Predictors of the Early 5-Year Course of Schizophrenia: A Path Analysis

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In this study, the effect of 19 possible predictor variables on 4 outcome variables was analyzed in young patients with recent-onset schizophrenia and related disorders (n = 64). Patients who participated in a 15-month intervention program were stratified into low and high parental expressed emotion and randomized over two intervention conditions: standard intervention and standard plus family intervention. Baseline variables were measured during the intervention. Outcome variables were measured over 5 years after discharge and comprised duration of psychotic episodes, living institutions for psychiatric patients, structural activities, and help from the family. From the 19 baseline variables, 6 had possible predictive value and were entered in a multivariate analysis. The resulting path model indicated that the score on the Strauss and Carpenter prognostic scale was predictive for duration of psychotic episodes. Diagnosis (schizophrenia vs. schizophrenia-related disorder) predicted help from the family. Age at first psychotic episode predicted living in institutions for psychiatric patients. Duration of psychotic episodes was associated with living in institutions for psychiatric patients and with help from the family but not with structural activities.

Key words: Course of illness/prognostic scale/predictors/longitudinal study/schizophrenia/path analysis

The course of schizophrenia is not uniform (Ciompi 1980). According to Kraepelin (1919), the course of “dementia praecox” is characterized by progressive deterioration. Bleuler (1911), who introduced the term schizophrenia, concluded that this deterioration occurs in only a subgroup of patients. Long-term studies showed 23 percent (Bleuler 1978) to 38 percent (Wing 1966) of first admitted patients to have favorable outcomes during the preneuroleptic era (Birchwood 1999). Later studies, during the neuroleptic era, showed 48.5 percent of the patients to have improved (Hegarty et al. 1994).

The heterogeneous outcome in schizophrenia implies that the search for predictors of the course of the illness has become an important goal, especially during early illness (Carpenter and Strauss 1991). Differentiated treatments become possible when robust predictors are identified. Predictors may also contribute to the development of theory regarding the pathogenesis of the illness.

The vulnerability-stress model of Zubin and Spring (1977) provided a framework for predictors and outcome in schizophrenia. This model assumes that schizophrenia occurs only in an individual vulnerable for psychosis and that environmental stressors are necessary to trigger a psychotic episode (Zubin et al. 1983). Expressed emotion (EE; Brown et al. 1972) in relatives is considered an environmental source of stress that can cause a psychotic episode (Zubin et al. 1983).

Although the vulnerability-stress model was elaborated by Nuechterlein et al. (1992a), it remained mainly hypothetical because most predictor studies tested monicausal hypotheses. For instance, a large body of research focused on EE as an environmental trigger of psychotic relapse (see Kavanagh 1992; Butzlaff and Hooley 1998 for reviews). A partial test of the vulnerability-stress model was done by Nuechterlein et al. (1992b). Parental EE, living with parents, illness onset age, psychotic relapse, and their interrelationships indicated that the association between EE and psychotic relapse is mediated by patient illness characteristics.

In the present study, we analyze the predictive effect of 19 variables regarding 4 outcome variables in young adults with recent-onset schizophrenia.

Predictor variables are clinical and sociodemographic data as measured during intervention and comprise risk and protective factors as found in earlier studies (Linszen et al. 1997). The Linszen et al. (1997) study, which began in 1986, investigated the treatment of young patients who came from low-EE and high-EE families. Half of the families received an additional family intervention, based on the behavioral family management approach of Falloon et al. (1984). The main goal of the family intervention was to lower high EE and thereby diminish the occurrence of psychotic relapse (Falloon et al. 1982). Although many studies have demonstrated the association between EE and psychotic relapse and the effect of family intervention on lowering high EE and reducing the occurrence of psychotic relapse, other studies failed to replicate this effect (see, for reviews, Kavanagh 1992; Mari and Streiner 1994; Pharoah et al. 2000). For this reason, variables other than EE have also been proposed as risk factors for psychotic relapse. These variables were reviewed by Linszen et al. (1997) and therefore included in our
intervention study (table 1): gender, education, prognostic scale of Strauss and Carpenter, premorbid adjustment scale of Goldstein, socioeconomic status, parental EE, one-parent household, age at first episode, type of illness onset, prior psychotic episodes, diagnosis, duration of untreated illness, psychopathology at end of inpatient intervention, and cannabis abuse during intervention. To these 14 possible predictors 4 variables were added.
in the present study because they appeared to be predictors of psychotic relapse in later studies and were assessed in the intervention study: prior admissions (Lay et al. 2000), ethnic group (McKenzie et al. 2001), living with parents before admission (Nuechterlein et al. 1992b), and compliance with antipsychotic medication (Robinson et al. 1999) during intervention. Intervention condition (standard intervention vs. standard plus family intervention) was included in the analysis because it had been shown to have an effect on living in institutions for psychiatric patients (Lenior et al. 2001).

Outcome variables were assessed with the Life Chart Schedule (WHO 1992) over a 5-year period after discharge from the 15-month intervention program. They comprise (table 1) duration of psychotic episodes, living in institutions for psychiatric patients, structural activities, and help from the family. We hypothesized that patients with a longer duration of psychotic episodes would live longer in institutions for psychiatric patients, would have shorter periods of structural activities, and would receive more help from their families than would patients with a shorter duration of psychotic symptoms (Lenior et al. 2001).

Method

Subjects. This followup study concerns the effect of a 15-month intervention program in the Adolescent Clinic of the Psychiatric Department of the Academic Medical Center in Amsterdam. The clinic is a unit from a university hospital and specializes in the treatment of young schizophrenia patients. The hospital is located in the Amsterdam suburbs. The majority of patients were referred to the clinic from inpatient and outpatient services in Amsterdam and rural areas around it.

Patients were eligible for the study if they (1) had an acute episode of schizophrenia, schizophreniform disorder, schizoaffective disorder, or other schizophreni-like psychotic disorder according to DSM–III–R criteria (APA 1987); (2) needed continuous antipsychotic medication; (3) were between 15 and 26 years old; (4) were living, or were in close contact (more than 35 hours face-to-face contact per week), with parents or other relatives. Patients with primary alcohol or drug dependence or with brief drug-related psychoses were excluded. Of the 164 patients referred from inpatient (44%) or outpatient (56%) services between 1986 and 1990, a group of 108 patients met these selection criteria. Of this group, 97 patients were admitted to the 3-month inpatient program, after informed consent was obtained from patients and parents.

Before the start of the controlled trial, at 3 months after admission, families were stratified into low and high EE and randomized over two conditions, standard intervention or standard plus family intervention, based on the behavioral family management approach of Falloon et al. (1984). The intervention program and the two intervention conditions have been described elsewhere (Linszen et al. 1996). Briefly, the program consisted of a 3-month inpatient phase and an outpatient phase of 12 months. In the family intervention, parents were supported and families received psychoeducation and training in communication skills and problem-solving techniques. All patients were put on a conventional antipsychotic medication regime intended to bring the acute or subchronic psychotic symptoms under control with minimization of side effects. Subsequently, this dosage served as maintenance medication (mean dosage of haloperidol equivalents during inpatient and outpatient intervention 3.5; standard deviation [SD] 1.1).

Of the 97 admitted patients, 21 patients dropped out of the intervention study before the controlled outpatient phase began. The patient group and comparisons between participants (n = 76) and nonparticipants (n = 21) have been described in detail elsewhere (Linszen et al. 1996). Briefly, the two groups did not differ significantly in demography, in medication, or in factors of clinical importance. However, participants scored better on the prognostic scale of Strauss and Carpenter (Kokes et al. 1977) than nonparticipants.

Of the 76 families that underwent the intervention program, 64 participated in the followup study, after written informed consent. Reasons for nonparticipation were refusal (n = 4), inability to be located (n = 2), suicide (n = 5), and fatal accident (n = 1). One suicide happened between discharge and 2.8 years after discharge, and four between 2.8 years and 7.9 years after discharge. Data were available in 51 cases from the patient and one or two parents, and in 11 cases from one or two parents without the patient. Two patients participated without their parent(s). The interviews took place 7.9 (range 6–10) years on average after discharge.

The mean age of the patients (44 men and 20 women) at admission was 20.7 (median 21; mode 22; range 16–26) years, whereas the mean age at the time of the followup interview was 30.4 (range 26–37) years. The mean duration of untreated illness before admission was 5.3 (median 2.0) months, and half of the patients (55%) had their first psychotic episode before admission (table 1). The onset of the illness was operationalized as the first occurrence of delusions, hallucinations, and/or formal thought disorders. Of the 25 percent of the patients who no longer lived with their parents before admission, 15 lived alone or with others, independently, and one lived in a psychiatric clinic. At discharge from the intervention program, the diagnoses (DSM–III–R; APA 1987) were schizophrenia 34 (53%), schizoaffective disorder 14 (22%), schizophreniform disorder 9 (14%), and other psychotic disorders (e.g., delusional disorder, atypical psychosis) 7 (11%).
Assessment of Predictor Variables. At the start of the intervention program, demographic data and illness characteristics as present before admission were assessed with the Psychiatric Symptoms and History Schedule (University of California 1984) with parents. They comprised (table 1) gender, education, prognostic scale of Strauss and Carpenter (Kokes et al. 1977), premorbid adjustment scale of Goldstein (Kokes et al. 1977), socioeconomic status (Hollingshead and Redlich 1958), ethnic group (Caucasian, not Caucasian), living with parents, one-parent household, age at first episode, type of illness onset (acute, subacute, chronic), prior psychotic episodes, prior admissions, and duration of untreated illness.

Shortly after admission, parental EE was assessed with the Camberwell Family Interview (Vaughn and Leff 1976). After being stratified into low and high parental EE, families were randomized over two intervention conditions: standard intervention and standard plus family intervention (Falloon et al. 1984). Diagnosis at discharge (DSM–III–R; APA 1987) was determined by examining all available data for the patient (Longitudinal Expert Assessment of Diagnosis procedure; Spitzer and Williams 1985). The psychopathology score was based on Brief Psychiatric Rating Scale (Lukoff et al. 1986) assessments of the previous 2 months of inpatient treatment (Breier et al. 1991). Cannabis abuse as present before admission was indexed as reported by patients and parents or by former treatment summaries and during intervention by patients and treatment staff. During the 15-month intervention program, the treating psychiatrist indexed medication compliance monthly. Data were rated on a 4-point scale, ranging from 1 (0%–24% compliance) to 4 (75%–100% compliance, including depot). As a possible predictor, the mean was calculated.

For details regarding assessments during intervention, see Linszen et al. (1994, 1997).

Assessment of Followup Data. Data over 5 years were assessed with the Life Chart Schedule (LCS; WHO 1992), which elicits data about symptoms, treatment, and social conditions (e.g., work, study, living arrangement) during a given period. Susser et al. (2000) showed that the LCS yields reliable ratings of the long-term course of schizophrenia when assessed by trained raters. Inconsistencies regarding symptoms and treatment (n = 3) were cross-checked with current therapists.

At the start of the interview, respondents (patients and/or parents) were asked to identify the points in time at which changes (e.g., in symptoms, in treatment) had occurred since discharge, and the data were plotted onto a time line. During the rest of the interview, this information served as a memory aid for responses to the more detailed questions of the structured interview.

In 1992, a first followup study that also included the LCS was carried out. At that time the followup period for the successively admitted and discharged patients differed (mean 34; range 17–55 months; Lenior et al. 1998). At the second followup, held in 1997–1998, the data were completed up to and including 5 years after discharge. If the patient and/or parent(s) had participated in 1992, which was the case for all except one patient, the data of that interview were first examined and completed for the 5-year period.

The course of the illness over 5 years was divided into psychotic and nonpsychotic episodes. A psychotic episode was characterized by clearly reported positive symptoms—that is, delusions, hallucinations, and/or formal thought disorders (Nuechterlein et al. 1986), with or without hospitalization. A nonpsychotic episode was a period without positive symptoms, with or without residual symptoms and/or negative symptoms. A nonpsychotic episode had to last at least 30 days (Wiersma et al. 1998). When a psychotic episode was not discontinued by a remission period of at least 30 days, the patient was considered to have chronic positive symptoms (60 months). The LCS data (including the written reports by the interviewers) were reviewed for psychotic episodes, rated by one of the authors (D.H.L.), and rated again by a psychiatrist who had not been involved with the patients. Of the 73 patients who completed the followup study (of whom 64 had been randomized over the two intervention conditions), there was disagreement for 6 (8%) of the patients, concerning clinical status (no psychotic episode, one or more psychotic episodes, chronic). For 16 (22%) patients, the number of months with psychotic symptoms differed (mean absolute difference 6.7; SD 6.8 months). A consensus between both raters was reached for the 22 patients about whom there was disagreement.

Regarding social functioning over the 5-year period, three composite scores were calculated from the LCS: (1) living in institutions for psychiatric patients (months in mental hospitals and/or sheltered homes); (2) structural activities (months of full-time job, part-time job, volunteer work, full-time study, and/or housekeeping); and (3) help from the family (sum score of help with activities of daily living, accompaniment to outpatient services, checks on intake of medication, and management of care). The four items regarding help from the family were scored as follows: 1, not at all; 2, for part of period; and 3, for majority of period.

Statistical Analysis. To test the predictive effect of 19 baseline variables regarding the 4 outcome variables, path analysis (Amos; Arbuckle and Wothke 1999) was used to build a path model in an exploratory way, using maximum likelihood estimation. Path analysis was chosen because duration of psychotic episodes was associated with the other 3 outcome variables (Lenior et al. 2001) and those associations cannot be seen in separate regression analyses. (With multiple regression analysis, several predictor or independent variables are regressed on only one dependent or outcome variable.) As in
multiple regression analysis, each association between variables is adjusted for other associations between variables in the model. For reasons of parsimony (Loehlin 1998), we first assessed the bivariate associations between the 19 possible predictor variables and the 4 outcome variables by Mann-Whitney tests (U M-W) for dichotomous predictor variables and by Spearman’s rank correlations (p) for continuous predictor variables. Second, the predictor variables that were significantly associated with one or more of the outcome variables were added, without arrows, to an initial path model, which means that the associations with other variables were fixed at zero. In the initial path model, duration of psychotic episodes was assumed to predict living in institutions for psychiatric patients, structural activities, and help from the family (no associations were assumed among living in institutions for psychiatric patients, structural activities, and help from the family). Third, parameters were freed (i.e., arrows were added) one at a time, as indicated by the largest modification index (MI; Sörbom 1989) calculated by the program. However, correlations between error terms as proposed by MI were not added to the model, because doing so was criticized by MacCallum et al. (1992). Finally, variables that were not associated with any other variable in the model were removed. The overall fit of the final model was assessed by $\chi^2$ and by root mean square error of approximation (RMSEA).1

As some of the continuous variables had bimodal distributions (months of untreated illness, duration of psychotic episodes, and living in institutions for psychiatric patients), the bivariate associations were tested using nonparametric tests. For path analyses these variables were normalized (Crocker and Algina 1986). Compliance with antipsychotic medication was dichotomized, as 43 of the patients were 100 percent compliant during intervention. Furthermore, in path diagrams the relationships are assumed to be linear. Because for some variables the relationships were nonlinear, several transformations were tried to linearize the relationships. The natural logarithm yielded the best solution, although the association between duration of psychotic episodes and living in institutions for psychiatric patients was not strictly linear. However, as stated by Loehlin (1998), mild departures from linearity may reasonably be approximated by linear relationships.

Results

Comparisons between participating patients ($n = 64$) and nonparticipants ($n = 12$) showed no significant differences in demography and medication, and in variables of clinical importance, except that all nonparticipating families were of low socioeconomic status (data not shown). No significant differences in baseline data between the two intervention conditions (33 from the standard condition; 31 from the standard plus family condition) were found (data not shown).

For the 64 patients who completed the followup study, the scores on the baseline data and outcome are shown in table 1. During the 5-year period, a quarter of the patients ($n = 16$) had no psychotic episode, half of them ($n = 34$) had one or more psychotic episodes, and almost a quarter ($n = 14$) had chronic positive symptoms (60 months). Eighteen patients (28%) lived the total 5-year period within the community, and two patients (3%) lived the whole period in institutions for psychiatric patients. Eight patients (13%) had no structural activities in the 5-year period, whereas five (8%) had structural activities for the whole followup period. For the 29 patients who had held a paid job (full-time and/or part-time) for some of the 5-year period (mean 9.9; SD 16.7 months), the level of the job was in 65.5 percent of the cases lower than the level of education.

In table 2 the associations between possible predictors and outcome variables are shown. A longer duration of psychotic episodes during followup was associated with a diagnosis of schizophrenia at discharge, with lower scores on the Strauss and Carpenter prognostic scale at the start of the intervention program, and with higher psychopathology scores (Breier et al. 1991) during the last 2 months of the inpatient phase of the intervention. Patients who received the additional family intervention, who were of lower socioeconomic status, and/or who were older when they had their first psychotic episode spent fewer months in institutions for psychiatric patients than did the other patients. Structural activities were not associated with any of the predictor variables. Finally, patients with a diagnosis of schizophrenia received more help from their families than did patients with schizophrenia-related disorders.

Intervention condition had no effect on the course of the illness in terms of duration of psychotic episodes. For patients whose families received the additional family intervention, the number of months spent in institutions for psychiatric patients was on average 10 months less than for patients from the standard condition. For structural activities and help from the family, no significant differences between the two intervention conditions were found. Parental EE did not predict the 5-year outcome,
except for a trend regarding duration of psychotic episodes: patients of high-EE families on average had 4 more months of psychotic episodes than patients of low-EE families.

The predictor variables that had a significant association with one or more of the outcome variables (table 2) were added, without arrows, to an initial model in which the number of months of psychotic episodes was assumed to predict living in institutions for psychiatric patients, structural activities, and help from the family. One at a time the following arrows were entered (parameters freed): correlation between diagnosis and prognostic scale (MI 17.43), age at first episode to living in institutions for psychiatric patients (MI 6.48), prognostic scale to duration of psychotic episodes (MI 5.06), and diagnosis to help from the family (MI 4.37). The other variables that had a significant association with one or more of the outcome variables (table 2: intervention condition, socioeconomic status, and psychopathology score) were removed from the model.

The resulting path model did not fit the data very well ($\chi^2 = 16.83; df = 14; p = 0.27; \text{RMSEA} = 0.06$). To obtain a better fit, correlations between the three predictor variables were added (as in multiple regression, correlations between predictor or independent variables are included implicitly). This model (figure 1) fits the data better ($\chi^2 = 12.89; df = 12; p = 0.38; \text{RMSEA} = 0.03$).

Figure 1 shows that the score on the prognostic scale as measured at intake is associated with diagnosis:
patients who had a diagnosis of schizophrenia at discharge had lower scores on the prognostic scale than patients with schizophrenia-related disorders. The score on the prognostic scale appears to be predictive for duration of psychotic episodes in a direct way: patients with higher scores on the prognostic scale had fewer months of psychotic episodes during followup than patients with lower scores. The indirect effects of the score on the prognostic scale are weak: on help from the family ($\beta = -0.28 \times 0.34 = -0.10$), on structural activities ($\beta = -0.28 \times -0.21 = 0.06$), and on living in institutions for psychiatric patients ($\beta = -0.28 \times 0.36 = -0.10$).

Diagnostic grouping is predictive for help from the family: during followup, patients with a diagnosis of schizophrenia received more help from their families than patients with schizophrenia-related disorders. Finally, age at first episode has predictive value for living in institutions for psychiatric patients: patients who were younger at their first episode spent more months in institutions for psychiatric patients than patients who were older.

The explained variances for the four outcome variables are low: duration of psychotic episodes 8 percent, living in institutions for psychiatric patients 24 percent, structural activities 4 percent, and help from the family 21 percent.

Discussion

The Strauss and Carpenter prognostic scale (Kokes et al. 1977) appeared to have the best predictive value regarding psychotic episodes during 5 years of followup, whereas indirectly, the score on this scale was only weakly predictive for the other outcome variables. This scale regards several areas of functioning: employment, social class, relationships, family history of psychiatric hospitalization, age of onset, and symptomatology. It has been reported (Möller et al. 1986; Jonsson and Nyman 1991) that single variables have limited prognostic value and often yield contradictory results but that combinations of variables predict outcome better. Although the predictive value of the Strauss and Carpenter scale was demonstrated in the 1980s (Stephens et al. 1980; Möller et al. 1986; Gaebel and Pietzcker 1987; Mackert and Flechtner 1989), the scale has not often been used lately. More recently, Händel et al. (1996) found the subscale “social functioning” from the Strauss and Carpenter scale to be predictive for course of illness and rehospitalization. In the aforementioned studies, patients were considerably older (mean age at admission from 28.8 years [Händel et al. 1996] to 35.4 years [Stephens et al. 1980]) than in our study (mean age at admission 20.7 years). The predictive value of the Strauss and Carpenter prognostic scale in this sample of young patients is especially important, because a poor course can be predicted in the early phase of the illness. This may eventually lead to differentiated interventions, based on the prognostic score, to improve a deteriorating course.

Although diagnosis (schizophrenia vs. schizophrenia-related disorder) as classified at discharge from the intervention was related to psychotic episodes in bivariate analysis, as was expected, it turned out to be not predictive for psychotic episodes in multivariate analysis. However, diagnosis was strongly related to the score on the prognostic scale, indicating that both diagnosis and the score on the prognostic scale reflect the severity of the illness. Furthermore, diagnosis was predictive for help from the family during followup. This may imply that parents recognize the more severe course of the illness in their offspring with a diagnosis of schizophrenia and therefore provide help in activities of daily living, as well as in matters of followup treatment.

A relationship between age at first episode and rehospitalization was found in previous studies (Borgå et al. 1991; Eaton et al. 1992; Haro et al. 1994). Haro et al. (1994) and Borgå et al. (1991) concluded that young age of onset is a strong predictor of chronicity and poor outcome. We found the negative relationship between age at first episode and living in institutions for psychiatric patients to be relatively independent of the course of the illness, expressed as months of psychotic episodes. The interpretation of this effect is not clear-cut. It may be that psychiatric services are aware of the bad prognosis for patients with an early onset of the illness and are more inclined to admit these patients than they are to admit patients with a later onset. It may also be that these services admit younger patients more frequently than older patients, an effect found by Tsoi and Wong (1991). Post hoc analysis of our data indicated that living in institutions for psychiatric patients was associated with

Table 1. Effects ($\beta$) of predictors on outcome during 5 years of followup: Results of path analysis ($n = 64$).

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<td>Diagnosis</td>
<td>$-0.34^{**}$</td>
<td>$0.26^{*}$</td>
<td>$-0.36^{**}$</td>
<td>$-0.53^{***}$</td>
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<td>Age at First Episode</td>
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<td>$-0.30^{**}$</td>
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<td>Help from the Family</td>
<td>$0.28^{**}$</td>
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<td>$-0.21$</td>
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<td>Living in Inst.</td>
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<td>Duration of Ps. Ep.</td>
<td>$-0.28^{*}$</td>
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<td>Social functioning</td>
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* $P<0.05$; **$P<0.01$; ***$P<0.001$ (two-tailed test)
age at admission at the intervention study ($\rho = -0.35; p = 0.004$). Thus, patients who were younger at admission, and consequently were younger during the followup period, spent more months in institutions for psychiatric patients than patients who were older. Another possibility is that younger patients are more often urged by their parents or the educational system to seek help from psychiatric services than are older patients. We found no relationship between age at first episode and management of care by parents ($\rho = -0.19; p = 0.14$). However, the association between age at admission and management of care was significant ($\rho = -0.29; p = 0.02$), indicating that younger patients received more help from their parents regarding treatment than did older patients.

No effect of the intervention condition was found in the multivariate analysis. Adding family intervention to the comprehensive standard intervention also had no effect on relapse during the 12-month outpatient phase of the intervention (Linszen et al. 1996). It was argued that the fact that there were family sessions during the 3-month inpatient phase of the intervention for both intervention conditions, and the fact that the family intervention began after patients were remitted or stabilized, prevented a differential intervention effect. It was also argued that, given the overall low relapse rate during the outpatient phase, the comprehensive standard intervention was effective in its own right. In a review study this supposition was confirmed by Pitschel-Walz et al. (2001). In the bivariate analysis the family intervention appeared to be effective in diminishing institutional care (Lenior et al. 2001). This effect was not found in the multivariate analysis, meaning that age at first psychotic episode was a stronger predictor for living in institutions for psychiatric patients than was intervention condition.

Parental EE as assessed at the beginning of the intervention was, among six possible predictors, associated with relapse during the 12-month outpatient phase of the intervention when narrow criteria for relapse were used (Linszen et al. 1997). In the 5-year followup period, EE was only weakly related to duration of psychotic episodes and did not emerge as an outcome predictor in the multivariate analysis. Most EE studies analyzed the predictive value of EE over relative short periods, generally 9 to 24 months (Kavanagh 1992). Only two studies evaluated EE and relapse over longer periods (i.e., 5 years). McCreadie et al. (1993) found no significant difference in relapse rate between patients from consistently high, fluctuating, and consistently low EE families. For the fluctuating-EE families, the relapse rates for patients from initially high EE and low EE families were not reported. However, when we recalculated the statistics for the relapse rates of patients from consistently high (4/7) and consistently low EE families (5/11), no significant difference was found ($\chi^2 = 0.23; df = 1; p = 0.63$). Huguelet et al. (1995) compared the annual relapse rates in patients from initially high and low EE families and found an association between EE and relapse during the third year; hence, it is unclear whether EE was predictive for the 5-year course. Given these results and the results of our study, it may be concluded that EE in relatives may not be predictive for psychotic episodes when studied over an extended period. Lenior et al. (2002) demonstrated that EE is not a stable characteristic in parents and may be a response to the course of the illness in their children.

The design of our study allowed us to fill in the vulnerability-stress model as proposed by Nuechterlein et al. (1992a) only partially, because we did not assess all factors. For instance, biological factors, the personal vulnerability factors, were not considered in our study. The personal protectors “coping and self-efficacy” and antipsychotic medication (during followup) as well as some environmental protectors and stressors were also not present, because these factors were not measured with the LCS. Furthermore, data on comorbidity and response to antipsychotic medication were not measured during intervention, and data about medication and other treatments during followup were missing. Although our model is far from complete, some remarkable differences from the original vulnerability-stress model emerged. First, the two variables diagnosis and age at first episode had an effect on the outcome variables that was relatively independent of the course of the illness (duration of psychotic episodes). Second, structural activities were not significantly associated with duration of psychotic episodes in the multivariate path analysis. The bivariate correlation between these two variables was significant, indicating that patients with more months of psychotic episodes had fewer months of structural activities (Lenior et al. 2001). However, this effect did not emerge in the multivariate analysis. The weak association between symptomatic outcome and work was reported earlier (Nuechterlein and Dawson 1984).

In the present model the associations between duration of psychotic episodes and the other outcome variables (see Kokes et al. 1977; Nuechterlein and Dawson 1984; Gaebel and Pietzcker 1987; Carpenter and Strauss 1991), and between baseline data and outcome variables (see Kokes et al. 1977; Jonsson and Nyman 1991; Wiersma et al. 1998; Lay et al. 2000), were of moderate magnitude, resulting in low explained variances. This implies that more variables, maybe personal vulnerability variables and environmental stressors and protectors as well as response to medication, are necessary to explain outcome in schizophrenia.

A major limitation of the present study is that followup data were collected retrospectively. Retrospective collection was necessary because after completion of the intervention program, there was no further contact between treatment staff and patients. The fact that the data were collected in two waves, in 1992 and in 1997/1998, covers this problem only partially. Furthermore, not for all...
families the patient and parent(s) participated in the study. This could have influenced the data. However, during the course of the data collection it appeared that the narratives of patients and parents did not differ in most cases. In only three cases were there inconsistencies that had to be cross-checked with therapists. This gave us confidence that parents could accurately report on their offspring.

We wanted to analyze the predictor variables in relation to the four outcome variables in an integrative way for two reasons: (1) to analyze the relative effects of the variables in the model (i.e., holding the effects of other variables in the model constant), and (2) to sustain the associations between the outcome variables. Therefore, path analysis was chosen. The process of adding parameters to the model was completely data driven and thus susceptible to capitalization of chance (MacCallum et al. 1992). This, and the fact that the sample size was relatively small, implies that the model may not be generalizable to other samples or to the population of schizophrenia patients as a whole.

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