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 ($P < 0{\cdot}001$).

The 'drop-out' rate (%) showed highly significant differences ($P < 0{\cdot}001$) 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	$P < 0{\cdot}01$
Percentage CATEGO S+	55·1	44·2	$P < 0{\cdot}001$
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.

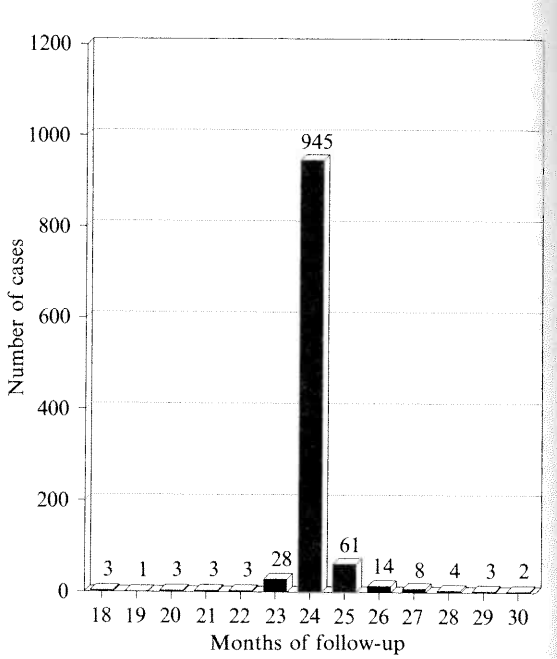


FIG. 4.1. Distribution of cases by number of months of follow-up within the range 18–30 months.

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 %; and that of cases with unremitting psychotic symptoms is 14·5 %.

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

Pattern of course	Centres in developed countries: 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	Centres in developing countries: Agr N = 76	Cal N = 140	Cha/R N = 50	Cha/U N = 110	Iba N = 98	All developing N = 474	All centres N = 1078
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	—	3·5	10·3	4·9	—	—	1·2	—	2·4	—	—	—	4·6	—	1·1	1·8
9 Not known	—	—	—	—	—	—	—	—	—	—	0·7	2·0	—	1·0	0·6	0·3
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

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

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 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.

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

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						
		0	1–5	6–15	16–45	46–75	76–100	Total
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	99·8
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	100·1
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, but 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*

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 = 3	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	2·9	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	14·7	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	2·9	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	26·5	25·0	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	23·5	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	29·4	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 remissions) 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 social 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).

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	36·8
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	18·7
In psychotic episodes 76–100 % of FU period	15·1	20·2
3 In complete remission 0 % of FU period	24·1	57·2
In complete remission 76–100 % of FU period	38·3	22·3
4 No antipsychotic medication throughout FU	5·9	2·5
On antipsychotic medication 76–100 % of FU period	15·9	60·8
5 Never hospitalized	55·5	8·1
Hospitalized for 76–100 % of FU period	0·3	2·3
6 Impaired social functioning throughout FU	15·7	41·6
Unimpaired social functioning for 76–100 % of FU period	42·9	31·6

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.

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.

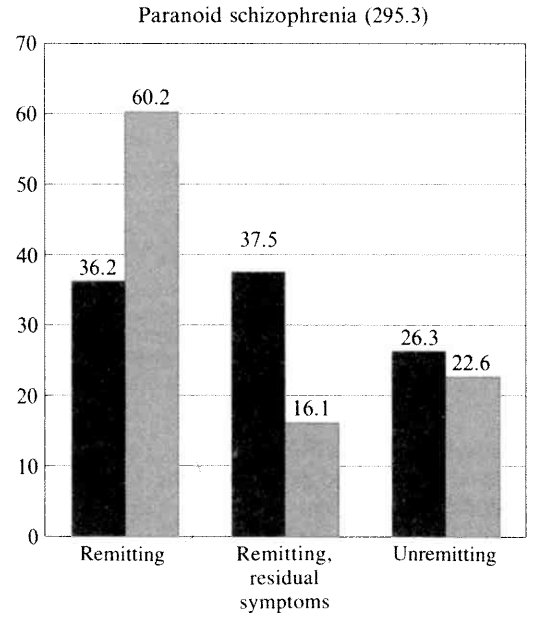
Comparisons on a centre by centre basis, as regards various course and outcome variables, are generally consistent with the overall trend outlined above. Such comparisons, however, are best considered in the context of other issues and the relevant data are presented in the remaining sections of this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

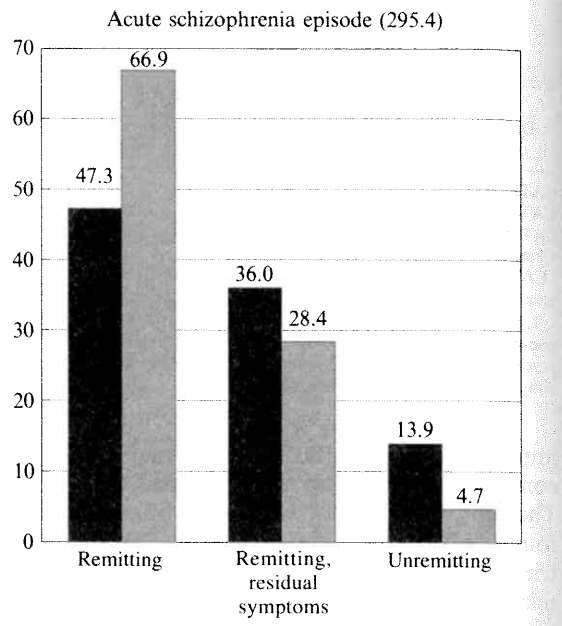
DIAGNOSIS AND SUBSEQUENT COURSE AND OUTCOME

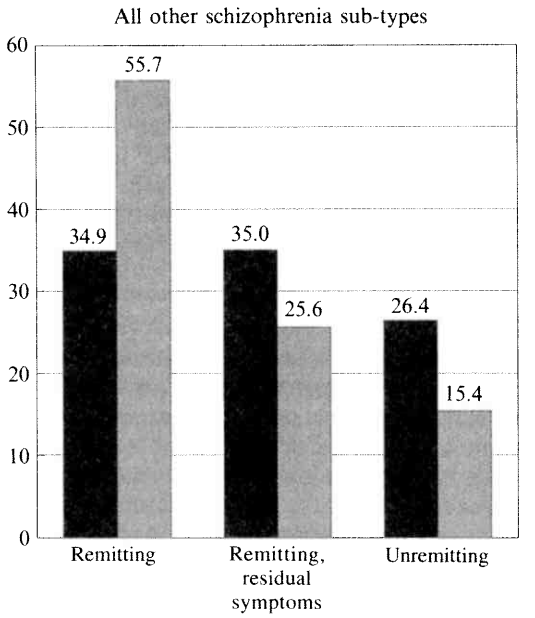
An important question concerns the extent to which 'caseness' for schizophrenia as defined by each one of the four diagnostic definitions of schizophrenia identified different two-year patterns of course and outcome. The four levels of diagnostic definition were: (i) clinical ICD-9 diagnosis of schizophrenia 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.







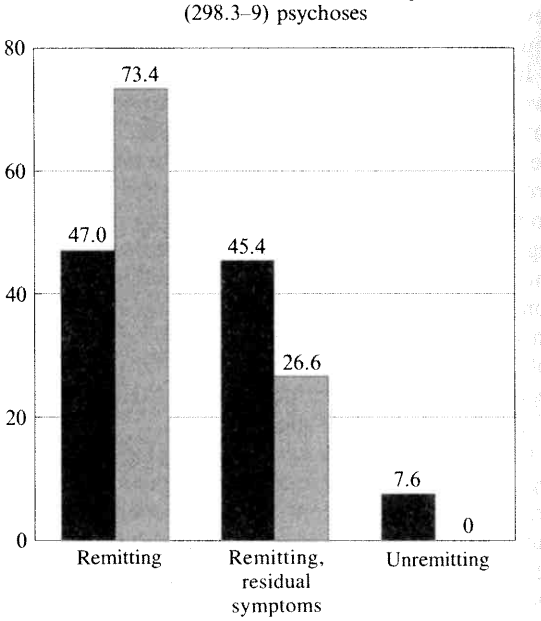


FIG. 4.2.1. Pattern of course (all patients with a follow-up) by clinical diagnosis made at field research centre on initial examination. Remitting: patterns 1, 3 and 5; Remitting, residual symptoms: patterns 2, 4 and 6; Unremitting: pattern 7. In Figs 4.2.1–4.2.6, ■ indicates 'developed countries', ▨ '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 examination (resulting in the assignment of a main clinical diagnosis) were grouped into five categories, with a view to ensuring a sufficient number of cases within each group. The five categories are:

(1) schizophrenia, paranoid type (ICD 295.3) – 261 patients;
(2) acute schizophrenic episode (ICD 295.4) – 218 patients;
(3) all other types of schizophrenia listed in ICD-9 (i.e. simple, hebephrenic, catatonic, latent, residual, schizoaffective, other, and unspecified) – 426 patients;
(4) paranoid states (ICD 297), acute paranoid reaction (ICD 298.3), psychogenic paranoid psychosis (ICD 298.4), other and unspecified reactive psychosis (ICD 298.8), unspecified psychosis (ICD 298.9) – 82 patients;
(5) all other diagnoses (i.e. paranoid or hallucinatory states induced by alcohol or drugs – ICD 291.3, 291.5, 292.1; paranoid or schizoid personality disorder – ICD 301.0, 301.2) – 91 patients.

The percentage distributions of the patients classified into the first four of these ICD-9 diagnostic groups are shown on Figs 4.2.1–6. There is a clear difference in the pattern of course distributions of cases diagnosed as paranoid schizophrenia and cases diagnosed as acute schizophrenic episode (Fig. 4.2.1). The seven principal patterns of course were grouped into fully remitting patterns (1, 3, and 5); remitting with residual symptoms (2, 4, 6); and unremitting (7). Patients with a diagnosis of paranoid schizophrenia show a considerably less favourable distribution on the pattern of course variable than patients with a diagnosis of an acute schizophrenic episode. The direction of this observed difference in prognosis between paranoid and acute schizophrenia is the same for patients in developing countries and for patients in developed countries. However, the size of the difference between the two diagnostic groups is greater within centres in developed countries. On the other hand, the general trend for patients in developing countries towards better course and outcome is so pronounced that, in fact, patients with a diagnosis of paranoid schizophrenia in the developing countries show a more favourable pattern of course than patients with acute schizophrenic episodes in the developed countries.

As regards the residual group of all other schizophrenia types, its breakdown by pattern of course indicates that these cases are closer to the paranoid type than to any other category in the developed countries, while in the developing countries they are more similar to the cases of acute schizophrenic episodes. The most favourable pattern of course is seen in the 4th group of paranoid states, psychogenic paranoid and unspecified psychoses.

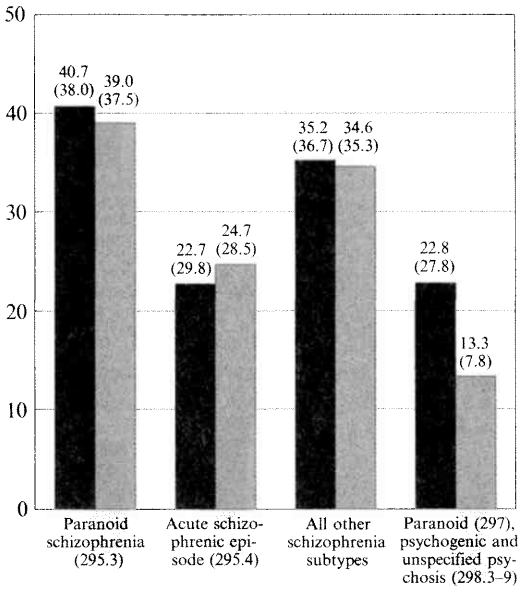


FIG. 4.2.2. Percentage of FU period in psychotic episodes (mean and S.D.) by clinical diagnosis on initial examination. (See Fig. 4.2.1.)

The distributions of the mean percentages of follow-up time during which patients were in psychotic episodes (Fig. 4.2.2) similarly indicate a favourable trend for acute psychotic episodes and an unfavourable trend for paranoid schizophrenia. In congruence with this finding, the mean percentage time in complete remission (Fig. 4.2.3) is greater for patients with acute schizophrenic episodes than for patients with paranoid schizophrenia. Both patients with paranoid schizophrenia and patients with acute schizophrenic episodes spent relatively brief mean periods of time (as percentage of the follow-up) in hospital (Fig. 4.2.4), although on this measure, too, the trend is less favourable for paranoid schizophrenia. There is a marked difference, as regards this variable, between

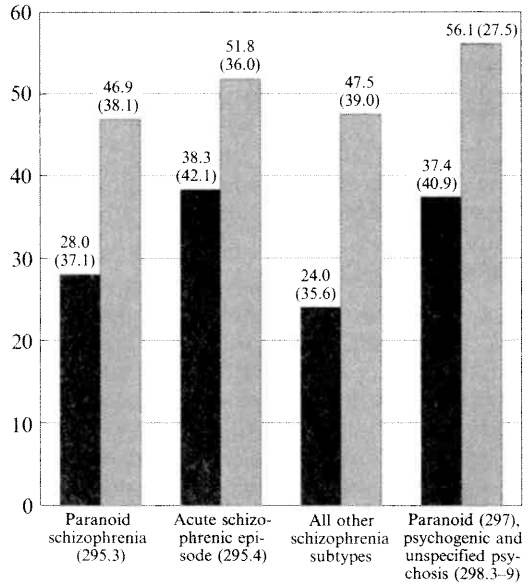


FIG. 4.2.3. Percentage of FU period in complete remission (mean and S.D.) by clinical diagnosis on initial examination. (See Fig. 4.2.1.)

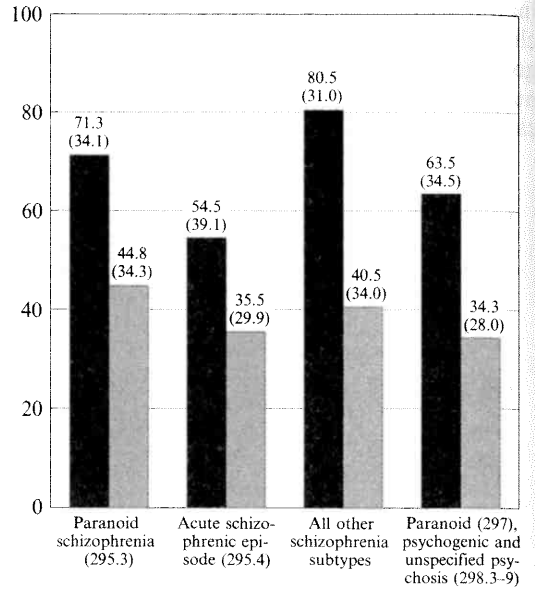


FIG. 4.2.5. Percentage of FU period on anti-psychotic medication (mean and S.D.) by clinical diagnosis on initial examination. (See Fig. 4.2.1.)

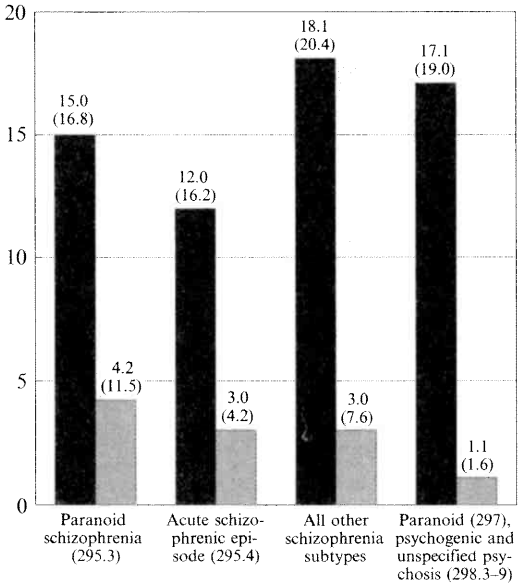


FIG. 4.2.4. Percentage of FU period in hospital admissions (mean and S.D.) by clinical diagnosis on initial examination. (See Fig. 4.2.1.)

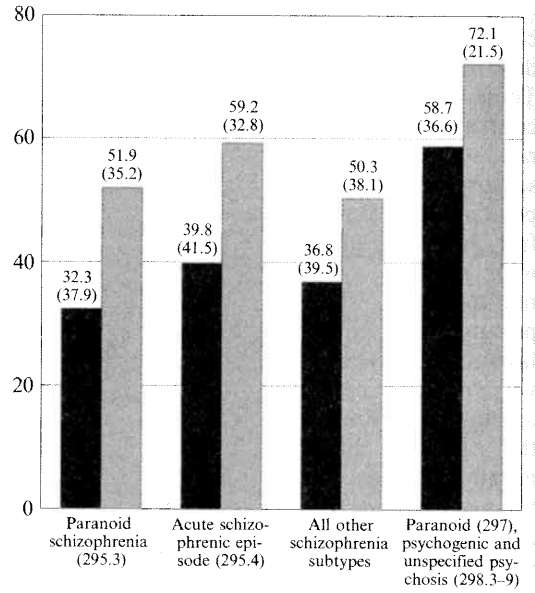


FIG. 4.2.6. Percentage of FU period in unimpaired social functioning (mean and S.D.) by clinical diagnosis on initial examination. (See Fig. 4.2.1.)

patients in developed countries and patients in developing countries falling into the category of other types of schizophrenia, the former being similar to the paranoid schizophrenics, and the latter having even shorter hospital admissions than acute schizophrenics. The distributions according to mean percentage follow-up time on antipsychotic medication (Fig. 4.2.5) follow the same general pattern. Finally, the mean proportions of time during the follow-up, in which the patients' social functioning was unimpaired (Fig. 4.2.6), show again, from a different perspective, the superior outcome of acute schizophrenic episodes as compared to paranoid schizophrenia.

The consistent pattern of the above findings suggests that the clinical subtyping of schizophrenia according to the 'conventional' clinical diagnostic criteria has clear predictive implications, especially as regards the prognostic distinction between the two diagnoses which were most frequently made in the present study, paranoid schizophrenia and acute schizophrenic episode. Patients meeting the inclusion criteria for schizophrenia and related disorders in developing countries indeed have a more favourable course and outcome on most measures than patients in developed countries, but the trends concerning differences in severity between the two diagnostic entities of paranoid schizophrenia and acute schizophrenic episode are very similar in the two kinds of setting. The results are less clear cut as regards the other diagnostic groupings.

The CATEGO classification and the course of schizophrenia

The CATEGO classification which reflects differences in symptom profiles of patients has important implications for the interpretation of data on the first-contact incidence of schizophrenia and related disorders in the different catchment areas of the study. Therefore, the relationship between CATEGO classes and the variables describing course and outcome needs an examination.

As pointed out above, the allocation of the patients included in the study to classification categories based on different subsets of CATEGO classes on initial examination did not identify subgroups of schizophrenic patients that are different from one another as regards two-year pattern of course. However, the initial CATEGO classification appeared to be related to another aspect of prognosis. As shown in Table 4.12, 23·7% of the patients who were assigned to CATEGO class S+ on the basis of the initial PSE had the same S+ CATEGO class on at least one of the subsequent two PSE examinations (at one year and at two years),

Table 4.12. *Occurrence of CATEGO class S+ and classes other than S+ at successive PSE examinations during the follow up of patients (a) initially categorized as S+ and (b) initially categorized as not S+*

Initial examination	1-year follow-up	2-year follow-up	*N*	%
		(*a*)		
S+	S+	S+	30	8·2
S+	Not S+	S+	17	4·6
S+	S+	Not S+	40	10·9
S+	Not S+	Not S+	279	76·2
		Total	366	100·0
		(*b*)		
Not S+	S+	S+	6	2·2
Not S+	Not S+	S+	11	4·1
Not S+	S+	Not S+	7	2·6
Not S+	Not S+	Not S+	244	91·0
		Total	268	100·0

while only 8·9% of the patients who, on initial examination, had a CATEGO class other than S+, were classified as S+ on any one of the follow-up assessments. This indicates that the symptomatological characteristics defining S+ ('the central schizophrenic syndrome') tend to recur, regardless of the fact that the occurrence of Schneiderian first-rank symptoms on initial examination did not predict a particular pattern of course of the disorder. This suggests that, while the occurrence of the constellation of symptoms defining S+ on a single occasion carries little prognostic weight, cases in which first-rank symptoms tend to be present on two or more consecutive cross-sections of the mental state may also differ in some of their other characteristics from cases in which S+ is followed or preceded by other CATEGO classes. From this follows the more general question whether particular CATEGO sequences or 'strings' composed of the classes assigned on the three consecutive cross-sections of the mental state of the patients might be significantly associated with course and outcome.

To explore this proposition, the actually occurring combinations of CATEGO classes during the follow-up were listed and ordered on the basis of purely clinical assumptions (Table 4.13). For example, it was hypothesized that patients who either had one of the three CATEGO classes S, P, or O on each of the three follow-up cross-sections, or had an S, P, or O

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	4·2
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 condition; 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-like psychosis') was modal in Agra, Chandigarh (rural and urban), and Ibadan, but not in Cali; in all of these centres, however, considerable percentages of the cases fell into categories 10 and 9. If anything, these data may indicate that the symptomatological manifestations of psychosis in the centres in developed countries tend to be more consistent over time than psychotic disorders in patients in the developing countries; further confirmation of this finding will however be necessary before it can be accepted with certainty.

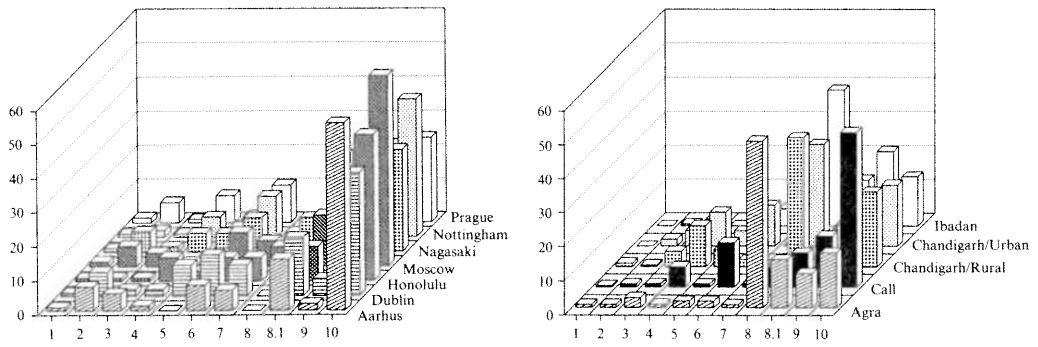


FIG. 4.3. Percentage distribution of specified sequences of CATEGO classes on initial and on two follow-up examinations by centre.

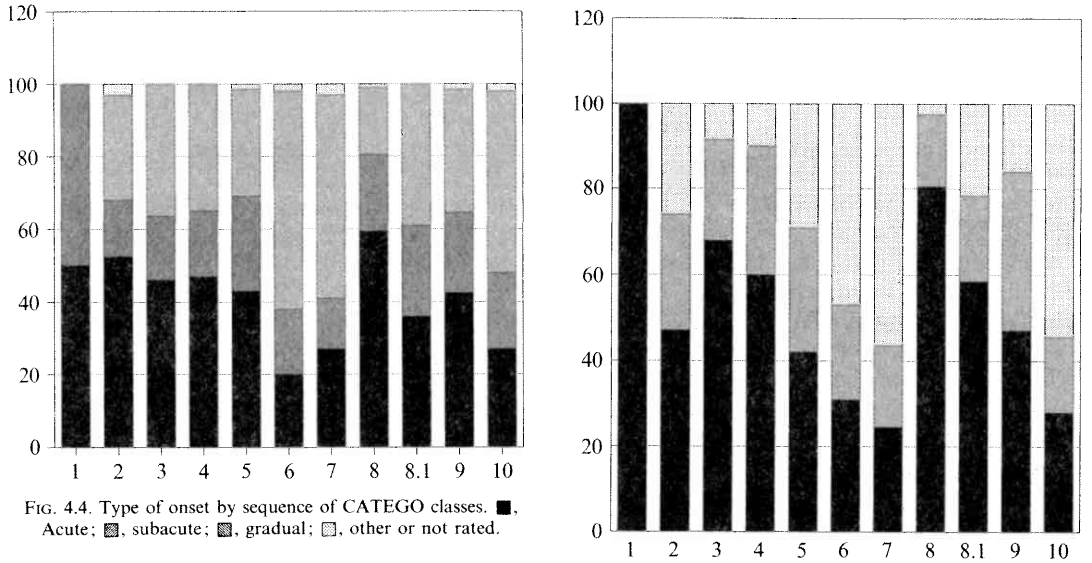


FIG. 4.4. Type of onset by sequence of CATEGO classes. ■, Acute; ▩, subacute; ▧, gradual; □, other or not rated.

FIG. 4.5. Pattern of course by sequence of CATEGO classes. ■, Mild, patterns 1–3; ▩, intermediate, patterns 4, 5; ▨, poor, patterns 6, 7.

The pooling of the data on patients in all of the centres shows that the CATEGO 'strings' are strongly associated with the mode of onset of the disorder (Fig. 4.4). For example, 50 or more per cent of the patients classified into types 8 ('schizophrenia-like'), 2 ('unipolar affective'), and 1 ('neurotic') had an acute onset, in contrast to types 10 ('schizophrenia'), and 7 and 6 ('schizoaffective'), in which over 50% of the patients had gradual onset.

No less important is the observed association between CATEGO 'strings' and the pattern of course. Fig. 4.5 indicates that 'mild' patterns of course (i.e. patterns 1, 2, and 3) characterize predominantly the disorders falling into the categories 1 ('neurotic'), 3 ('bipolar affective'), 4 ('atypical affective'), and 8 ('schizophrenia-like'), in contrast to the 'poor' patterns of course occurring most frequently in patients classified into categories 7 ('schizoaffective') and 10 ('schizophrenia').

Table 4.14. *Variables used in the analysis of predictors of course and outcome and number of patients for whom data were available*

Variables	Categories	Source of information	No. of patients
Outcome variables			
Pattern of course	Good – patterns 1–3	Synopsis table	500
	Intermediate – patterns 4–5		222
	Poor – patterns 6–7		334
Percentage follow-up time psychotic	< 15%	Synopsis table	527
	16-44%		266
	> 45%		276
Percentage follow-up time in complete remission	< 15%	Synopsis table	491
	16–44%		100
	> 45%		475
Percentage follow-up time in incomplete remission	< 15%	Synopsis table	571
	16–44%		168
	> 45%		325
Percentage follow-up time when social functioning was unimpaired	< 15%	Synopsis table	347
	16–44%		109
	> 45%		544
Percentage follow-up time in hospital	< 5%	Synopsis table	556
	6–15%		298
	> 15%		224
Percentage follow-up time on antipsychotic medication	< 15%	Synopsis table	265
	16–44%		196
	> 45%		617
Explanatory variables			
Gender	Male	PPHS	574
	Female		504
Age	< 25 years	PPHS	509
	> 25 years		569
Marital status	Single, widowed, divorced, married		655
	Common-law marriage, separated		408
Type of household	One person, unrelated persons	PPHS	116
	Nuclear family		694
	Extended family, joint family		231
Setting (level of industrialization)	Developing country	PPHS	604
	Developed country		474
Frequency of contact with relatives	None	PPHS	426
	Rare		328
	Frequent		273
Frequency of contact with close friends	None	PPHS	598
	Rare		251
	Frequent		171
Frequency of contact with casual friends	None	PPHS	458
	Rare		371
	Frequent		171
Avoidance of patient by family members	None	PPHS	705
	Some		138
	Marked		52
Avoidance of patient by relatives	None	PPHS	634
	Some		74
	Marked		26
	Increased contact		46
Avoidance of patient by close friends	None	PPHS	457
	Some		74
	Marked		36
	Increased contact		16
Avoidance of patient by casual friends	None	PPHS	556
	Some		91
	Marked		57
	Increased contact		14
Affective relationship to spouse (among married, common law, separated patients)	Never had close relationship (No interest shown)	PPHS	112
	Never close but showed interest		66
	Only casual contact		62
	Relationship before onset only		164
	Relationship after onset		43

Table 4.14. (*cont.*)

Variables	Categories	Source of information	No. of patients
Overall adjustment in childhood	Good adjustment	PPHS	690
	Transient problems		166
	Persistent problems		32
Overall adjustment in adolescence	Good adjustment	PPHS	593
	Transient problems		200
	Persistent problems		74
Street drug use	No use, none suspected	PPHS	878
	Sporadic use known or suspected		63
	Five or more instances known or suspected		82
Number of months since onset of disorder	Continuous variable	PPHS	986
CATEGO class	S+	PSE+CATEGO program	594
	Not S+		484
Main diagnosis			
Group 1	295.3	DPS	307
Group 2	295.1, 295.6		111
Group 3	296.7, 295.4, 295.2		328
Group 4	Other schizophrenia		159
Group 5	Non-schizophrenia (other diagnosis)		173
Type of onset	Acute	Synopsis table	405
	Sub-acute		216
	Slow		402

The conclusion which can be drawn from these data is that, while the CATEGO classification of PSE symptoms at the point of the initial examination does not predict the subsequent pattern of course, the sequential pattern of CATEGO classes determined on two or three follow-up examinations is predictively associated with an independently derived measure of the course of the disorder. Classes S, P, and O, if and when they recur, are clinical markers of a relatively poor prognosis, while the appearance of affective or neurotic CATEGO classes at any point in time, with or without an S, P, or O class on a single occasion, is associated with a more favourable evolution of the disorder.

It may be argued that in a general sense the CATEGO classes and the different patterns of course are not entirely unrelated (e.g. a CATEGO class representing psychosis could be *a priori* expected to be associated with a less favourable course than a class representing a neurotic illness). However, apart from the general criteria defining a psychotic and a non-psychotic episode, no specific symptomatology data were used in the operational definition of the pattern of course; the assessment of the latter was based only on a review of the longitudinal characteristics of the disorder. In contrast, the PSE/CATEGO assessment, as used in this study, presupposes the sampling of symptoms on a short-term (one month) basis, without any reference to the history of symptoms outside that period. The finding of an association between the pattern emerging from consecutive 'point' assessments by CATEGO, and the pattern emerging from longitudinal data should qualify the statement made above about the lack of predictive power for the CATEGO classification. It should also caution against the conclusion that symptomatology is not predictive of course and outcome; such a conclusion could only be made if a single cross-section of the mental state were considered. The data reported here advise strongly against prognostic judgements based on isolated cross-sections of the disorder.

PREDICTORS OF TWO-YEAR COURSE AND OUTCOME

The principal method used to identify predictors of two-year course and outcome was that of log-linear analysis. Log-linear modelling is a general term applying to a set of statistical techniques developed for analysing multidimensional cross-classifications. The particular technique used here is known as polytomous logit, or a log-odds model. It predicts the log-odds of a certain outcome measured by a discrete variable by using a linear combination of effects due to the explanatory variables.

The log-odds model makes no distributional

Table 4.15. *Effect of type of onset and setting on seven outcome variables*

Outcome variable	Explanatory variable	*N*	Effect on good outcome: Coefficient	Effect on good outcome: χ^2	Effect on good outcome: Estimated partial derivative	Effect on poor outcome: Coefficient	Effect on poor outcome: χ^2	Effect on poor outcome: Estimated partial derivative
Pattern of course	Type of onset							
	Acute	403	+0·445***	23·88	+0·111	−0·543***	24·92	−0·116
	Sub-acute	216	+0·052	0·25	+0·013	−0·197	2·74	−0·04
	Gradual[a]	389	−0·497		−0·124	+0·740		+0·158
	Setting							
	Developing country[a]	449	+0·227		+0·057	−0·290		−0·062
	Developed country	559	−0·227***	11·43	−0·057	+0·290***	14·63	+0·062
Percentage follow-up time in psychotic episode	Type of onset							
	Acute	404	+0·540***	34·27	+0·135	−0·573***	22·77	−0·107
	Sub-acute	215	+0·163	2·47	+0·041	−0·314*	5·50	−0·059
	Gradual[a]	398	−0·703·		−0·175	+0·887		+0·166
	Setting							
	Developing country[a]	450	−0·048		−0·010	+0·149		+0·028
	Developed country	567	+0·048	0·50	+0·010	−0·149	3·50	−0·028
Percentage follow-up time in complete remission	Type of onset							
	Acute	400	+0·495***	28·32	+0·123	−0·458***	21·96	−0·113
	Sub-acute	210	+0·240*	5·09	+0·059	−0·330**	8·71	−0·082
	Gradual[a]	405	−0·735		−0·182	+0·788		+0·195
	Setting							
	Developing country[a]	571	+0·355		+0·880	−0·524		−0·130
	Developed country	444	−0·355***	26·80	−0·088	+0·524***	54·28	+0·130
Percentage follow-up time in incomplete remission (and non-psychotic episode)	Type of onset							
	Acute	400	−0·020	0·05	−0·005	−0·047	0·21	−0·010
	Sub-acute	210	−0·068	0·42	−0·017	−0·009	0·01	−0·002
	Gradual[a]	404	+0·088		+0·022	+0·056		+0·012
	Setting							
	Developing country[a]	596	+0·306		+0·076	−0·542		−0·114
	Developed country	445	−0·306***	20·72	−0·076	+0·542***	48·23	+0·114
Percentage follow-up time in hospital	Type of onset							
	Acute	402	+0·162	2·29	+0·040	−0·054	0·18	+0·008
	Sub-acute	213	−0·019	0·02	−0·005	−0·128	0·81	+0·021
	Gradual[a]	411	−0·143		−0·036	+0·182		−0·030
	Setting							
	Developing country[a]	574	+1·243		+0·310	−1·423		−0·235
	Developed country	452	−1·243***	245·49	−0·310	+1·423***	91·30	+0·235
Percentage follow-up time on antipsychotic medication	Type of onset							
	Acute	402	+0·313**	8·76	+0·057	−0·203*	4·43	−0·049
	Sub-acute	213	−0·108	0·70	−0·020	+0·109	0·94	+0·027
	Gradual[a]	411	−0·205		−0·037	+0·094		+0·023
	Setting							
	Developing country[a]	574	+0·685		+0·125	−0·792		−0·193
	Developed country	452	−0·685***	70·39	−0·125	+0·792***	125·72	+0·193
Percentage follow-up time in unimpaired social functioning	Type of onset							
	Acute	375	+0·447***	21·10	+0·111	−0·478***	19·30	−0·107
	Sub-acute	198	+0·202	3·35	+0·050	−0·170	1·98	−0·038
	Gradual[a]	380	−0·649		−0·161	+0·648		+0·145
	Setting							
	Developing country[a]	446	+0·204		+0·051	−0·433		−0·097
	Developed country	507	−0·204**	8·40	−0·051	+0·433***	32·23	+0·097

[a] Excluded category; * significant at 0·05 level; ** significant at 0·01 level; *** significant at 0·001 level.

assumptions and can handle interactions between variables easily. It differs from the more conventional methods of analysing the relationships between categorical variables, such as the chi-square tests, in the manner in which the dependent variable is represented in the model. While the traditional methods represent the dependent variables in terms of proportions of subjects falling into specified categories, the log-odds model uses the natural logarithm of the ratio of frequencies for any two categories of the dependent (outcome) variable. The log-odds model, therefore, explores how the odds (expressed in a log form) that a subject will appear in one outcome category rather than in another are linked to the explanatory, or predictor, variables. By comparing the natural logarithms of the odds, rather than the proportions of cases in each category, the log-odds model has the effect that the distance between the proportions is 'stretched' as they approach the values of zero and one. For example, in a log-odds model a distance between 0·1 and 0·2 will be about twice the distance between 0·5 and 0·6 (Kritzer, 1979).

The log-odds model for polytomous data, when the dependent variable has n categories, can be written as a set of $n-1$ equations:

$$\ln \frac{P_j}{1-P_j} = u_j + \sum_i \beta_{ij} X_i;$$

where j represents categories of the dependent variable, P_j is the frequency of responses in category j, u_j is a consonant, X_is are the explanatory variables, and β_{ij}s are the coefficients to be estimated. The model was implemented using maximum likelihood techniques and the SAS version 5 CATMOD procedure.

The results presented below include both the estimated coefficients β_{ij} as well as the estimated partial derivative evaluated at the sample mean which can be used to approximate the percentage point change in the dependent variable per unit change in the explanatory variable. (For categorical variables the formula for the estimated partial derivative is an approximation – Peterson & Kronmal, 1985.)

Table 4.14 lists all variables used in the predictor analysis and their categorization. Seven measures of course and outcome were used, namely pattern of course, percentage of the follow-up period during which the subject

was in psychotic episodes, percentage of the follow-up period in complete remissions, percentage of follow-up period in incomplete remissions, percentage of the follow-up period in hospital admissions, percentage of the follow-up period on anti-psychotic medication, and percentage of the follow-up period in unimpaired social functioning.

The main reason for using seven different outcome variables was that one variable, by itself, could not capture the multi-faceted nature of outcome. It was felt that examining a profile of outcome variables will give a much better understanding of the course and outcome of the disorder. In the analysis, not only was statistical significance considered, but also the consistency of the relationship with seven outcome measures. Thus, if an explanatory variable had a consistently significant relationship with the majority of outcome variables, this was considered strong evidence for believing that the variable in question was indeed an important predictor of the outcome of the disorder. If the relationship was inconsistent, the evidence was considered to be weaker.

The analysis was carried out in two steps. First, the relationship between outcome and type of onset (acute, sub-acute, gradual) and the setting (developed/developing country) was examined. As the second step, other explanatory variables were tested, one at a time, controlling for the type of setting (developed/developing) and type of onset.

EFFECTS OF THE PRINCIPAL EXPLANATORY VARIABLES

The results of the first step of the analysis in which type of onset and type of setting (developed/developing country) were used as explanatory variables are presented in Table 4.15. The first response function in these tables concerns predictors of good outcome, and the second response function concerns predictors of poor outcome. The coefficients for the log-linear model are presented, as well as the estimated partial derivatives which measure the estimated percentage point change in the probability of having either a good outcome or poor outcome for a unit change in the explanatory variable. The partial derivatives are obtained by multiplying the coefficient by $P(1-P)$, where P is the mean probability of good outcome or poor outcome depending on the response function.

The type of setting, (i.e. centres in developed countries or centres in developing countries) was shown to be a highly significant predictor of all outcome measures with the exception of the percent time spent in psychotic episodes. Patients living in developing countries were significantly more likely to have a more favourable outcome than patients living in developed countries, on six of these outcome measures. Because of the correlation between the variable describing the setting (developed/developing country) and many of the other explanatory variables it was necessary to control for the variable 'setting' when examining other predictors.

Three categories of the type of onset were considered: acute (development of florid psychotic state within a week); sub-acute (development of a psychotic state within a month); and gradual (slow, incremental development of psychotic symptoms over periods exceeding one month). Type of onset stood out as a significant predictor of five out of the seven outcome variables, namely the pattern of course, percentage of time spent in psychotic episodes, time (%) spent in complete remissions, time (%) spent in unimpaired social functioning, and time (%) on anti-psychotic medication. Patients with acute onsets had the most favourable outcomes on these five measures, while patients with gradual onsets had the least favourable outcomes. Those with sub-acute onsets were in the middle.

Since mode of onset appeared to be a highly significant predictor, and the proportion of patients with acute, sub-acute and gradual onsets varied between centres, it was decided to control for the type of onset in all subsequent analysis. It should be mentioned that the interactions between type of onset and 'setting' (developed or developing country) were examined and found to be insignificant for two of the most important outcome variables, pattern of course and percentage of time psychotic. (They were not examined for the other outcome variables.)

ADDITIONAL EXPLANATORY VARIABLES

The results of the second step of the predictor analysis are presented in Tables 4.16 and 4.17.

Table 4.16. *Summary of predictors and cause-and-outcome variables: predictors of good outcomes*

Predictors	Course and outcome variables: Pattern of course	% of FU in psychotic episodes	% of FU in complete remission	% of FU in incomplete remission	% of FU in hospital	% of FU antipsychotic medication	% of FU unimpaired social functioning[a]
Age	NS	NS	NS	NS	**	NS	*
Sex	*	*	**	NS	NS	NS	**
Marital status	**	***	***	*	***	***	***
Type of household	NS	NS	NS	NS	NS	NS	NS
Setting (developed *v.* developing country)	***	NS	***	***	***	***	***
Type of onset	***	***	***	NS	NS	**	***
N months since onset	NS	NS	**	NS	NS	NS	***
Diagnostic group (ICD-9)	*	**	***	***	NS	***	***
CATEGO class on initial examination	NS	NS	NS	NS	*	NS	NS
Adjustment in childhood	NS	NS	**	NS	NS	NS	***
Adjustment in adolescence	NS	***	***	***	NS	NS	***
Drug use	*	*	***	NS	NS	*	***
Heterosexual relationships	NS	NS	*	NS	*	NS	NS
Affective relationships with spouse	NS	NS	NS	NS	NS	NS	NS
Contact with relatives	NS	NS	*	NS	NS	NS	*
Contact with close friends	*	*	***	NS	**	**	***
Contact with casual friends	*	**	*	NS	NS	***	*
Avoidance by family members	NS	NS	*	**	NS	NS	NS
Avoidance by close friends	NS	NS	NS	NS	NS	NS	NS
Avoidance by casual friends	NS	NS	NS	NS	NS	NS	NS

* Significant at $P \leqslant 0{\cdot}05$; ** significant at $P \leqslant 0{\cdot}01$; *** significant at $P \leqslant 0{\cdot}001$; NS not significant.
[a] Not ascertained for Nagasaki.

Each additional variable was entered in a separate model in which setting and type of onset were controlled for. When the additional variables were added to the model, there were very few changes in the significance of the coefficients for mode of onset or for setting. The percentage of time spent in hospital had particularly large centre specific variation. Therefore for this outcome measure, there were two runs: one run controlling for individual centres, and one run controlling for developed or developing country setting. Since there were very few differences between these two runs, only the runs controlling for setting are reported.

Age

Age was significantly related to only two of the outcome measures, percentage of follow-up time in which social functioning was unimpaired and percentage of follow-up time spent in hospital. Patients at least 25 years-of-age at the initial examination were more likely to spend more than 45% of the follow-up period with unimpaired social functioning, and were more likely to have spent very little time (< 5% of follow-up period) in hospital than younger patients.

Gender

Gender was significantly related to pattern of course, percentage of time psychotic, percentage of time in complete remission, percentage of time of unimpaired social functioning, and percentage of time in hospital. Female subjects tended to have more favourable outcomes than male subjects on those five outcome variables.

Marital status

Marital status was significantly related to all seven measures of outcome. Patients who were married at the point of initial examination (including married, common law-married, and married but separated) had the better outcomes on all measures, and patients not married at the time of initial examination (i.e. never married, widowed, or divorced) had the worst outcomes. Significance was generally high. The consistency of the relationship and the high levels of significance indicate that marital status is an important predictor of outcome.

Number of months between onset and initial examination

The number of months since the onset of the

Table 4.17. *Summary of predictors and course-and-outcome variables: predictors of poor outcome*

Predictors	Course and outcome variables: Pattern of course	% of FU in psychotic episodes	% of FU in complete remission	% of FU in incomplete remission	% of FU in hospital	% of FU antipsychotic medication	% of FU unimpaired social functioning*
Age	NS	NS	NS	NS	*	NS	NS
Sex	**	**	**	NS	*	NS	***
Marital status	***	***	**	NS	***	NS	***
Type of household	NS	NS	NS	NS	NS	NS	NS
Setting (developed *v.* developing country)	***	NS	***	***	***	***	**
Type of onset	***	***	***	NS	NS	*	***
N months since onset	NS	*	***	NS	NS	NS	***
Diagnostic group (ICD-9)	**	***	**	*	NS	***	***
CATEGO class on initial examination	NS	NS	NS	*	NS	NS	NS
Adjustment in childhood	NS	NS	**	NS	NS	NS	*
Adjustment in adolescence	***	***	***	NS	NS	NS	**
Drug use	**	**	**	NS	NS	***	**
Heterosexual relationships	NS	NS	**	NS	NS	*	NS
Affective relationships with spouse	NS	NS	NS	NS	NS	NS	NS
Contact with relatives	NS	NS	NS	NS	NS	***	**
Contact with close friends	*	***	***	NS	NS	***	***
Contact with casual friends	*	***	*	NS	NS	**	*
Avoidance by family members	NS	**	***	NS	NS	NS	***
Avoidance by close friends	NS	NS	NS	NS	NS	NS	NS
Avoidance by casual friends	NS	NS	NS	NS	NS	NS	NS

* Significant at 0·05; ** significant at 0·01; *** significant at 0·001; NS not significant.
[a] Not ascertained for Nagasaki.

disorder is particularly difficult to estimate in the case of patients with gradual onsets. Therefore, several consistency checks were applied to the data to ascertain the accuracy of the information. The results indicate that the length of illness before initial examination was associated with the percentage of time in psychotic episodes during the follow-up, percentage of time in complete remission, and percentage of time that social functioning was unimpaired. The longer the time since onset, the more likely the patient was to have spent a longer period of time in a less favourable state. However, this variable was not significantly related to the remaining three outcome variables.

Main clinical diagnosis on initial examination

In the predictor analysis, the patients were divided into five diagnostic groups:

(1) paranoid schizophrenia ICD 295.3 (the diagnosis of shift-like progressive type according to the Moscow criteria was also included here);
(2) hebephrenic and residual schizophrenia ICD 295.1 and 295.6 (including the continuous progressive type according to the Moscow criteria);
(3) schizoaffective, catatonic, and acute types ICD 295.7, 295.2 and 295.4 (including the Moscow diagnosis of periodic or recurrent schizophrenia);
(4) other schizophrenia subtypes;
(5) other diagnoses.

Diagnosis was a significant predictor of all outcome variables except for percentage of follow-up time in hospitals. In general, patients in group 5 tended to have the best outcomes, and patients in group 2 had the worst outcomes. (An exception to this was the percentage of time spent in incomplete remission.) Group 3 had the second best outcome (or a very close third) in terms of pattern of course, percentage of time psychotic, percentage of follow-up time spent in unimpaired social functioning, and percentage of time on anti-psychotic medication. However, although group 3 spent relatively little time in psychotic episode, this group spent the most time in incomplete remission, and relatively little time in complete remission.

CATEGO class

Patients classified as S+ were significantly more likely to have spent more than 45% of the follow-up period in incomplete remission and were less likely to have spent < 5% of follow-up time in hospital, than those in other CATEGO classes. These were the only statistically significant relationships found between the seven outcome measures, and the classification S+.

Overall adjustment in childhood

The overall adjustment in childhood was significantly related to only two of the seven outcome variables, namely percentage follow-up time in complete remission, and in unimpaired social functioning. Those with good adjustments in childhood had the best outcomes on these two measures, those with persistent problems had the worst outcomes, and those with transient problems were in the middle.

Adjustment in adolescence

Three categories were considered: those with good adjustment in adolescence, those with transient problems, and those with consistent problems. There was a significant relationship between adjustment in adolescence and five of the seven outcome variables (the exceptions were percentage follow-up time on anti-psychotic indication, and percentage follow-up time in hospital). Those with good adjustment consistently had more favourable outcomes (on these five variables) than those with persistent problems. Those with transient problems were usually in the middle, but not consistently so.

Use of 'street' drugs

The use of 'street' drugs was significantly related to five of the seven outcome variables (exceptions were percentage of follow-up time in incomplete remission, and percentage of follow-up time in hospital). For four of the outcome measures the use of street drugs was less likely to be associated with a favourable outcome. However, the percentage of time on anti-psychotic medication was shorter for those who used 'street' drugs than for those who did not.

Heterosexual relationship

For those patients who were single, divorced, or widowed, information was asked about the extent of their relationship with the opposite sex, both before and after the illness. This variable was not significantly related to four of the seven outcome variables. However there was a significant relationship with percentage of follow-up time in complete remission, percentage of follow-up time in hospital, and percentage of time on anti-psychotic medication. Those who were able to have a heterosexual relationship even after falling ill had the most favourable outcomes.

Social isolation

There were two ways in which the social isolation of the patients was considered. The first was whether other persons in the 'social field' of the patient (relatives, friends, household members) were avoiding him or her. There were no significant relationships found between any of the outcome variables and avoidance of the patient by either close or casual friends. There were three outcome measures that were significantly related to avoidance of the patient by family members; however, these relationships were not consistent with one another.

The frequency of contact with close friends, casual friends and relatives was used as another indicator of social isolation. Patients with frequent contact with close friends had significantly more favourable outcomes on six outcome measures (the exception being percentage of follow-up time in incomplete remission). Those with no contact with close friends had the least favourable outcomes, and those with rare contact with close friends were in the middle. For contact with casual friends the general pattern was similar, but the levels of significance were lower, and the relationships were significant for only five of the outcome measures. (Pattern of course, percentage follow-up time psychotic, percentage of time in complete remissions, percentage of follow-up time that social functioning was unimpaired, and percentage of time on anti-psychotic medication.) There was a significant association between frequency of contact with relatives for only three of the outcome variables, (percentage time that social functioning was unimpaired, percentage follow-up time in complete remission, and percentage of time on anti-psychotic medication). Here again, the more frequent the contact, the better the outcome.

Variables unrelated to any outcome measure

The following variables did not appear to be significantly related to any of the seven outcome measures used in the analysis:

(1) type of household;
(2) affective relationship to spouse;
(3) avoidance of the patient by either close or casual friends.