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The Predictability of Relapses in Schizophrenic Patients*

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Summary. The objective of this study was to identify clinically relevant predictors of short-term (2 years) outcome in schizophrenic patients and to gather these predictors into one simple prognosis model for the course of the disease. Ninety-nine schizophrenic outpatients classified according to DSM-III criteria were observed for 3 years with regard to their relapse (rehospitalization) frequency. Predictors of both a high and a low relapse risk permitting a prognostic assessment of the individual case were based on various sources: case history data, especially those relating to the previous course of the disease; social and therapeutic situation; psychopathological findings; emotional family atmosphere; and prognosis scales.

Key words: Predictability – Relapses – Schizophrenics patients prognosis

Introduction

The concern of predictor research in schizophrenic patients is to permit reliable assessment of the future course of the disease. Clinical and social information has been used in an attempt to find characteristics indicating a specific course of the illness. Research into such predictors has produced many new findings during the past 15 years (Biehl et al. 1986; Möller et al. 1982a, b; Pietzcker and Gaebel 1983; Strauss and Carpenter 1977; Huber et al. 1979; Ciompi and Müller 1976; Johnstone et al. 1979; Who 1979). Predictors of the course of the disease were found in five areas: previous course of the disease (onset, type of psychotic manifestation, discharge findings, remission, residual symptoms; Möller and von Zerssen 1985); psychopathological findings (Biehl et al. 1986; Möller and von Zerssen 1985); premorbid social adjustment (e.g. Möller et al. 1984; Biehl et al. 1986; Ciompi 1981; Huber et al. 1979); emotional family atmosphere (Vaughn and Leff 1976b; Buchkremer et al. 1986; Nuechterlein et al. 1986; Jenkins et al. 1986; Moline et al. 1985); social or professional integration (Strauss and Carpenter 1977).

One finding in common in these studies was that a predictor invariably correlated with only specific aspects of the course of the illness (e.g. of the clinical *or* of the social course). Therefore predictor research to date (not restricted to therapy response) has provided more findings of a general theoretical nature than aids to individual prognostics. From the clinical practitioner's point of view, the essential objective of predictor research is the formulation of a valid but simple prognostic model relating to a manageable period of time. The search for such models involves the application of multivariate statistical methods. Depending on the specific methods selected, the psychiatrist often has difficulty in assessing the validity of a prognostic model or even in using it correctly. This applies in particular to prognosis scores obtained from multivariate regression analyses and formulated as a linear function (e.g. Möller and von Zerssen 1985). Assessment of the validity of such a score is also unlikely to be elucidated by data on its account for the variance (in %).

A more favourable solution is the formulation of a simple prognosis schedule (e.g. hierarchic) based on a small number of dichotomous predictors. One example is the prognostic model introduced by Vaughn and Leff (1976b) within the framework of EE research, a model whose widespread use and acceptance is due in part to its simplicity and comprehensibility. Such a model permits patients to be classified simply into high-, medium- or low-risk groups.

Prior to the development of new prognostic models, however, the facilities for therapy and prophylaxis currently availabe give rise to the question whether individual prognostics are necessary at all. Is indication-based assignment to a specific therapy not adequate from the

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clinical point of view? The following arguments suggest that this question should be answered in the negative.

Any forced psychosocial therapeutic intervention may put the patient under strain and thus involve the risk of psychotic symptoms recurring (Stevens 1973; Wing 1982). For this reason it is advisable to be aware of the individual relapse risk, especially prior to incisive psychotherapeutic or sociotherapeutic interventions. This also applies to neuroleptic therapy. Although the effects of long-term neuroleptic therapy in relapse prevention are now undisputed, a cautious, reserved approach to uncritical long-term neuroleptic therapy is on the increase (Möller 1987; Kapfhammer and Rüther 1988) and new means of relapse prevention are being investigated. A distinction can currently be made between four different neuroleptic-based relapse prevention strategies (cf. Pichot and Möller 1987): neuroleptic long-term therapy (standard dose); no neuroleptic long-term therapy; prophylactic early intervention (interval therapy); low-dose therapy.

One fundamental problem in individual prediction of outcome is, however, that hardly any patients who have not undergone neuroleptic therapy are currently available for outcome studies. The substantiated relapse-prophylactic effect of neuroleptics makes comparative studies impossible for ethical reasons.

Medication-free therapy, prophylactic early intervention and low-dose therapy are high-risk strategies that imply a special degree of cooperation of the patients and their relatives with the psychiatrist (Buchkremer and Schulze Mönking 1986; Buchkremer and Windgassen 1987). Another essential precondition for a high-risk therapeutic strategy is the opportunity to assess *the relapse risk individually*. Predictor research is thus focused on the search for variables that are capable of predicting an acute psychotic relapse (Atakan et al. 1990).

The *objective* of this study was to identify clinically relevant predictors of relapse (especially rehospitalization) and to gather these predictors into one simple prognostic model for the course of the disease in chronic schizophrenic patients.

Methods

Ninety-nine schizophrenic outpatients classified according to DSM-III criteria (72 male, 27 female) and their relatives ($n = 151$) were included in a random assignment controlled intervention study funded by the Ministry of Research and Technology of the Federal Republic of Germany (Buchkremer and Schulze Mönking 1987).

The mean age was 30.5 years (SD = 13.4). With a mean duration of the disease being 6.1 years (SD = 4.4), the mean number of previous episodes was 2.7 (SD = 1.3). The mean GAS rating as a measure of psychosocial disturbance was 53.1 (SD = 15.2). The study covered a total of 151 relatives of these patients (15 partners, 80 mothers, 54 fathers, 2 siblings). Seventy-five of these were classified as high EE and 76 as low EE according to the Camberwell Family Interview (CFI) (Buchkremer and Rath 1989).

The objective of the study was to evaluate the efficiency of therapeutic relatives' group with regard to relapse prevention. As no significant differences in the relapse risk and rehospitalization rate were found, however, between the randomized patient subgroups with relatives in therapeutic family groups and those without, the group is evaluated as a whole. The results of that study are awaiting publication.

Inclusion and Exclusion Criteria. For inclusion in the study, patients had to have been stabilized on a neuroleptic drug within the 2 previous years, following at least two acute psychotic manifestations or one psychotic manifestation succeeded by a progressively negative course without remission. The last period of hospitalization had to have been concluded at least 2 months previously and the psychopathological findings stabilized for at least 4 weeks. The specified age range was from 16 to 49 years. The patients had to be living in a close-knit family unit (e.g. with parents or marital partner). Patients with an additional psychiatric diagnosis were excluded from the study.

Prognostic Criteria. "Relapse" as a criterion can be described at different levels such as psychopathological findings, social adaptation or subjective state of well-being. Reducing the complex process of a relapse to only one level involves a number of problems but is necessary for methodological reasons. In this study, interest was focused on the first *rehospitalization* within 2 years after the beginning of the study for the following reasons:

1. Rehospitalization is a relevant criterion. (Any rehospitalization takes the patient from his natural environment and increases the risk of social isolation).
2. Rehospitalization is an easily measured (dichotomous) criterion (The investigators had no influence on whether and when a patient was rehospitalized).
3. Rehospitalization correlates significantly with other prognostic criteria such as deterioration in the psychopathological findings or social adaptation. (The predictors of these criteria were also examined; they are not described in detail in this paper, however, as there was no fundamental difference in the results).

In this study, the criterion "relapse" therefore implies rehospitalization as a matter of principle. It was defined as inpatient hospitalization for more than 36 h or treatment at a day hospital for more than 5 days.

Assessment Instruments. Past history and follow-up schedules [including Past History and Sociodemographic Description Schedule (PHSD) and AMDP past history schedule 1–3]; psychopathological findings (AMDP) with the T-transformed syndrome characteristics (Baumann and Stieglitz 1983; Gebhardt et al. 1983); Paranoid Depressivity Scale (PDS; von Zerssen and Koeller 1975); medication questionnaire (recording of drug intake); Global Assessment Scale (GAS; Endicott et al. 1976); Clinical Global Impressions (CGI, CIPS 1979); Muenster Family Questionnaire (MFB; Buchkremer et al. 1986, assessment of the emotional family atmosphere); Camberwell Family Interview (CFI; Vaughn and Leff 1976a); Family Conflict Inventory (FKI; Kreisman et al. 1979); Muenster Prognosis Score (MPS; Schulze Mönking et al. 1986, estimation of the rehospitalization risk); prognosis scale according to Strauss and Carpenter (1974) and to Phillips (for translation into German see Pietzcker and Gaebel 1978).

Data collection on the course of the disease was undertaken 6, 12, 18, 24 and 36 months after the initial examination by the same investigators.

Dropouts. The patients for whom not all patient-related data could be recorded in the various follow-ups had to be excluded from the study. The absence of family-related data in the follow-ups did not lead to drop out.

Complete records were kept on 89 of the 99 patients throughout a 3-year follow-up. There were 14 dropouts from specific data on emotional family atmosphere (MFB) and 22 dropouts from data on intra-family conflicts (FKI).

The *statistical analysis* was done by the Statistics and Data Center for Clinical Trials at the Department of Medical Biometry and Medical Informatics of the University of Heidelberg. The statistical methods chosen for the evaluation of the predictors depended on the form of criterion available. If there was a dichotomous criterion, the assessment of quantitative predictor variables

was performed with the U-test of Mann-Whitney-Wilcoxon. For qualitative predictors we used the chi-square test, or in the case of low cell frequencies the exact Fisher test. Because of the problems of multiple testing, all P values are understood to be descriptive, since no adjustment for the error of the first kind was applied.

The prognostic value of a predictor can be characterized by means of easily interpreted parameters, provided that the predictor is dichotomous. The data referring to the correlation between prediction and true course of the disease can be combined in a simple 2×2 table (a, b, c, d are absolute frequencies; $n = a + b + c + d$) where "course" denotes the event "rehospitalization within 2 years" and "predictor" the unfavourable value of the predictor.

		Course	
		+	−
Predictor	+	a	b
	−	c	d

As a parameter for the quality of the prediction, the accuracy is calculated as the percentage of correct predictions $(a + d)/n$. Other frequently used parameters are sensitivity $a/(a + c)$ and specificity $d/(d + b)$, which give the rate of correct predictions in respect of patients without or with hospitalization. More adequate for the clinician are the so-called *predictive values* of the "positive" (favourable) $[a/(a + b)]$ or the "negative" (unfavourable) prediction $[c/(c + d)]$. It has to be pointed out that the predictive values calculated from one study may not be applicable to another group of patients with a different rehospitalization rate. In order to apply this concept to a quantitative predictor, an appropriate cut-off point for dichotomization has to be chosen. The parameters specified above vary depending on the choice of this cut-off point where a higher sensitivity coincides with a lower specificity and vice versa. As a criterion for selecting optimal dichotomization the predictive accuracy (A) was applied in this paper. For further analysis we chose that cut-off point yielding maximum accuracy.

Choosing a reference interval of 2 years for rehospitalization excludes the possibility of differentiating between early and late rehospitalizations within that interval. We therefore did a second series of analyses with a dependent variable "time to first rehospitalization".

This is a so-called censored variable, meaning that its value is unknown for some patients, either because a patient was not rehospitalized within the follow-up period or because he/she dropped out early in the study. Statistical methods under the name "survival analysis" have been developed to permit an unbiased estimate of the distribution function of a censored variable as well as non-parametric tests for the comparison of two distributions. The graphical presentation of the distribution is based on the *Kaplan-Meier method* in the form of a so-called survival curve (cf. Fig. 2). The survival curve shows the percentage of patients not rehospitalized up to each point in time. Patients without rehospitalization are included in the calculation of the curve, provided that they have been followed up within the study. The median is usually chosen as the location parameter of the distribution; it can be read off directly from the survival curve. The so-called *log rank test* is most appropriate for testing two or more groups with respect to the location of the survival distributions, because it gives more weight to long-term differences in the survival curves than the *generalized Wilcoxon test.* These methods are set out clearly and concisely by Pocock (1983).

Multivariate Evaluation. The search for predictors out of a set of more than 50 potential predictor variables requires a well-structured strategy. When the number of variables and their combinations exceeds the number of patients, the number of prognostic models used for comparison has to be severely restricted because chance constellations of data might otherwise be misinterpreted as real associations. The following guidelines were taken into account in analysis: partitioning of the set of variables into different sections; preselection of possible predictors by means of univariate analyses within each section; elimination of highly correlated predictors, taking content or measurability as criteria; combination of a limited number of predictors in simple models.

We restricted the combination of different predictors to a maximum of three variables because we observed that the addition of a fourth predictor led to inconsistencies because of small subgroups and yielded no significant improvement in the accuracy of a prognostic model. As simple and therefore suitable prognostic models, we chose hierarchic classification tree models. Selection of these models was not performed automatically by a computer program (e.g. CART) but step by step, taking the above-stated guidelines into account.

Results

Table 1 lists predictor variables under the headings of case history, social and therapeutic situation, psychopathological findings, family and prognosis scales, and checks for significance over periods of 12 and 24 months. The greatest predictive power is shown by overall psychopathological findings, emotional family atmosphere, social adaptation and the prognosis scales.

Table 2 lists in hierarchical form established predictors according to accuracy (A), positive (PV+) and negative (PV-) predictive values, the criterion being rehospitalization with 24 months. (Accuracy rates of over 80% were achieved for the 12-month observation period as well.)

Predictors under the headings of psychopathology (especially disturbed thinking and attention), social adaptation and the MPS offer maximum accuracy (A: > 70%). Rehospitalizations can best be predicted using predictors with high negative predictive values (PV−: > 80%). These are found under the headings of emotional family atmosphere, psychopathology and social adaptation.

The clinically significant question of probable absence of relapse (rehospitalization) can best be answered by using predictors with as high a positive predictive value as possible. A regular employment contract permits a reliable prediction from the clinical standpoint that the patient will not be rehospitalized within the next 2 years. Other factors predicting a low relapse risk within 2 years are the MPS, low degree of hostility or of disturbed thinking and attention, good social adaptation and a minimum of problems within the family.

The predictors selected by univariate analysis for each section are to be gathered below into simple prognostic models, taking content or measurability as criteria.

Case History

If a patient has at least one grade 1 or grade 2 relative suffering from a psychiatric disease requiring therapy, he/she has a significantly increased rehospitalization risk at least in the short term (12 months). In contrast, patients who have previously (i.e. prior to commencement of the study) been relapse-free for more than 1 year are significantly less likely to be rehospitalized within the 2-year follow-up. No other case history data proved to be of prognostic significance. Various combinations of case history variables resulted in the hierarchical classification tree model shown in Fig. 1.

Table 1. Predictors of rehospitalization within 12 or 24 months after initial examination (*P* value of dichotomized variables: chi-square-test; *P* value of quantitative variables: U-test)

	12 months *P*-value	24 months *P*-value
Case history ($n = 89$)		
Age (years)	0.066	0.248
Age at onset of disease (years)	0.506	0.631
Sex	0.348	0.991
Psychiatric disease in grade 1 or 2 relatives	0.038	0.082
Social class	0.069	0.427
Education	0.589	0.688
Professional qualification	0.148	0.066
Onset of disease	0.226	0.114
Total hospitalization period	0.721	0.067
Frequency of hospitalization	0.555	0.814
Absence of relapse	0.018	0.051
Social and therapeutic situation ($n = 89$)		
Psychiatric care	0.224	0.220
Frequency of social contacts	0.286	0.055
Work paid at standard rates	0.025	0.003
Neuroleptic therapy	0.004	0.024
GAS	0.0000	0.0000
Psychopathological findings ($n = 89$)		
Total AMDP score	0.0000	0.0000
Apathetic syndrome	0.002	0.004
Disturbed attention and thinking	0.0001	0.0001
Depressive syndrome	0.001	0.004
Hostility syndrome	0.007	0.0003
Paranoid-hallucinatory syndrome	0.003	0.001
CGI	0.0000	0.0000
Family ($n = 89$)		
MFB index ($n = 79$)	0.002	0.0001
Emotional over-involvement	0.425	0.154
Criticism	0.473	0.157
Hostility	0.199	0.104
Rejection	0.063	0.221
Warmth	0.440	0.045
Resignation	0.043	0.003
CFI: EE index ($n = 89$)	0.051	0.066
FKI: Problem ($n = 77$)	0.004	0.004
Prognosis ($n = 89$)		
MPS	0.0000	0.0000
Strauss-Carpenter scale	0.001	0.0001
Phillips scale	0.087	0.088

AMDP; CFI, Camberwell Family Interview; CGI, Clinical Global Impressions; FKI, Family Conflict Inventory; GAS, Global Assessment Scale; MFB, Muenster Family Questionnaire; MPS, Muenster Progressive Score

The predictive accuracy is not improved by any other predictors obtained from the case history (professional qualification, genetic factors).

Summing up, a high relapse risk can be predicted among schizophrenic patients that had to be rehospitalized in the 12 months prior to the initial examination and had been hospitalized for a total period of more than 1 year in the past. A low relapse risk cannot be predicted so accurately.

Table 2. Hierarchy of predictors according to predictive accuracy (A) and to positive (PV+) and negative (PV−) predictive values over a 24-months observation period

Predictor	Accuracy (A)	Pos. pred. value (PV+)	Neg. pred. value PV−)
MPS	75%	$n = 39:69\%$	$n = 50:80\%$
GAS	74%	$n = 40:67\%$	$n = 49:80\%$
Total AMDP score	73%	$n = 44:64\%$	$n = 45:80\%$
Work paid at standard rates	67%	$n = 16:75\%$	$n = 73:66\%$
Intra-family problems	67%	$n = 31:65\%$	$n = 48:69\%$
Strauss-Carpenter scale	66%	$n = 45:58\%$	$n = 44:75\%$
Absence of relapse (in previous year)	65%	$n = 38:58\%$	$n = 51:71\%$
CGI	63%	$n = 56:54\%$	$n = 33:79\%$
Family warmth (MFB)	61%	$n = 47:53\%$	$n = 38:71\%$
Family resignation (MFB)	58%	$n = 61:54\%$	$n = 24:88\%$
Neuroleptic therapy	58%	$n = 74:47\%$	$n = 14:86\%$
AMDP subscales:			
Apathetic syndrome	70%	$n = 40:62\%$	$n = 49:76\%$
Disturbed attention and thinking	72%	$n = 36:67\%$	$n = 53:75\%$
Depressive syndrome	67%	$n = 36:61\%$	$n = 53:72\%$
Hostility syndrome	70%	$n = 30:67\%$	$n = 59:71\%$
Paranoid-hallucinatory syndrome	67%	$n = 32:62\%$	$n = 57:70\%$

The survival curves derived from the case histories (Fig. 2) develop their maximum predictive power after about 20 months, after which time the curves come close together again.

Social and Therapeutic Situation

The extent of social contacts is of little prognostic value. Work paid at standard rates proved to be the best long-term predictor of a low relapse risk. Non-compliance in neuroleptic therapy is a reliable predictor of rehospitalization.

The classification tree model for assessment of the rehospitalization risk can be derived from the current social and therapeutic situation (Fig. 3).

Summing up, the marked significance of drug compliance as an outcome predictor can be emphasized. If neuroleptics are rejected by the patient despite long-term neuroleptic therapy being indicated (cf. Möller 1987), a high risk of rehospitalization within 2 years is to be assumed. A patient taking the indicated neuroleptics has a lower relapse risk if he/she holds a job paid at standard rates or at least has adequate social contacts.

The corresponding survival curves (Fig. 4) show that assessment of the relapse risk based on the social and therapeutic situation develops its maximum predictive value after about 17 months.

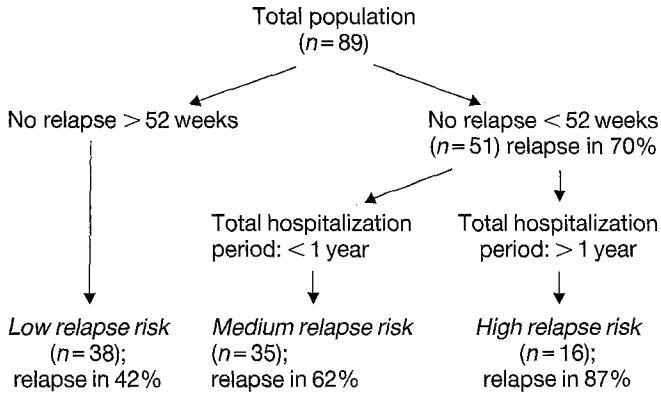

Fig. 1. Case-history based classification tree model for prediction (percentage) of rehospitalization within 2 years

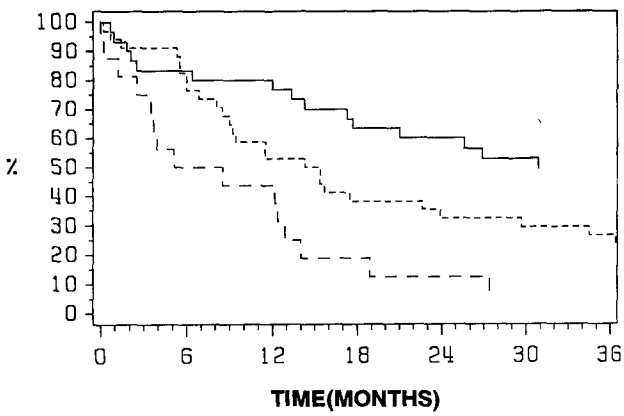

Fig. 2. Survival curves derived from case histories of patients with low ($n = 30$; median 30.9; |——|), medium ($n = 34$; median 14.3; |----|) and high ($n = 16$; median 5.1; |- - -|) rehospitalization risk (Log rank test: $P = 0.0002$)

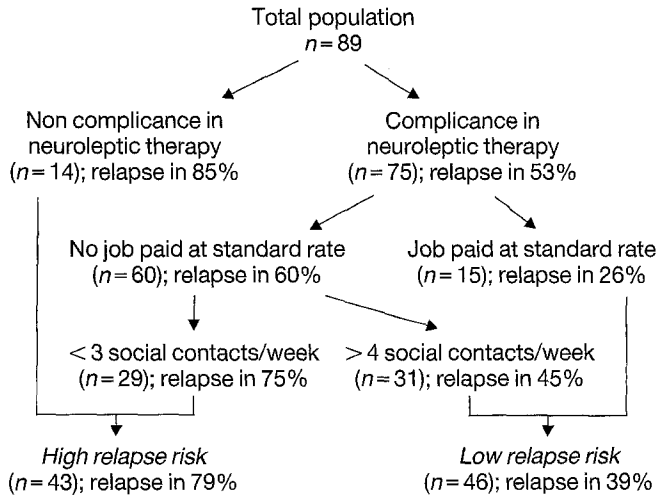

Fig. 3. Classification tree model derived from current social and therapeutic situation for prediction (percentage) of rehospitalization within 2 years

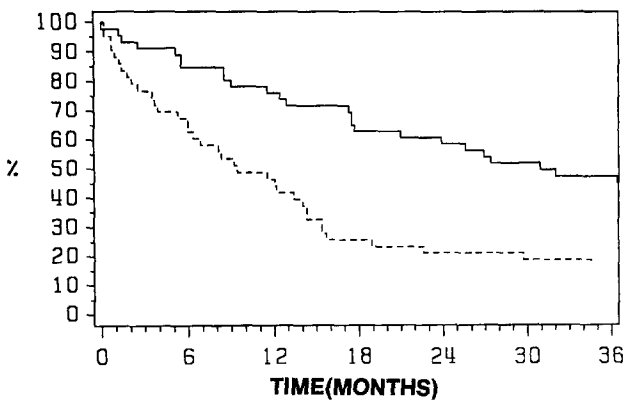

Fig. 4. Survival curves derived from social and therapeutic situation of patients with low ($n = 46$; median 30.9; |——|) or high ($n = 43$; median 9.4; |----|) rehospitalization risk. (Log rank test: $P = 0.0003$)

Psychopathological Findings

These findings represent a special area within the predictor variables, as the characteristics themselves belong to the course of the disease. It is therefore not surprising that the relapse rate is higher among patients with a more extensive syndrome at the outset of the study. The fact that the total AMDP score, however, is also of higher predictive value in the long term (two years) indicates that psychopathological symptoms are lasting prognostic characteristics. The AMDP subscales representing the individual syndromes yield similarly good results. These findings conform with those published by Möller and von Zerssen (1985). The GAS and the CGI, both of which also refer to psychopathological disturbances, also provide reliable relapse prognoses. These two scales have, however, a high degree of correlation. The self-rating of the patient in respect of paranoid (P-score) and depressive (D-score) symptoms, while not providing long-term predictors of rehospitalization, does offer reliable short-term ones (not illustrated).

The prognostic value can be improved still further by combining the psychopathological overall impression (total AMDP score) and social adaptation (GAS). The classification tree model in Fig. 5 shows that the rehospitalization risk among patients with only few psychopathological symptoms but with poor social adaptation is equally high as among those with severe psychopathological disturbances. This is confirmed by the survival and hospitalization curves (Fig. 6).

Family

Special weight was given to the field of family variables, as this study was designed to examine the efficiency of therapeutic groups involving relatives of patients. The best predictors in this respect were obtained from the self-ratings of the relatives concerning intra-family problems and conflicts (FKI), following a detailed interview (CFI and MFB), and from behaviour observation, evaluated in the Muenster Family Questionnaire (MFB), with the extent of resignative behaviour providing the most accurate prediction of rehospitalization. The CFI index has been shown elsewhere to permit a reliable prediction

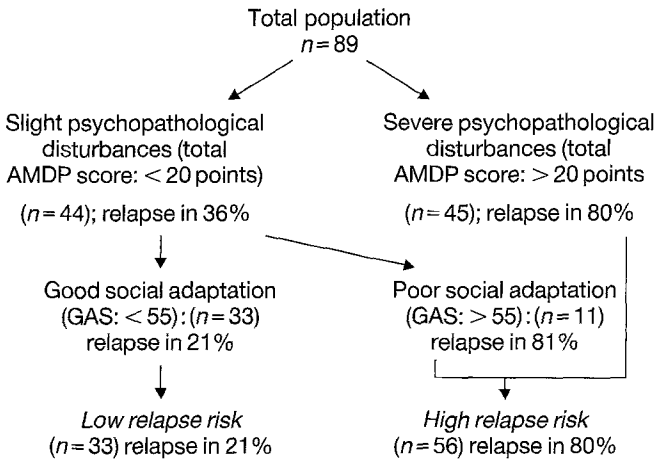

Fig. 5. Classification tree model derived from psychopathological findings (AMDP, GAS) for prediction (percentage) of rehospitalization within 2 years

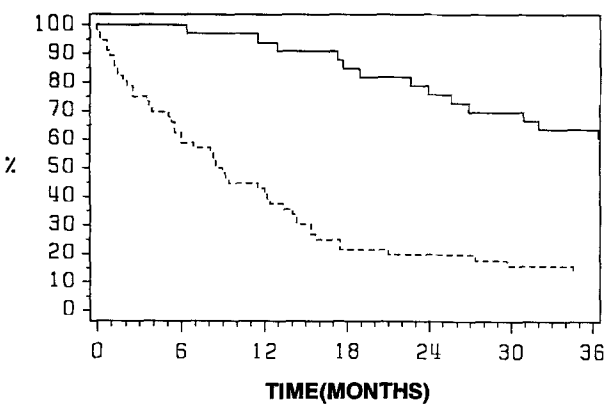

Fig. 6. Survival curves derived from psychopathological findings and socal adaptation of patients with low ($n = 33$; median 42.6; |——|), or high ($n = 56$; median 8.5; |----|) rehospitalization risk. (Log rank test: $P = 0.0001$)

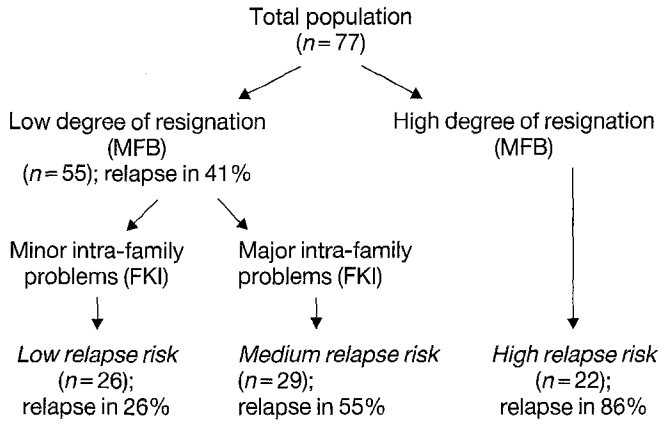

Fig. 7. Classification tree model derived from emotional family atmosphere (MFB, FKI) for prediction (percentage) of rehospitalization within 2 years

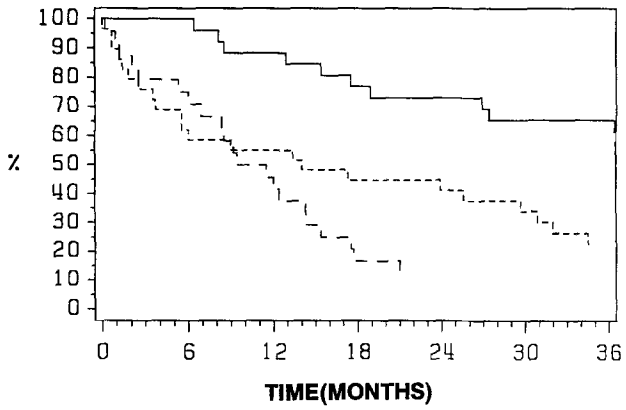

Fig. 8. Survival curves derived from emotional family atmosphere of patients with low ($n = 26$; median 42.6; |——|), medium ($n = 29$; median 14.0; |----|) and high ($n = 24$; median 9.4; |- - -|) rehospitalization risk. (Log rank test: $P = 0.0001$)

of relapses, as already claimed in earlier Anglo-American studies (cf. Vaughn and Leff 1976b; Goldstein 1985; Buchkremer et al. 1986).

The emotional family atmosphere (MFB) combined with the self-ratings of the relatives (FKI) can also produce a classification tree model of high predictive value (Fig. 7). The extent of expressed emotions within the family (according to the CFI index) does not improve the predictive accuracy of this classification tree model, even in conjunction with other predictors.

Summing up, it can be stressed that a high rehospitalization risk can be predicted by the emotional family atmosphere, in particular by the extent of resignation. A medium and a low relapse risk can furthermore be differentiated by taking the subjective ratings of the relatives (concerning the extent of intra-family problems and conflicts) into account.

The survival curves (Fig. 8) show that the extent of family resignation is the only factor of significance in determining whether the rehospitalization risk is high or low in the first 9 months. Only after this period can a medium-risk and a high-risk group be differentiated in addition on the basis of subjective assessment of the relatives concerning the extent of family problems.

Prognosis

The prognostic validity of the Strauss-Carpenter scale has been confirmed, although its predictive values are below those of the MPS. The prognoses provided by the MPS are just as reliable as those derived from the overall psychopathological symptoms (AMDP). The rehospitalization rates among patients with a favourable prognosis ($n = 39$) were 8% during the 1st year and 30% after 2 years. The corresponding figures for patients with an unfavourable prognosis ($n = 50$) were 60% and 80% respectively. The efficiency of the MPS in predicting rehospitalization is reflected in the survival curves (Fig. 9).

The MPS is exemplary of the way in which various predictor fields (number of hospitalizations, psychopathological findings, premorbid development, stability of social environment) can be combined to provide reliable short-term and long-term prediction of rehospitalization by relatively simple means (cf. Schulze Mönking et al. 1986).

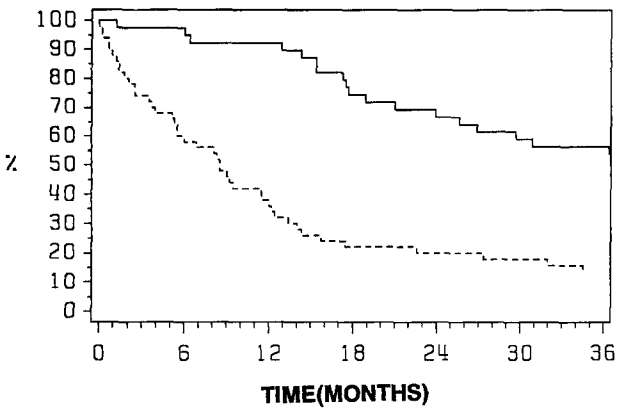

Fig. 9. Survival curves derived from MPS of patients with favourable ($n = 39$; median 40.3; |——|) and unfavourable ($n = 50$; median 8.5; |----|) prognosis. (Log rank test: $P = 0.0001$)

Global Prognosis Score

The predictive accuracy (A) for the 2-year period can be further increased by gathering the results of the different "classification tree models" into one global prognosis score (GPS).

In the classification tree models (case history, social and therapeutic situation, psychopathological findings, family), 1 point is given for a low and 2 points for a medium relapse risk. 3 points are given for a high relapse risk in the sections case history and family, and 2 points in the sections social and therapeutic situation and psychopathology. Patients whose emotional family atmosphere cannot be assessed are given the maximum value of 3 points in the "family" section. A value of less than 6 is predictive of a favourable prognosis, a value of 6 or more of an unfavourable prognosis.

Only 6 (16%) of the 37 patients assessed by this GPS as having a favourable prognosis relapsed within the 2-year follow-up period, whereas 46 (88%) of the 52 assessed as having an unfavourable prognosis were rehospitalized. This corresponds to a predictive accuracy of 88%.

Discussion

When evaluating and interpreting the results, the selection criteria of the sample covered in this study have to be taken into account; most of the patients were male, not acutely ill, of outpatient status and had a considerable relapse risk. They were undergoing neuroleptic therapy at least at the outset of the study and were living in a family unit. In other words, non-cooperative schizophrenic patients and those living alone were virtually excluded from the study. The prognostic findings thus apply only to the specific population detailed above. On the other hand, the findings conform broadly with those of other studies (e.g. Möller et al. 1984; Möller and von Zerssen 1985; Strauss and Carpenter 1977; Huber et al. 1979; Biehl et al. 1986; Atakan et al. 1990), so that a cautious generalization of the results would appear admissible.

In conclusion, it is pointed out once again that rehospitalization was selected as the target criterion in this study for different reasons. It was, however, not only a deterioration in the psychopathological findings that led to rehospitalization but also disturbances in social adaptation and changes in the patients' environment.

A group of patients with a medium-term (more than 2 years) high relapse risk (> 80%) can be identified from their *case histories* (Derissen 1989). Frequent hospitalizations in the past are reliable predictors of frequent hospitalizations in the future.

The data were collected within the framework of a study examining the effects of therapeutic relatives' groups on relapse rate. Although no significant differences in rehospitalization rate was found between the randomized control group and the patient group undergoing therapy involving relatives, the possibility cannot be ruled out that the results have been influenced by the therapy.

The rehospitalization risk can also be predicted from the *current social and therapeutic situation.* Patients refusing to take neuroleptics despite medical advice have a high relapse risk (PV−: > 80%). On the other hand, there is only a low rehospitalization risk among patients holding down a job paid at standard rates or having an adequate number of social contacts while undergoing neuroleptic therapy. It is interesting to note that adequate social contacts can obviously compensate for a lack of paid work. It appears to be the extent rather than the type of social stimulation that influences the course of the disease, with a moderate level apparently being most favourable.

Any conclusions that could be drawn on rehospitalization risk from the premorbid personality were only trend-relevant. This is in contrast to studies on the long-term course of the disease (Huber et al. 1979; Ciompi 1981).

The *psychopathological findings* are exceptionally reliable predictors of short-term and long-term rehospitalization. Systematic objective assessment (according to the AMDP system) is essential for this purpose, however, so that a dichotomized prediction can be made, following evaluation using a cut-off point. In scientific issues this is not problematic, but in clinical practice it may represent a virtually unsurmountable obstacle. As the social handicaps determined from the psychopathology can be assessed without difficulty and with equal precision by means of the GAS, however, such an assessment might be suitable for the psychiatrist not engaged in scientific work.

In the psychopathological findings, emphasis is to be placed on disturbed thinking and attention as accurate predictors with high prognostic values. In contrast to the predictive qualities of disturbed emotions and drive that have been found in other studies too (e.g. Möller et al. 1982a, b), disturbed thinking and attention have not been included previously in the short-term or long-term predictors. In most outcome studies, patients were examined after remission of an acute psychotic episode while still hospitalized (cf. Möller et al. 1982a, b; Huber et al. 1979). It is the post-remission exhaustion syndrome (Heinrich 1967), characterized in particular by disturbed emotions and drive, that is predominant at this stage of the disease. Those patients examined within the

scope of the present study, on the other hand, were at various stages of the disease; most of them had not been hospitalized within the previous 12 months (according to the inclusion and exclusion criteria applied). The conspicuous psychopathological characteristics were therefore more heterogeneous, so that the prognostic significance of various types of disturbance could be examined. The prognostic validity of disturbed thinking and attention emphasizes the role of cognitive disturbances in the course of the disease and supports the hypothesis put forward by those working in experimental psychology that disturbances in processing information characterize the vulnerability of schizophrenia in a special way (cf. Nüchterlein and Dawson 1984; Zubin and Spring 1977; Martin and Sterne 1976; Rutter et al. 1977; Knight et al. 1979).

Disturbed emotions and drive as well as paranoid-hallucinatory symptoms have a significant link with impending rehospitalization. The absence of these symptoms, however, provides little indication of a low relapse risk (cf. Pogue-Geile 1989).

Although the *emotional family atmosphere* was not recorded in the acute phase of the illness, in contrast to all previous EE research, it nevertheless proved to be a predictor of rehospitalization within 2 years. (A paper dealing with the correlation between EE indices and rehospitalization rates is in preparation.) Keeping this in mind, the MFB, which is easy to use in the psychiatric practice too, was shown to provide a more reliable prognosis than the far more complex CFI. Schizophrenic patients whose relatives display a high degree of resignation or expect severe problems within the family are likely to be rehospitalized within 2 years in more than 80% of cases. Worried families lead to social overstimulation of the patient and thus to relapses. Resigned families, in contrast, offer too little care and warmth so that the protective effect of a more balanced emotional family atmosphere is lost. The psychiatrist keeping in touch with the entire family (e.g. within the scope of a home visit) is therefore in a good position to assess the rehospitalization risk from the emotional family atmosphere. This predictor analysis demands among other things that concrete therapeutic work involving relatives should counteract not only emotional over-involvement but also resignation on the part of relatives.

An easily applied *prognosis scale* can also help the clinical psychiatrist to assess the rehospitalization risk. Besides the internationally recognized Strauss-Carpenter scale, the MPS proved in this study to be practicable and of prognostic validity.

A further interlinking of the various predictor sections (case history, social and therapeutic situation, psychopathological findings, emotional family atmosphere) by a GPS led to acute psychotic relapses or rehospitalization within 2 years being predicted with greater accuracy (A = 88%) in this study, too. This astonishingly good result is presumably somewhat "over-optimistic", as it was validated on the test sample and not on independent data. (This result is currently being examined within the scope of a further BMFT study.) The actual predictive accuracy will probably prove not to be much more than 85%.

What is the cause of these inaccuracies? One important factor may well be the incalculable, unpredictable inter-relationships between environmental influences, e.g. interpersonal conflicts, pharmacotherapy or psychotherapy (Glass et al. 1989; Schooler and Kane 1986; Karley et al. 1989), life events, professional situation and vulnerability. Not until prognostically valid trait markers are available can the inter-relationships between vulnerability and psychosocial factors be examined in more detail. Another factor may well be the heterogeneity of the population covered by the study. Finally, the frequent interferences of various predictors may be a reason for the residual inaccuracy. For instance, a compliant patient with a steady job might be living in a high EE family. In this example there is competition between a positive factor (with a high PV+) and a negative one (with a high PV−).

Despite the accuracy rates of some predictors not being very high, just over 60%, the positive or negative predictive values may be of great clinical significance for the samples concerned.

This can be illustrated by the following example. The predictive accuracy derived from recording the emotional family atmosphere (resignation) was only 58%. The negative predictive value, however, was 88%. This means that a valid prediction based on this variable (PV+: 54%) is hardly possible for the patient group whose relatives do not have a resigned attitude towards the schizophrenic member of the family. Patients with a family assessed as resigned, however, have a high probability (PV−: 88%) of rehospitalization within a 2-year period.

When assessing the individual relapse risk, it is therefore not sufficient to seek predictors in one section only. Assessments should rather be made in as many sections as possible and gathered into one GPS. This is the only means of obtaining an adequately valid individual prognosis that can serve as a rationale for specific therapeutic strategies.

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