carry ready-made assumptions and implications. Until not too long ago the diagnosis of schizophrenia carried with it hopelessness concerning any successful therapeutic outcome, and depressions carried the implication that only ECT could be useful. It is only after getting to know each individual patient that we realize that very few schizophrenics are therapeutically hopeless and very few depressed patients need ECT.

Until we are able to diagnose according to etiology and pathogenesis there will be a need for many different types of diagnostic systems, depending on one's point of view and particular frame of reference—descriptive, dynamic, cognitive, etc. But we cannot do without a system of diagnosis that is accepted by all in the field at least for certain purposes. The APA *Diagnostic and Statistical Manual of Mental Disorders* serves this purpose. This study has lit a light in a tiny corner of the manual that heretofore was dark. The team of investigators set out in search of a syndrome. I think they found it.

Establishment of Diagnostic Validity in Psychiatric Illness: Its Application to Schizophrenia

BY ELI ROBINS, M.D., AND SAMUEL B. GUZE, M.D.

A method for achieving diagnostic validity in psychiatric illness is described, consisting of five phases: clinical description, laboratory study, exclusion of other disorders, follow-up study, and family study. The method was applied in this paper to patients with the diagnosis of schizophrenia, and it was shown by follow-up and family studies that poor prognosis cases can be validly separated clinically from good prognosis cases. The authors conclude that good prognosis "schizophrenia" is not mild schizophrenia, but a different illness.

SINCE BLEULER (3), psychiatrists have recognized that the diagnosis of schizophrenia includes a number of different disorders. We are interested in distinguishing these various disorders as part of our long-standing concern with developing a valid classification for psychiatric illnesses(6, 7, 10, 11). We believe that a valid classification is an essential step in science. In medicine, and hence in psychiatry, classification is diagnosis.

One of the reasons that diagnostic classification has fallen into disrepute among some psychiatrists is that diagnostic schemes have been largely based upon a priori principles rather than upon systematic studies. Such systematic studies are necessary, although they may be based upon different approaches. We have found that the approach described here facilitates the development of a valid classification in psychiatry. This paper illustrates its usefulness in schizophrenia.

The Five Phases

1. Clinical Description

In general, the first step is to describe the clinical picture of the disorder. This may be a single striking clinical feature or a combination of clinical features thought to be associated with one another. Race, sex, age at onset, precipitating factors, and other items may be used to define the clinical picture more precisely. The clinical picture thus does not include only symptoms.

2. Laboratory Studies

Included among laboratory studies are chemical, physiological, radiological, and anatomical (biopsy and autopsy) findings. Certain psychological tests, when shown to be reliable and reproducible, may also be considered laboratory studies in this context. Laboratory findings are generally more reliable, precise, and reproducible than are

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clinical descriptions. When consistent with a defined clinical picture they permit a more refined classification. Without such a defined clinical picture, their value may be considerably reduced. Unfortunately, consistent and reliable laboratory findings have not yet been demonstrated in the more common psychiatric disorders.

3. Delimitation from Other Disorders

Since similar clinical features and laboratory findings may be seen in patients suffering from different disorders (e.g., cough and blood in the sputum in lobar pneumonia, bronchiectasis, and bronchogenic carcinoma), it is necessary to specify exclusion criteria so that patients with other illnesses are not included in the group to be studied. These criteria should also permit exclusion of borderline cases and doubtful cases (an undiagnosed group) so that the index group may be as homogeneous as possible.

4. Follow-Up Study

The purpose of the follow-up study is to determine whether or not the original patients are suffering from some other defined disorder that could account for the original clinical picture. If they are suffering from another such illness, this finding suggests that the original patients did not comprise a homogeneous group and that it is necessary to modify the diagnostic criteria. In the absence of known etiology or pathogenesis, which is true of the more common psychiatric disorders, marked differences in outcome, such as between complete recovery and chronic illness, suggest that the group is not homogeneous. This latter point is not as compelling in suggesting diagnostic heterogeneity as is the finding of a change in diagnosis. The same illness may have a variable prognosis, but until we know more about the fundamental nature of the common psychiatric illnesses marked differences in outcome should be regarded as a challenge to the validity of the original diagnosis.

5. Family Study

Most psychiatric illnesses have been shown to run in families, whether the investigations were designed to study hereditary or environmental causes. Independent of the question of etiology, therefore, the finding of an increased prevalence of the same disorder among the close relatives of the original patients strongly indicates that one is dealing with a valid entity.

We hope it is apparent that these five phases interact with one another so that new findings in any one of the phases may lead to modifications in one or more of the other phases. The entire process is therefore one of continuing self-rectification and increasing refinement leading to more homogeneous diagnostic grouping. Such homogeneous diagnostic grouping provides the soundest base for studies of etiology, pathogenesis, and treatment. The roles of heredity, family interactions, intelligence, education, and sociological factors are most simply, directly, and reliably studied when the group studied is as homogeneous as possible.

We will demonstrate by examining certain studies that these principles concerning the validity of psychiatric diagnosis may be applied to schizophrenia. These studies show that it is possible to systematically divide cases of schizophrenia into a poor prognosis group and a good prognosis group. Further, these studies suggest that this differentiation is not simply a matter of severity of illness but that the two groups represent different illnesses.

Nomenclature

Psychiatrists have recognized for many years that among patients given the diagnosis of schizophrenia there are two main groups—one with a poor prognosis and the other with a better prognosis. Different investigators have referred to these two groups by different diagnostic terms. The more common terms for poor prognosis cases are chronic schizophrenia, process schizophrenia, dementia praecox, and nuclear schizophrenia. For good prognosis cases, they are acute schizophrenia, reactive schizophrenia, schizo-affective psychosis, atypical psychosis, and schizophreniform psychosis.

Diagnostic Validation by Follow-Up Studies

Table 1 summarizes those studies reported in English in which the authors attempted to define patients systematically into poor prognosis groups or good prognosis groups. These studies were prospective or retrospective. In the retrospective studies, the author,

TABLE 1
Follow-Up Studies of Patients Given the Diagnosis of Schizophrenia

AUTHORS	COUNTRY	NUMBER OF CASES	DURATION OF FOLLOW-UP (YEARS)	FOLLOW-UP RESULTS (IN PERCENT) WELL	SYMPTOMS + INCAPACITY
CASES PREDICTED TO HAVE A POOR OUTCOME					
1. Clark and Mallett (4)	England	76	3	11	73
2. Eitinger and associates (5)	Norway	110	5-15	1	84
3. Stephens and Astrup (13)	U.S.A.	143	5-13	7	55
4. Astrup and associates (1)	Norway	435	6-22	15	68
5. Astrup and Noreik (2)	Norway	273	>5	6	66
6. Vaillant (14)	U.S.A.	35	2	14	--
7. Vaillant (15)	U.S.A.	48	8-15	13	74
		60	1-2	7	62
8. Johanson (8)	Sweden	100	10-18	<12	>88
9. Robins and Smith (12)	U.S.A.	35	6	9	91
CASES PREDICTED TO HAVE A GOOD OUTCOME					
1. Eitinger and associates (5)	Norway	39	5-15	36	23
2. Stephens and Astrup (13)	U.S.A.	74	5-13	38	3
3. Astrup and associates (1)	Norway	398	6-22	--	26
4. Astrup and Noreik (2)	Norway	306	>5	--	17
5. Vaillant (14)	U.S.A.	30	2	83	--
6. Vaillant (15)	U.S.A.	24	8-15	83	17
		28	1-2	64	11

without knowledge of the outcome, made a prediction concerning prognosis based upon the original clinical manifestations in the clinical records. In the selection of patients for all of these studies, cases of organic brain syndrome (including delirium), mental deficiency, obsessional neurosis, and typical manic-depressive illness were excluded. It is worth noting that similar results were obtained in different countries. This implies that the findings probably have universal application.

Patients with the diagnosis of schizophrenia who were predicted to have a poor outcome did so in from 55 to 91 percent of cases, whereas they were well at follow-up in from one to 15 percent of cases only (table 1). Clinical features of the cases in these studies associated with a poor prognosis are summarized in table 2.

Patients with the diagnosis of schizophrenia who were predicted to have a good outcome were found to have a poor prognosis in only three to 26 percent of cases, whereas they were well in 36 to 83 percent of cases (table 1). Clinical features associated with a good prognosis are summarized in table 2.

It is evident that in table 1, the figures do not add up to 100 percent except in three studies. This is because in the remaining studies, although the patients were not well, it was not possible to determine their incapacity. Therefore, we did not include them in the tables. It seems evident from the data in table 1 that, using the appropriate criteria, predicting a poor outcome is more likely to be correct than is predicting a good outcome.

The error in prediction for each group (poor outcome and good outcome) suggests two possibilities: either each group is not homogeneous, i.e., it includes patients with

TABLE 2
Prognostic Features in Schizophrenia

FEATURES ASSOCIATED WITH A POOR PROGNOSIS	FEATURES ASSOCIATED WITH A GOOD PROGNOSIS
1. Insidious onset (more than six months of symptoms)	1. Prominent depressive symptoms
2. Hebephrenic clinical picture	2. Family history of affective disorders
3. "Massive" persecutory delusions	3. Absence of a family history of schizophrenia
4. Clear sensorium	4. Good premorbid adjustment
5. Schizoid personality	5. Confusion
6. Family history of schizophrenia	6. Acute onset (less than six months of symptoms)
7. Striking emotional blunting	7. Precipitating factors
	8. Concern with dying and guilt

more than one illness, or each group represents a separate illness with a variable prognosis. The family studies described below permit, to a considerable extent, the resolution of these alternatives.

Diagnostic Validation by Family Studies

There are many family studies of schizophrenia in the literature. We have limited ourselves for the present purpose to only two studies. We selected only studies in which the following three criteria were met: 1) There was a clinical differentiation made of poor prognosis from good prognosis index cases. 2) There was a follow-up of the index cases to establish the validity of the original differentiation. 3) There was a systematic study of schizophrenia and affective disorders among first-degree relatives. Since we believe that such family studies are very important in establishing diagnostic validity, we regret that there are so few to report.

The two pertinent studies are presented in table 3. The most striking finding in these studies is the great preponderance of affective disorders among the first-degree relatives of patients with a good prognosis. This indicates that many of the index cases with a good prognosis did not have schizophrenia but suffered from a different illness—an affective disorder. On the other hand, the finding of an increased prevalence of schizophrenia among the first-degree relatives of the good prognosis cases (eight percent in Kant's [9] series and 20 percent in Vaillant's [14] series) indicates that some of the good prognosis cases did, in fact, suffer from schizophrenia.

Another striking finding in these studies is the preponderance of schizophrenia among the first-degree relatives of patients with a poor prognosis (32 percent schizophrenia versus six percent affective disorder in Kant's[9] series, and 23 percent schizophrenia versus seven percent affective disorder in Vaillant's [14] series).

The only finding inconsistent with the two points just made is the similarity of the prevalence of schizophrenia among the relatives of good prognosis and poor prognosis index cases in Vaillant's (14) series. We have no explanation for this inconsistency. It suggests that Vaillant's (14) series of good prognosis cases included more patients with schizophrenia than did Kant's (9).

Discussion

In this paper, we have reviewed selected studies written in English in which attempts were made to separate cases diagnosed as schizophrenia into two groups: one with a poor prognosis and the other with a good prognosis. These studies indicate that it is possible to achieve this separation with a high degree of success. The failure to achieve 100 percent success in predicting outcome and the overlap in the results of the family studies indicate that the criteria used for the separation need further refinement. The impressive results achieved, however, by using the method described in this paper for establishing diagnostic validity indicate that the method has great power.

The method shows its power not only by its ability to separate the two groups quite well but also by pointing up its failures, thus indicating where additional study is needed. This additional study may involve further refinement of clinical studies, of follow-up studies, or of family studies.

TABLE 3
Family Studies of Poor Prognosis Versus Good Prognosis Cases

AUTHOR	COUNTRY	NUMBER OF CASES	PERCENT OF INDEX CASES WITH PSYCHIATRIC ILLNESS IN FIRST-DEGREE RELATIVES	
			SCHIZOPHRENIA	AFFECTIVE DISORDER
Kant (9)	U.S.A.	50 good prognosis	8	38
		versus		
		50 poor prognosis	32	6
Vaillant (14)	U.S.A.	30 good prognosis	20	50
		versus		
		30 poor prognosis	23	7

Even though at this time laboratory studies have not contributed reliably to the diagnosis of schizophrenia, without such reliable laboratory studies a completely satisfactory classification of schizophrenia may not be possible despite the refinements of clinical and family studies. Thus, as indicated earlier in the paper, a fully validated diagnostic classification will probably also require reliable laboratory studies. We hope we have demonstrated, however, that even in the absence of such laboratory studies, careful clinical, follow-up, and family studies have contributed importantly to our knowledge of schizophrenia. We believe that similar studies will accomplish as much in other psychiatric illnesses.

Summary

A method for achieving a high degree of diagnostic validity for psychiatric illness was described. The method was applied to schizophrenia. It was shown that it is possible to separate poor prognosis from good prognosis cases of schizophrenia. Poor prognosis cases have a predominance of schizophrenia among their psychiatrically ill first-degree relatives. Good prognosis cases have a predominance of affective disorder among their psychiatrically ill first-degree relatives. Therefore, apparent "schizophrenia" with a good prognosis is not a mild form of schizophrenia, but is a different illness. Research in schizophrenia, whether genetic, psychodynamic, clinical, sociological, chemical, physiological, or therapeutic, must take this differentiation into account.

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