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The International Pilot Study of Schizophrenia: five-year follow-up findings¹

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SYNOPSIS A five-year follow-up of the patients initially included in the International Pilot Study of Schizophrenia was conducted in eight of the nine centres. Adequate information was obtained for 807 patients, representing 76% of the initial cohort. Clinical and social outcomes were significantly better for patients in Agra and Ibadan than for those in the centres in developed countries. In Cali, only social outcome was significantly better.

INTRODUCTION

The International Pilot Study of Schizophrenia (IPSS) is a transcultural psychiatric investigation of 1202 patients in nine countries - Colombia, Czechoslovakia, Denmark, India, Nigeria, China, Union of Soviet Socialist Republics, United Kingdom and the United States of America.

The IPSS sample was recruited from successive admissions or referrals to psychiatric facilities in the different centres and thus was not necessarily representative of the wider population of schizophrenic and other psychiatric patients in the community.

The first publication related to this study (WHO, 1973) presented a detailed account of the origins of the study as well as description of the place of the IPSS in the World Health Organization's long-term programme in epidemiological and social psychiatry. The results of a two-year follow-up of the original cohort of patients were published in a second volume (WHO, 1979). The initial phase of the study, which occupied the period between April 1968 and September 1969, demonstrated the feasibility of a large-scale international collaborative study, which required the field workers involved

to apply standardized interviews in eight different languages. Despite this linguistic diversity, satisfactory inter-rater reliability was achieved for the schedules used. It was discovered that patients with characteristic patterns of signs and symptoms, closely corresponding to descriptions of schizophrenia in the most widely used textbooks, were found in each of the settings. In seven of the nine centres, the diagnostic term schizophrenia was applied by the research psychiatrists to a group of patients whose clinical characteristics were very similar across these centres. In the two remaining centres, Washington and Moscow, the psychiatrists included broader clinical groupings under the rubric of schizophrenia. This was confirmed by the use of a computer program, CATEGO (Wing *et al.* 1974), which functioned as a reference classification with which to compare the diagnostic practices in each of the centres. Agreement between the centres on a core group of patients diagnosed as schizophrenia was sufficient to justify comparison of the outcome of patients in the various centres.

A two-year follow-up study of the original cohort was successfully completed although the proportion of patients with complete assessments was rather low in some of the centres, notably London and Ibadan. In London there were difficulties due to insufficient staff, while in Ibadan problems arose in tracing rural patients. Of the 1202 patients given an initial examination, it was possible to obtain sufficient information about 77% to include them in the basic follow-

¹ This paper on the 5-year follow-up of patients included in the International Pilot Study of Schizophrenia of the WHO was prepared on behalf of the collaborating investigators (see Appendix).

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up analyses. In presenting the material, the Agra, Cali and Ibadan centres will be referred to as centres in developing countries because of the prevailing socio-economic conditions in India, Colombia and Nigeria. Taipei has not been included as a centre in a developing country because the characteristics of medical care facilities and the principal causes of death in the city resemble those of a centre in a developed country. Aarhus, London, Moscow, Washington and Prague are referred to as centres in developed countries.

Using this convention, the two-year follow-up data revealed that patients with an initial diagnosis of schizophrenia had a considerably better course and outcome in centres in developing countries than in centres in developed countries (WHO, 1979). This remained true whether clinical outcome, social outcome, or a combination of the two was considered. A strikingly good outcome characterized schizophrenic patients in Agra, where over 90% were followed-up, as well as in Ibadan, where the follow-up rate was 50%. The poorest outcome was evident in Aarhus, where a similar definition of schizophrenia was applied as in Agra and Ibadan. Hence neither the relative success of the follow-up, nor the diagnostic practices of the psychiatrists can account for the markedly better outcome for schizophrenia in the developing countries.

Another artefactual explanation for this finding cannot be excluded, namely that patients who chose to attend the sparse facilities in the centres in developing countries were selected, by themselves or relatives, on the basis of a good prognosis. The follow-up data, as yet unpublished, from the WHO Determinants of Outcome study (Sartorius *et al.* 1986) provide evidence against this possibility, since they relate to a strict epidemiological sample making a first contact with psychiatric facilities, yet still demonstrate a better outcome for schizophrenic patients in developing countries.

We present here the findings from the five-year follow-up of the IPSS, which not only confirm the two-year results, but amplify them, since a more complete follow-up was achieved in some of the centres. The centre in Taipei ceased participating in the IPSS before the five-year follow-up study was completed so that data from that centre are not included in this paper.

METHOD

Instruments

Four main types of schedule were used during the follow-up phase of the IPSS: the Present State Examination (PSE), the Follow-up Psychiatric History schedule (FUPH), the Follow-up Social Descriptions schedule (FUSD) and the Follow-up Diagnostic Assessment schedule (FUDA). The PSE was originally devised by Wing *et al.* (1974) and was translated from English into the seven other languages of the IPSS with the usual precautions (WHO, 1973). The development of the other three schedules is described in the second IPSS publication (WHO, 1979). The main purposes of the five-year FUPH were to collect information on the course of the patient's illness in the interval between initial examination and the five-year follow-up, and to provide an account of any socioeconomic changes affecting the patient during the same period. The FUDA schedule requires the psychiatrist assessing the patient at follow-up to state his diagnosis of the patient using follow-up information only, and to reformulate the diagnosis using all the information available. In addition to interviews with the patient, information was obtained from family members, health records and health professionals.

Reliability of instruments

This was established for the instruments used for initial assessment and for the follow-up schedules by interviews being regularly rated by a number of research workers, both within centres and between centres. Various measures of reliability of rating were presented for the two-year follow-up data (WHO, 1979). With respect to the PSE, the intracentre reliability was extremely high for all 129 units of analysis derived from the PSE items (intraclass correlation coefficient, agreement ratio 0.87). The intercentre reliability was about 5% lower than in the intracentre exercises, but still very satisfactory.

For the various measures of course and outcome, with the exception of social outcome, the inter-rater agreement ranged from 0.58 to 0.75. When social outcome was analysed as a trichotomous variable, low levels of reliability resulted. Therefore the categories were collapsed into 'severe impairment' and 'all other out-

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Table 1. Number of patients in each centre with a PSE at five-year follow-up

	Aarhus	Agra	Cali	Ibadan	London	Moscow	Praque	Washington	All centres
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Followed up	8 (6)	37 (26)	10 (8)	59 (41)	45 (35)	20 (14)	17 (14)	62 (47)	258 (24)
Not followed up	4 (3)	6 (4)	10 (8)	2 (1)	1 (1)	0 (0)	3 (2)	0 (0)	26 (2)
Not in PSE	113 (87)	88 (63)	102 (80)	53 (37)	55 (43)	48 (34)	98 (78)	67 (51)	624 (59)
Within 6 months of follow-up	5 (4)	9 (6)	5 (4)	31 (21)	26 (20)	72 (51)	7 (6)	2 (2)	157 (15)
More than 6 months after follow-up	130	140	127	145	127	140	125	131	1065

Table 2. Distribution of all patients assessed at five-year follow-up by ICD diagnosis and centre

ICD diagnosis	Aarhus	Agra	Cali	Ibadan	London	Moscow	Praque	Washington	All centres
22 - Puerperal psychosis	2	—	—	—	—	1	—	—	3
23 - Simple schizophrenia	6	2	1	1	2	—	5	3	20
24 - Hebephrenic schizophrenia	11	—	19	8	7	—	3	—	48
25 - Catatonic schizophrenia	2	15	12	6	3	—	—	—	38
26 - Paranoid schizophrenia	26	11	17	28	44	12	30	33	201
27 - Acute schizophrenia	—	8	27	4	—	11	4	6	60
28 - Latent schizophrenia	3	—	3	—	—	11	2	2	21
29 - Residual schizophrenia	—	—	—	—	1	—	2	—	3
30 - Schizo-affective	1	14	7	15	7	4	15	6	69
31 - Other schizophrenia	1	3	6	2	—	28	3	2	45
32 - Unspecified schizophrenia	—	20	—	5	—	—	1	—	26
33 - Agitated depression	1	3	1	—	—	—	—	—	5
34 - Manic-depressive depression	17	3	1	5	4	9	18	1	58
35 - Manic-depressive manic	19	16	3	2	3	1	7	1	52
36 - Other affective disorder	4	—	—	1	3	1	—	2	11
37 - Paranoid states	9	—	—	1	—	—	8	—	18
38 - Other psychoses	1	—	—	1	—	6	1	1	15
39 - Reactive depression	13	—	2	1	—	5	3	—	24
40 - Unspecified psychosis	2	—	—	—	—	—	—	—	2
41 - Depressive neurosis	2	6	5	2	8	8	6	8	45
42 - Other neurosis	2	2	12	—	—	23	—	4	43
43 - Personality disorders	—	—	—	—	—	—	—	—	—
All	122	103	117	86	82	120	108	69	807
Percentage of initial cohort	94	74	92	59	65	86	86	53	76

comes, which resulted in inter-rater agreement of 0.75.

The checks on inter-rater reliability of the schedules continued between the two-year and five-year follow-ups, but analyses of the data are not available. While it is possible that rater drift occurred over the long follow-up period of this study, there is no reason why this should have produced a systematic bias affecting the assessment of outcome in one centre differently from the others.

Completeness of follow-up

The absence of the Taipei centre from the five-year follow-up removed 137 patients from the initial cohort of 1202, leaving 1065 to be followed-up in the remaining eight centres.

From Table 1 it can be seen that 59% of patients were examined with the PSE within six months either side of the five-year follow-up point. No patient was seen earlier than the limit, but 15% were interviewed more than five and a

Table 3(a). Distribution of Centre diagnoses in original cohort and five-year follow-up sample

	Original cohort		Follow-up sample	
	N	%	N	%
Schizophrenia	727	68.3	531	65.8
Mania	64	6.0	52	6.4
Other	274	25.7	224	27.8

Table 3(b). Distribution of CATEGO classes in patients given diagnosis of schizophrenia

CATEGO class	Original cohort		Follow-up sample	
	N	%	N	%
S+	443	60.9	323	60.8
S. P. O	581	79.9	421	79.3
Other	146	20.1	110	20.7

Table 3(c). Sex distribution of original cohort and five-year follow-up sample

	Original cohort		Follow-up sample	
	N	%	N	%
Centre schizophrenia				
Female	357	49.1	261	49.1
Male	370	50.9	270	50.9
All diagnoses				
Female	582	54.6	443	54.9
Male	483	45.4	364	45.1

Table 3(d). Age distribution of original cohort and five-year follow-up sample

	Original cohort		Follow-up sample	
	N	%	N	%
Centre schizophrenia				
Age < 30	430	59.2	312	58.8
Age > 30	296	40.8	219	41.2
All diagnoses				
Age < 30	573	53.9	425	52.7
Age > 30	491	46.1	382	47.3

half years after the initial examination. The longest duration of follow-up, recorded for a single patient, was seven years and three months. In all, 74% of the original cohort were given a PSE at the five-year follow-up, a creditable success rate and very similar to the 76% reinterviewed at the two-year follow-up.

Table 3(e). Marital status of original cohort and five-year follow-up sample

	Original cohort		Follow-up sample	
	N	%	N	%
Centre schizophrenia				
Married or cohabiting	298	41.1	210	39.6
Single/widowed/divorced	427	58.9	320	60.4
All diagnoses				
Married or cohabiting	508	47.8	383	47.5
Single/widowed/divorced	555	52.2	423	52.5

Table 3(f). Type of onset of original cohort and five-year follow-up sample

	Original cohort		Follow-up sample	
	N	%	N	%
Centre schizophrenia				
Sudden	99	13.6	72	13.6
Slow/insidious	623	85.7	457	86.1
All diagnoses				
Sudden	158	14.8	119	14.8
Slow/insidious	897	84.2	683	84.6

In addition to the patients assessed with all the instruments including the PSE, for another 26 individuals information was obtained by using only the FUPH and FUSD schedules. Thus, sufficient information to characterize outcome over five years was obtained for a total of 807 patients, representing 76% of the initial cohort.

A frequent reason for not tracing or not assessing patients at the five-year follow-up was death. A total of 52 patients, or 4.9% of the original cohort, died during the follow-up period. There may have been additional deaths among patients who were not traced. Suicide (ascertained and suspected) was the commonest cause of death among the study patients, accounting for 38% of all known deaths. It is well-established that the suicide risk in schizophrenia is as high as in affective illnesses (e.g. Tsuang *et al.* 1979) and this is borne out in the IPSS. In two of the centres (Ibadan and Agra) the percentage of patients who died was 9.0 and 7.1 respectively. The centre with the lowest

Original cohort sample

Follow-up sample

N	%
210	39.6
320	60.4
383	47.5
423	52.5

Final cohort and sample

Follow-up sample

N	%
72	13.6
57	86.1
119	14.8
683	84.6

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Of the 807 patients satisfactorily assessed at five-year follow-up 531 (65.8%) had an initial centre diagnosis of schizophrenia and 126 (15.6%) a diagnosis of an affective psychosis. Among the 1065 patients originally assessed, excluding the patients from the Taipei centre, a diagnosis of schizophrenia was given to 727 (68.3%) and of affective psychosis to 154 (14.5%). These figures suggest that successful follow-up is not influenced by initial diagnosis.

The initial diagnostic distribution of these 807 patients is shown for each centre in Table 2. The striking variation in distribution between centres is likely to be due to a combination of selection factors and, in the case of the subtypes of schizophrenia, differences in diagnostic practices. However, the high proportion of catatonic schizophrenia in Agra, Cali and Ibadan reflects a genuine difference in the prevalence of this subtype between developing and developed countries (Leff, 1988). It can be seen from Table 2 that sufficient outcome data were obtained from a low of 53% of the initial cohort in Washington to a high of 94% in Aarhus. It is reassuring that in one of the centres in a developing country, Cali, the success rate in obtaining follow-up data was over 90%.

Potential bias introduced by incomplete follow-up

Since patients lost to follow-up may bias the remainder of the sample either towards a better or a worse outcome, it is necessary to compare the patients successfully followed up with the original cohort. In particular such a comparison must include factors commonly associated with the prognosis of the major psychiatric illnesses. Age, sex and marital status are almost invariably identified as influencing the outcome of the whole range of psychiatric conditions, while type of onset is particularly important in schizophrenia. Tables 3(a-f) show the comparison of the five-year follow-up sample with members of the original cohort on all those variables, as well as on the distributions of Centre diagnoses (made by the research psychiatrists in each centre) and CATEGO diagnoses (made by the computer program). In each instance the value of the variable was that determined at initial interview.

In none of these comparisons did the sample followed-up differ significantly from the original cohort. In fact for most of the variables, the distributions are virtually identical. These results eliminate one interpretation of the findings.

RESULTS

Clinical course and outcome of patients with an initial diagnosis of schizophrenia

The IPSS was deliberately focused on schizophrenia, and we will present outcome data mainly for this group. However, comparisons will also be made with other diagnostic groups.

PSE at five-year follow-up

The PSE covers one month preceding the interview. When given at a follow-up of a cohort of schizophrenic patients, it will only record active symptoms over that period. Usually a high proportion of patients are in a quiescent phase. However, those with chronic symptoms and those who happen to be in an acute episode at the time will be identified by a PSE assessment. Some patients suffer from neurotic symptoms when not in a psychotic phase, and these have been included in Fig. 1. Patients have been divided into those who at five-year follow-up had at least one clearly psychotic or three possibly psychotic symptoms; those who were symptomatic but did not fulfil these criteria and those with no symptoms recorded by the PSE. Chi-square analysis indicates that the differences among the centres are statistically significant ($P < 0.001$). The highest proportion of asymptomatic patients was found in both Agra and Ibadan, amounting to two-thirds of the sample seen at follow-up. The highest proportion of actively psychotic patients (nearly 60%) was shown by the samples from Aarhus and Moscow, which also had the lowest proportion of asymptomatic patients (under 5%).

Time spent in a psychotic episode

The cross-sectional data from the PSE at the five-year follow-up need to be supplemented by information of a more longitudinal nature. The follow-up psychiatric histories provide this type of data, and were used to estimate the percentage of the follow-up period that each patient spent in a psychotic episode. A psychotic episode was one which the psychiatrists completing the

