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Schizophrenia: manifestations, incidence and course in different cultures

A World Health Organization Ten-Country Study

This monograph presents the findings of a WHO Collaborative Study on the Determinants of Outcome of Severe Mental Disorders (DOS). The study was designed to investigate further some of the findings of the WHO International Pilot Study of Schizophrenia (IPSS) which produced the unexpected finding that patients suffering from schizophrenia in the centres in developing countries appear to have a more favourable outcome at both two and five years follow-up than initially similar patients in centres in developed countries. The DOS was carried out in field centres in Aarhus (Denmark), Agra and Chandigarh (India), Cali (Columbia), Dublin (Ireland), Honolulu and Rochester (United States of America), Ibadan (Nigeria), Moscow (USSR), Nagasaki (Japan), Nottingham (United Kingdom), and Prague (Czechoslovakia). Six of these centres had also taken part in the IPSS.

One of the major achievements of the IPSS had been the demonstration that large-scale cross-cultural studies using standardized methods of interviewing, symptom rating and diagnosis are possible. The study reported here rested upon the same methodological foundations but used an epidemiological approach. In each of the twelve centres of the DOS, all individuals from a defined catchment area making a lifetime first contact with specified psychiatric, medical or other agencies because of symptoms of a possibly schizophrenic illness were identified, assessed, and followed up for two years.

The finding of a better outcome of patients in developing countries was confirmed, as was the existence of a substantial proportion of patients (often more than half) with undoubted initial schizophrenic symptoms but a good outcome at two years. About one-third of all patients in the study were never admitted to a psychiatric hospital, and of those that were admitted the majority were in hospital for only short periods.

The Study also produced evidence about the incidence rates of schizophrenia. Significant differences were found between centres in the incidence of schizophrenia using a broad definition, although the rates ranged only from 1.5 to 4.2 per 100 000 population aged 15-54. In contrast, the incidence of schizophrenia using a narrow definition based on the presence of a limited number of 'classical' symptoms in the present mental state (category S+ of the CATEGO program derived from the PSE-9 interview) was not significantly different between centres.

This study confirms that schizophrenic illnesses are ubiquitous, appear with similar incidence in different cultures and have clinical features that are more remarkable by their similarity across cultures than by their difference. They are illnesses with variable outcomes which are more favourable in the developing countries and depend on genetic, developmental and environmental influences whose exact nature, interaction and relative importance have yet to be identified.

Chapter 4 Two-year course and outcome

The medium-term course and outcome of the disorders manifested by the original 1379 subjects who met the inclusion criteria of the project and had been assessed at the initial examination were evaluated by means of two follow-up examinations, scheduled at one year and at two years from the date of the first assessment (the date of the initial PSE was taken as the reference point).

In each research centre, the patients and, in most instances, also key informants, were invited for a follow-up interview; if no response to the letter of invitation resulted, the patients were visited at their homes. Every attempt was made to trace subjects who had changed their place of residence, and to collect at least a minimum of information on those who could not be re-interviewed. The latter represented a minority (301 out of 1379 study subjects, or an overall 'drop-out' rate of 21.8%) of the original patient series. The analysis of follow-up data reported in this chapter is, therefore, based on a total of 1078 cases (the totals in the tables which follow may not add up to this figure because of missing data on some patients in specific tabulations).

The sociodemographic and diagnostic characteristics of the patients who were not re-assessed did not deviate in any systematic manner from those of the patients who were available for follow-up. The principal characteristics of the patients who dropped out and were not re-assessed are shown in Table 4.1. There were no significant differences between patients re-assessed and patients not re-assessed on variables such as age, gender, marital status, and type of onset. Patients with reported use of street drugs were over-represented among the 'drop-outs' and the difference was significant at the 0.01 level. Considering diagnostic classification, there was no difference at the level of the 3-digit ICD-9 diagnosis, but patients falling into CATEGO classes other than S+ were more likely to be lost to the follow-up than class S+ cases ($P < 0.001$).

The 'drop-out' rate (%) showed highly significant differences ($P < 0.001$) among the

Table 4.1. Characteristics of the patients who completed the follow-up and of those who did not

Variable	Followed up (N = 1078)	Not followed up (N = 301)	Difference
Mean age (years)	27.9	26.6	NS
Sex (M/F)	1.1	1.3	NS
Percentage single	61.6	62.8	NS
Percentage acute onset	39.2	41.3	NS
Percentage using drugs	14.2	20.9	$P < 0.01$
Percentage CATEGO S+	55.1	44.2	$P < 0.001$
Percentage ICD 295.3 ¹	28.8	28.9	NS
Percentage ICD 295.4 ²	24.1	22.8	NS

¹ Paranoid; ² Acute schizophrenic episode.

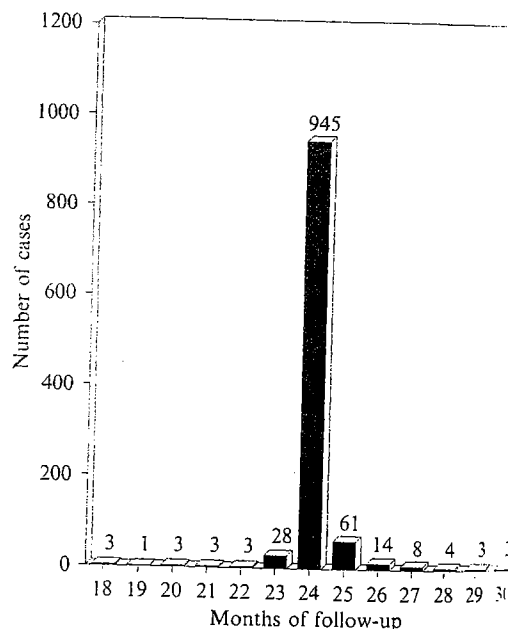


Fig. 4.1. Distribution of cases by number of months of follow-up within the range 18-30 months.

field research centres: Aarhus 19.2, Agra 6.4, Cali 9.7, Chandigarh (rural) 5.6, (urban) 30.9, Dublin 14.9, Honolulu 57.4, Ibadan 31.0.

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The differences in the proportions of patients who were followed up were unrelated to the developing/developed country dichotomy.

The 1078 cases with a complete follow-up assessment (78.2% of the original series) provided sufficient data to enable the evaluation of the main variables describing the course and outcome of schizophrenic disorders over a period of an average length of two years following the initial examination. The actual range of the follow-up was between 18 and 30 months (i.e. it allowed for a deviation of up to 6 months either way from the target date for completion of the follow-up which had been set at 24 months after the first assessment). The distribution of cases by the completed number of months of follow-up within the permissible range of 18 to 30 months is shown on Fig. 4.1.

METHODS AND INSTRUMENTS USED ON FOLLOW-UP EXAMINATIONS

Every patient, available for a follow-up assessment, had a PSE interview. Both patient and informant provided information for the Follow-Up Psychiatric and Personal History Schedule (FU-PPHS); in many instances this information was supplemented with data from hospital or clinic notes. Apart from an updating review of the main demographic and social data about the patient, the FU-PPHS contains a month-by-month chart of symptomatology, treatment, and life events, which was designed to enable a reconstruction of the course of the condition over the preceding 12 months. Upon completion of the PSE and the FU-PPHS, the investigators were required to record their overall impressions and conclusions in the Follow-Up Diagnostic and Prognostic Schedule (FU-DPS), and to write a narrative summary of the patient's progress. An additional instrument, the WHO Disability Assessment Schedule (WHO-DAS) was also rated at follow-up examinations, and the results of the analysis of the data obtained with it will be reported in subsequent publications.

The extensive data collected on follow-up examinations were processed and tabulated at WHO Headquarters, and reviewed at a meeting of the collaborating investigators. An agreement

was reached on how to aggregate the large number of variables that had been followed up, and each centre produced its own summary chart of the main course and outcome characteristics on every patient. These summary charts were coded and double-checked for consistency against the original dataset at WHO Headquarters, any discrepancies between the centres and WHO Headquarters were resolved through correspondence or discussion. The information used in the analyses presented below has, therefore, been subjected to multiple checks.

GENERAL DESCRIPTION OF THE TWO-YEAR COURSE AND OUTCOME

The following variables were assessed with a view to describing the general features of the 2-year course and outcome of the study patients: (1) pattern of course (a composite rating of the number of discrete psychotic and non-psychotic episodes observed over the follow-up period, and of the number and clinical quality of the remissions, if any); (2) proportion of the total length of the follow-up period during which the patient was in psychotic episodes; (3) proportion of the follow-up period during which the patient was in a complete remission (symptom-free); (4) proportion of the follow-up period during which the patient was on anti-psychotic medication; (5) proportion of the follow-up period during which the patient was in psychiatric hospital; and (6) proportion of the follow-up period during which the social functioning of the patient was unimpaired. Each of these variables had an operational definition, and the ratings provided by the centres were checked at Headquarters.

The results described below apply to all patients who met the original inclusion criteria and completed the follow-up, i.e. to the patients falling into the 'broad' diagnostic category of schizophrenia, which was based on the presence of either an eligible clinical (centre) diagnosis in ICD-9 terms, or a CATEGO class S, P, or O on initial examination.

Pattern of course

The categories used to classify the course of the disorder were as follows.

- 1, single psychotic episode followed by a complete remission;

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P < 0.001

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Table 4.3. Distribution of cases by percentage of follow-up spent in psychotic episodes

Centre	No. of patients	Percentage of time in psychotic episodes					Total
		1-5	6-15	16-45	46-75	76-100	
Aar	80	26.3	17.5	27.5	7.5	21.3	100.1
Dub	57	14.0	50.9	19.3	1.8	14.0	100.0
Hon	29	34.5	20.7	13.8	—	31.0	100.0
Mos	164	17.7	31.7	24.4	7.3	18.9	100.0
Nag	69	4.4	18.8	30.4	11.6	34.8	100.0
Not	86	24.4	25.6	19.8	7.0	23.3	100.1
Pra	87	17.2	47.1	25.3	2.3	8.1	100.0
Roc	31	32.3	35.5	22.6	—	9.7	100.1
Agr	76	23.7	34.2	17.1	4.0	21.2	100.2
Cal	139	6.5	26.6	22.3	17.3	27.3	100.0
Cha/R	49	27.5	35.3	27.5	3.9	5.9	100.1
Cha/U	107	23.4	37.4	21.5	6.5	11.2	100.0
Iba	96	20.8	53.1	19.8	4.2	2.1	100.0
All	1070	18.8	33.6	22.7	7.0	17.9	100.0

and that of cases with unremitting psychotic symptoms is 14.5%.

Proportion of the follow-up period spent in psychotic episodes

The proportions of the cases which fall into the different percentiles of the total follow-up time spent in psychotic episodes (obtained by summing up the duration of all discrete episodes) are presented in Table 4.3. Nearly identical proportions (18.8% and 17.9%) of patients fall into the extremes of very short (up to 5% of the length of the follow-up period) and very long (76-100% of the period) total duration of the psychotic episodes. Within these two extreme categories, there is marked variation in the share of each field research centre. Thus, the proportions of patients who spent in psychotic episodes less than 5% of the follow-up period vary from 4.4% in Nagasaki to 34.5% in Honolulu. Higher proportions (over 20%) were observed in all of the centres in developing countries except Cali, and also in three of the centres in developed countries (Aarhus, Honolulu and Nottingham). As regards the subjects who spent 76-100% of the time in psychotic episodes, their proportions range from 2.1% in Ibadan to 34.8% in Nagasaki; these proportions generally tend to be higher in the centres in developed countries (except for Dublin and Prague) but they are similarly high in two of the centres in developing countries (Agra and Cali).

Proportion of the follow-up period in complete remission

The percentage of time during which patients are symptom-free is not simply the reciprocal value of the percentage of time spent in psychotic episodes because a certain number of subjects had non-psychotic episodes or incomplete remissions, in addition to having been psychotic for some of the time. However, there is a fair correspondence between the distributions of cases over 'time psychotic' and 'time in complete remission' (Table 4.4).

Overall, 29.4% of the patients were symptom-free (complete remission for 76-100% of the time; on the other hand, 42.9% never attained a complete remission during the follow-up. The proportion of cases in complete remission over 46-100% of the follow-up period is 44.6%.

The extremes of the distributions by centre are illustrated by Nagasaki and Ibadan where 7.3% and 73.1% respectively of the patients fell within the range of 76-100% symptom-free time, and by Ibadan and Moscow, with 7.5% and 77.4% respectively of the patients not having had any symptom-free interval during the follow-up.

Proportion of time on antipsychotic medication

This measure of the course of psychotic disorders is based on a month-by-month review of the treatment chart contained in the FU-PPHS in which every prescribed medication was recorded; the study design did not envisage

Table 4.4. Distribution of cases by percentage of the follow-up period spent in complete remission

Centre	No. of patients	Percentage of time spent in complete remission						Total
		0	1-5	6-15	16-45	46-75	76-100	
Aar	80	70.0	—	—	1.3	11.3	17.5	100.1
Dub	56	55.4	—	—	10.7	12.5	21.4	100.0
Hon	28	57.1	3.6	3.6	7.1	14.3	14.3	100.0
Mos	164	77.4	1.2	1.2	1.2	4.3	14.6	100.0
Nag	69	65.2	—	2.9	10.1	15.5	7.3	99.9
Not	86	30.3	—	3.5	10.5	16.3	39.5	100.0
Pra	87	29.9	—	—	9.2	21.8	39.1	100.0
Roc	31	54.8	—	—	12.9	3.2	29.0	100.0
Agr	76	21.1	1.3	2.6	1.3	10.5	63.2	99.9
Cal	138	37.0	0.7	5.8	24.6	21.7	10.1	100.0
Cha/R	50	28.0	—	2.0	8.0	32.0	30.0	100.0
Cha/U	108	23.2	0.9	6.5	14.8	25.0	29.6	100.0
Iba	93	7.5	2.2	—	6.5	10.8	73.1	100.1
All	1066	42.9	0.8	2.5	9.4	15.2	29.4	100.2

Table 4.5. Distribution of cases by percentage time of the follow-up during which the patients were prescribed antipsychotic medication

Centre	No. of patients	Percentage of time on psychotic medication						Total
		0	1-5	6-15	16-45	46-75	76-100	
Aar	80	3.8	—	6.3	16.3	23.8	50.0	100.2
Dub	56	5.4	1.8	8.9	8.9	19.6	55.4	100.0
Hon	29	6.9	10.3	20.7	24.1	3.5	34.5	100.0
Mos	164	—	0.6	3.7	3.7	4.3	87.8	100.0
Nag	70	2.9	—	4.3	10.0	17.1	65.7	100.0
Not	84	3.6	9.5	10.7	25.0	13.1	36.9	99.8
Pra	86	1.1	2.3	8.0	14.8	21.6	52.3	100.1
Roc	31	6.5	6.5	22.6	12.9	25.8	25.8	100.1
Agr	76	4.0	32.9	32.9	22.4	5.3	2.6	100.1
Cal	139	3.6	9.4	18.0	36.0	23.0	10.1	100.1
Cha/R	49	8.2	14.3	28.6	26.5	18.4	4.1	100.1
Cha/U	109	13.8	7.3	15.6	20.2	24.8	16.5	100.2
Iba	96	—	4.2	11.5	19.8	25.0	40.6	100.1
All	1069	3.9	6.9	13.1	18.3	17.1	40.6	99.9

plasma level monitoring or determination of metabolite excretion in the urine. Therefore, the actual extent of compliance with the prescribed medication was not known. Nonetheless, this variable is informative as a measure of the estimated need for pharmacological treatment and maintenance which, in turn, reflects the psychiatrist's perception of the severity of the course of the illness. However, the variable also reflects different treatment practices in different locations.

The data (Table 4.5) show a considerable variation among the centres in this respect. There is a marked tendency within the centres in developed countries to maintain patients on

antipsychotic medication for much longer periods of time, as compared to centres in developing countries. Between 34.5% (Honolulu) and 87.8% (Moscow) of the patients in the developed countries were prescribed neuroleptic for 76-100% of the follow-up period. In the developing countries, the corresponding proportions were in the range between 2.6% (Agra) and 16.5% (Chandigarh, urban area), with the exception of Ibadan where a relatively high proportion (40.6%) were prescribed neuroleptic treatment for 76-100% of the time. However, since compliance was not monitored, and the impression of the Ibadan investigators was that few patients actually adhered to the treatment as

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