

# A Prospective Study of Factors Influencing Adherence to a Continuous Neuroleptic Treatment Program in Schizophrenia Patients During 2 Years

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## Abstract

Dropout from prophylactic neuroleptic treatment is one major reason for relapse in schizophrenia patients. There is a lack of prospective studies on factors that predict medication adherence. We investigated factors suspected to predict dropout from continuous neuroleptic treatment in a 2-year prospective study involving 122 outpatients with a *DSM-III-R* diagnosis of schizophrenia. Forty-two (34.4%) were classified as patient-related dropouts. No significant difference between compliant patients and dropouts was found with regard to sociodemographic variables, except that compliant patients were significantly older. Also, no differences in psychopathology were seen at the beginning of treatment, but compliant patients had a longer duration of illness. Compliant patients had higher doses of neuroleptics in the initial stabilization phase and correspondingly showed more extrapyramidal signs. Physicians rated compliant patients from the beginning as more cooperative. These patients also showed significantly higher scores in positive treatment expectations. In a stepwise regression analysis, positive illness concepts, the global assessment of functioning (GAF), and the physicians' view of patients' cooperation predicted 19 percent of the variance. We concluded that the prediction of dropouts is insufficient and remains largely an unsolved problem. Future research should focus more on context factors in the search for clinically meaningful explanations of patient dropout from treatment.

**Keywords:** Compliance, long-term medication, schizophrenia, illness concepts, dropouts, neuroleptic drugs, health service research, medication adherence.

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## Introduction

Schizophrenic illnesses are typically long-term illnesses. Ninety percent of patients suffer successive relapses and finally never experience full recovery (Gaebel and Pietzcker 1984). Many studies showed that the rate of relapse in schizophrenic psychoses can be reduced from about 75 percent to 20 percent by neuroleptic medication (Kissling 1992). Therefore, it is internationally recommended that prophylactic treatment start immediately after the first episode and be continued for at least 2 years. Following the first relapse it should be continued for 5 or more years (Kissling 1991).

Despite this therapeutic recommendation, there is a high dropout rate from continuous medication. Noncompliance rates are reported to be between 10 percent and 60 percent (Johnson 1977; Axelrod and Wetzler 1989). Dropping out can involve taking medication on an irregular basis or stopping medication altogether. Irregularity in taking neuroleptics is of secondary importance, because the persistence of efficacy, or the therapeutic window of neuroleptics, is sufficient to prevent immediate relapse even if some tablets are not taken. In contrast, patient dropout from treatment is very significant, because in almost all cases it results in relapse (Forrest et al. 1964; Kane 1989; Verghese et al. 1989). Learning how to foster and ensure patient compliance is, therefore, a primary therapeutic task in the treatment of schizophrenia patients; knowledge of how to improve compliance could contribute as much to treatment as the introduction of neuroleptics itself did (Kissling 1994).

Haynes and colleagues (1979) and Fenton and colleagues (1997), in their reviews, come to the conclusion that compliance is a multidetermined phenomenon; they list up to 200 different factors said to influence patient

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compliance. There are four main groups of factors for schizophrenia patients:

1. sociodemographic variables (age, gender, occupation, level of education, and social status);
2. illness-related variables (type and severity of symptoms, illness insight, course of illness);
3. treatment-related variables (complexity of treatment, adverse medication effects, length of treatment); and
4. patient's general values and attitudes (illness attitudes).

These factors pertain mostly to long-term treatment of schizophrenia patients, which has to be discussed separately from the management of acute phases of schizophrenic psychoses, where, for instance, dysphoric reactions in the initial application of neuroleptic medication (van Putten 1974; van Putten et al. 1981, 1984) and paranoid delusions (Wilson and Enoch 1967) are seen as important problems.

**Sociodemographic Variables.** Most studies did not show a relation between compliance and sociodemographic variables such as gender (Lin et al. 1979; Buchanan 1992; Razali and Yahya 1995), age (Lin et al. 1979), income (Razali and Yahya 1995), or occupational status (Buchanan 1992). Only a few authors report a positive relationship to older age (Schwartz and Wang 1962; Linden 1987) or female gender (Linden 1987)

**Illness-Related Variables.** Schizophrenic illnesses are frequently accompanied by symptoms that inhibit the patient's ability to cooperate. Noncompliance is reported to be related to disturbances in social adaptation and interaction behavior (van Putten et al. 1976; Marder et al. 1983), to lack of insight into their condition (van Putten et al. 1976; Lin et al. 1979; Bartkó et al. 1988), and to a lack of feeling ill (Bartkó et al. 1988).

On admission, noncompliant patients achieved higher total scores on the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham 1962; Marder et al. 1983). McEvoy et al. (1984) emphasized that they showed more hallucinations, more thought disorders, more aggressive behavior, and more productive-psychotic symptoms (psychoticism). In addition, noncompliant patients also showed more delusions of grandeur (van Putten et al. 1976; Bartkó et al. 1988).

On the other hand, symptoms of depressivity and anxiety are reported as accompanying better compliance (van Putten et al. 1976; McEvoy et al. 1984; Bartkó et al. 1988). In contrast to these findings, Pan and Tantam (1989) observed significantly poorer compliance in cases of high depressivity.

**Treatment-Related Variables.** Treatment-related variables are also responsible for noncompliance. There is a

general notion that unwanted side effects have a negative influence on compliance (van Putten et al. 1984; Marder and May 1986). There are reports that some patients discontinue prescribed neuroleptic medicines because of side effects such as sexual dysfunction, sedation, or extrapyramidal symptoms (Hoffmann et al. 1974; del Campo et al. 1983). In most studies with schizophrenia patients, however, no significant difference in frequency or intensity of side effects was found in general (Linden 1987) or specifically—for instance, akathisia (McEvoy et al. 1984; Buchanan 1992; Fleischhacker et al. 1994) or parkinsonism (McEvoy et al. 1984; Buchanan 1992; Fleischhacker et al. 1994). However, it remains unclear whether in these studies the chosen instruments of measurement (Abnormal Involuntary Movement Scale [AIMS], Extrapyramidal Symptom Scale [EPS]) are sensitive enough to measure the subjective experience under neuroleptics.

This aspect is the focus of research on the quality of life in patients under neuroleptic therapy (Awad and Hogan 1994; Lindström 1994; Naber 1995). Lindström (1994) showed that reduced affective modulation, reduced intensity of feelings, and subjectively experienced thought inhibition are related to reduced compliance. This reduction in quality of life was not observed in patients under clozapine. Therefore, patients treated with clozapine are said to show better compliance (Naber 1995). Marder et al. (1983) also observed that compliant patients under neuroleptic medication report a higher feeling of subjective well-being.

Other authors report that the number of positive effects of neuroleptics are of greater significance for compliance than the unwanted effects of the medication (Adams and Howe 1993). Linden (1987) demonstrated that patients who could name more positive effects of their neuroleptic medication showed better compliance in spite of reporting more side effects. Falloon (1984) reported that schizophrenia patients showed better compliance as their knowledge of their own illness increased.

Finally, the complexity of the treatment carried out is seen as important. In essence, the number of errors in taking medication increases with the number of times the tablets must be taken per day (Gateley 1968; Gundert-Remy et al. 1977), whereas taking tablets once a day increases regularity of intake (Porter 1969; Mendels and Schless 1977). In this regard, Razali and Yahya (1995) observed significantly improved compliance in schizophrenia patients if the medication was to be taken only once or twice daily. In this context also depot medication seems to have a beneficial impact on compliance (Glazer and Kane 1992), and, by extension, the rate of relapse. Another new development with possibly positive effects on compliance is the introduction of new atypical neu-

roleptics, which some claim to be better tolerated and accepted by patients. Data on long-term effects in this respect are pending.

The physician-patient relationship is another aspect of treatment-related variables. Eisenthal and colleagues (1979) examined 130 patients in a psychiatry walk-in clinic and pointed out that a positive physician-patient relationship fosters patient compliance. The physician must understand the patient's wishes and allow him or her to participate in discussions about the therapy.

**Patients' General Values and Attitudes (Illness Attitudes).** Great importance is given in the literature to psychological variables. Compliant patients are described as individuals who are concerned about their health (Becker 1979; Apsler and Rothman 1984) and who expect or have personally experienced improvement of their condition as a result of the medication (van Putten 1974; Peterson et al. 1982; Ginath et al. 1983; Conrad 1985). The "Health Belief Model" summarizes the process by which the patient weighs the cost of treatment against benefits, assuming adherence to the treatment if the benefits are seen to be greater than the costs and risks (Becker and Maiman 1975; Becker et al. 1977; Becker 1985). Compliant patients consider the medication to be helpful in treating their illness and have a positive attitude toward medication (Marder and May 1986; Albus 1995; Razali and Yahya 1995). Conversely, noncompliant patients see no reason for taking medication because they may not consider themselves to be ill, or they may see taking the medication as the wrong way to solve their problems (Johnson and Freeman 1973; Johnson 1977; Soskis 1978; Marder et al. 1983, 1984). A biologically oriented model of illness (in which schizophrenia is viewed primarily as a metabolic disorder) also increases medication compliance, whereas a psychosocial model of illness (in which schizophrenia is seen as the consequence of problems an individual has with his or her environment) reduces compliance (Albus 1995). Illness and treatment attitudes can also be related to subjective experiences of drug effects, as described earlier. Under this perspective, Hogan and colleagues (1983) have published a medication attitude scale that was retrospectively correlated with medication compliance in schizophrenia patients.

This research argues for a close relationship between compliance and the evaluation of or attitudes toward the illness. Attitudes and illness concepts can be understood as the sum of opinions, interpretations, explanations, and predictions with regard to the state of an individual's health (Wilms et al. 1985). These attitudes are largely independent of psychopathology and should not be confused with psychopathological symptoms such as "lack of insight into the illness." Central

dimensions of illness concepts were summarized by Linden and colleagues (1988) in the Illness Concept Scale (ICS). It encompasses seven dimensions with particular relevance to compliance in schizophrenia treatment: trust in medication, trust in physician, idiosyncratic assumptions, guilt, negative expectations, chance control, and susceptibility.

Mayr and Soyka (1992) concluded in a review that factors influencing compliance in schizophrenia patients are sufficiently well-known and that the focus of scientific work should be therapeutic improvement of compliance. This, however, contradicts our knowledge of the literature. Assumptions about relationships between so-called causal factors and compliance come from cross-sectional or even retrospective studies; prospective studies are largely missing. Searching the literature through Medline for the period 1983 to 1997, we found only three studies that had been conducted prospectively (Bartkó et al. 1988; Frank and Gunderson 1990; Buchanan 1992) with either small numbers of patients or restricted assessment.

Bartkó and colleagues (1988) studied the differences in the psychopathology of 26 compliant and 32 noncompliant schizophrenia patients on discharge from the hospital. All patients were medicated by depot neuroleptics. They found that lack of feeling ill, lack of insight into the illness, grandiosity, and disturbance in social adjustment correlate with insufficient compliance. Buchanan (1992) found in a prospective investigation of 61 schizophrenia patients that a positive attitude toward medication and a generally optimistic outlook improve compliance. Frank and Gunderson (1990) showed in a 2-year course that patients with good initial treatment alliance are also cooperative in the further course of treatment. None of the studies says anything about the predictive power of any of these variables. Thus, in spite of the importance of this topic, there are virtually no studies trying to predict non-compliance and/or evaluating the predictive power of selected variables.

We therefore report here on the first prospective 2-year study with a sufficiently large patient sample, examining the influence of sociodemographic, treatment-related and illness-related variables, and illness concepts on the compliance of schizophrenia patients in long-term treatment with neuroleptics.

## Methods

The data reported here come from the Acute Neuroleptic Interval Medication (ANI) study. Details of the design and objectives of this study have been reported elsewhere (Pietzcker et al. 1993). The ANI study is a prospective multicenter study. Patients were recruited and treated at the university outpatient clinics and in psychiatric prac-

tices in Berlin, Düsseldorf, München, and Göttingen. Patients were included after a stabilization phase of at least 3 months after the most recent acute episode. All patients had to fulfill research diagnostic criteria (RDC) for schizophrenic psychosis (Spitzer et al. 1978). Patients were randomly assigned to three different treatment strategies with neuroleptics: continuous medication, early intervention treatment, and crisis intervention. In the following we will only refer to the 122 who had been assigned to continuous treatment. In these cases physicians explained to the patients from the outset that a continuous 2-year neuroleptic therapy was planned. The goal in this treatment arm was to give 100 mg or more of chlorpromazine equivalent per day. Selection of neuroleptics was done by the treating psychiatrist according to his clinical judgment. It was also possible to use oral or/and depot preparations. In the stabilization phase 24 patients were treated by depot neuroleptics only, 42 by oral medication only, and 56 by a combination.

Essential sociodemographic variables were recorded. Psychopathology was assessed by the BPRS (Overall and Gorham 1962) and AMDP (Association for Methodology and Documentation in Psychiatry) ratings (including lack of feeling for the illness, lack of insight into the illness, and rejection of treatment) (Guy and Ban 1982).

Any side effects of the neuroleptic medication were recorded on the AIMS (Guy 1976) and the EPS (Simpson et al. 1970). The dosage of neuroleptics prescribed in the stabilization and treatment phase was calculated in chlorpromazine equivalents. For self-evaluation, a visual analogue scale was used to record the patient's satisfaction with treatment, the physician-patient relationship, the extent of subjective suffering, and the richness of life in the preceding year (Aitken 1969). In addition, the psychiatrist estimated the patient's willingness to cooperate using a visual analogue scale.

Illness concepts were measured by the ICS (Linden et al. 1988). The ICS consists of seven dimensions with 29 items, each of which could be answered on a 5-step Likert type scale ranging from "do not agree at all" to "agree fully." Dimensions are as follows: (1) trust in medication (TM) reflects a patient's confidence that a particular medication can yield positive changes in his or her own health (external control attribution); (2) trust in physician (TP) refers to the patient's belief that the physician is helpful (external control attribution, significant others); (3) negative expectations (NE) measures assumptions that the treatment poses risks and burdens (sensitizer); (4) guilt (GT) measures the degree to which the patient feels responsible for the state of his or her health (internal control attribution); (5) idiosyncratic assumptions (IA) refers to dysfunctional concepts that may be part of the patient's illness concept (dysfunctional beliefs); (6) chance control

(CC) measures the degree to which the patient sees his or her health status as depending on chance (external control attribution, chance); (7) susceptibility (SC) describes the extent to which the patient sees himself or herself as threatened by the illness (susceptibility). The total ICS score was computed using the following equation:  $ICS = TP + TM - GT + SC - IA - NE + CC$ .

The 122 patients were subdivided into compliant patients and dropouts. Patients who went through the 2-year treatment period according to plan were classified as compliant. Patients who did not come to two consecutive prearranged appointments and did not respond to written requests to do so, or came but openly refused to continue the medication, were classified as dropouts.

To compare the groups, *t* tests or chi-square tests were used. Calculations were done with SPSS.

## Results

Of the 122 patients, 70 (57.4%) adhered to neuroleptic medication for 2 years. Forty-two (34.4%) were classified as patient-related dropouts (i.e., appointments were not kept or continuation of medication was refused). Of the 42, 34 dropped out during the first and 8 during the second year of treatment. Ten patients (8.2%) were classified as technical dropouts (i.e., a change of residence meant that they could no longer participate in the study). They were excluded from further analyses.

**Sociodemographic Variables.** There were no significant differences between compliant and noncompliant patients with regard to sex, family status, education level, occupational qualification, and occupational status (table 1). Compliant patients, however, were significantly older ( $p < 0.05$ ).

**Illness-Related Variables.** Patient groups did not differ in severity of illness at treatment outset (table 2). They were also similarly depressed and anxious. "Lack of insight into the illness" and "lack of feeling for the illness" (AMDP) were also similarly seen in dropouts and compliant patients. Both groups reportedly had a good relationship with their physicians. The rate of alcohol and drug addiction was also similar. Dropout patients had rejected treatment somewhat more frequently in the past. The duration of illness was significantly longer in schizophrenia patients adhering to treatment ( $p < 0.01$ ) (table 3). Additionally, compliant patients had a better social functional level (predictive power of GAF about 5%).

**Treatment-Related Variables.** Compliant patients received a significantly higher neuroleptic dosage in the run-in 3-month stabilization phase (average: 296.30 as

**Table 1. Sociodemographic variables**

	Compliant	Dropout	Chi square, <i>p</i> < 0.05	<i>t</i> value	<i>t</i> tail significance
Age, mean ± SD	35.71 ± 9.25	32.10 ± 9.21		2.01	0.047*
Family status ( <i>n</i> = 112)					
Single	43	30	NS		
Married	18	8			
Divorced/separated	9	4			
Sex ( <i>n</i> = 112)					
Female	39	22	NS		
Male	31	20			
Education ( <i>n</i> = 110)					
Junior high	30	13	NS		
High school	14	16			
College	24	13			
Occupational qualification ( <i>n</i> = 100)					
No diploma	17	14	NS		
Trade school	31	17			
Technical school	7	4			
University	7	3			
Occupational status ( <i>n</i> = 74)					
Housewife	10	6	NS		
Skilled worker	12	4			
Worker	11	4			
Civil servant	19	8			

Note.—SD = standard deviation.

\**p* < 0.05.

against 190.74 mg chlorpromazine equivalent; *p* < 0.05). Correspondingly more extrapyramidal symptoms were observed in these patients (*p* < 0.05).

The physician's judgment about the lack of willingness of the patient to cooperate in the therapeutic process was significantly higher in the group of dropouts (*p* < 0.001). None of the other treatment-related variables significantly differed (table 3). Whether the last hospitalization was initiated by the patient or the physician does not seem to be significant. Similarly, the mode of hospital admission, voluntary or involuntary, had no relation to the patient's compliance. The patient's evaluation of his or her last treatment is also not significantly related to compliance.

**Illness Concepts.** The ICS total score was significantly higher among compliant schizophrenia patients (*p* < 0.005) (table 4). Compliant patients trusted their physicians significantly more. They expected that physicians would be helpful in treatment (*p* < 0.05). Idiosyncratic assumptions were clearly more frequent among dropouts (*p* < 0.05). In addition, compliant patients showed a tendency to feel less responsible for their illness (less internal control attribu-

tion) and to have more trust in the effectiveness of the medication (more external control attribution).

**Regression Analysis.** We calculated a multivariate regression analysis to test the common explanatory power of the variables that showed significant differences in univariate testing between compliant patients and dropouts (table 5). Education, age, gender, BPRS total score, GAF, EPS, duration of illness (alternatively age at initial onset of illness), therapists' evaluation as to the extent of patients' cooperation, and the total ICS score were included in a stepwise multiple regression analysis. Only three variables could explain part of the variance. The therapists' evaluation as to patients' cooperativeness explained 8 percent of the variance, the GAF an additional 5 percent, and the total ICS score 4 percent of the variance. In absolute terms, 19 percent of the variance was explained by all variables together.

## Discussion

This study has several unique features and strengths. It is the largest prospective study on patient adherence to con-

**Table 2. Illness-related variables**

	Compliant	Dropout	t value	t tall significance	Chi square, p < 0.05
BPRS thought processes, mean ± SD	5.17 ± 2.28	4.71 ± 1.61	1.24	0.219	
BPRS anxiety/depression, mean ± SD	7.03 ± 2.78	7.05 ± 2.88	-0.03	0.972	
BPRS lack of energy, mean ± SD	8.47 ± 3.52	7.71 ± 2.94	1.22	0.224	
BPRS activation, mean ± SD	4.2 ± 1.58	4.0 ± 1.85	0.59	0.560	
BPRS hostility/mistrust, mean ± SD	3.93 ± 1.79	4.55 ± 1.93	-1.69	0.095	
BPRS total score, mean ± SD	28.80 ± 8.13	28.02 ± 6.79	0.54	0.588	
GAF, mean ± SD	62.43 ± 13.15	66.14 ± 11.02	-1.60	0.112	
SRS degree of subjective complaint, mean ± SD	1.83 ± 1.38	1.62 ± 1.31	0.80	0.424	
SRS fullness of life last year, mean ± SD	2.03 ± 0.76	2.07 ± 0.71	-0.30	0.764	
AMDP lack of feeling for the illness, mean ± SD	0.07 ± 0.31	0.14 ± 0.42	-0.96	0.340	
AMDP lack of insight into the illness, mean ± SD	0.21 ± 0.54	0.26 ± 0.63	-0.41	0.683	
AMDP rejection of treatment, mean ± SD	0.01 ± 0.12	0.19 ± 0.67	-1.69	0.099	
Alcohol dependency (n = 112)					
Yes	5	7			NS
No	64	35			
Medication dependency (n = 111)					
Yes	4	3			NS
No	66	39			

Note.—AMDP = Association for Methodology and Documentation in Psychiatry Rating Scale; BPRS = Brief Psychiatric Rating Scale; GAF = global assessment function; SD = standard deviation; SRS = Satisfaction Rating Scale.

tinuous neuroleptic treatment in schizophrenia patients using a thorough multilevel, multivariate assessment in the search for predictors of dropouts.

Prospective studies on compliance in the long-term treatment of schizophrenia patients are rare. Most reports are of limited value for a number of reasons: samples were relatively small, studies were retrospective or cross-sectional, the basis for subdivision into compliant and noncompliant patients was often based "only" on the impression of physicians or nursing staff, and selected items are limited. The point in time at which the investigations were carried out was frequently too early (i.e., immediately after admission to inpatient care, because subjective experience in a state of acute psychotic exacerbation is of subordinate importance for the long-term treatment of schizophrenia patients). Also, the few prospective studies (Bartkó et al. 1988; Buchanan 1992)

were begun immediately after discharge from the hospital, when many patients have not yet reached a stable psychopathological condition.

The present study took most of these points into consideration, and the number of patients was sufficiently large. This was a prospective study into which patients were admitted only after a 3-month stabilization period and in which noncompliance was defined by treatment dropout during the study itself. The assessment includes many items that have been discussed so far in connection with inadequate patient compliance.

The study also has some limitations. It refers in essence to treatment and not medication compliance. It may be that some patients who went through the whole treatment time still did not take their medication or that, on the other side, some of the dropouts are not primary but secondary noncompliant patients (i.e., that they

**Table 3. Treatment-related variables**

	Compliant	Dropout	t value	t tail significance	Chi square, p < 0.05
Dose of neuroleptic in stabilization phase, mean ± SD	296.30 ± 254.63	190.74 ± 126.95	2.92	0.004	
EPS, mean ± SD	1.51 ± 2.40	0.74 ± 1.39	2.06	0.042	
Number of admissions to psychiatric hospitals, mean ± SD	1.96 ± 0.46	1.92 ± 0.40	0.38	0.705	
SRS contact with physician, mean ± SD	21.43 ± 15.04	26.06 ± 15.56	-1.56	0.124	
SRS evaluation of lack of patient's cooperation, mean ± SD	0.81 ± 0.58	1.36 ± 0.88	-3.58	0.001	
Duration of illness (years), mean ± SD	8.14 ± 7.91	4.74 ± 5.01	2.79	0.006	
Mode of last hospital admission (n = 100)					
Voluntary	58	33			NS
Involuntary	4	5			
Initiator of last hospital admission (n = 49)					
Physician	12	2			NS
Patient	21	14			
Effect of last treatment (n = 64)					
Good	31	16			NS
Moderate	12	2			
Meager	1	2			
Success of treatment during last stationary admission (n = 111)					
Good	52	33			NS
Moderate	11	6			
Poor	7	2			

Note.—EPS = Extrapyramidal Symptom Scale; SD = standard deviation; SRS = Satisfaction Rating Scale.

**Table 4. Conception of illness**

	Compliant, mean ± SD	Dropout, mean ± SD	t value	t tail significance
TP	12.43 ± 2.77	11.14 ± 2.98	2.18	0.032
TM	14.24 ± 3.68	12.72 ± 4.61	1.73	0.088
GT	3.61 ± 2.34	4.78 ± 3.25	-1.94	0.057
IA	8.82 ± 2.48	10.03 ± 2.78	-2.21	0.031
SC	6.74 ± 2.83	7.11 ± 2.64	-0.66	0.509
NE	7.33 ± 3.93	8.24 ± 4.21	-1.09	0.278
CC	9.23 ± 4.51	8.22 ± 4.37	1.12	0.265
ICS total	70.87 ± 10.82	64.13 ± 11.73	2.90	0.005

Note.—CC = chance control; GT = guilt; IA = idiosyncratic assumptions; ICS = Illness Concept Scale; NE = negative expectations; SC = susceptibility; SD = standard deviation; TM = trust in medication; TP = trust in physician.

**Table 5. Stepwise multivariate regression analysis**

Step	Variable	$r^2$	$t$ value	$t$ significance
1	SRS evaluation of lack of patient's cooperation	0.086	2.94	0.004**
2	GAF	0.139	2.44	0.016*
3	ICS total	0.174	-2.11	0.038*
4-8	Education	0.190	0.25	0.804
	Gender		-0.13	0.896
	Duration of illness		-1.22	0.225
	EPS		-0.27	0.979
	BPRS total score		-0.15	0.920

Note.—BPRS = Brief Psychiatric Rating Scale; EPS = Extrapyramidal Symptom Scale; GAF = global assessment function; ICS = Illness Concept Scale; SRS = Satisfaction Rating Scale.

\* $p < 0.05$ ; \*\* $p < 0.001$ .

stopped treatment not because of noncompliance but because of a psychotic relapse). Also, in spite of the large number of variables there are still important areas that have not been addressed in this study (e.g., family support, psychoeducation, and type of housing [supervised vs. independent]) that surely also can influence patient compliance (Xiang et al. 1994; Lehman et al. 1998). A further restriction of the present study is that all patients who did not give written informed consent or who refused to participate in a study from the outset were excluded. This means that the study sample is biased toward cooperative patients so that all results regarding noncompliance must be seen as underestimates of the problem. Group differences would probably be more pronounced if initial "study refusers" could have been included as well.

The present study yielded a number of surprising results not reported previously. Some authors report no connection between compliance and sociodemographic variables (age, gender, education). In a retrospective investigation of 225 schizophrenia patients, Razali and Yahya (1995) report that after admission to the hospital, those treated for less than 5 years show better compliance. Similar to Linden (1988), our study showed that compliance improves with age ( $p < 0.05$ ). One interpretation could be that patients accumulate experience with their psychotic illness and that they learn that there is a connection between relapse and interruption of neuroleptic drug intake. We also found that dropouts have been ill for a shorter period of time. But data on the number of prior hospitalizations and compliance are inconclusive, as some authors found that frequent (Pan and Tantam 1989; Sellwood and Tarrier 1994) and others found that fewer hospitalizations (McEvoy et al. 1984) are related to non-compliance. Similar to Hogan and colleagues (1983), our

study did not find a connection between compliance and the number of hospitalizations.

Better education could mean better access to illness-related information. If compliance is related to knowledge, then education and occupational status should also influence compliance. However, similar to Buchanan (1992) and Lin et al. (1979), we found no significant difference in this respect.

Another important result is the influence of medication and side effects on compliance. While most authors assume that unwanted medication effects have no influence on compliance (Marder et al. 1983; McEvoy et al. 1984; Buchanan 1992), some reports do regard poorer compliance to be a result of burdensome side effects (Albus 1995). In contrast, we even found significantly more neuroleptic side effects and clearly higher neuroleptic dosages in the group of compliant patients during the run-in stabilization time of 3 months. This observation is in line with the findings of Linden (1987), who also saw more side effects in compliant patients. The explanation for this finding is that compliant patients take more medication and, therefore, have more side effects, while dropouts may generally have a greater irregularity of drug intake and, thus, a lower rate of drug exposure and fewer side effects. The explanation could also be that compliant patients, for psychological reasons, better accept the treatment as well as an increased number of side effects, whereas dropouts may be less tolerant of side effects and insist on reducing their medication dose early in the course of illness. Our data can only show the paradoxical phenomenon of fewer side effects in dropouts. Further research into this matter is needed.

We found no prognostic relation between psychopathological symptoms and compliance, either in the BPRS total score or in selected symptoms (disturbance of



formal thought processes; insight into illness; paranoid anxiety, etc.). In addition, compliant patients were not rated as being more severely ill and did not have better contact with their physicians. This finding contrasts with those of a number of authors who report a significant increase in psychopathological symptoms—such as delusions of grandeur, disturbance of formal thought processes, and lack of insight into illness—in noncompliant patients (van Putten et al. 1976; Lin et al. 1979; Bartkó et al. 1988).

Various authors conclude that schizophrenia patients have more difficulties implementing coherent actions because of disturbances in their formal thought processes, (Marder et al. 1983); that they are too locked into their productive-psychotic experience to take medication regularly (McEvoy et al. 1984); that they have a partial feeling of well-being despite being in a state of psychosis (van Putten et al. 1976; Bartkó et al. 1988); and that they are incapable of understanding that they are ill (lack of insight into their illness) (Lin et al. 1979; Bartkó et al. 1988). The difference between these reports and our findings can be explained by the fact that we studied the predictive power of psychopathology at the end of a stabilization phase. This does not contradict the fact that acute psychopathological states can interfere with the ability of patients to see the necessity of treatment and guarantee medication intake.

In the present study, the treating physicians generally rated their patients' ability and willingness to cooperate as good, which can be understood as a result of the patient selection process because physicians were more likely to select patients with good compliance. Still, noncompliant patients were recognized at an early state as being noncooperative. Eight percent of the variance in noncompliance can be predicted by initial physician rating. The treating physicians apparently successfully took into account all compliance-related variables in the behavior of their patients in the sense of a global clinical judgment. No other study reports on the validity of this "clinical global impression" rating, although many reports in the literature consider the physicians' impression as a criterion to operationalize and define compliance. In spite of being significant, this measure does not seem to have enough predictive power to be useful as a criterion variable.

Illness concepts have often been reported to have an important influence on the compliance of schizophrenia patients. Albus (1995) comes to the conclusion that a biological illness model and a positive attitude toward medication in general lead to better compliance. Moreover, Buchanan (1992) reports that the compliance of schizophrenia patients can be favorably influenced by a confident attitude toward medication effectiveness. This was confirmed by our study. Nevertheless, only 4 percent of

the variance can be explained by the patients' illness concepts. Patients are more compliant if they trust their physician's recommendations and the efficacy of their medication. This must be taken into account in the long-term treatment of compliance. As a consequence, Kemp and colleagues (1996) recommend cognitive-based psychotherapy to change attitudes and to improve compliance. They stress that it is necessary to achieve acceptance of the long-term medication by altering the patient's illness concept.

Although there is a long tradition of research into compliance and the great clinical importance of noncompliance with long-term neuroleptic medication is well accepted, there is a surprising paucity of prospective research. In summary, our results are disappointing. In spite of several significant results (for age, duration of illness, dosage of treatment, and illness-related attitudes, for instance), the overall predictive power of all the variables that have been thoroughly assessed in this study is, by and large, insufficient. The conclusion must be that future research should focus more on context factors in the search for clinically meaningful explanations of patient dropout from treatment.

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