to illustrate these last two points. The shaded area in the center may represent similarities among schizophrenic patients brought together from diverse cultural and socioeconomic backgrounds. Thus, the features of schizophrenia that are more related to incidental, or local, variables would appear outside of the shaded area and the general attributes found in schizophrenic patients across cultures would fall in the shaded area. The same is true when this diagram illustrates a study design using psychiatrists from several diagnostic schools. The shaded area would represent those signs and symptoms commonly believed indicative of schizophrenia. For example, if loose associations are diagnostic of schizophrenia in one country but not in others, while delusions of passivity are regarded as critical schizophrenic indicators in all countries, then

Figure 1. Venn diagram. [1]
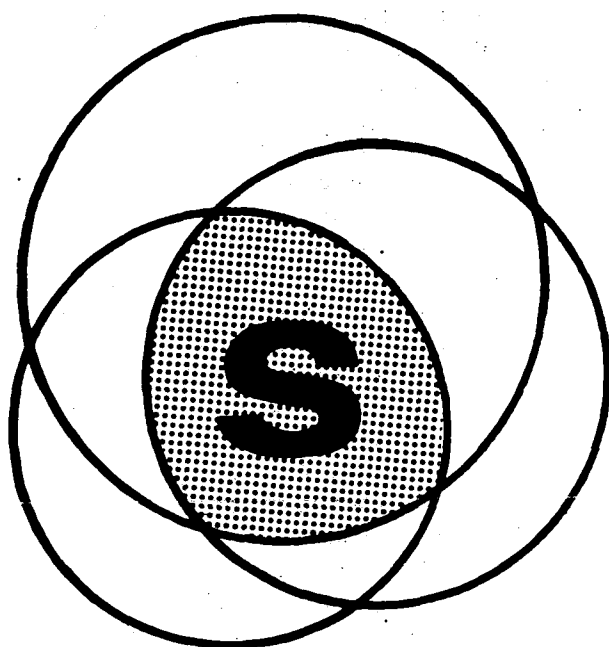
only the latter would fall within the shaded area. An analysis of variance and stepwise discriminate function analysis would assign highest value to those signs and symptoms located within the shaded area.

Following the rationale outlined in the preceding paragraph, each of the 1,119 IPSS patients was assigned to a schizophrenic or nonschizophrenic category. Eighty-three of the original 1,202 patients were assigned such diagnoses as paranoid states, unspecified reactive psychosis, and paraphrenia. Because we had little confidence in assigning this 6 percent of the sample to either the schizophrenic or nonschizophrenic group, and their incorrect inclusion in either group might obscure the distinctions between schizophrenia and nonschizophrenia, these patients were excluded from our analyses. A country-by-country randomization of patients was carried out to establish two cohorts, each containing approximately 405 schizophrenic and 155 nonschizophrenic patients. One cohort was omitted from data analysis so that it could later be used to replicate or refute highly discriminating signs and symptoms derived from the other cohort.

A series of analyses was undertaken with cohort A. The PSE data base, consisting of 230 symptoms and 130 signs, was arrayed as 443 overlapping variables. The 443 variables contained numerous single items thought to be relevant to the distinction between schizophrenia and nonschizophrenia (e.g., thought broadcast) or regarded as having general psychopathologic interest (e.g., anxiety). Psychopathologic dimensions were also formed by combining related items. Thus, we would analyze a dimension that contained maximum information regarding the presence or absence of depression as well as examine some individual depressive items (e.g., depressed facies) for discriminating power.

An analysis of variance (ANOVA), using these 443 variables, was done with cohort A. The ANOVA program assigns an F value to each variable, which indicates the variable's power to discriminate between the schizophrenic and nonschizophrenic groups when examined independently of all other variables. Thus, when the variables are ranked from highest to lowest F value, they are depicted in order of their inherent discriminating capacity. We examined the 150 most discriminating variables, all of which are discriminating at the $p < .01$ level, and reduced them to 69 by eliminating obvious overlap. For example, the following 3 variables were included in the 150: 1) The patient

hears his thoughts spoken aloud, 2) he feels that other patients can know what he is thinking without his actually saying it, and 3) he has a mysterious thought-communication dimension comprised of the above two items. It was determined that the overlap between these three variables was extensive, and we would be justified in further data analysis to use only the most discriminating of these three variables. In this way, the 150 most discriminating variables were reduced to 69. Table 4 lists the 24 most discriminating variables in descending order from the ANOVA. These variables have the greatest difference between mean ratings in the two diagnostic groups, and all are significant discriminators at $p < .001$ or better.

A second method for determining variables is to examine the ratio between a symptom's occurrence in the schizophrenic group versus the nonschizophrenic group. The group means for each variable were calculated by assigning a score of 1 if present and 0 if absent. An examination of the ratio of means reveals those signs and symptoms that have the highest odds of being associated with a schizophrenic diagnosis. Thus, a symptom that occurs in 10 percent of the schizophrenics and in 1 percent of the nonschizophrenics will be less

discriminating on the ANOVA than a symptom that occurs in 60 percent of the schizophrenics and in 10 percent of the nonschizophrenics. The former occurrence, however, has higher odds of being associated with a schizophrenic diagnosis (10:1 compared to 6:1). Table 5 shows the ratio of the mean rating in the schizophrenic and nonschizophrenic group for the 24 symptoms with the highest schizophrenic to nonschizophrenic ratios. Many of the symptoms are generally regarded as characteristic of schizophrenia, but they may occur so infrequently as to be of little practical use in the differential diagnosis of schizophrenia.

The third analysis undertaken was a stepwise discriminate function analysis. This program reduces the redundancy between discriminating signs and symptoms. The first step in a discriminate function run shows the diagnostic assignments based on the single most discriminating symptom from the ANOVA (restricted affect). However, the second symptom added is chosen by its power to increase discrimination between the schizophrenic and nonschizophrenic groups, given the presence of the first symptom. Thus, symptoms are added stepwise and take into account the symptoms already included. For example, in the ANOVA, both persecu-

Table 4. Discriminating symptoms of schizophrenia (ANOVA).

Restricted affect	Thoughts aloud	Apophany
Poor insight	Auditory hallucinations	Unreliable information
Abnormal explanations	Apathy	Irrelevance
Persecutory ideas	Voices speak to patient	Blocking
Suspiciousness	Depressed facies	Vagueness
Widespread delusions	Waking early	Remoteness from reality
Poor rapport	Preoccupied, inattentive	Incomprehensibility
Preoccupied with delusions	Thought alienation	Bizarre delusions

Table 5. Twenty-four discriminating symptoms of schizophrenia (ratio of means).

Thoughts broadcast	Remoteness from reality	Thought withdrawal
Denies delusions though present	Audible thoughts	Frequence of auditory hallucinations
Lack of affective reaction to disordered thoughts	Thought alienation	Perseveration
	Stereotypic	Hallucinated voices speak sentences
Voices arguing	Made feelings	Restricted affect
Preoccupied, inattentive	Incoherent speech	Hallucinated voices sound human
Idiosyncratic speech	Neologisms	Nonverbal auditory hallucinations
Thought intrusion	Blocking	Unreliable information
Apathy		

tory ideas and suspiciousness were highly discriminating. A stepwise discriminate function analysis would be expected to reduce sharply the discriminating power for suspiciousness, if the system is already taking into account the presence or absence of persecutory ideas. Table 6 lists the 12 most discriminating symptoms ranked in order of their entry on this stepwise program. Note that here, for the first time, signs and symptoms more prevalent in nonschizophrenia appear, thus forming criteria for differential diagnosis.[5]

Table 7 shows the results of using the 12 discriminating signs and symptoms from the stepwise discriminant function analysis to make diagnostic assignments.[6] The nine signs and symptoms more prevalent in schizophrenia are scored 1 point each if present, and the three symptoms—waking early, depressed facies, and elation—more prevalent in the nonschizophrenic group are scored 1 point each when absent. Thus, the most stringent criteria for our assignment to schizophrenia would be a total score of 12 (i.e., 9 schizophrenic symptoms present and 3 nonschizophrenic symptoms absent). Table 7 demonstrates that a meaningful split between schizophrenic and nonschizophrenic diagnostic assignments results when one determines that five or more, or six or more, of these symptoms are present. At these levels, a very substantial number of diagnosed schizophrenic patients would be judged schizophrenic, while relatively few of the patients assigned nonschizophrenic diagnoses would be relegated to the schizophrenic group by these criteria. The percentages in the left-hand, or schizophrenic, column can guide the clinician on the applicability of this system in a schizophrenic population. For example, he might expect 80 percent of acute and subacute schizophrenic patients to have at least five of these symptoms. In the right-hand, or nonschizophrenic, column, the percentages indicate the degree of error one might anticipate when making diagnostic assignments with this system. For example, if a patient with five or more of these symptoms is assigned automatically to a schizophrenic category, one might expect that 13 percent of nonschizophrenic patients would be erroneously assigned to schizophrenic groups. The latter

Table 6. Twelve differential symptoms.

Restricted affect	Elation (-)
Poor insight	Widespread delusions
Thoughts aloud	Incoherent speech
Waking early (-)	Unreliable information
Poor rapport	Bizarre delusions
Depressed facies (-)	Nihilistic delusions

point is critical whenever diagnostic certainty is combined with a fatalistic approach to schizophrenia, which can launch the negative therapeutic expectation described by the societal-reaction theorists (Becker 1963, Erikson 1964, Goffman 1961, Gruenberg 1969, Scheff 1966, and Wing and Brown 1970).

The advantages of using such a flexible system are as follows: 1) These 12 signs and symptoms are operationalized, and reliable judgments regarding their presence or absence can be made (see appendix I). 2) The system is simple enough to encourage its use by various research groups in describing their subjects, thus enhancing the opportunity for comparability of groups in replication studies. 3) One can choose the cutoff level (e.g., the presence of five or more symptoms, or six or more symptoms) according to his needs. For example, in a busy emergency room, a 1st-year resident might make a diagnostic judgment, assisted by this system, that would apply to 80 percent of the schizophrenic patients, and incorrectly include as schizophrenic only 13 percent of nonschizophrenic patients. More stringent criteria could be used by a research group that is trying to draw 10 "certain" schizophrenic patients from a pool of 50. One might then choose to include only patients who have seven or more symptoms and thus have a high degree of confidence that the 10 patients chosen would not represent nonschizophrenic diagnoses.[7]

Such a promising system would ordinarily have to await extensive data collection by other groups to

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[5] A flexible system for the diagnosis of schizophrenia based on these 12 symptoms has been reported elsewhere (Carpenter, Strauss, and Bartko 1973).

[6] Similar analyses were performed, using the best 12 symptoms from the ANOVA and ratios (tables 4 and 5), but the results were less successful and therefore are not presented.

[7] The use of 12 symptoms rather than another number was largely fortuitous. We wanted enough symptoms to give a good discrimination of schizophrenia, but few enough to be readily taught and used. Removal of each symptom sequentially, therefore, using each combination of 11 of these symptoms, revealed that each of the 12 symptoms contributed substantively. Sequential addition of four other highly discriminating symptoms did not appreciably improve the system. Therefore, the 12 symptoms are like the four forward gears on a Volkswagen—three (11) are not enough and five (13) are too many.

Table 7. Twelve symptoms for differential diagnosis, cohort A.

Symptoms	Percentage schizophrenic (N=407)	Percentage nonschizophrenic (N=152)
Five or more	80	13
Six or more	66	4
Seven or more	44	1

determine whether its basic claims are replicable. The IPSS, however, includes a sufficient number of cases to initially establish two substantial cohorts. This flexible diagnostic system, based on highly discriminating signs and symptoms, was derived from cohort A. It was then applied to cohort B—a group of patients evaluated with the same methodologic techniques, but who did not contribute to the derivation of this 12-point system. Table 8 depicts the results of this replication attempt. An almost identical split again occurs when one examines patients who have five or more, six or more, or seven or more of these symptoms. At the six or more level, the percentage split is essentially the same as in cohort A. Tables 7 and 8 are not statistically different ($\chi^2 = 5.1$, $df = 5$, $p < .40$). We regard this result as confirmatory evidence for the general applicability of this system when dealing with acute and subacute patients drawn from functional psychoses, borderline, and severe (hospitalized) neurotic and personality diagnostic groups. It is yet to be determined to what extent the system will apply in chronic, institutionalized cases or will distinguish between organic and functional psychoses. It was more successful, however, in diagnostic assignments with IPSS patients than was a similar system using discriminating symptoms from Schneider, the ANOVA, or ratio of means.

Summary (Part I)

The nine-nation methodology of the IPSS provides an opportunity for scientific assessment of established diagnostic schools. To illustrate the strength of a multination design, data analyses previously done in evaluating the diagnostic approaches of Schneider and Langfeldt were summarized. Schneider's system is built on highly discriminating signs and symptoms; but when the system is used inflexibly, as advocated by Schneider, to assign any case with an FRS to a schizophrenic diagnosis, substantial diagnostic discrepancy accrues. Using more flexible rules for his diagnostic system results in a significant differential between schizophrenic and nonschizophrenic patients and provides an estimate of false positive and false negative assignments at each level of stringency of criteria chosen.

Langfeldt's diagnostic school is particularly noteworthy for its success in discriminating between good- and poor-outcome patients (schizophrenic and schizophreniform psychoses). The methodology of the IPSS permits a clear separation of sign and symptom data from other prognostic data and thus provides an opportunity for testing the basic tenets of Langfeldt's system. Evaluation of outcome in the American patients did not support Langfeldt's characteristic symptoms as

Table 8. Twelve symptoms for differential diagnosis, cohort B.

Symptoms	Percentage schizophrenic (N=404)	Percentage nonschizophrenic (N=156)
Five or more	81	22
Six or more	63	6
Seven or more	39	1

discriminators between the good- and poor-outcome schizophrenic groups.

A rationale for using cross-cultural research methodologies in a renewed search for highly discriminating signs and symptoms was provided. Biased patient populations and diagnostic schools may be highlighted when a study is done in a single center, but are weakened with a cross-cultural or multicenter design. Furthermore, the large number of cases that can be generated in a multicenter study permit a division of the patients into two randomized cohorts. A series of analyses established the most successful signs and symptoms for discriminating between schizophrenia and nonschizophrenia in cohort A. A flexible system, based on these 12 discriminating signs and symptoms, was presented. Replication of this work, using cohort B—a group of patients who did not contribute to the derivation of the discriminating signs and symptoms—was successful. This system is particularly advantageous, since it is operationalized by a few questions that a psychiatrist can be taught to score reliably from a single psychiatric interview. It can be readily applied at various levels of diagnostic stringency and in each instance provides an estimate of false negative and false positive diagnostic assignments.

The Authors

William T. Carpenter, Jr., M.D., is Acting Chief, Section on Psychiatric Assessment, National Institute of Mental Health, Bethesda, Md.; John S. Strauss, M.D., is Director, Clinical Psychiatry Research Programs, University of Rochester School of Medicine and Dentistry, Rochester, N.Y.; and John J. Bartko, Ph.D., is Mathematical Statistician, Theoretical Statistics and Mathematics Branch, National Institute of Mental Health, Bethesda, Md.

available from nimh

It's Good to Know about Mental Health, a brochure recently released by the National Institute of Mental Health, attempts to define mental health and describes some of the causes and warning signs of mental disorders, such as prolonged anxiety, depression, tension-caused physical symptoms, and perfectionism. The booklet gives a number of simple suggestions for keeping or achieving good mental health. It also describes the kinds of mental illness and where and how the mentally ill can obtain help. Single courtesy copies are available from Public Inquiries, Room 15C-17, National Institute of Mental Health, 5600 Fishers Lane, Rockville, Md. 20852.

Definition of Terms in Mental Health, Alcohol Abuse, Drug Abuse, and Mental Retardation, a revised, updated edition of a manual defining basic terms in mental health and related areas of concern, has been published by NIMH. The 123-page manual provides a common language for the exchange of information among concerned disciplines. The lack of commonly understood definitions has made it difficult to compare programs in terms of work done, costs, facilities, staff, and persons served. The manual, if widely used, should make possible enhanced sharing of information on program planning and evaluation. It is designed to be useful to program planners and developers, program administrators, statisticians, budget officers, and others involved in funding and cost accounting. The manual, NIMH Mental Health Statistics Series C, No. 8, DHEW Publication No. (ADM) 74-38, is available from the Survey and Reports Section, Biometry Branch, Room 18C-25, National Institute of Mental Health, 5600 Fishers Lane, Rockville, Md. 20852.