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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 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,

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.

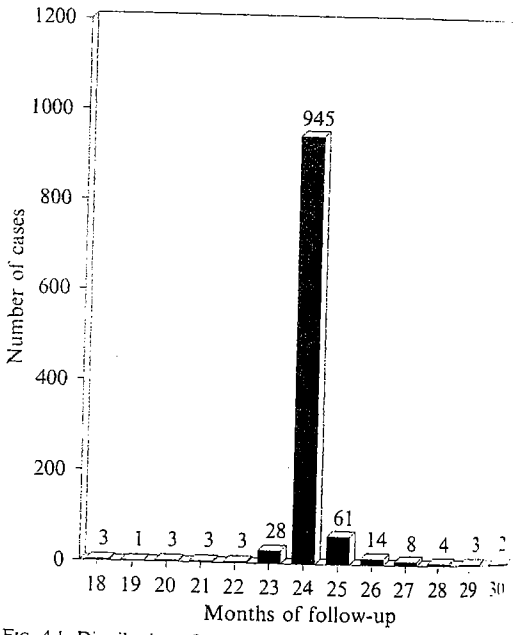

FIG. 4.1. Distribution of cases by number of months of follow-up within the range 18–30 months.

Moscow 16·8, Nagasaki 35·2, Prague 18·7, Rochester 43·6.

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;

2, single psychotic episode followed by an incomplete remission;
3, single psychotic episode followed by one or more non-psychotic episodes, with complete remissions between all or most of the episodes;
4, single psychotic episode followed by one or more non-psychotic episodes, with incomplete remissions between all or most of the episodes;
5, two or more psychotic episodes, with complete remissions between all or most of the episodes;
6, two or more psychotic episodes, with incomplete remissions between all or most of the episodes;
7, continuous psychotic illness (no remission); psychotic symptoms present most of the time;
8, continuous non-psychotic illness (no remission); psychotic symptoms may be present for some time but non-psychotic symptoms predominate throughout;
9, information inadequate for rating the pattern of course.

The distribution of the patients over these different patterns of 2-year course is shown in Table 4.2. Considering the entire series of cases with completed follow-up, the majority of the patients (50·3 %) had a single psychotic episode, i.e. fell into one of the patterns 1–4. A substantial proportion (33·1 %) had two or more psychotic episodes, i.e. pattern 5 or 6, and only a minority (14·6 %) of the patients had an unremitting, continuous psychotic illness (pattern 7). However, there was significant variation among the centres. For example, the percentages of cases with single psychotic episodes (patterns 1–3) in the course of the follow-up ranged from 27·5 in Aarhus to 75·0 in Chandigarh (rural area); those patients with two or more psychotic episodes (patterns 5 and 6) were in the range between 19·2 (Chandigarh, rural area) and 52·5 (Aarhus); and those subjects with continuous psychotic illness were in the range between 2·0 (Ibadan) and 32·9 (Nagasaki).

The individual patterns can be combined in different ways to obtain more global descriptors of the course of the disorder. A summation of the cases of patterns 1, 3 and 5 indicates that the proportion of remitting schizophrenic illnesses with complete remission is high and amounts to no less than 48·1 % of all cases. The proportion of patients with incomplete remissions is 35·3 %;

Table 4.2. *Pattern of course (all patients who were followed up), by centre (percentage distribution)*

Pattern of course	Centres in developed countries									Centres in developing countries							All centres N = 1078
	Aar N = 80	Dub N = 57	Hon N = 29	Mos N = 164	Nag N = 70	Not N = 86	Pra N = 87	Roc N = 31	All developed N = 604	Agr N = 76	Cal N = 140	Cha/R N = 50	Cha/U N = 110	Iba N = 98	All developing N = 474	
1 Single psychotic episode, complete remission	12·5	14·0	3·5	7·9	5·7	29·1	32·2	19·4	15·5	54·0	24·3	42·0	27·3	51·0	37·0	25·1
2 Single psychotic episode, incomplete remission	13·8	17·5	17·2	24·4	21·4	10·5	10·3	19·4	17·2	...	22·9	10·0	12·7	4·1	11·6	14·8
3 Single psychotic episode, non-psychotic episodes complete remission	1·2	8·8	13·8	4·9	2·9	8·1	11·5	3·2	6·6	4·0	2·1	16·0	10·9	5·1	7·6	6·4
4 Single psychotic episode non-psychotic episodes, incomplete remission	...	5·3		13·4			5·5	6·5	5·2	...	2·1	8·0	2·7	1·0	2·3	4·0
5 2+ psychotic episodes, complete remission	13·8	14·0	6·9	5·5	20·0	23·3	23·0	16·1	14·8	19·7	18·6	8·0	18·2	25·6	19·1	16·6
6 2+ psychotic episodes incomplete remission	38·7	24·7	20·7	24·4	17·1	10·5	9·2	25·8	20·9	4·0	12·1	10·0	13·6	10·2	10·5	16·5
7 Continuous psychotic illness, no remission	20·0	13·3	27·6	14·6	32·9	18·6	6·9	9·7	17·4	18·4	17·1	4·0	10·0	2·0	11·1	14·5
8 Continuous non-psychotic illness							1·2		2·4				4·6		1·1	1·8
9 Not known											0·7	2·0		1·0	0·6	0·3

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 1–5	6–15	16–45	46–75	76–100	Total
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						
		0	1–5	6–15	16–45	46–75	76–100	Total
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	99·9
Nag	69	65·2	—	2·9	10·1	15·5	7·3	100·0
Not	86	30·3	—	3·5	10·5	16·3	39·5	100·1
Pra	87	29·9	—	—	9·2	21·8	39·1	100·0
Roc	31	54·8	—	—	12·9	3·2	29·0	99·9
Agr	76	21·1	1·3	2·6	1·3	10·5	63·2	100·0
Cal	138	37·0	0·7	5·8	24·6	21·7	10·1	99·9
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						
		0	1–5	6–15	16–45	46–75	76–100	Total
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	100·1
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 neuroleptics 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

Table 4.6. *Distribution of cases per percentage time of the follow-up spent in a psychiatric hospital*

Centre	No. of patients	Percentage of time in psychiatric hospital						
		0	1–5	6–15	16–45	46–75	76–100	Total
Aar	80	5·0	28·8	28.8	25·0	8·8	3·8	100·2
Dub	57	15·8	21·1	43·8	14·0	3·5	1·8	100·0
Hon	29	6·9	65·5	13·8	13·8	—	—	100.0
Mos	164	1·8	13·4	47·6	34·8	1·8	0·6	100·0
Nag	70	28·6	4·3	22·8	25·7	7·1	11·4	99·9
Not	86	10·5	27·7	38·4	20·9	3·5	—	100·0
Pra	87	—	5·8	40·2	47·1	6·9	—	100·0
Roc	31	—	32·2	54·8	6·5	3·2	3·2	99·9
Agr	76	73·7	11·8	5·3	5·3	2·6	1·3	100·0
Cal	139	23·7	46·8	27·3	2·2	—	—	100·0
Cha/R	45	91·1	6·7	2·2	—	—	—	100·0
Cha/U	109	80·7	11·0	6·4	1·8	—	—	99·9
Iba	97	69·1	10·3	17·5	3·1	—	—	100·0
All	1070	31·0	20·2	27·9	16·8	2·7	1·4	100·0

prescribed, it is highly unlikely that the good outcome of the majority of the cases in that centre was in any way related to a high medication rate.

On the other hand, very few patients in any centre had been considered in no need of neuroleptic treatment (3·9% of the total study population). The percentage ranged from 0% in Moscow to 13·8% in Chandigarh (rural area). All in all, 40·6% of the subjects in the study were presumed to be on anti-psychotic drug treatment continuously, i.e. 76–100% of the length of the follow-up period.

Proportion of time spent in psychiatric hospital

In contrast to anti-psychotic medication, the total length of time during which a patient is admitted to hospital can be determined with accuracy. Although the probability of occurrence and the length of an hospital admission may be influenced by the availability of beds and by the pressure of the local caseload, none of the centres participating in the study reported any serious difficulties in admitting project patients when necessary. It can be assumed, therefore, that in most of the centres, in both developed countries and developing countries, the proportion of time during which patients were in hospital was related to the severity of symptoms and the degree of social dysfunction.

The data (Table 4.6) indicate that, in the majority of the study centres, very few patients with a diagnosis of schizophrenia are maintained continuously in hospital. In the total sample, there were only 1·4% who spent between 76% and 100% of the follow-up period in hospital, and there was no centre, except Nagasaki, where this percentage exceeded 3·8. Not a single case in the developing countries had been continuously in hospital throughout the follow-up period. Although 69% of the study patients were admitted at some point to hospital, 48·1 remained there for less than 15% of the follow-up period (20·2% were hospitalized for less than 5% of the time). It should be noted that nearly one-third (31·0%) of the patients had never been admitted to hospital. Across the centres, however, this percentage varied from 0% in Prague to 91·1% in Chandigarh (rural area).

The highest percentages of patients with no hospital admissions during the follow-up were, apart from rural Chandigarh, in the urban area of Chandigarh (80·7%) and in Agra (73·7%). Higher rates of hospitalization occurred in several of the centres in developed countries, e.g. Nagasaki and Aarhus, which had the highest proportions of patients treated in hospital for 46–100% of the period (18·5% and 12·6% respectively), whereas Prague and Moscow had the highest proportions (87·3% and 82·4% respectively) of patients hospitalized for 6–45% of the follow-up period.

Unimpaired social functioning as a proportion of the follow-up period

This variable was assessed on the basis of all available information (recorded in the FU-PPHS) from the patient, key informants, and

Table 4.7. *Distribution of cases by percentage of the follow-up time during which social functioning was unimpaired*

Centre	No. of patients	Percentage of time of unimpaired social functioning						Total
		0	1–5	6–15	16–45	46–75	76–100	
Aar	80	35·0	—	8·8	10·0	15·0	31·3	100·1
Dub	56	51·8	—	1·8	14·3	8·9	23·2	100·0
Hon	28	53·6	7·1	7·1	3·6	14·3	14·3	99·9
Mos	164	58·5	0·6	—	3·1	12·2	25·6	99·9
Nag[1]	0	—	—	—	—	—	—	—
Not	86	30·2	—	3·5	5·8	18·6	40·7	99·8
Pra	87	17·2	—	1·1	11·5	25·3	44·8	99·9
Roc	31	58·1	—	—	12·9	6·5	22·6	100·1
Agr	76	21·1	1·3	2·6	1·3	7·9	65·8	100·0
Cal	138	12·3	2·2	8·7	28·3	26·8	21·7	100·0
Cha/R	50	9·6	—	3·9	13·5	26·9	46·2	100·0
Cha/U	108	25·0	—	6·5	13·0	23·2	32·4	100·1
Iba	96	9·4	—	2·1	7·3	15·6	65·6	100·0
All	1000	30·1	0·7	3·9	10·9	17·7	36·7	100·0

[1] This item was not rated in the Nagasaki Centre.

any other relevant sources. Social functioning was considered to be unimpaired if, in the judgement of the rater, the patient's overall performance of social and occupational roles was commensurate with that expected of an 'average' person of the same age, sex, social and educational background, and culture.

Of all patients who completed the follow-up, 36·7% were rated as unimpaired in their social functioning for 76–100% of the entire period; a nearly identical proportion (30·1%) were in some degree impaired throughout the follow-up period (Table 4.7).

The proportions of patients who were unimpaired for 76–100% of the time ranged from 14·3% in Honolulu to 65·8% in Agra. At the other extreme, the percentages of subjects who were socially impaired during the entire period of the follow-up, varied between 9·4 in Ibadan and 58·5 in Moscow.

Sex differences in course and outcome

There were surprisingly few sex-related differences in course and outcome when data from centres in developed and developing countries were aggregated. When considered separately for centres in developed and developing countries, some suggestions of gender differences appeared, e.g. as regards the pattern of course, there was an excess of female subjects falling into pattern 1 (single psychotic episode, followed by a complete remission), in both developed and developing countries (Table 4.8). In the developing countries, there was a relative predominance of males in pattern of course 6 (two or more psychotic episodes with incomplete remissions between most of them), while in the developed countries males were over-represented in pattern 7 (continuous psychotic illness). On the remaining variables, such as percentage of the follow-up period spent in psychotic episodes, percentage time in complete remission, percentage time on antipsychotic medication, percentage time in hospital treatment, and percentage time of unimpaired social functioning, there were virtually no differences between the sexes (Table 4.9) when location was not considered.

Thus, it could be said that there was an over-representation of females in the most favourable pattern of course, and an over-representation of males in the two least favourable patterns, so that on the whole the course of schizophrenia when analysed from the point of view of individual variables (i.e. not controlling for location), exhibited few consistent associations with the gender of the patient. This conclusion, however, needs to be qualified in the light of findings from the multivariate analysis of predictors of course and outcome, reported below. Sex did emerge as a predictor, but the magnitude of the effect was not of an order that would justify regarding it as a key prognostic factor.

Table 4.8 A. *Pattern of course by sex (percentage distribution): centres in developed countries*

	Aar	Dub	Hon	Mos	Nag	Not	Pra	Roc	All developed countries	Both
Pattern of course										

Table 4.8 A. *Pattern of course by sex (percentage distribution): centres in developed countries*

Pattern of course[1]	Aar		Dub		Hon		Mos		Nag		Not		Pra		Roc		All developed countries		
	M N = 47	F N = 33	M N = 30	F N = 27	M N = 21	F N = 8	M N = 61	F N = 103	M N = 36	F N = 34	M N = 56	F N = 30	M N = 28	F N = 59	M N = 16	F N = 15	M N = 295	F N = 309	Both M+F N = 604
1	6·4	21·2	13·3	14·8	4·8	—	9·8	6·8	8·3	2·9	26·8	33·3	17·9	39·0	12·5	26·7	13·2	18·2	15·7
2	14·9	12·1	13·3	22·2	19·0	12·5	29·5	21·4	27·8	14·7	10·7	10·0	14·3	8·5	12·5	26·7	18·6	26·2	17·4
3	2·1	—	6·7	11·1	9·5	25·0	1·6	6·8	2·8	2·9	8·9	6·7	10·7	11·9	6·3	—	5·4	7·1	6·2
4	—	—	3·3	7·4	—	—	8·2	16·5	—	—	—	—	3·6	6·8	12·5	—	3·1	7·4	5·3
5	14·9	12·1	20·0	7·4	9·5	—	3·3	6·8	13·9	26·5	25·0	20·0	32·1	18·6	12·5	20·0	15·9	13·6	14·7
6	38·3	39·4	23·3	25·9	19·0	25·0	19·7	27·2	11·1	23·5	10·7	10·0	10·7	8·5	25·0	26·7	19·7	22·7	21·2
7	23·4	15·2	16·7	7·4	28·6	25·0	24·6	8·7	36·1	29·4	17·9	20·0	7·1	6·8	18·8	—	23·0	12·3	17·1
8	—	—	3·3	3·7	9·5	12·5	3·3	5·8	—	—	—	—	3·6	—	—	—	2·0	2·6	2·3
9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Total	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0

[1] See Table 4.2 for definition of numbered patterns.

Table 4.8 B. *Pattern of course by sex (percentage distribution): centres in developing countries*

Pattern of course[1]	Agr		Cal		Cha/R		Cha/U		Iba		All developing countries		
	M N = 49	F N = 27	M N = 90	F N = 50	M N = 25	F N = 25	M N = 60	F N = 50	M N = 55	F N = 43	M N = 279	F N = 195	Both M+F N = 474
1	55·1	48·1	20·0	32·0	48·0	36·0	18·3	38·0	43·6	60·5	33·3	42·6	37·1
2	—	—	24·4	20·0	8·0	12·0	13·3	12·0	5·5	2·3	12·5	10·3	11·6
3	4·1	3·7	—	6·0	4·0	28·0	8·3	14·0	5·5	4·7	3·9	10·3	6·5
4	—	—	1·1	4·0	8·0	8·0	5·0	—	—	2·3	2·1	2·6	2·3
5	18·4	22·2	18·9	18·0	4·0	12·0	16·7	20·0	25·5	25·6	18·3	20·0	19·0
6	6·1	—	14·4	8·0	20·0	—	18·3	8·0	16·4	2·3	14·7	4·6	10·6
7	14·3	25·9	20·0	12·0	4·0	4·0	11·7	8·0	1·8	2·3	12·2	9·7	11·2
8	—	—	—	—	—	—	8·3	—	—	—	1·8	—	1·1
9	—	—	1·1	—	4·0	—	—	—	1·8	—	1·1	—	0·6
Total	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0	100·0

[1] See Table 4.2 for definition of numbered patterns.

Table 4.9. *Distribution of selected course variables (percentages) by sex: all patients with a follow-up, all centres*

Course variables		Percentage of the follow-up period						
		0	1–5	6–15	16–45	46–75	76–100	Total
Percentage time in psychotic episodes	M(N = 610)	—	20·3	32·1	21·0	7·9	18·7	100·0
	F(N = 514)	—	18·9	36·4	22·0	5·4	17·3	100·0
	M+F(N = 1124)	—	19·7	34·1	21·4	6·8	18·1	100·0
Percentage time in complete remission	M(N = 609)	44·2	0·3	3·4	10·0	13·8	28·2	100·0
	F(N = 511)	40·7	1·2	1·0	9·8	17·8	29·5	100·0
	M+F(N = 1120)	42·6	0·7	2·8	9·9	15·6	28·8	100·0
Percentage time on antipsychotic medication	M(N = 610)	4·1	7·0	13·1	16·8	19·9	39·2	100·0
	F(N = 514)	6·1	7·4	12·7	20·4	14·9	38·6	100·0
	M+F(N = 1124)	5·0	7·2	12·9	18·4	17·6	38·9	100·0
Percentage time in hospital treatment	M(N = 610)	30·3	21·0	28·5	15·1	3·3	1·8	100·0
	F(N = 513)	34·6	19·8	25·2	17·3	2·7	0·4	100·0
	M+F(N = 1125)	32·3	20·4	27·0	16·1	3·0	1·2	100·0
Percentage time of unimpaired social functioning	M(N = 571)	30·5	0·4	5·8	11·7	16·8	34·8	100·0
	F(N = 475)	28·8	1·0	1·2	11·4	18·9	38·5	100·0
	M+F(N = 1046)	29·7	0·7	3·7	11·6	17·8	36·5	100·0

Differences between developing countries and developed countries

The examination of the follow-up results for such differences was an important task, considering the findings of the IPSS which indicated, for the first time on a large scale and with the use of standardized methods, that the course and outcome of disorders diagnosed as schizophrenic were more favourable in the developing countries than in the developed countries. In view of the importance of replicating these findings, this issue was addressed in the Outcome Study on a larger and more representative series of patients, and with more refined methods. The principal results in this respect, from the point of view of simple univariate analysis, are presented on Table 4.10 which shows proportions of patients who had met the inclusion criteria and during the follow-up fell into the extreme ends of the distributions of the six major variables describing course and outcome.

As regards the 'best possible' outcomes, in five out of six comparisons, the proportions of patients in the centres in developing countries falling into these categories are considerably higher than the proportions of patients in the centres in developed countries. For example, the percentage of patients in the developing countries who exhibited a remitting course over the two years of the follow-up (i.e. patterns 1, 3 and 5), was 62·8, as compared with 36·9 in the developed countries. The percentage of patients who were symptom-free (in complete remission) for over three-quarters of the length of the follow-up period was 38·3 in the developing countries and 22·3 in the developed countries. Similarly, the percentage of patients in developing countries who functioned without

Table 4.10. *Percentage of patients in the developing countries and in the developed countries falling into selected categories of course and outcome variables*

Course and outcome category	Developing countries	Developed countries
1 Remitting course with full remission (1+3+5)	62·7	36·9
Continuous or episodic psychotic illness, without full remission (2+4+6+7)	35·7	60·9
2 In psychotic episodes 1–5% of FU period	18·4	35·7
In psychotic episodes 76–100% of FU period	15·1	34·2
3 In complete remission 0% of FU period	24·1	57·7
In complete remission 76–100% of FU period	38·3	22·3
4 No antipsychotic medication throughout FU	5·9	2·1
On antipsychotic medication 76–100% of FU period	15·9	46·6
5 Never hospitalized	55·5	1·1
Hospitalized for 76–100% of FU period	0·3	1·1
6 Impaired social functioning throughout FU	15·7	41·1
Unimpaired social functioning for 76–100% of FU period	42·9	7·1

Table 4.11. *Pattern of course by initial diagnostic classification of the cases (percentage distribution)*

Diagnostic classification on initial examination	Pattern of course									Total	*N*
	1	2	3	4	5	6	7	8	9		
CATEGO class S+	24·0	16·9	6·4	4·0	15·0	16·1	15·7	1·7	0·2	100·0	626
CATEGO classes S, P, O+	24·3	16·2	6·8	4·2	15·4	15·9	15·0	2·1	0·1	100·0	859
CATEGO classes S, P, O	24·9	15·4	7·1	4·3	15·6	15·8	14·5	2·2	0·2	100·0	968
Clinical ICD-9 diagnosis *or* CATEGO classes S, P, O	25·4	15·3	7·1	4·0	15·8	16·0	14·1	2·0	0·3	100·0	1134

1, Single psychotic episode, complete remission; 2, Single psychotic episode, incomplete remission; 3, Single psychotic episode one or more non-psychotic episodes, complete remissions; 4, Single psychotic episode, one or more non-psychotic episodes, incomplete remission; 5, 2+ psychotic episodes, complete remissions; 6, 2+ psychotic episodes, incomplete remissions; 7, Continuous psychotic illness; 8, Continuous non-psychotic illness; 9, Missing data.

impairment for 76–100% of the time was 42·9, compared with 31·6 in the developed countries. The only category for which no difference was found between developing and developed countries was that of the proportion of cases with relatively brief psychotic illnesses, i.e. with a total length of time in psychotic episodes less than 5% of the follow-up period (18·4 in the developing countries and 18·7% in the developed countries).

In the range of categories characterizing the 'worst possible' outcome, the proportions of patients in the centres in developed countries were consistently higher than the corresponding proportions of patients in the centres in developing countries: 38·3% compared to 21·6% as regards cases with continuous or episodic psychotic illness without complete remission; 41·6% compared to 15·7% as regards presence of impaired social functioning throughout the follow-up; and 20·2% compared to 15·1% as regards being in psychotic episodes for 76–100% of the length of the follow-up.

Comparisons on a centre by centre basis, as regards various course and outcome variables, are generally consistent with the overall trend outlined above. Such comparisons, however, are best considered in the context of other issues and the relevant data are presented in the remaining sections of this chapter.

DIAGNOSIS AND SUBSEQUENT COURSE AND OUTCOME

An important question concerns the extent to which 'caseness' for schizophrenia as defined by each one of the four diagnostic definitions of schizophrenia identified different two-year patterns of course and outcome. The four levels of diagnostic definition were: (i) clinical ICD-9 diagnosis of schizophrenia or of a specified related disorder, or CATEGO class S, P, or O; (ii) CATEGO classes S, P, or O; (iii) CATEGO classes S, P, or O+; and (iv) CATEGO class S+. It has been shown that each one of these four alternative diagnostic definitions, and especially (i) and (iv), was related to a different level of severity of the florid or 'positive' psychotic symptoms of schizophrenia. If diagnosis-related differences in the course and outcome of the disorders could likewise be demonstrated, the hypothesis that the diagnostic classification of schizophrenia possesses predictive validity would receive considerable support.

Diagnostic inclusion criteria and course and outcome

Table 4.11 provides a clear answer to this question: there are virtually no differences between the percentage distributions over the different categories of the variable pattern of course between the patients series meeting each one of the four sets of inclusion criteria of 'caseness'. The 'restrictive' definition of schizophrenia based on CATEGO S+ on initial examination does not select cases that are in any way different, as regards pattern of course, from the cases identified by the 'broad' diagnostic category based on either a clinical ICD-9 diagnosis or on a CATEGO class S, P, or O. Put in a different way, this finding suggests that the pattern of course is unrelated to the degree of symptomatological specificity of the inclusion criteria for schizophrenia adopted in this study.

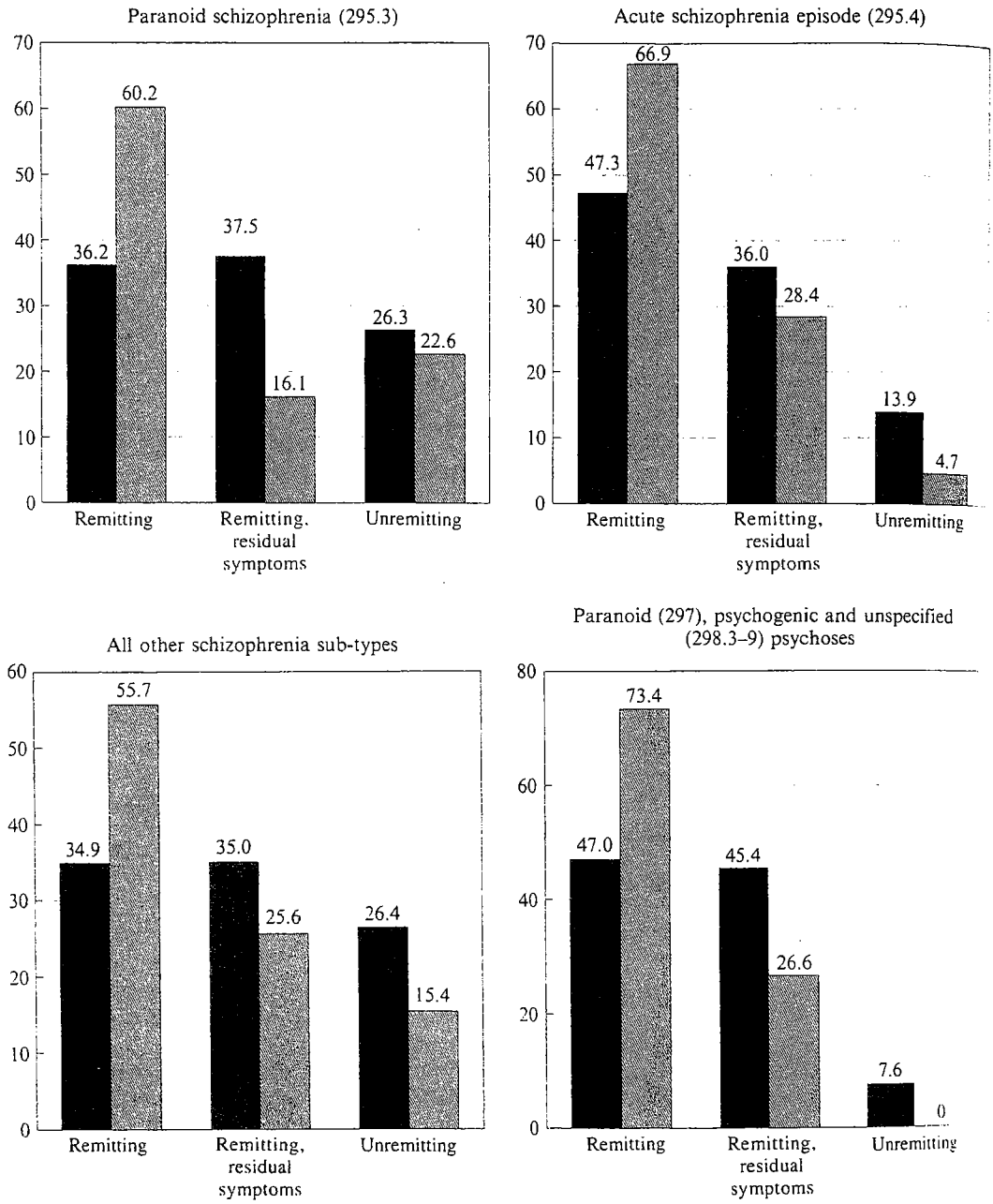

FIG. 4.2.1. Pattern of course (all patients with a follow-up) by clinical diagnosis made at field research centre on initial examination. Remitting: patterns 1, 3 and 5; Remitting, residual symptoms: patterns 2, 4 and 6; Unremitting: pattern 7. In Figs 4.2.1–4.2.5 ■ indicates 'developed countries', ▨ 'developing countries'.

Course and outcome according to clinical diagnostic subtype

The next question to be considered is whether the different clinical diagnoses, made by the psychiatrists in the field research centres on the basis of the initial examination PSE, previous history, and any other data, bear any prognostic implications. For the purposes of this analysis all diagnostic assessments made on initial exam-

Table 4.13. *Types of 'strings' of CATEGO classes occurring in the follow-up study*

Code number	Combination of CATEGO classes observed on the three examinations	*N*	%
10	S, P or O on each of the three occasions, *or* S, P or O on any two occasions and missing PSE on remaining occasion	365	35·2
9	S, P or O on any two occasions; on the remaining one occasion: A, B, X, NO	119	11·5
8·1	S, P or O on one occasion; on the remaining two occasions: either missing PSE data, or A, B, X, or NO *and* missing PSE data	140	13·5
8	S, P or O on one occasion; on the remaining two occasions: either twice A or B, or twice X or NO, or A, B and X, NO	168	16·2
7	S, P or O on one occasion and M on another occasion, with missing PSE data on the remaining one occasion; *or* S, P or O on two occasions and M on the remaining one occasion	28	2·7
6	S, P or O on one occasion and D, R or N on another occasion, with missing PSE data on the remaining one occasion; *or* S, P or O on two occasions and D, R or N on the remaining one occasion	89	8·6
5	S, P or O on one occasion and M on both remaining occasions; *or* S, P or O on one occasion, M on another occasion, and either D, R, N or A, B, X, NO on the remaining one occasion	28	2·7
4	S, P or O on one occasion, D, R, or N on another occasion, and either D, R, N or A, B, X, NO on the remaining one occasion	43	4·1
3	M on one occasion, either M or D, R, N or A, B, X, NO on another occasion, and missing PSE data on the remaining one occasion; *or* M on at least one occasion, and any combination of M, D, R, N, A, B, X, NO on one or two occasions	22	2·1
2	D, R or N on one occasion, missing PSE data on the remaining two occasions; *or* D, R, or N on one occasion and either D, R, N or A, B, X, NO on another occasion, with missing PSE data on the remaining one occasion, *or* D, R, or N on at least one occasion, and any combination of D, R, N, A, B, X, NO on one or two occasions	33	3·2
1	A or B on one occasion, A, B or X, NO on another occasion, with missing PSE data on the remaining one occasion; *or* A or B on at least one occasion, and any combination of A, B, X, NO on one or two occasions	2	0·1
		1037	100·0

S, Schizophrenic psychosis; P, Paranoid psychosis; O, Borderline and doubtful psychosis; M, Manic and mixed affective psychosis; D, Depressive psychosis; R, Retarded depression; N, Neurotic depression; A, Anxiety state; B, Obsessional neurosis; H, Hysterical conditions; X, Other; NO, No abnormality.

class on any two occasions and missing data on the other one, would be different, as regards course and outcome, from patients who had an S, P, or O class on one occasion only, and a non-psychotic CATEGO class on the remaining two occasions. The rest of the syndrome list presented in Table 4.13 was constructed in a similar way, and descriptive clinical labels were assigned to the different 'strings' before examining the course and outcome of the patients with those 'strings'. The clinical labels were chosen as a matter of convenience only, and have no terminological implications outside this context. The different combinations of CATEGO classes were grouped according to the following clinical concepts.

CATEGO 'string'	Corresponding clinical concept
10, 9	Schizophrenia
8.1, 8	Schizophrenia-like disorder
7, 6	Schizoaffective disorder
5, 4	Atypical affective disorder
3	Bipolar affective disorder
2	Unipolar affective disorder
1	Neurotic disorder

The numbers of patients and the percentages given in Table 4.13 indicate that with such use of the CATEGO classification (i.e. considering only the serial or consecutive PSE data and ignoring other diagnostically relevant information), not more than 5·5% of all included patients remain outside those sequences of CATEGO classes in which there is at least one S, P, or O. When the frequency with which each of the CATEGO 'strings' occurred in the course of the study in the individual catchment areas is examined it can be seen that 'string' 10 ('schizophrenia') was clearly predominant in all the centres in developed countries. In the centres in the developing countries 'string' 8 ('schizophrenia-

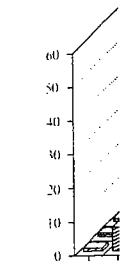

FIG. 4.3. I

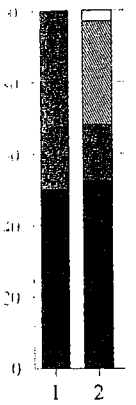

FIG. 4.4. Type
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