Psychoeducation and Compliance in the Treatment of Schizophrenia: Results of the Munich Psychosis Information Project Study

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Objective: The present study examined whether psychoeducational groups for patients with schizophrenic disorders and for their families can reduce rehospitalization rates and improve compliance.

Method: 236 inpatients who met DSM-III-R criteria for schizophrenia or schizoaffective disorder and who had regular contact with at least 1 relative or other key person were randomly assigned to 1 of 2 treatment conditions. In the intervention condition, patients and their relatives were encouraged to attend psychoeducational groups over a period of 4 to 5 months. The patients' and relatives' psychoeducational programs were separate, and each consisted of 8 sessions. Patients in the other treatment condition received routine care. Outcomes were compared over 12-month and 24-month follow-up periods. The study was conducted from 1990 to 1994.

Results: It was possible to significantly reduce the rehospitalization rate after 12 and 24 months in patients who attended psychoeducational groups compared with those receiving routine care ($p < .05$). Patients who attended psychoeducational groups showed better compliance than patients under routine care without psychoeducation.

Conclusions: The results suggest that a relatively brief intervention of 8 psychoeducational sessions with systematic family involvement in simultaneous groups can considerably improve the treatment of schizophrenia. Psychoeducation should be routinely offered to all patients with schizophrenia and their families.

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Rehospitalization rates of patients with schizophrenia on treatment with oral antipsychotic medication average 42% in the first year after index discharge.[1] It has been conclusively demonstrated in numerous scientific studies that there is a massive informational and motivational deficit on the part of patients with schizophrenia with respect to relapse prevention using antipsychotics. More than 50% of all rehospitalizations may be attributable to medication noncompliance.[1–4] It is unfortunate that compliance rates are low, because research has shown that the 12-month relapse rates of patients without antipsychotic long-term treatment are much higher (70%–80%) than the relapse rates of patients with antipsychotic long-term treatment (10%–20%).[5–7] A number of factors that tend to cause drug noncompliance in patients with schizophrenia have been described, such as informational deficits, poor insight into illness, cognitive deficits, psychopathology, negative attitude or subjective response to medication, side effects or fear of possible side effects, drug and alcohol abuse, inadequate discharge planning, and a poor patient/doctor relationship. The families of patients with schizophrenia are also often against medical treatment and do not support the patients adequately when compliance problems occur.[8,9] The reduction of noncompliance or treatment nonadherence is one of the most important aims in current psychiatry and especially in the treatment of schizophrenia.

A meta-analysis on the efficacy of interventions in enhancing adherence in psychosis[10] has shown that these interventions can double the likelihood of adherence to medications and to scheduled appointments.

Psychoeducational patients' and relatives' groups appear to be one of the successful intervention strategies for improving compliance.[11,12] In addition, these groups satisfy the patients' and relatives' needs for information about the disease and about possible treatments, and they provide emotional relief and help in coping with the disease as well.[11,12]

While numerous studies have shown a positive effect of several forms of interventions for reducing noncompliance shortly after implementation, data on the long-term impact of such interventions are still scarce.[10]

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We report here on a German prospective, randomized, multicenter study (Psychosis Information Project [PIP]-Study) involving 236 inpatients that was carried out to answer the question of whether psychoeducational groups for patients with schizophrenic disorders and for their families can improve long-term outcomes. The PIP-Study was intended to correct the lack of studies with long-term follow-ups and examined whether the benefits of psychoeducation are maintained over a period longer than 6 months. The present article describes the effects of psychoeducational groups (intervention group) in comparison with routine care (control group) on compliance and rehospitalization rates over a 24-month follow-up period.

METHOD

Subjects

The study was conducted from 1990 to 1994 at the inpatient wards of 3 German psychiatric hospitals (Department of Psychiatry and Psychotherapy of the University of Munich, Department of Psychiatry and Psychotherapy of the Technical University of Munich, and the Psychiatric State Hospital in Haar). The 3 study hospitals performed a screening of all admitted patients who fulfilled clinical DSM-III-R/ICD-9 (295) criteria for schizophrenia or schizoaffective disorder.

Inclusion criteria were as follows: diagnosis of schizophrenia or schizoaffective disorder (DSM-III-R/ICD-9), indication for at least a 12-month antipsychotic relapse prevention, age of 18 to 65 years, willingness to be treated for at least 1 year in the outpatient department of the hospital, and general willingness to involve one of the key persons in the patient's life (relatives or close friends).

Exclusion criteria were as follows: distance from patient's home to hospital > 150 km, no regular contact with relatives (< 30 minutes/week), regular substance abuse (< 6 months before admission), pregnancy, IQ < 80, lack of competence in German, and no remission in the last 2 years.

Institutional review board approval was obtained for the study, and patients gave written informed consent prior to participation. The consent agreement included the willingness to involve at least 1 relative (or key person) in the study. The relatives then gave their written informed consent as well. We recruited 236 patients for the study, i.e., 10% of the patients who passed the screening procedure. Patients who did not participate did not meet the inclusion criteria (7.0%), had no relatives to involve in the study (32.2%), had a chronic illness with no expectation of a remission during their inpatient stay (17.0%), had regular substance abuse (8.8%), were living at a distance of more than 150 km from the hospital (9.3%), did not speak German sufficiently well (5.7%), had an IQ less than 80 (2.6%), were pregnant (0.4%), refused to take part in the study (9.5%; most [54%] of the refusals can be traced to the fact that the patients wished to be treated by their psychiatrist and did not want to come to the study center for outpatient treatment), or were excluded for other reasons (7.5%).

Randomization Procedures

In each of the study centers, we integrated 8 to 12 patients into a group, and through block randomization each group was allocated either to the intervention group or to the control group. The study centers could learn to which treatment condition the group was assigned via telephone. The randomization list for each study hospital was generated by a computerized random sampling in the study evaluation center. The treating study psychiatrists were blind to the randomization.

Exclusions and Dropouts

Of the 236 patients included in the study, 26 (11%) were belatedly excluded from the study population as protocol violators because they no longer fulfilled the inclusion criteria or exclusion criteria arose (change of diagnosis: 6 patients; no indication for antipsychotic relapse prevention: 1 patient; no remission during inpatient stay: 11 patients; distance from patient's home to hospital because of relocation: 8 patients). Sixteen study patients (7%) withdrew their consent before outpatient treatment could begin. For these patients, only the assessments at study entry exist.

Of the remaining 194 study patients (intervention group: 102, control group: 92), 163 patients remained in the study until the 12-month follow-up was completed (intervention group: 81, control group: 82). Twenty-four month follow-up data are available for 153 patients (intervention group: 79, control group: 74). The 41 dropout patients must be considered as intervention-related dropouts. They either discontinued the outpatient treatment (32 patients) or did not sufficiently participate in the psychoeducational group sessions (patient and relative attended fewer than 4 group sessions; N = 8), and 1 patient committed suicide.

Dropout rates were comparable in both groups (23% in the intervention group vs. 20% in the control group; not significant). Dropout patients did not differ from the study completers in regard to sociodemographic or illness-related variables such as diagnosis, duration of illness, number of previous hospitalizations, or severity of the illness at study entry. Figure 1 shows a CONSORT[13] flow diagram of the study disposition.

Study Intervention

In addition to routine treatment, patients and relatives in the intervention group were encouraged to attend psychoeducational groups.

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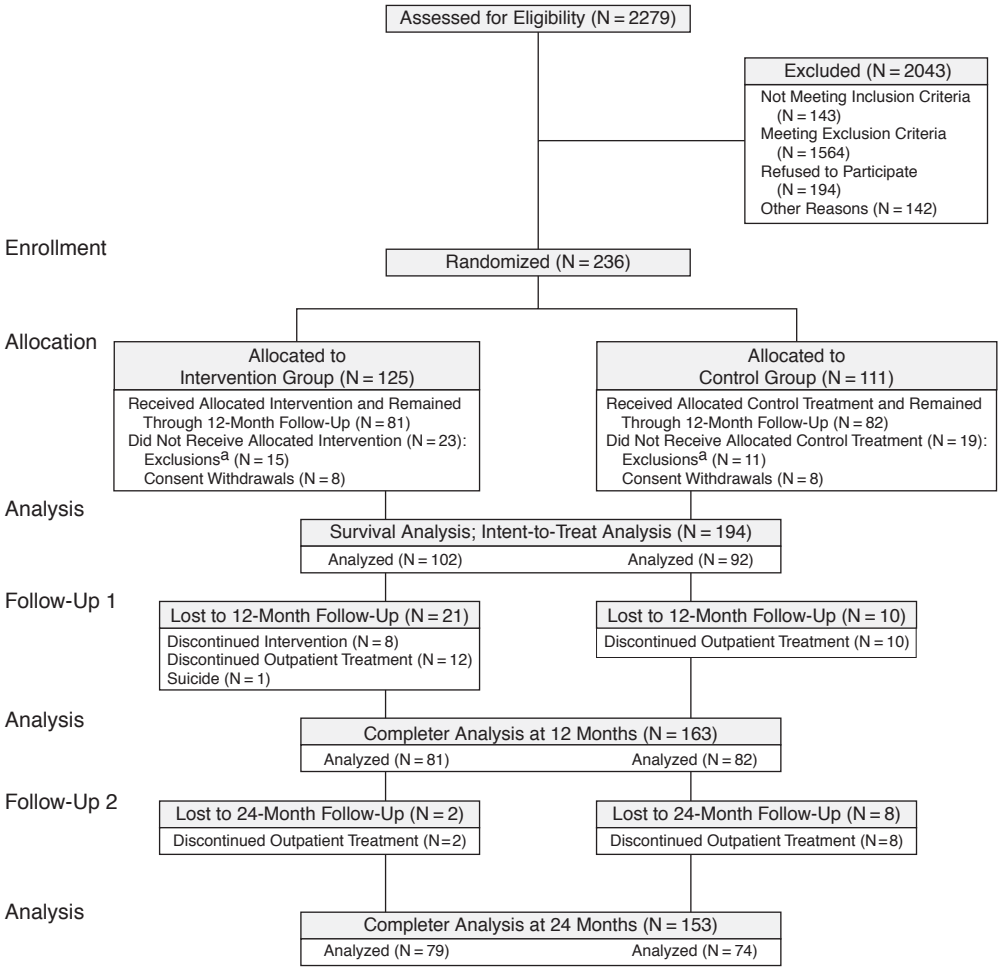
Figure 1. CONSORT Flow Diagram of the Progress Through the Phases of the Study



[a]Change of diagnosis: 6 patients; no indication for antipsychotic relapse prevention: 1 patient; no remission at inpatient stay: 11 patients; distance from patient's home to hospital due to relocation: 8 patients.

In the first period of the study, the research associates developed a curriculum for the psychoeducational groups.[14] The intervention therapists included 9 psychiatrists and 1 clinical psychologist, who were experienced psychotherapists as well and who were trained in psychoeducation. Integrity of the manner in which the intervention was implemented in each of the study centers was ensured by holding supervision sessions and by the therapists' observing one another in the groups at regular intervals.

The total program of the psychoeducational patients' groups consisted of 8 one-hour group sessions. Sessions 1 to 4 took place weekly, mostly during the patients' inpatient stay but after fading of the acute symptoms, and sessions 5 to 8 took place monthly, predominantly during the outpatient period of the study. Comprehensive information was given about symptoms, etiology, acute treatment, relapse prevention, and psychosocial treatment of schizophrenia; adequate coping strategies were discussed; and individual crisis plans were drawn up. Furthermore, patients had the opportunity to discuss current questions or day-to-day problems concerning the illness. By establishing a good group cohesion, the psychoeducational groups also made possible self-help effects for the group members.

The psychoeducational relatives' groups were designed for the patients' "key relatives." Additional relatives and friends could also join the group. Eight biweekly 90-minute sessions were planned for the relatives. The relatives' groups started meeting soon after randomization, because at this time the relatives need information and help the most and their motivation to participate is highest. Information in the relatives' groups was of the same tenor as in the patients' groups. Also discussed was how the family members can better help the patient with schizophrenia and how they can obtain support and emo-

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Table 1. Compliance Ratings

Very good	Oral: patient took the drugs very regularly Depot: patient always came punctually to take the injections
Good	Oral: patient took the drugs quite regularly, missed taking them only a few times (once or twice a week) Depot: patient usually came to take the injections, sometimes had to be reminded by a phone call, but did not delay longer than a week
Mediocre	Oral: patient did not take the drugs regularly, often missed taking them (nearly every second day or over a period of 1 or 2 weeks), insisted on a dose reduction that is not justifiable from the therapeutic standpoint Depot: patient did not come for injections, had to be reminded by phone calls very often and delayed longer than a week, insisted on a dose reduction that is not justifiable from the therapeutic standpoint
Bad	Oral: patient did not take the drugs at all, or only very sporadically, or reduced the dose by himself to an unacceptable extent Depot: patient did not come to take the injections in spite of several phone calls, or patient came, but refused the injection

tional relief for themselves. Especially in this "exchange of experiences" section, the groups had a more or less self-help character. The psychoeducational groups lasted over a period of 4 to 5 months.

Patients and relatives in the intervention group received informational material that was developed especially for the study. In 4 brochures, all psychoeducational topics were described in detail and in a language understandable by laymen. The material was later published as a guidebook.[15]

Drug Treatment

After remission of the acute symptoms, the patients in both study groups received maintenance antipsychotic medication. After discharge, they received outpatient treatment at the study hospital. Choices of substances and doses were made according to individual clinical needs with a fixed minimum dose of 100 mg of chlorpromazine equivalents. Additional drugs were given on an as-needed basis. At least 1 appointment per month was planned for every study patient.

Outcome Measures

The main outcome criteria were compliance and rehospitalization rates 12 and 24 months after index discharge. Compliance was assessed by the treating psychiatrists and was scored on an ordinal 4-point compliance scale that was exactly operationalized (Table 1). To validate the psychiatrists' compliance ratings, plasma drug level measurements were made.

Secondary outcome measures were the number of rehospitalizations, the number of days in the hospital, psychopathology (Brief Psychiatric Rating Scale [BPRS][16]), and global functioning (Global Assessment Scale [GAS][17]).

Additional outcome criteria such as gain in knowledge, changes in illness concept, families' expressed emotion status, satisfaction with treatment, and other subjective ratings were analyzed as well, but are reported elsewhere.[14,18–22]

Data were recorded at study entry, on discharge, and at 6, 12, 18, and 24 months after index discharge. Additionally, the course of the illness, the treatment, and the patients' compliance were documented at the monthly appointments and at all further appointments.

Data Analysis and Statistical Methods

We consider the study intervention to be more effective than standard care if rehospitalizations can be prevented or retarded within the 1-year and 2-year follow-up periods. Rehospitalization outcomes were analyzed using the survival model by Kaplan-Meier with log-rank statistics. In addition, the rehospitalization rates of the intervention and the control groups were computed for the 2 endpoints, and significance was tested with Fisher exact test. Fisher exact test was also employed for other comparisons between the study groups and for the comparisons between study patients and dropout patients involving dichotomous variables. Chi-square tests according to Pearson were used for group comparisons involving categorical variables with more than 2 alternative answers. The Mann-Whitney U test was used for analyzing compliance data. For continuous variables, equal variance t tests or nonparametric procedures (Wilcoxon test) for independent samples according to distributional characteristics were used.

The survival analysis refers to the total sample of study patients who started the outpatient treatment and who were not among the protocol violators (N = 194). For rehospitalization rates, the results of both the intent-to-treat analysis and the completer analysis are indicated. All other findings and post hoc analyses refer to the completers' data. The criterion for considering results to be statistically significant was set at $\alpha = .05$ (2-tailed). The statistical package used was SPSS for Windows, version 11.5 (SPSS Inc.; Chicago, Ill.).

RESULTS

Sample Characteristics

Table 2 lists the sociodemographic and clinical variables of the 236 study patients. There were no statistically significant differences in baseline sociodemographic and psychopathologic variables between the intervention and control groups.

It was possible to analyze data of 125 relatives; 60% of the study relatives were female with a mean age of 49 years. They were mostly the patients' parents (57%), approximately a quarter were partners (26%), and the rest represented adult children, siblings, or friends (17%).

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Table 2. Description of Study Patients

Characteristic	Intervention Group (N = 125)	Control Group (N = 111)	p	Total (N = 236)
Age, mean, y	33	34	.508	33
Female, %	51	57	.434	54
Marital status, %				
Never married	69	68	.889	68
Married	19	21	.746	20
Other	12	11	.841	12
Education, %				
Elementary/grade school	36	38	.682	37
High school	36	28	.165	32
Other	28	35	.446	31
Regular job, full/part time, %	36	35	.787	35
Diagnosis (ICD-9 no.), %				
295.1	10	8	.820	9
295.2	4	3	.726	3
295.3	55	66	.111	60
295.4	3	2	.687	3
295.6	1	3	.345	2
295.7	26	19	.214	23
297.2	1	0	1.000	0
Baseline clinical status				
GAS score, mean	49	49	.876	49
BPRS total score, mean	43	41	.240	42
Duration of illness, mean, y	7	7	.856	7
Previous hospitalizations, mean	3	4	.140	4
First admission, %	28	18	.110	24

Abbreviations: BPRS = Brief Psychiatric Rating Scale, GAS = Global Assessment Scale.

Figure 2. Survival Analysis for Rehospitalization During 24-Month Follow-Up Period (N = 194)

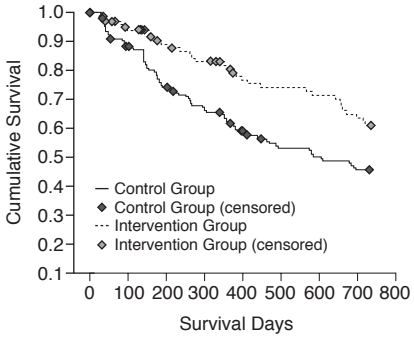

Table 3. Rehospitalization Rates at 12 and 24 Months, Differentiated According to the Number of Previous Psychotic Episodes

Psychotic Episodes	Rehospitalization Rates at 12 Months, % (N = 163) Intervention Group	Control Group	p	Rehospitalization Rates at 24 Months, % (N = 153) Intervention Group	Control Group	p
1	15	13	1.00	37	39	1.00
2–5	18	47	.006	34	65	.008
6 or more	38	36	1.00	63	58	1.00

About 60% of the relatives were living with the patient. About three quarters of the relatives (72%) had had no prior experience with offers for families such as self-help groups, family therapy, or relatives' groups.

Medication

We recommended antipsychotic relapse prevention treatment of at least 1 year to all study patients. As the treating doctors were responsible for the choice of the antipsychotic drug and the treatment was dependent on the special needs of the individual patients, 21 different antipsychotics were used in the study. More than half of the patients (63%) received oral medication in the 24-month follow-up period, and the others received either depot medication only or both depot and oral medication. There were no significant differences between the study groups on this point ($\chi^2 = 1.063$, df = 2, p = .588). The proportions of patients treated with atypical antipsychotics (clozapine, risperidone, zotepine) were also comparable in both groups (intervention group: 28%, control group: 29%; $\chi^2 = 1.096$, df = 2, p = .578).

Rehospitalization Outcomes

The main study criterion was rehospitalization during the first and second years after index discharge. The survival analysis considering the time up to the first rehospitalization showed a significant difference in favor of the intervention group within the first year (log rank = 6.91, df = 1, p = .009) and within 2 years (log rank = 5.93, df = 1, p = .015).

Figure 2 shows the results of the survival analysis for the 24-month period. The rehospitalization rate at the 12-month follow-up for the intervention group was 21% (N = 17) compared to 38% (N = 31) in the control group (total N = 163, p = .025). At the 24-month follow-up, 41% (N = 32) of the intervention group and 58% (N = 43) of the control group had to be rehospitalized (total N = 153, p = .036). In the intent-to-treat analyses with all dropouts assessed as rehospitalizations (worst-case scenario), the differences were not statistically significant (N = 194; 1-year follow-up: 37% vs. 45%, p = .301; 2-year follow-up: 54% vs. 66%, p = .107).

Post hoc analyses showed a significant correlation between the number of previous psychotic episodes and rehospitalizations. Data on previous psychotic episodes (according to clinical judgment) were collected at study entry, taking into account all episodes with and without medical treatment, inclusive of the index episode. The greater the number of episodes, the higher the probability for rehospitalization in the first year after index discharge (r = 0.178, N = 163, p = .023) and after 2 years (r = 0.187, N = 153, p = .022). Table 3 lists the rehospitalization rates for the intervention and the control groups differentiated into 3 classes according to the number of previous psy-

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Table 4. Number of Rehospitalizations and Number of Days in Hospital After 12 and 24 Months

	After 12 Months (N = 163)			After 24 Months (N = 153)		
Variable	Intervention Group Mean (SD)	Control Group Mean (SD)	p	Intervention Group Mean (SD)	Control Group Mean (SD)	p
No. of rehospitalizations	0.3 (0.7)	0.6 (0.8)	.086	0.6 (1.1)	1.1 (1.4)	.031
No. of days in hospital	17 (46.6)	30 (54.4)	.105	39 (90.4)	78 (127.2)	.034

chotic episodes. A clear effect of the psychoeducational groups was seen in the group of patients with 2 to 5 previous psychotic episodes.

Number of Rehospitalizations and Days in Hospital

It was possible to significantly ($p < .05$) reduce the number of rehospitalizations and the number of days in hospital between index discharge and the 24-month follow-up (Table 4). After 1 and 2 years, the patients in the control group had on the average nearly twice as many rehospitalizations as the patients of the intervention group. In addition, the number of days they had to spend in hospital was twice as great as in the intervention group.

Doses of Antipsychotics and Compliance

To obtain comparability, doses of antipsychotics were converted into chlorpromazine units (CPZ units; modified dose equivalence list by Jahn and Mussgay[23]). Three study patients had to be excluded from this evaluation because we had insufficient information as to their antipsychotic doses. Within the first year after index hospitalization, the study patients received a mean of 275 CPZ units per patient and day. There were no significant differences between the study groups ($F = 1.814$, $p = .180$). The results for the second year after index discharge are comparable.

Patients who were rehospitalized during the 24-month follow-up period had received significantly higher antipsychotic doses ($F = 5.933$, $p = .016$). Analyzing the data of the subgroup of patients who were rehospitalized in the first year after index discharge revealed a mean dose of 252 CPZ units per patient and day. Control patients took significantly fewer CPZ units in the outpatient period up to their first rehospitalization than the patients of the intervention group (205 vs. 334 CPZ/day; $t = 2.14$, $p = .038$).

The treating doctors assessed the patients' compliance at every appointment (see Table 1 for compliance rating scale). At discharge, the rates of patients with very good or good compliance were comparable in both study groups (Table 5). After 12 and 24 months, compliance rates were significantly lower in the control group ($p < .01$), whereas in the intervention group the rate of compliance remained at the same level.

The treating doctors' compliance ratings for the period up to the 12-month follow-up were computed to an average compliance value (mean compliance). In spite of the generally good compliance of all study patients, a significant difference between the study groups was found. For the patients attending psychoeducational groups, a mean compliance of 1.7 (SD = 0.6) was computed, and for the patients not attending psychoeducational groups, a mean compliance of 2.1 (SD = 0.8) was computed (Mann-Whitney U test: $Z = 2.96$, $p = .003$). There was a significant association ($r = 0.218$, $N = 163$, $p = .005$) between mean compliance and first-year rehospitalization, predominantly in the control group ($r = 0.229$, $N = 82$, $p = .038$). In the intervention group, the correlation did not attain significance ($r = 0.142$, $N = 81$, $p = .207$). Thus, the patients who did not attend psychoeducational groups were less compliant, and their noncompliance resulted in a higher rehospitalization rate.

Table 5. Patients With Very Good/Good Compliance at Discharge and After 12 and 24 Months

	Intervention Group		Control Group		
Timepoint	%	N/N	%	N/N	p
Very good/good compliance at discharge	85	69/81	81	64/79[a]	NS
Very good/good compliance after 12 months	80	65/81	58	46/79	< .01
Very good/good compliance after 24 months	80	58/73	55	34/62	< .01

[a]Total N = 79 because data were missing for 3 patients.
Abbreviation: NS = nonsignificant.

To analyze this association in more detail, we performed an intraindividual comparison of the compliance of patients who were admitted to a psychiatric hospital in the first year after index discharge. We compared their mean compliance 2 months before rehospitalization with their mean compliance during 2 other, randomly chosen months. For this calculation, we excluded 2 patients who did not have enough compliance ratings.

In the intervention group, the mean compliance before rehospitalization of 2.05 (SD = 0.9) corresponded to the mean compliance of 2.04 (SD = 1.1) found in the comparison period ($N = 17$; Wilcoxon test: $Z = 0.410$, $p = .682$). In the control group, however, the mean compliance before rehospitalization of 2.66 (SD = 1.2) was significantly worse than the compliance in the comparison period of 2.28 (SD = 0.9) ($N = 29$; Wilcoxon test: $Z = 2.059$, $p = .039$).

We conducted regular plasma drug level measurements to verify the doctors' compliance ratings. Four hundred

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thirty-four blood samples of 64 study patients who had received an oral medication (flupenthixol, haloperidol, clozapine, perazine) were analyzed. Plasma drug levels correlated significantly with the patients' indications about their antipsychotic doses ($r = 0.52$, $p < .001$). Analyzed plasma drug levels also corresponded to the compliance ratings in 99.5% of the cases. Two blood samples (0.04%) of 2 different patients (3%) showed plasma drug levels with the value "0," although medication was prescribed and compliance was assessed as "good" or "very good" at the time of the blood sample. As both patients belonged to the control group, this finding supports the conclusion that the patients not attending psychoeducational groups show worse compliance.

Psychopathology

To assess the psychopathology of the study patients, we used the BPRS. We found that the patients in the intervention group, who showed mean values comparable to those of the control group at study entry and at index discharge (study entry: 41 vs. 38, $N = 162$, $p = .105$; discharge: 30 vs. 31, $N = 159$, $p = .494$), achieved significantly better BPRS total scores than the patients of the control group after 12 months (26 vs. 32, $N = 149$, $p < .001$) and after 24 months (28 vs. 34, $N = 134$, $p < .01$).

We also found a significant effect regarding the global social functioning assessed with the GAS. At study entry and at discharge, mean GAS scores of the study groups did not differ in the intervention group and the control group (study entry: 49 vs. 51, $N = 162$, $p = .284$; discharge: 67 vs. 64, $N = 161$, $p = .099$), but at the following measurement points, significant differences between these groups were registered. After 12 months, the mean GAS score in the intervention group increased to 78 and in the control group to 68 ($N = 150$, $p < .001$). Twenty-four months after index discharge, values of 75 and 66, respectively, were computed ($N = 133$, $p < .01$).

We found a statistical association between compliance and BPRS scores and between compliance and GAS scores 12 and 24 months after index discharge. BPRS total scores were higher in noncompliant patients (12 months: $N = 153$, $r = 0.536$, $p < .001$; 24 months: $N = 132$, $r = 0.413$, $p < .001$), and GAS scores were higher in compliant patients (12 months: $N = 149$, $r = –0.348$, $p < .001$; 24 months: $N = 131$, $r = –0.383$, $p < .001$).

DISCUSSION

The Munich PIP-Study is one of the largest studies to examine the effects of psychoeducational interventions in schizophrenia. Our data suggest that psychoeducation has an important influence on patients' compliance and can reduce rehospitalization rates considerably. After 2 years, patients in the intervention group still showed advantages in regard to psychopathology and social adjustment.

The group of patients with 2 to 5 previous psychotic episodes received the greatest benefit. Patients in the intervention group with 6 or more episodes did not show a positive effect. It may be that a short intervention of 8 psychoeducational sessions is not sufficient to improve their outcome, particularly as measured with objective and easy-to-measure criteria such as rehospitalization. Perhaps psychoeducational programs adapted for this special target group with a longer duration, more redundancies, and simple lay models of illness as well as additional topics may lead to better results. Furthermore, it should be examined whether other outcome criteria besides relapse and rehospitalization rate, such as "days spent in hospitals," "treatment satisfaction," "psychosocial functioning," or "quality of life," show similar significant differences between patients with 2 to 5 or more previous psychotic episodes.

Our findings confirm the results of other studies on psychoeducation and psychoeducational family interventions in schizophrenia, which are summarized in several reviews and meta-analyses.[24–26] A specific feature of our study is that a relatively brief program of 8 psychoeducational sessions for patients and 8 sessions for their relatives was able to produce these effects. Bäuml et al.[18] demonstrated that these effects could be maintained even up to 7 years after index discharge. Rehospitalization rates increased in both groups (54% vs. 88%), but the difference between patients with and without psychoeducation was still significant. This corresponds to the long-term results of a psychoeducational family intervention[27] and a comprehensive psychosocial intervention package including psychoeducation, cognitive therapy, and a relatives' group.[28]

The question of how many psychoeducational sessions are necessary at the minimum to achieve significant effects has not yet been answered. Varying the numbers of standardized psychoeducational sessions and the impact this might have on rehospitalization rates have not been examined. Imparting information has generally led to significant knowledge gain. In a study by Macpherson et al.,[29] 3 sessions of education produced a higher knowledge gain than a single session and significantly increased insight, but did not improve compliance. Pitschel-Walz et al.[26] found in their meta-analysis that long-term psychoeducational family interventions with a treatment duration of 9 to 24 months appeared to be more successful in regard to relapse rates than short-term interventions with a treatment duration of 2 to 10 weeks, although the short-term interventions also showed a significant effect. In practice, the 8-session program of the Munich PIP-Study represents a good compromise between the somewhat more effective but costly long-term interventions and the brief educational programs, which are easy to set up, but less effective.

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Which therapeutic factors contribute most to this success of psychoeducation is still an open question. In their article on interventions to improve medication adherence in schizophrenia, Zygmunt et al.[30] concluded that psychoeducation and family interventions without accompanying behavioral components and supportive services are not likely to improve medication adherence. Even if all psychoeducational programs provide information as a core item, psychoeducation is certainly more than doctors merely imparting information about medication. In psychoeducational groups—at least in the program that was used in our study—therapists and participants work together closely on an illness concept in order to build up a basis for compliant behavior. Changes in illness concept (Illness Concept Scale)[31] through psychoeducation have already been demonstrated.[21,32] Psychoeducation aims at empowering patients to deal with their illness in a positive way. As experts on their own illness, they become capable of making an informed decision on their treatment and become responsible for changing their own behavior in order to support recovery and to prevent a relapse and rehospitalization. In this respect, psychoeducation acts as an emancipatory endeavor[12] that is made together with patients and their relatives as partners on equal terms in order to optimize coping with the illness and to enhance the patient's chance of living a "normal life." To fully evaluate these important psychosocial factors, further research is needed using outcome criteria that go beyond compliance and relapse, such as empowerment, coping strategies, and quality of life.

Possible limitations in evaluating the results of this study should be recognized. It was possible to recruit only a small percentage of all patients screened for the study; hence, our results are valid for only a portion of the population. Our study sample probably represents a group of patients who are in general a bit more cooperative than others, as seen by the fact that they are willing to take part in a scientific study; besides, they are at an advantage in having relatives who are willing to care for them. These selection effects apply to both study groups, though, and in spite of this selection process we were still able to find significant results between the intervention and control groups.

A further limitation of our study derives from the fact that it was performed in the early 1990s when typical antipsychotics still dominated the medical treatment of schizophrenia. With the arrival of several atypical antipsychotics and their lower rates of extrapyramidal effects and tardive dyskinesia, it was suggested that the improved side effect profile of these new drugs would lead to better compliance. Indeed, some studies were able to demonstrate that the use of atypical antipsychotics was associated with moderately higher compliance rates,[33–35] but others could find no significant differences in compliance between patients given conventional and atypical antipsychotics.[36–39] A comprehensive review studying the prevalence of and risk factors for medication nonadherence revealed that despite the benefits of the atypicals, 60% (median of 39 study reports) of all patients received "persistent" therapy, regardless of medication type.[40] The new agents reduce the risk of neurologic side effects, but on the other hand, other side effects such as weight gain,[41] sedation, postural hypotension, and sialorrhea may contribute to the high level of noncompliance in patients prescribed atypical antipsychotics. Although adverse effects play an important role in a patient's decision to discontinue antipsychotic treatment, there are various other factors that have an impact on adherence and noncompliance as well.[9,38,40,42] Thus, psychoeducation, as one form of compliance intervention providing educational, behavioral, and affective components, is a strategy that has not lost its importance with the increased use of atypical antipsychotics.

Until now, there was no ideal way to measure compliance. Using doctors' compliance ratings as a sole measure is often criticized because some research has shown that clinicians overestimate their patients' compliance.[43,44] In our study, we used the doctors' compliance ratings as one of the main outcome measures, but to correct for this objection we combined them with plasma drug level measurements. We found a good agreement between the doctors' impressions and the objective measurements. In contrast to those of other authors, the evaluation by Basan et al.,[45] using the same compliance rating, showed that the doctors' impression of the patients' future compliance was the best predictor for later treatment dropout. Nevertheless, it will still be necessary to use multiple sources in the future to assess compliance, such as concentration monitoring, pill counts, patients' self-reports, family reports, and clinicians' ratings.

One important possible source of bias should also be discussed: the study psychiatrists were blinded, but they might have learned of the study condition through seeing the patients regularly. This is a problem that often occurs in psychotherapy studies. The patients may spontaneously talk about their group experiences. Therefore, it cannot be ruled out that the blind was in some cases not maintained, and this may constitute a bias in favor of the intervention group. A comparable problem usually occurs in medication studies: in spite of blinding procedures, psychiatrists can often recognize the study medication from the side effect profile.

In scientific randomized studies, an intent-to-treat approach is usually required. To meet these standards, we used different evaluation strategies. The intent-to-treat analysis did not show that the rehospitalization rate was lower in patients of the intervention group, whereas the survival analysis and the completer analysis were both able to demonstrate the superiority of the intervention group. The additional result of the intent-to-treat analysis

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may place restrictions on our findings. On the other hand, we assessed all dropout patients as treatment failures for the intent-to-treat analysis, which may represent a worst-case scenario. In the intervention group, about twice as many patients dropped out in the first year after index hospitalization in comparison with the control group. This might explain the negative result of the intent-to-treat analysis. In their study, Basan et al.[45] found no significant differences between the relapse rate of the patients who dropped out (66%) and those who continued the long-term treatment (53%). Dropout is not always connected with a bad outcome, and therefore our intent-to-treat analysis may underestimate the effect of psychoeducation. Furthermore, for the practitioners working with persons suffering from schizophrenia, the most important question is how much patients can profit by taking part regularly in psychoeducational sessions. They want to know whether it is worthwhile to implement psychoeducational interventions and motivate patients and relatives to join these groups. In our study, the effects were greatest when both the patients and their relatives took part in the group sessions regularly, and the knowledge gain correlated with the number of sessions.[11,22] Our study clearly demonstrated that psychoeducation is an effective intervention for patients and relatives provided they make use of it.

As a consequence, psychoeducation should be routinely offered to all patients with schizophrenia and their families. In routine clinical practice, however, psychoeducation is not yet a matter of course. A recent survey that included all psychiatric hospitals in Germany, Austria, and Switzerland (N = 622) revealed that psychoeducation for patients with schizophrenia had been offered by 83% of the responding institutions in the year 2003,[46] but only about 21% of their patients and 2% of the relatives actually attended psychoeducational groups, and an average dropout rate of 25% was reported. Assuming furthermore that many of those hospitals who did not reply (about 46%) do not offer psychoeducation, it would thus still appear necessary to encourage psychiatric professionals to offer psychoeducation in order to inform patients and their families about schizophrenia, to support them with coping strategies, and to improve compliance with medication for relapse prevention. The psychoeducational approach presented here is particularly suitable for implementation and satisfies the standards for psychoeducation that were established by the German Expert Group on Psychoeducational Interventions for Schizophrenic Disorders.[47] Our experiences with the psychoeducational program and the positive results of the Munich PIP-Study have strongly influenced the development of these standards.

Further research must be done to answer the questions of how psychoeducation can be better disseminated in different psychiatric settings (inpatient, outpatient) and adapted for special target groups (actively psychotic patients, patients with many previous psychotic episodes, patients with double diagnoses, etc.), how patients and relatives can be better motivated to join psychoeducational group sessions, and which strategies may prevent dropouts.

Drug names: clozapine (Clozaril, FazaClo, and others), haloperidol (Haldol and others), risperidone (Risperdal).

REFERENCES

1. Schooler NR. Relapse and rehospitalization: comparing oral and depot antipsychotics. J Clin Psychiatry 2003;64(suppl 16):14–17
2. Kissling W, Leucht S. Results of treatment of schizophrenia: is the glass half full or half empty? Int Clin Psychopharmacol 1999;14(suppl 3): S11–S14
3. Jeffreys SE, Harvey CA, McNaught AS, et al. The Hampstead Schizophrenia Survey 1991, 1: prevalence and service use comparisons in an inner London health authority, 1986–1991. Br J Psychiatry 1997;170: 301–306
4. Weiden P, Glazer W. Assessment and treatment selection for "revolving door" inpatients with schizophrenia. Psychiatr Q 1997;68:377–392
5. Kissling W. Ideal and reality of neuroleptic relapse prevention. Br J Psychiatry Suppl 1992;18:133–139
6. Gaebel W, Pietzcker A. One-year outcome of schizophrenic patients: the interaction of chronicity and neuroleptic treatment. Pharmacopsychiatry 1985;18:235–239
7. Kane JM, Aguglia E, Altamura AC, et al. Guidelines for depot antipsychotic treatment in schizophrenia. European Neuropsychopharmacology Consensus Conference in Siena, Italy. Eur Neuropsychopharmacol 1998; 8:55–66
8. Rettenbacher MA, Hofer A, Eder U, et al. Compliance in schizophrenia: psychopathology, side effects, and patients' attitudes toward the illness and medication. J Clin Psychiatry 2004;65:1211–1218
9. Fenton WS, Blyler CR, Heinssen RK. Determinants of medication compliance in schizophrenia: empirical and clinical findings. Schizophr Bull 1997;23:637–651
10. Nosé M, Barbui C, Gray R, et al. Clinical interventions for treatment non-adherence in psychosis: meta-analysis. Br J Psychiatry 2003;183: 197–206
11. Bäuml J, Pitschel-Walz G, eds. Psychoedukation bei Schizophrenen Erkrankungen. Stuttgart, Germany: Schattauer; 2003
12. Wiedemann G, Klingberg S, Pitschel-Walz G, et al. Psychoeducational interventions in the treatment of patients with schizophrenic disorders. Nervenarzt 2003;74:789–808
13. CONSORT Group. CONSORT Flowchart. Available at: http://www.consort-statement.org/Downloads/flowchart.pdf. Accessibility verified Feb 20, 2006
14. Bäuml J, Pitschel-Walz G, Kissling W. Psychoedukative gruppen bei schizophrenen psychosen für patienten und angehörige. In: Stark A, ed. Verhaltenstherapeutische Ansätze im Umgang mit Schizophren Erkrankten. Tübingen, Germany: dgvt-Verlag; 1996:217–255
15. Bäuml J. Psychosen aus dem Schizophrenen Formenkreis. Ein Ratgeber für Patienten und Angehörige. Berlin, Germany: Springer; 1994
16. Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. Psychol Rep 1962;10:799–812
17. Endicott J, Spitzer RL, Fleiss JL, et al. The Global Assessment Scale: a procedure for measuring overall severity of psychiatric disturbance. Arch Gen Psychiatry 1976;33:766–771
18. Bäuml J, Pitschel-Walz G, Basan A, et al. Die auswirkungen des Protektiven potentials von angehörigen auf den langzeitverlauf schizophrener psychosen: ergebnisse der 7-Jahreskatamnese der Münchner PIP-Studie. In: Binder W, Bender W, eds. Die Dritte Dimension in der Psychiatrie-Angehörige, Betroffene und Professionelle auf Einem Gemeinsamen Weg. Cologne, Germany: Claus Richter Verlag; 2003:129–159
19. Bäuml J, Pitschel-Walz G, Bindl W, et al. Belastungen von angehörigen: vergleich von patienten mit und ohne psychoedukation [abstract]. Nervenarzt 2003;74(suppl 2):S50
20. Pitschel-Walz G, Boerner R, Mayer C, et al. Psychoeducational groups for schizophrenic patients and their relatives: influence on knowledge, attitudes and familial expressed emotions [abstract].

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Pharmacopsychiatry 1993:26
21. Pitschel-Walz G, Boerner R, Mayer C, et al. Effects of psychoeducational groups for schizophrenic patients and their relatives on knowledge, compliance and relapse [abstract]. Pharmacopsychiatry 1995:28
22. Pitschel-Walz G. Die Einbeziehung der Angehörigen in die Behandlung Schizophrener Patienten und ihr Einfluß auf den Krankheitsverlauf. Frankfurt am Main, Germany: Peter Lang; 1997
23. Jahn T, Mussgay L. Die statistische kontrolle möglicher medikamenteneinflüsse in experimentalpsychologischen schizophreniestudien: ein vorschlag zur berechnung von chlorpromazinäquivalenten. Z Klin Psychol 1989;18:257–267
24. Mojtabai R, Nicholson RA, Carpenter BN. Role of psychosocial treatments in management of schizophrenia: a meta-analytic review of controlled outcome studies. Schizophr Bull 1998;24:569–587
25. Pekkala E, Merinder L. Psychoeducation for schizophrenia. Cochrane Database Syst Rev 2002:CD002831
26. Pitschel-Walz G, Leucht S, Bäuml J, et al. The effect of family interventions on relapse and rehospitalization in schizophrenia: a meta-analysis. Schizophr Bull 2001;27:73–92
27. Tarrier N, Barrowclough C, Porceddu K, et al. The Salford Family Intervention Project: relapse rates of schizophrenia at five and eight years. Br J Psychiatry 1994;165:829–832
28. Hornung WP, Feldmann R, Klingberg S, et al. Long-term effects of a psychoeducational psychotherapeutic intervention for schizophrenic outpatients and their key-persons: results of a five-year follow-up. Eur Arch Psychiatry Clin Neurosci 1999;249:162–167
29. Macpherson R, Jerrom B, Hughes A. A controlled study of education about drug treatment in schizophrenia. Br J Psychiatry 1996;168: 709–717
30. Zygmunt A, Olfson M, Boyer CA, et al. Interventions to improve medication adherence in schizophrenia. Am J Psychiatry 2002;159: 1653–1664
31. Linden M, Nather J, Wilms HU. Zur definition, bedeutung und messung der krankheitskonzepte von patienten: die krankheitskonzeptskala (KK-Skala) für schizophrene patienten. Fortschr Neurol Psychiatr 1988;56:35–43
32. Hornung WP, Schonauer K, Feldmann R, et al. Medication-related attitudes of chronic schizophrenic patients: a follow-up study after psycho-educational intervention. Psychiatr Prax 1998;25:25–28
33. Dolder CR, Lacro JP, Dunn LB, et al. Antipsychotic medication adherence: is there a difference between typical and atypical agents? Am J Psychiatry 2002;159:103–108
34. Menzin J, Boulanger L, Friedman M, et al. Treatment adherence associated with conventional and atypical antipsychotics in a large state Medicaid program. Psychiatr Serv 2003;54:719–723
35 Rosenheck R, Chang S, Choe Y, et al. Medication continuation and compliance: a comparison of patients treated with clozapine and haloperidol. J Clin Psychiatry 2000;61:382–386
36. Cabeza IG, Amador MS, Lopez CA, et al. Subjective response to antipsychotics in schizophrenic patients: clinical implications and related factors. Schizophr Res 2000;41:349–355
37. Diaz E, Neuse E, Sullivan MC, et al. Adherence to conventional and atypical antipsychotics after hospital discharge. J Clin Psychiatry 2004;65:354–360
38. Freudenreich O, Cather C, Evins AE, et al. Attitudes of schizophrenia outpatients toward psychiatric medications: relationship to clinical variables and insight. J Clin Psychiatry 2004;65:1372–1376
39. Olfson M, Mechanic D, Hansell S, et al. Predicting medication noncompliance after hospital discharge among patients with schizophrenia. Psychiatr Serv 2000;51:216–222
40. Lacro JP, Dunn LB, Dolder CR, et al. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. J Clin Psychiatry 2002;63:892–909
41. Weiden PJ, Mackell JA, McDonnell DD. Obesity as a risk factor for antipsychotic non-compliance. Schizophr Res 2004;66:51–57
42. Perkins DO. Predictors of noncompliance in patients with schizophrenia. J Clin Psychiatry 2002;63:1121–1128
43. Lam YF, Velligan DI, DiCocco M, et al. Comparative assessment of antipsychotic adherence by concentration monitoring, pill count and self-report [poster]. Presented at the 9th biennial International Congress on Schizophrenia Research; March 29–April 2, 2003; Colorado Springs, Colo
44. Byerly M, Fisher R, Whatley K, et al. A comparison of electronic monitoring vs clinician rating of antipsychotic adherence in outpatients with schizophrenia. Psychiatry Res 2005;133:129–133
45. Basan A, Pitschel-Walz G, Bäuml J. Psychoedukative Gruppen bei schizophrenen patienten und anschließende ambulante langzeitbehandlung. Fortschr Neurol Psychiatr 2000;68:537–545
46. Rummel-Kluge C, Pitschel-Walz G, Bäuml J, et al. Psychoeducation in schizophrenia: results of a survey of all psychiatric institutions in Germany, Austria, and Switzerland. Schizophr Bull. In press
47. Bäuml J, Behrendt B, Bender M, et al. Arbeitsgruppe Psychoedukation. Konsensuspapier zu psychoedukativen interventionen bei schizophrenen erkrankungen. In: Bäuml J, Pitschel-Walz G, eds. Psychoedukation bei Schizophrenen Erkrankungen. Stuttgart, Germany: Schattauer; 2003: 1–35

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