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ORIGINAL PAPER

The Munich 15-year follow-up study (MUFUSSAD) on first-hospitalized patients with schizophrenic or affective disorders: comparison of psychopathological and psychosocial course and outcome and prediction of chronicity

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Abstract Given the limited explanatory power of the available neurobiological findings, results of long-term follow-up studies should still be considered as one criterion among others in the development of psychiatric classification systems regarding schizophrenia and affective disorders. A total of 323 first hospitalized inpatients of the Psychiatric Department of the University Munich were recruited at index time and followed up after 15 years. The full follow-up evaluation including several standardized assessment procedures (AMDP, PANSS, SANS, DAS, GAS) could be performed in 197 patients. The patients originally diagnosed according to ICD-9 were re-diagnosed according to ICD-10 and DSM-IV, using SCID among others. Schizophrenic patients had a much poorer outcome than affective or schizoaffective patients in terms of negative syndrome, deficit syndrome, psychosocial impairments and GAS results, and a higher prevalence of a chronic course. The logistic regression analyses performed to find optimized predictor combinations for the prognosis of a chronic course found, for example, the total Strauss–Carpenter Scale score, male gender and several other psychopathological syndromes to be relevant predictors. The findings reflect some long-term related validity for the differentiation between schizophrenia and affective disorders. The Strauss–Carpenter Scale, male gender as well as several psychopathological syndromes are the most relevant predictors for chronicity.

Keywords Schizophrenia · Affective disorder · Classification · Prediction

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Introduction

There is a long and rich tradition of long-term follow-up research especially on schizophrenic patients, and, to a lesser degree, also on patients with affective disorders. Examples are the catamnestic study on schizophrenia by M. Bleuler, the catamnestic study on schizophrenia by G. Huber and the follow-up study on unipolar/bipolar disorders by J. Angst, to mention only a few master pieces of catamnestic works [3, 7, 44]. Only a few follow-up studies investigated in a comparative way the long-term course of patients with schizophrenic and affective disorders to investigate long-term outcome differences of patients with schizophrenic and patients with affective disorders. Most were retrospective follow-up studies [64, 65, 67, 99] or, if prospective, they referred to relatively small sample sizes or relatively short follow-up durations [74, 77]. In this respect, the study by Harrow et al. [36, 37] appears to be the only exception. All the comparative studies found a poorer outcome of schizophrenic patients compared to patients with affective disorders.

In addition to these very few comparative long-term follow-up studies, several follow-up studies focusing only on schizophrenia have been performed during the 2–3 decades, most of them using a prospective design. These studies have contributed to the increase of knowledge on the course and outcome of schizophrenia in a significant way, underlining the heterogeneity of outcome and thus indirectly contributing to the understanding of potential outcome differences between schizophrenia and affective disorders [6, 10, 13, 14, 22, 24, 25, 34, 41, 58, 83, 90, 92, 93, 98, 102].

Studies focussing only on unipolar or bipolar affective disorders indicate that there is much more heterogeneity in the outcome of affective disorders than traditionally believed, including also poor outcome to a certain percentage, especially in patients with psychotic symptoms or even mood incongruent psychotic symptoms [15, 16, 26, 35, 48–52, 55, 91, 95].

Particularly with regard to the planned revisions of DSM-IV and ICD-10 [23, 72], it appears to be useful to gather further empirical data on the validity of the differentiation between schizophrenic and affective psychoses in terms of a comprehensive psychopathological and psychosocial outcome description. In view of the limited explanatory power of the available neurobiological findings, results of follow-up studies should continue to be considered in the development of psychiatric classification systems [71].

For the above-mentioned reasons, the Munich 15-year follow-up study on first-hospitalized patients with schizophrenic and affective disorders (MUFSSAD) focussed on the outcome differences in psychopathological symptoms and disturbances of social functioning. The main aim was to determine similarities and differences between schizophrenic, schizoaffective patients and patients with affective disorders, regarding the longitudinal symptom pattern at admission and discharge of the index hospitalization and at follow-up as well as the psychosocial outcome, all measured in a comprehensive standardized rating approach. Another aim was to describe the most relevant outcome predictors for schizophrenic patients, schizophrenic spectrum patients and the total sample, including affective disorder patients.

This study was performed at a time when patients were treated almost exclusively with first generation antipsychotics (FGAs), apart from the second-level administration of clozapine (which was introduced as early as the 1970s in Germany) in treatment-refractory patients. Thus, where schizophrenia is concerned, the therapeutic results of the study primarily refer to the impact of FGAs, naturally in combination with clinical management and psychosocial support. Regarding the possible impact of neuroleptic treatment on naturalistic follow-up data, the review by Wyatt should be considered [106].

Methods

Patient sample, study design and assessment methods

The study was approved by the ethics commission of the medical faculty of the Ludwig-Maximilian University, Munich, Germany. First-hospitalized patients admitted to the Psychiatric University Hospital in the years 1980 through 1982 were enrolled if they fulfilled the following criteria: diagnosis of a schizophrenic or affective disorder (ICD-9: 295.x, 296.x, 297.x, 298.x) without psychiatric comorbidity, i.e. without a psychosis of organic cause or an addictive disorder; age 65 years or younger at the time of enrolment; living in Greater Munich; and mother tongue German. It was planned to recruit at least 120 schizophrenic patients and at least 120 patients with a schizoaffective or affective psychosis. Because of the known differential diagnosis problems, patients with reactive psychoses and paranoid states were also included.

In principle, the follow-up study had an ex post prospective design, i.e. data were collected from every patient during the hospital stay in a prospective and standardized way (using standardized assessment procedures), as part of a huge electronic routine documentation system. Such a database involving thousands of patients can be used to answer different questions at any time. This type of study is methodologically much more sound and convincing than the typical retrospective evaluation of clinical record data, where the non-standardized data are collected from written reports and put into the study datasheet. The latter method of retrospective reconstruction of clinical treatment data has a high risk of bias. Furthermore, it relies on data that were not originally collected using standardized assessment procedures. Thus, the ex post prospective design is methodologically superior to such a retrospective design.

The core study was a cross-sectional 3-point measurement of AMDP and GAS: at admission to and discharge from the first hospitalization and at the 15-year follow-up. The data about the first hospitalization, including standardized rating scales, were taken from the comprehensive documentation system of the Psychiatric University Hospital, Munich. At follow-up, these instruments were enriched by internationally accepted psychopathological scales and by scales assessing social functioning, among other things.

At the time of admission to and discharge from the first hospitalization (1980–1982), patients underwent standardized assessment by the treating physician: psychopathology was recorded by using the Arbeitsgemeinschaft für Methodik und Dokumentation (AMDP) system [5, 73, 84], the global level of symptom severity by the Clinical Global Impression (CGI) and the level of global psychosocial functioning with the Global Assessment Scale (GAS) [21].

Age, sex and psychosocial and anamnestic parameters were documented by means of a standardized Basic Documentation System (BADO). The Strauss–Carpenter Scale [96] was filled out retrospectively on the basis of the medical records by an outcome blind investigator.

At follow-up, 15 years after index hospitalization, the AMDP system and GAS were again applied, and the CGI was also measured. In addition, the Positive and Negative Syndrome Scale (PANSS) [54] and the Scale for the Assessment of Negative Symptoms (SANS) [1] were applied. Furthermore, extrapyramidal symptoms were documented with the Abnormal Involuntary Movement Scale (AIMS) [27] and Simpson–Angus Scale [94]. The GAS was additionally applied retrospectively for every month in the 2 years before the 15-year follow-up evaluation.

Detailed findings on the psychosocial functioning ability were recorded in a semi-structured interview at the 15-year follow-up by using the German version of the Disability Assessment Schedule (DAS), the DAS-M [53]. The five parts of the interview cover general behaviour and role-specific areas of the patient's life, giving an overall estimate of the psychosocial impairment and also collect biographical information. The degree of impairment in the various areas can be graduated on the DAS from '0' (no functional impairment) to '4' (very severe functional impairment), and the manual gives additional advice on how to rate the severity of each parameter.

Besides the results of the standardized assessments performed cross-sectionally at various points in time, the longitudinal evaluations included additionally recorded information on various aspects of disease course, which, among other things, were summarized in an epicrisis for each individual patient.

The literature includes multiple attempts to type the course and outcome of functional psychoses in such a global evaluation. For example, in his long-term study performed over several decades Bleuler [7] divided the course into eight types; Watt et al. [100] categorized course into only four types, which corresponded to the fact that they performed a shorter follow-up study over 5 years. In our study, we differentiated the course into three types. In accordance with Harrison et al. [34], the differentiation between a chronic and non-chronic course was operationalized among others by means of the GAS. Similar approaches were, for example, used in the Vermont Longitudinal Study [33] to differentiate between a favourable and an unfavourable course as well as in others [100]. Möller et al. [74] showed that the GAS is suitable for use as a global outcome parameter and correlates closely with other cross-sectional outcome dimensions; the correlation with longitudinal outcome dimensions is less pronounced. In this study, the course types were operationalized as follows:

Single episode: The symptoms of the index episode remitted completely. There were no more signs of a functional psychosis in the remainder of the study period.

Episodic-remitting course: Further episodes of a schizophrenic or affective disorder occurred during the study. In the 2 years before the follow-up evaluation, the GAS was not continually below 61.

Chronic course: There was no complete remission of symptoms during the study period with or without further episodes of a functional psychosis. In the two years before the follow-up evaluation, the GAS was continually below 61.

All available sources of information (personal interview, relations, treating physician, medical records) were included to assign the patients to one of these course types [46]. The typology is rather crude and of course arbitrary but quite meaningful from a clinical-pragmatic viewpoint.

As mentioned earlier, the study used ICD-9 diagnoses since the ICD-9 was the obligatory clinical diagnostic system at the time of first hospitalization of the patients. At follow-up, investigators blind to the patients' outcome used the detailed medical records to deduce diagnoses according to the research criteria of the ICD-10 [101] and DSM-IV. For details of the results, see Möller [75]. The symptoms listed in the SCID [105] were chosen as the standardized frame of reference. If there was any doubt about a diagnosis, we tried to obtain a consensus of two experienced psychiatrists on the evaluation. The diagnostic classification was based only on the information that was available at the time of the first hospitalization [75]. In psychiatric research, especially in follow-up studies, diagnoses have frequently been deduced from written case reports [33]. This approach also forms the basis for the Operation Criteria Checklist for Psychotic Illness (OPCRIT) system, which is used in genetic research [17, 68, 104]. The SCID was additionally used in the exploration of the patients at the follow-up evaluation as a fully structured diagnosis instrument, and the cross-sectional and life-time diagnoses were established with the SCID computer algorithm.

The patients' acute episode in the hospital was treated according to the standard clinical practice at the time of the study. Schizophrenic patients were primarily treated with FGAs. Clozapine, the first atypical antipsychotic, was used only in refractory patients. In case of moderate to severe depressive syndromes, antidepressants (mostly TCAs) were administered as co-medication, and in case of psychotic depression, neuroleptics. Co-medication with a benzodiazepine was administered for agitation, anxiety and insomnia. Manic syndromes were treated with neuroleptics, sometimes in co-medication with lithium or carbamazepine. ECT was given in case of a catatonic schizophrenic

syndrome or to severely drug-resistant depressive patients. Long-term treatment also followed the clinical guidelines and standards of that time: oral or depot FGAs for schizophrenic patients and antidepressants (mostly TCAs) for patients with unipolar affective disorder. Bipolar disorder patients underwent long-term treatment with a mood stabilizer, mostly lithium or carbamazepine. Long-term treatment of schizoaffective patients was similar to that of patients with affective disorder; neuroleptics were applied only in cases with predominant schizophrenic symptoms. It is important to note in this context that in this naturalistic study the research group had no influence on the patients' treatment, neither during the index hospitalization nor during following hospital stays or outpatient treatment periods. Furthermore, a high rate of non-compliance would have to be expected during long-term treatment.

Statistics

To analyse the rating scale data (AMDP, PANSS, SANS, DAS, GAS, CGI), the total scores or, if relevant, the subscores were calculated. For the AMDP system, which is a very comprehensive rating system covering the full spectrum of psychopathological symptoms of psychiatric disorders, neither a total score analysis nor the consideration of all 9 subfactors seemed to be of relevance to the question at hand [4, 73, 84]. Therefore, the analyses concentrated on four selected AMDP syndromes of specific relevance for the disorders being investigated: paranoid-hallucinatory syndrome, negative syndrome, depressive syndrome and manic syndrome. For the DAS, the mean scores in the different domains were calculated as well as the frequencies of patients with severe/very severe psychosocial impairments.

In principle, the data were analysed only descriptively using analyses of frequency and means. Tests of statistical significance were mostly not performed because of the abundance of different variables and the large number of questions investigated, to avoid excessive multiple testing, with the associated problem of correcting false positive significances, which is difficult to solve.

The model of logistic regression analysis was chosen to answer the question whether at the time of the first hospitalization demographic and psychopathological (i.e. dimensional) variables predicted a chronic long-term course.

Results

Description of the original sample and the follow-up sample

A total of 323 patients were recruited at index time. Fifteen years after the first hospitalization, information on the further course of the disorders could be obtained from 298 of the initial sample of 323 patients. However, a follow-up evaluation including standardized assessment was not possible in 101 people: 43 patients had died (suicide was known to be the cause in 10 of these patients); 18 patients refused to participate and therefore it is only known that they were alive; for 40 people only incomplete follow-up data could be obtained, for example because they had moved abroad permanently. There were no statistically significant differences at baseline in age, sex or distribution of diagnoses between the sample with a complete follow-up evaluation using standardized assessment instruments ($n = 197$), that with incomplete follow-up data ($n = 101$) and that with no data ($n = 25$). The average age of the whole sample at the time of first hospitalization was 35.0 years (women: 36.4 years; men: 30.5 years).

The patient cohort with a complete follow-up evaluation also in terms of rating scale data ($n = 197$) was composed of 141 women (72%) and 56 men (28%); the diagnoses of this cohort were as follows: 64 patients had schizophrenia (F20); 12 patients had a delusional disorder (F22); 30 patients had an acute transient psychotic disorder (F23); 30 patients had a schizoaffective disorder (F25); and 61 patients had an affective disorder (F30, 31, 32, 33). The diagnoses refer to the ICD-10 index diagnoses.

Course of psychopathological syndromes

The comprehensive measurement of psychopathological symptoms with the AMDP system at three points in time (admission to index hospitalization, discharge from index hospitalization, 15-year follow-up) resulted in syndrome profiles for each cross-sectional assessment. Interesting information about the changes in psychopathological syndromes and syndrome patterns over time can be gained from a comparison of these profiles. Only the four domains of the AMDP most relevant for a study on schizophrenic/schizoaffective disorders were evaluated: paranoid-hallucinatory syndrome, negative syndrome, depressive syndrome and manic syndrome. Their analysis focussed on schizophrenia, schizoaffective and affective disorders, considering both ICD-10 and DSM-IV diagnosis.

Since the AMDP dimensions consist of different numbers of symptoms and the raw values therefore differ, the values are expressed as a percentage of the respective syndrome score maximum to make the results comparable. The results for schizophrenic, schizoaffective and affective patients (ICD-10 diagnoses) are shown in Fig. 1. The syndrome profiles at admission to index hospitalization show an obvious difference between schizophrenic and affective disorders: in the group of schizophrenic disorders the paranoid-hallucinatory syndrome is much higher and the mean depression syndrome score is much lower

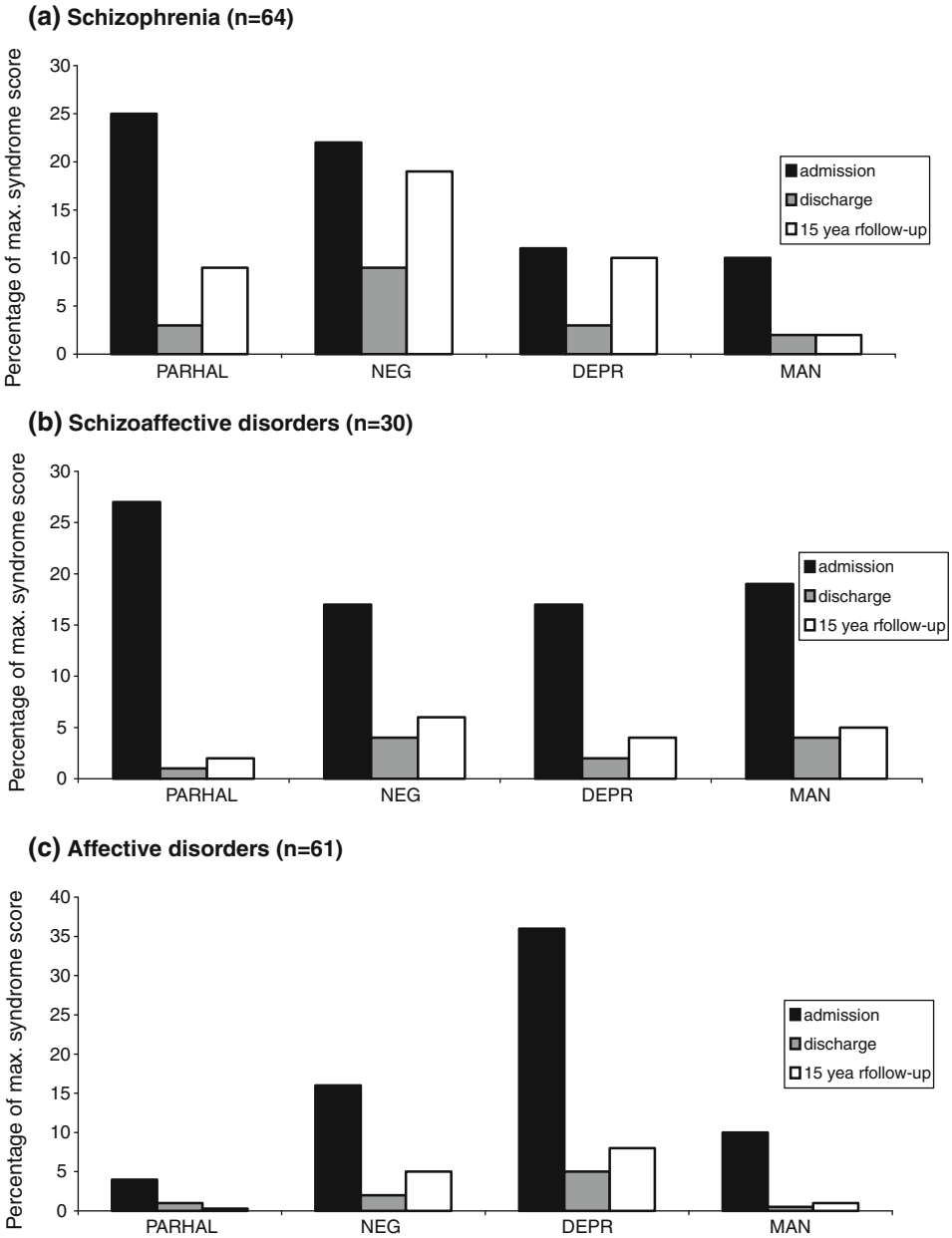

Fig. 1 Course of AMDP syndromes for schizophrenia, schizoaffective disorders and affective disorders (ICD-10). Mean values. *PARHAL* paranoid-hallucinatory syndrome, *NEG* negative syndrome, *DEPR* depressive syndrome, *MAN* manic syndrome

compared to the group of affective disorder. There is also a clear difference regarding the mean negative syndrome score—the schizophrenic patients have a higher one—whereas the mean manic syndrome score shows no relevant difference. The schizoaffective group is similar to the schizophrenic group in terms of the mean paranoid-hallucinatory syndrome score, the mean negative syndrome score is somewhat less pronounced, the mean depressive syndrome score and the mean manic syndrome score are higher than in the schizophrenic group. However, the depressive syndrome score does not reach the magnitude of the respective score in the group of affective disorders, while the manic syndrome is much higher than in the depressive group.

Between index admission and discharge the schizophrenic patients' mean score in the paranoid-hallucinatory syndrome showed a marked reduction of positive symptoms. This is in line with the well-known efficacy of first generation antipsychotics (FGAs) in positive symptoms. At the 15-year follow-up, positive symptoms had increased from the level at discharge from the index hospitalization but had not reached the severity measured at index admission. The increase was mostly associated with symptoms that were more or less chronic during the follow-up period. The mean score of the negative syndrome declined to a lesser degree between admission and discharge than that of the paranoid-hallucinatory syndrome. It is well known that the efficacy of FGAs is not as good in

negative symptoms as in positive symptoms. Nevertheless, there was a clear reduction of negative symptoms, the main reason for which may have been a reduction of acute negative symptoms associated with the reduction of acute positive symptoms [76]. At the 15-year follow-up, there was a marked increase in negative symptoms, almost to the level measured at index admission. The negative symptoms present at the 15-year follow-up were mainly more or less chronic symptoms that persisted during the follow-up period. The mean score of depressive syndromes in the group of schizophrenic patients showed a decline from admission to discharge and an increase from the index admission to follow-up, possibly partially associated with the changes in the amount of negative syndromes. The mean score of the manic syndrome decreased from index admission to discharge and had not increased again at follow-up.

The patients with affective disorders showed only a low average score in the paranoid-hallucinatory syndrome at all three evaluations (Fig. 1). At index admission, the mean score for the depressive syndrome was much higher than that of the other syndromes; it declined markedly between admission and discharge and increased again only slightly at follow-up. The average score of the manic syndrome was much lower than that of the depressive syndrome; it decreased markedly between admission and discharge and hardly increased again at follow-up. These improvements between index admission and discharge can be seen as a result of the acute efficacy of both antidepressants and antimanic medication. The only slight increase in affective symptoms at follow-up may have been associated with long-term treatment with antidepressants and mood stabilizers. Of course, the good long-term prognosis of affective disorders also has to be considered. It was not tried to differentiate between unipolar and bipolar patients because the groups would have become too small.

When the three diagnostic groups' syndrome profiles and their course between admission and discharge were compared, there was a clear contrast between the schizophrenic and the affective disorder patients: the former were predominantly characterized by the paranoid-hallucinatory and the negative syndrome and the latter by the depressive syndrome. Interestingly, the manic syndrome did not differentiate between the two groups, perhaps because some symptoms of the manic syndrome can even be present in a group of more or less core schizophrenic patients or the manic syndrome score includes symptoms like excitement or aggressiveness which are not per se specific for mania. There were some negative symptoms in depressive patients, too, although the average scores at index admission and discharge were obviously lower than in schizophrenic patients.

At follow-up, there was a clear differentiation between schizophrenic and depressive patients insofar as schizophrenic patients had a relatively high mean score in the negative syndrome at follow-up and a higher mean negative syndrome score than at index discharge, whereas depressive patients had a very low mean depressive syndrome score at follow-up and there was obviously no relevant increase between index discharge and follow-up.

In summary, this means that at index admission, the mean scores of both the paranoid-hallucinatory and the negative syndrome were higher in the schizophrenic than in the affective disorder patients; the mean score of the depressive syndrome was much lower in the schizophrenic than in the affective disorder patients. At admission, the patients with schizoaffective disorders showed a pattern quite similar to that of the schizophrenic patients, although scores in the depressive and especially the manic syndrome were higher. At follow-up, the patients with schizoaffective disorder had lower scores than the schizophrenic patients in nearly all dimensions, especially the paranoid-hallucinatory and the negative syndrome. At follow-up, the much higher mean score in the negative syndrome and the higher mean score in the paranoid-hallucinatory syndrome differentiated most clearly between the schizophrenic and the affective disorder patients.

As to the DSM classification (Fig. 2), the results for the schizophrenic and the affective disorder patients were nearly identical to those found with the ICD-10 classification. The results were even very similar for the schizoaffective group, which may have been expected to differ because of the differences between the diagnostic concepts in ICD-10 and DSM-IV (Tables 1, 2).

Differentiated description of psychopathological outcome at follow-up, with a special focus on negative symptoms

For the outcome description at follow-up, negative symptoms were assessed with other instruments (PANSS and SANS) in addition to the AMDP system to allow better comparison of the results with those in the international literature (Table 3). At follow-up schizophrenic patients had a higher PANSS total score (on average about 20 points more) at follow-up than schizoaffective and affective disorder patients, who had nearly identical mean PANSS scores. Schizophrenic patients had higher scores than the other two groups in all PANSS subscores.

The higher degree of negative symptoms in schizophrenic patients at follow-up was clearly shown by the SANS total score, which was nearly 3–4 times higher in schizophrenic patients than in the other two groups. Schizoaffective and affective disorder patients had almost

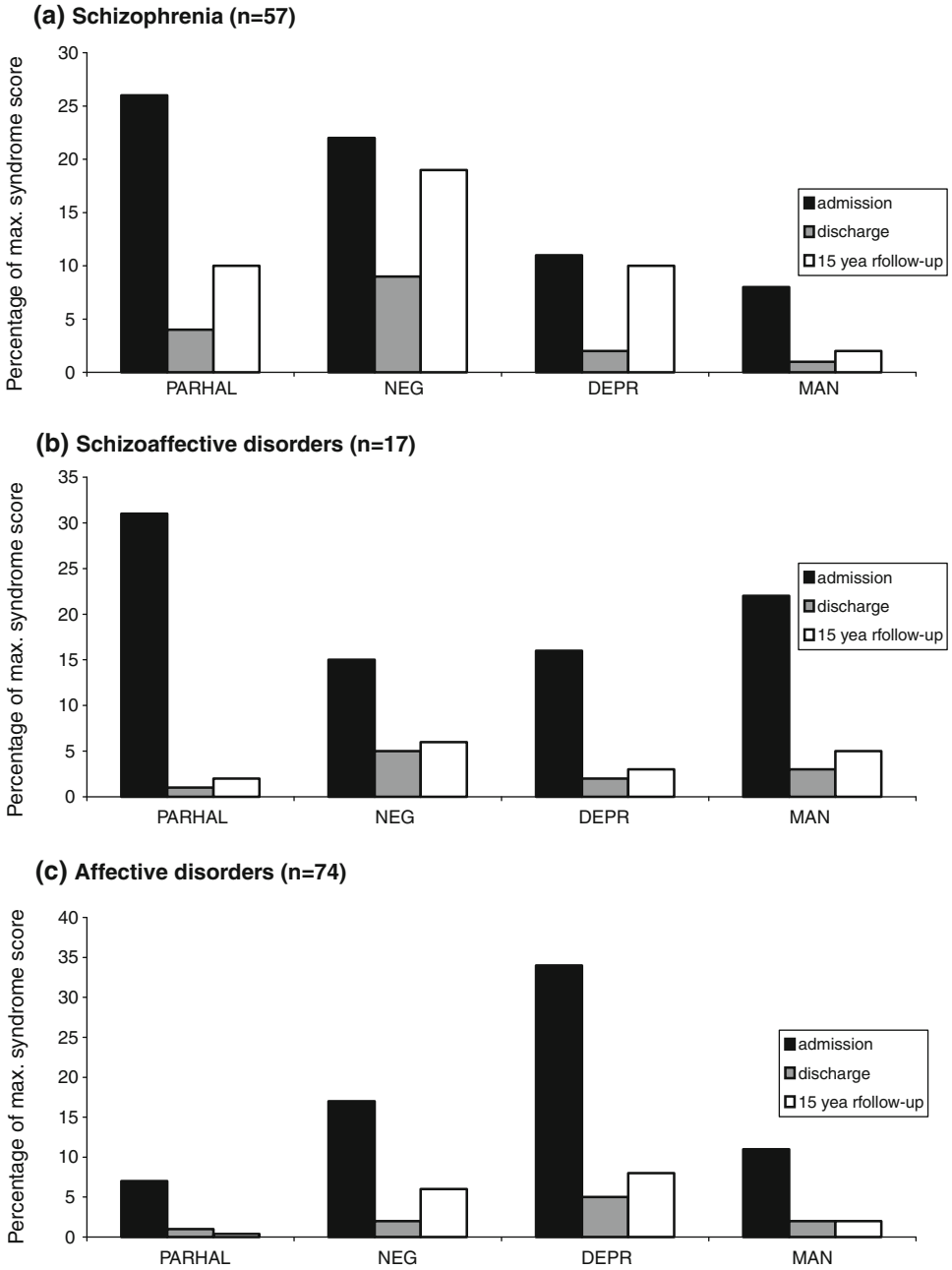

Fig. 2 Course of AMDP syndromes for schizophrenia, schizoaffective disorders and affective disorders (DSM-IV). Mean values. *PARHAL* paranoid-hallucinatory syndrome, *NEG* negative syndrome, *DEPR* depressive syndrome, *MAN* manic syndrome

similar scores, whereby the schizoaffective group showed a slight tendency towards higher values.

The means of the HAMD-D total scores at follow-up (Table 3) were generally quite low, although they were somewhat higher in the schizophrenic group than in the affective and schizoaffective group. The mean Young Mania total scores were low in all three groups.

There were no relevant differences between ICD-10 and DSM-IV diagnoses in any of the above parameters.

The results of the different scales measuring negative symptoms (PANSS, SANS and the negative and apathy syndromes of the AMDP system) correlated highly and significantly with each other (correlation coefficient > 0.70, $P < 0.01$ significance level), which indicates that the different scales measure a similar psychopathological dimension.

At follow-up, patients with at least one negative symptom were found in a large number of patients. When assessed with the AMDP system, patients with at least one negative symptom were found in 75% of the group of schizophrenic patients, 68% of the schizoaffective patients and 44% of the patients with affective disorders. The findings with the SANS scale were comparable to those with the AMDP system: 78% of the patients with schizophrenia, 74% of those with schizoaffective and 47% of those with affective disorders had negative symptoms in

the SANS scale. In contrast, the percentage of patients with at least one negative symptom in the PANSS scale was lower: 59% of the schizophrenic group, 53% of the schizoaffective group and 34% of the affective group. In summary, the findings indicate that negative symptoms, when assessed with different instruments, were more frequent and expressed at follow-up to a greater degree in schizophrenia than in both other diagnostic categories, but were not specific for schizophrenia.

Table 1 Index sample ($n = 323$)

Age	35.0 years (SD: 13.1)
Sex	231 (72% female)
GAS	34.0 (SD: 11.3)
Admission	
Discharge	63.9 (SD: 14.1)
Marital status (%)	
Single	46
Married, stable partnership	37
Separated, divorced	6
Widowed, living alone	3
Other/no information	8
Living arrangements (%)	
Private apartment	95
Assisted living	0.3
Home	2
Other/no information	3
School education (%)	
No certificate	5
Special school	5
Secondary modern school without qualification	18
Secondary modern school with qualification	25
General certificate of secondary education	22
Final secondary school examinations	22
Other/no information	3
Job qualification (%)	
No qualification	35
Apprenticeship	43
School for master craftsmen	6
University	11
Other/no information	5

Ex post the deficit syndrome concept [11] was applied to test whether narrower concepts of the negative syndrome resulted in higher specificity for schizophrenia: the respective symptoms were described on the basis of the rating scale data. Cases were excluded that fulfilled the symptom criteria but had concomitant parkinsonian symptoms. It has to be considered that this approach does obviously not fully fit all criteria of the deficit syndrome suggested by Carpenter et al. [12], but it seems a very meaningful approximation. The AMDP deficit syndrome was defined according to the symptomatic criteria defined by Kirkpatrick [56]: it included the symptoms affective rigidity, blunted affect, mutism, lack of drive and social withdrawal. In order to meet the criteria for an AMDP-based deficit syndrome, two of the AMDP symptoms listed above had to be present with a rating of '2' or more (0 = normal to 3 = severely impaired). The SANS-based deficit syndrome was defined according to Mayerhoff et al. [66] as a rating of '3' or more on at least two of the first four global categories (affect, alogia, avolition, anhedonia). Patients were classified as suffering from a 'questionable deficit syndrome' if they fulfilled these symptomatic criteria and also had significant signs of parkinsonism (akinesia, tremor, rigidity) on the Simpson–Angus scale. 'Significant signs' were defined as akinesia, tremor or rigidity rating of '2' or more on the Simpson–Angus Neurological Scale. The definition of the AMDP-based deficit syndrome seems to be highly specific for schizophrenia. No patient with an affective disorder fulfilled the criteria for the syndrome at either discharge or follow-up but there was a high proportion of the schizophrenic patients as well as a lower proportion of the schizoaffective patients fulfilling all criteria. For schizophrenia and schizoaffective disorders, the results concerning the SANS-

Table 2 Diagnoses according to ICD-9, ICD-10 and DSM-IV ($n = 323$)

Diagnostic group	ICD-9 diagnoses	ICD-10 diagnoses	DSM-IV diagnoses
Schizophrenia	Schizophrenia ($n = 128$)	Schizophrenia ($n = 105$)	Schizophrenia ($n = 94$)
'Transient psychoses'	Schizoaffective psychoses ($n = 65$)	Schizoaffective disorders ($n = 41$)	Schizoaffective disorders ($n = 22$)
			Schizophreniform disorders ($n = 29$)
	Reactive psychoses ($n = 18$)	Acute and transient psychotic disorders ($n = 54$)	Brief psychotic disorders ($n = 12$)
			Other psychotic disorders ($n = 19$)
Delusional disorders	Paranoid states ($n = 39$)	Delusional disorders ($n = 28$)	Delusional disorders ($n = 33$)
Affective disorders	Unipolar depression ($n = 59$)	Unipolar depression ($n = 71$)	Unipolar depression ($n = 79$)
	Manic/bipolar disorder ($n = 14$)	Manic/bipolar disorder ($n = 24$)	Manic/bipolar disorder ($n = 35$)

Table 3 Positive, negative, manic and depressive symptoms at follow-up for the three diagnostic groups in ICD-10 and DSM-IV

	Schizophrenia		Schizoaffective disorders		Affective disorders	
	ICD-10 ($n = 64$)	DSM-IV ($n = 57$)	ICD-10 ($n = 30$)	DSM-IV ($n = 17$)	ICD-10 ($n = 61$)	DSM-IV ($n = 74$)
PANSS						
Total score	62.0 (±23.9)	62.8 (±23.9)	41.2 (±14.9)	40.0 (±16.0)	36.5 (±10.6)	38.0 (±12.2)
Positive subscore	15.8 (±8.9)	16.1 (±8.7)	9.5 (±5.5)	9.9 (±7.0)	7.1 (±2.4)	7.5 (±2.6)
Negative subscore	17.5 (±8.6)	17.9 (±8.5)	10.3 (±4.8)	10.3 (±4.2)	8.4 (±3.1)	9.0 (±4.5)
Global psycho-pathological subscore	29.7 (±11.1)	30.1 (±11.1)	21.7 (±9.5)	20.2 (±7.4)	21.0 (±6.8)	21.6 (±6.8)
SANS						
Total score	41.5 (±28.2)	41.9 (±27.3)	13.5 (±14.5)	13.1 (±12.8)	9.1 (±12.1)	11.2 (±17.3)
HAM-D						
Total score	8.6 (±6.3)	8.7 (±6.3)	4.2 (±5.3)	3.2 (±4.3)	5.9 (±7.7)	5.8 (±7.3)
Young Mania Scale						
Total score	3.0 (±3.8)	3.0 (±3.9)	2.9 (±3.9)	3.5 (±4.5)	2.4 (±4.5)	2.3 (±4.1)

based deficit syndrome were similar to those of the AMDP-based deficit syndrome; however, 6% of the patients with an affective disorder met the criteria for the SANS deficit syndrome.

Comprehensive assessment of psychosocial outcome

Besides psychopathological outcome, outcome in terms of social functioning is of great importance. We therefore assessed psychosocial outcome by using the comprehensive and well-validated scale DAS-M, for details see Bottlender [8].

The following results refer to 177 patients: 61 with a schizophrenic disorder (mean age: 32.22 years, SD: 11.96; 59% women); 58 patients with a schizoaffective disorder (mean age: 32.84 years, SD: 11.33; 81% women); and 58 patients with an affective disorder (mean age: 38.62 years, SD: 11.11; 77.6% women).

The DAS results at the 15-year follow-up are presented for the three diagnostic groups—schizophrenic, schizoaffective and affective disorders (Fig. 3). The average disability scores of the patients with a schizophrenic disorder are in almost all areas considerably higher than the average disability scores of the patients in the other two diagnostic groups. The profiles of the patients with affective disorders are almost identical to those of the patients with schizoaffective disorders—apart from the impairments in their role as parents.

The analysis of the proportion of patients with severe or very severe psychosocial impairments (categories 3 and 4) showed a similar picture: patients with schizophrenic psychosis had pronounced impairments in almost all areas much more frequent than patients with an affective or schizoaffective disorder. As expected, the control test,

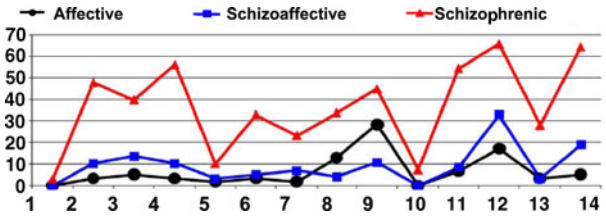

Fig. 3 Mean values of different DAS dimensions. *1* Self-care, *2* spare time activities, *3* pace of daily routines, *4* communication/social withdrawal, *5* considerateness and frictions, *6* behaviour in emergencies, *7* housekeeping activities, *8* marriage or similar relations, *9* sexual relationship, *10* parenting role, *11* heterosexual role behaviour, *12* work role behaviour, *13* general interests/need for information, *14* global estimate of social adjustment

which calculated the frequency of patients without psychosocial deficits, found the complementary result, i.e. in almost all areas; patients with an affective or schizoaffective disorder were without psychosocial deficit much more often than patients with a schizophrenic disorder.

One of the important results of the analysis was that a much larger proportion of the schizophrenic patients were affected by psychosocial impairments (64%) than was the case in affective or schizoaffective patients. Nevertheless, in the global evaluation also 19% of the schizoaffective and 5% of the affective disorder patients had severe or very severe psychosocial impairments at the follow-up evaluation. A more differentiated analysis of the DAS data was presented by Bottlender et al. [8].

Global outcome and other course and outcome parameters

Global outcome was measured using the Global Assessment Score (GAS). Severe symptoms of illness and

Table 4 Global outcome for the three diagnostic groups

	Schizophrenia		Schizoaffective disorders		Affective disorders	
	ICD-10 ($n = 64$)	DSM-IV ($n = 57$)	ICD-10 ($n = 30$)	DSM-IV ($n = 17$)	ICD-10 ($n = 61$)	DSM-IV ($n = 74$)
Global assessment score						
GAS at follow-up	45.6 (±19.7)	45.3 (±19.5)	60.0 (±20.9)	59.4 (±22.4)	67.7 (±18.6)	66.8 (±18.8)
Highest GAS (year before FU)	55.0 (±18.4)	53.7 (±18.3)	68.6 (±18.0)	69.1 (±18.3)	73.3 (±13.7)	72.3 (±14.7)
Lowest GAS (year before FU)	42.0 (±19.4)	40.8 (±18.2)	48.3 (±20.0)	45.9 (±21.7)	54.8 (±22.0)	54.1 (±21.3)
CGI at follow-up	5.4 (±1.7)	5.4 (±1.6)	4.2 (±1.8)	4.4 (±2.0)	3.8 (±1.8)	3.9 (±1.8)
Number of rehospitalizations	2.8 (±2.7)	2.7 (±3.2)	3.2 (±3.0)	3.0 (±3.0)	1.9 (±1.9)	2.1 (±2.2)

reduced functioning, defined as a GAS rating lower than 51, were seen at follow-up in 34% of the schizophrenic, 26% of the schizoaffective and only 3% of the affective patients. Findings for the average GAS were pointing in the same direction as well as the GAS area scores (Table 4). However, in this mean score analysis, the group of schizoaffective disorders was quite close to that of affective disorder. The direction of these findings was comparable with those of the highest GAS for the year before follow-up, suggesting that the group differences of the detected impairments were relatively stable over time. There was quite a large difference between the highest and lowest average GAS in the year before follow-up in all three groups: the difference was 13 in the schizophrenic group and about 20 in the affective and schizoaffective groups. A comparison of the respective ICD-10 and DSM-IV diagnoses found no significant differences in the reported tendencies.

These findings on cross-sectional global outcome at follow-up underline the poorer outcome of patients with schizophrenic disorders, compared with patients with affective disorders. The outcome of schizoaffective patients is closer to that of schizophrenic patients than to that of affective patients.

Schizophrenic patients had a higher number of rehospitalizations than affective disorders, while schizoaffective patients are more similar to schizophrenic patients in this respect (Table 4).

Predictors of outcome in ICD-10/DSM-IV schizophrenic and schizophrenic spectrum disorders

The following analyses focussed on schizophrenia patients s.str. as well as on schizophrenia related spectrum disorder patients, according to ICD-10 and DSM-IV diagnosis. For details, see Möller [75]. Of the patients with an ICD-10 diagnosis of schizophrenia, 57% had a chronic course and 39% an episodic-remitting course. Merely 3% of the patients had a single episode. Of the patients with a delusional disorder, 50% had a chronic and 50% an episodic-remitting course. In contrast to these two diagnostic groups, only 20% of the patients with an acute transient psychotic disorder had a chronic course; beside the proportion with an episodic-remitting course (50%), the relatively high proportion of single episodes (30%) is particularly noteworthy. The majority (87%) of the schizoaffective disorders showed an episodic-remitting course; merely 10% of the cases showed a chronic course and 3% were a single episode. The pattern of the prognostic relevance of the DSM-IV diagnoses is similar. Of the patients with a diagnosis of schizophrenia, 61% had a chronic course, 37% an episodic-remitting one and merely 2% a single episode. Of the patients with a delusional disorder, 44% had a chronic course, 50% an episodic-remitting course and 6% a single episode. In contrast, only 21% of cases of a schizophreniform disorder had a chronic course; beside the proportion with an episodic-remitting course (52%), the relatively high proportion of single episodes (26%) is particularly noteworthy. The patients with a schizoaffective disorder mostly had an episodic-remitting course (88%); a chronic course or single episode both occurred infrequently (6% each).

In order to identify the optimized set of predictors for the outcome of schizophrenia s.str. or schizophrenia spectrum disorders, the model of logistic regression analysis was chosen. The aim was to predict whether the course would be chronic or not chronic in terms of course types described earlier. Gender, age, GAS-values (at admission, at discharge of index manifestation and the highest value in the year before admission), the Strauss–Carpenter total score, duration of untreated psychosis, and the total scores of paranoid-hallucinatory, negative, depressive and manic syndrome (at admission and at discharge) were entered as independent variables.

The first model was calculated for all patients who fulfilled diagnostic criteria for schizophrenia according to ICD-10 criteria (Table 5). The overall predictive validity (correct identification of the future course) was 75%, Nagelkerkes R^2 was 0.376. The paranoid-hallucinatory syndrome at admission and the negative syndrome at discharge played a significant role in predicting the long-term

Table 5 Logistic regression model for the prediction of outcome (non-chronic course) for schizophrenia according to ICD-10 ($n = 64$)

Variable	Coefficient	SE	Wald	*df*	*P* value	OR	95% CI
Sex	0.471	0.732	0.414	1	0.520	1.601	0.381–6.725
Age	0.006	0.043	0.022	1	0.881	1.006	0.926–1.094
GAS–admission	−0.045	0.047	0.929	1	0.335	0.956	0.871–1.048
GAS—discharge	0.037	0.042	0.801	1	0.370	1.038	0.957–1.127
GAS—before admission	0.004	0.038	0.012	1	0.913	1.004	0.933–1.081
Strauss–Carpenter	0.131	0.072	3.343	1	0.068	1.140	0.991–1.312
DUP > 6 months	0.006	0.930	0.000	1	0.995	1.006	0.162–6.226
PARHAL—admission	**−0.181**	**0.081**	**4.949**	**1**	**0.026**	**0.834**	**0.711–0.979**
PARHAL—discharge	0.048	0.169	0.079	1	0.779	0.779	0.753–0.1461
NEG—admission	0.188	0.097	3.754	1	0.053	1.206	0.0.998–1.458
NEG—discharge	**−0.377**	**0.156**	**5.849**	**1**	**0.016**	**0.686**	**0.505–0.931**
MAN—admission	0.300	0.195	2.369	1	0.124	1.350	0.921–1.978
MAN—discharge	−0.344	0.588	0.343	1	0.558	0.709	0.224–2.243
DEPR—admission	−0.181	0.107	2.909	1	0.088	0.833	0.676–1.028
DEPR—discharge	0.354	0.304	1.353	1	0.245	1.424	0.785–2.586
Constants	−5.852	5.366	1.189	1	0.275	0.003	

Predictive validity: 75%, Nagelkerkes R^2: 0.376

Table 6 Logistic regression model for the prediction of outcome (non-chronic course) for schizophrenia according to DSM-IV ($n = 57$)

Variable	Coefficient	SE	Wald	*df*	*P* value	OR	95% CI
Sex	0.329	0.917	0.129	1	0.719	1.390	0.231–8.381
Age	0.048	0.060	0.651	1	0.420	1.049	0.934–1.179
GAS—admission	0.015	0.058	0.064	1	0.800	1.015	0.905–1.138
GAS—discharge	0.010	0.048	0.044	1	0.834	1.010	0.920–1.110
GAS—before admission	0.016	0.042	0.141	1	0.707	1.016	0.936–1.102
Strauss–Carpenter	0.086	0.079	1.183	1	0.277	1.090	0.933–1.272
DUP > 6 months	0.059	0.989	0.004	1	0.958	1.061	0.152–7.381
PARHAL—admission	**−0.216**	**0.091**	**5.636**	**1**	**0.018**	**0.806**	**0.674–0.963**
PARHAL—discharge	0.102	0.183	0.314	1	0.575	1.108	0.674–0.963
NEG—admission	0.190	0.132	2.050	1	0.152	1.209	0.932–1.567
NEG—discharge	**−0.420**	**0.192**	**4.799**	**1**	**0.028**	**0.657**	**0.452–0.957**
MAN—admission	0.255	0.205	1.537	1	0.215	1.290	0.863–1.929
MAN—discharge	−0.174	0.645	0.073	1	0.787	0.840	0.238–2.973
DEPR—admission	−0.240	0.124	3.755	1	0.053	0.787	0.617–1.003
DEPR—discharge	0.249	0.402	0.384	1	0.535	1.283	0.583–2.821
Constants	−4.652	6.262	0.552	1	0.485	0.010	

Predictive validity: 72%, Nagelkerkes R^2: 0.409

course. The same was true when the regression model was calculated for patients who fulfilled DSM-IV criteria for schizophrenia (Table 6). The predictive validity was 72%, Nagelkerkes R^2 was 0.409. To summarize, a high level of paranoid-hallucinatory symptoms at admission and of negative symptoms at discharge were predictive of an unfavourable outcome in terms of a chronic course type. This was true for both ICD-10 and DSM-IV.

The analogous calculations were performed for schizophrenia spectrum disorders according to ICD-10 criteria (schizophrenia, delusional disorders, acute and transient psychotic disorders, schizoaffective disorders). The overall predictive validity was 71%, Nagelkerkes R^2 was 0.257 (Table 7). Beside male sex, only the total score of the Strauss–Carpenter prognostic score played a significant role in prediction of the long-term course. The same was

Table 7 Logistic regression model for the prediction of outcome (non-chronic course) for schizophrenic spectrum disorders according to ICD-10 ($n = 136$)

Variable	Coefficient	SE	Wald	*df*	*P* value	OR	95% CI
Sex	**1.125**	**0.482**	**5.447**	**1**	**0.020**	**3.080**	**1.197–7.924**
Age	0.010	0.021	0.256	1	0.613	1.011	0.970–1.094
GAS—admission	−0.020	0.027	0.542	1	0.462	0.980	0.930–1.034
GAS—discharge	−0.012	0.024	0.232	1	0.630	0.988	0.943–1.036
GAS—before admission	0.001	0.038	0.005	1	0.943	1.001	0.933–1.081
Strauss–Carpenter	**0.078**	**0.037**	**4.467**	**1**	**0.035**	**1.082**	**1.006–1.163**
DUP > 6 months	0.345	0.523	0.434	1	0.510	1.411	0.506–3.933
PARHAL—admission	−0.022	0.036	0.036	1	0.546	0.979	0.913–1.050
PARHAL—discharge	−0.050	0.092	0.292	1	0.589	0.952	0.795–1.140
NEG—admission	0.017	0.052	0.103	1	0.748	1.017	0.918–1.127
NEG—discharge	−0.104	0.094	1.209	1	0.271	0.901	0.749–1.085
MAN—admission	−0.038	0.069	0.300	1	0.273	0.963	0.840–1.103
MAN—discharge	0.265	0.242	1.201	1	0.271	0.901	0.811–2.094
DEPR—admission	−0.085	0.058	2.134	1	0.144	0.919	0.819–1.127
DEPR—discharge	0.071	0.304	0.300	1	0.712	1.074	0.736–1.566
Constants	−2.886	5.366	0.989	1	0.320	0.056	

Predictive validity: 71%, Nagelkerkes R^2: 0.257

Table 8 Logistic regression model for the prediction of outcome (non-chronic course) for schizophrenic spectrum disorders according to DSM-IV ($n = 123$)

Variable	Coefficient	SE	Wald	*df*	*P* value	OR	95% CI
Sex	**1.170**	**0.501**	**5.448**	**1**	**0.020**	**3.220**	**1.206–8.598**
Age	0.006	0.023	0.062	1	0.803	1.006	0.961–1.052
GAS—admission	−0.022	0.029	0.587	1	0.444	0.978	0.925–1.035
GAS—discharge	−0.009	0.035	0.124	1	0.725	0.001	0.944–1.041
GAS—before admission	0.004	0.020	0.043	1	0.835	1.004	0.966–1.044
Strauss–Carpenter	**0.079**	**0.038**	**4.305**	**1**	**0.038**	**1.082**	**1.004–1.166**
DUP > 6 months	0.338	0.546	0.384	1	0.536	1.402	0.481–4.085
PARHAL—admission	−0.027	0.037	0.515	1	0.473	0.974	0.905–1.047
PARHAL—discharge	−0.013	0.094	0.018	1	0.893	0.987	0.821–1.188
NEG—admission	0.060	0.063	0.913	1	0.339	1.062	0.939–1.201
NEG—discharge	−0.188	0.106	3.155	1	0.076	0.829	0.673–1.020
MAN—admission	−0.028	0.073	0.150	1	0.699	0.972	0.842–1.122
MAN—discharge	0.226	0.300	0.570	1	0.450	1.254	0.697–2.257
DEPR—admission	−0.081	0.064	0.913	1	0.201	0.922	0.814–1.044
DEPR—discharge	0.127	0.202	1.392	1	0.531	1.135	0.764–1.687
Constants	−3.096	3.013	1.056	1	0.304	0.045	

Predictive validity: 71%, Nagelkerkes R^2: 0.241

true when the regression model was calculated for schizophrenia spectrum disorders according to DSM-IV criteria (schizophrenia, delusional disorders, schizophreniform disorders, schizoaffective disorders, other psychotic disorders). The predictive validity was 71%, Nagelkerkes R^2 was 0.241 (Table 8). To summarize, for schizophrenic spectrum disorders male gender and high values in the Strauss–Carpenter prognostic score were predictive of an unfavourable outcome in terms of a chronic course type. This was true for both ICD-10 and DSM-IV.

In order to identify predictors for the outcome of in the whole sample including affective disorders the model of logistic regression analysis was applied again (Table 9). The aim was to predict whether the course would be

Table 9 Logistic regression model for the prediction of outcome (non-chronic course) for the whole follow-up sample ($n = 197$)

Variable	Coefficient	SE	Wald	*df*	*P* value	OR	95% CI
Sex	**1.009**	**0.439**	**5.294**	**1**	**0.21**	**2.743**	**1.161–6.481**
Age	−0.003	0.017	0.023	1	0.878	0.997	0.964–1.032
GAS—admission	−0.027	0.021	1.575	1	0.209	0.973	0.933–1.015
GAS—discharge	−0.024	0.019	1.664	1	0.197	0.976	0.940–1.013
GAS—before admission	0.015	0.018	0.660	1	0.417	1.015	0.979–1.052
Strauss–Carpenter	**0.074**	**0.035**	**4.533**	**1**	**0.033**	**1.077**	**1.006–1.152**
DUP > 6 months	−0.219	0.490	0.199	1	0.656	0.804	0.308–2.099
PARHAL—admission	0.026	0.031	0.691	1	0.406	1.077	0.965–1.092
PARHAL—discharge	−0.047	0.084	0.313	1	0.576	0.954	0.809–1.125
NEG—admission	−0.003	0.048	0.003	1	0.953	0.997	0.907–1.096
NEG—discharge	−0.032	0.088	0.135	1	0.264	1.281	0.814–1.151
MAN—admission	−0.092	0.063	2.144	1	0.143	0.912	0.806–1.032
MAN—discharge	0.248	0.222	1.246	1	0.264	1.281	0.829–1.978
DEPR—admission	**−0.091**	**0.046**	**3.861**	**1**	**0.049**	**0.913**	**0.833–1.000**
DEPR—discharge	−0.055	0.150	0.134	1	714	0.946	0.705–1.271
Constants	−2.192	2.858	0.588	1	0.443	0.112	–

Predictive validity: 78%, Nagelkerkes R^2: 0.329

chronic or not chronic in terms of course types described earlier. Gender, age, GAS-values (at admission, at discharge and the highest value in the year before admission), the Strauss–Carpenter total score, duration of untreated psychosis, and the total scores of paranoid-hallucinatory, negative, depressive and manic syndrome (at admission and at discharge) were entered as independent variables. The overall predictive validity (correct identification of the future course) was 78%, Nagelkerkes R^2 was 0.329. Gender, the total score of the Strauss–Carpenter prognostic score at admission and the score of depressive syndrome at admission played a significant role in the prediction of the long-term course. Male sex and a higher core of the Strauss–Carpenter scale were predictive for an unfavourable outcome in the sense of a chronic course, while the depressive syndrome at admission pointed in the opposite direction.

Discussion

The psychopathological outcome of schizophrenia patients shows clear differences compared to patients with affective disorders. During the index periods, the syndrome profile of schizophrenic patients was predominantly characterized by the paranoid-hallucinatory syndrome and the negative syndrome, whereas for the affective patients the depressive syndrome was of higher relevance. At 15-year follow-up, the schizophrenic patient had a much higher negative syndrome score and a higher score in the paranoid-hallucinatory syndrome than the patients with affective disorders. The schizoaffective patients showed some similarities with the schizophrenic patients, especially regarding the paranoid-hallucinatory syndrome, but also with the affective disorder patients in terms of depressive and manic symptoms. The general results were independent from the diagnostic systems used, either ICD-10 or DSM-IV. Taken together, these findings reflect some validity for the diagnostic differentiation between schizophrenic affective disorders as well as for using psychopathological syndromes to subtype functional psychoses.

The results are more or less in good accordance with published results from other studies following a similar comparative approach [36, 37, 64, 65, 74, 77, 99]. In terms of psychopathological symptoms, especially the importance of negative symptoms as a characteristic component of schizophrenia and their relevance for disturbances in social functioning was described in several studies [12, 19, 30, 42, 43, 56, 78, 85, 96]. Also the relevance of positive/paranoid-hallucinatory symptoms for schizophrenia and its outcome was widely discussed in the literature [20, 38, 39, 59, 62, 88, 89]. Depressive symptoms were not only described as a core symptom of affective disorders but also as a relevant psychopathological dimension for schizophrenic spectrum disorders, even of core schizophrenia [30, 31, 70, 79].

The findings on a higher degree of psychosocial impairment in schizophrenic patients compared to patients with affective and schizoaffective disorders are in good accordance with those of other studies [37, 77]. For example, Marneros et al. [63] used a comparative approach in their 25-year follow-up study of affective,

schizoaffective and schizophrenic patients. They found that schizophrenic patients had a significantly higher degree of psychosocial impairment, both globally and in specific areas, than patients with affective and schizoaffective disorders. Furthermore, the degree of impairment in schizoaffective patients rather resembled that of the patients with affective disorder than that of those with schizophrenic disorder. Similar results were reported by Möller et al., in two different studies for the 5- to 8-year course of schizophrenic, schizoaffective and affective disorders [77, 81]. From a methodological point of view it should be underlined that in our study apparently a more comprehensive description of different domains of disturbances in social functioning depicts more precisely the amount of disabilities compared to a more global rating [8, 73, 77]. Also other studies indicated a high relevance of social malfunctioning, and disability at the long-term outcome of schizophrenia [20, 29, 32, 45]. In a large WHO study in 349 patients, Wiersma et al. found that after 15 years of illness only 14% of the patients had no impairment of psychosocial functioning but 59% had obvious or severe impairment. These percentages are almost identical to those found in our study [103]. The measuring of social functioning and disability, additionally to the assessment of psychopathological symptoms, is without doubt of great importance regarding patients suffering from schizophrenia and affective disorders [40].

Based on a logistic regression analysis including some relevant psychopathological and psychosocial characteristics from the index period, from psychosocial parameters as well as the Strauss–Carpenter scale, the following predictors were identified as most relevant predictors for a chronic course:

- in the schizophrenic group: a high score of the paranoid-hallucinatory syndrome at admission and a high score of the negative syndrome at discharge were predictive for an unfavourable outcome in terms of chronic course type
- in the schizophrenic spectrum group: male gender and high values in the Strauss–Carpenter scale were predictive for an unfavourable outcome in terms of a chronic course type
- in the whole group of schizophrenic and affective disorder patients: male gender, the total score of the Strauss–Carpenter scale and the score of the depressive syndrome at admission played a significant role in the prediction of long-term outcome, the first two pointing at an unfavourable outcome, the latter in the opposite direction.

Altogether, in each of the predictor combinations a predictive validity of slightly more than 70% could be reached for schizophrenia s.str. or the schizophrenic spectrum group, independent on whether the classification followed ICD-10 or DSM-IV criteria. The predictor analysis in the whole sample including affective disorders reached even 78% predictive validity. This seems promising. However, given the fact that a multivariate analysis always optimizes the predictive result to the respective sample, the result has to be replicated in an independent sample, both in terms of the size of predictive power as well as in terms of selection of predictors.

The results fit the respective results in the follow-up literature [10, 14, 24, 25, 28, 33, 47, 77, 78, 80, 93, 97]. For example, male gender has repeatedly been described in the schizophrenia literature as predictor of poor outcome. The results regarding the prognostic impact of paranoid-hallucinatory symptoms in schizophrenia follow-up studies are inconsistent [81]. The predictive power of the negative syndrome as a predictor of poor outcome at discharge was found in several studies [2, 78, 80]. The depressive syndrome as a predictor of positive outcome in the mixed group of schizophrenic, schizoaffective and affective patients possibly underlines that patients with depressive disorder but also possibly schizophrenic patients with a depressive component [70, 77] might have more favourable outcomes.

Interestingly, symptoms viewed as symptoms of schizophrenia like the paranoid-hallucinatory syndrome and the negative syndrome demonstrated prognostic relevance in some of the predictor models. The relevance of affective symptoms for the differentiation of psychiatric disorders and for the prediction of outcome was described by several authors [30, 31, 86, 87].

Altogether, these results seem to demonstrate some validity of the clinical differentiation of schizophrenic and affective disorders [71] in terms of psychopathological dimensions and especially in terms of outcome differences: Schizophrenia patients have shown a much poorer outcome in terms of psychopathological symptoms and social disabilities. However, there is no ‘point of rarity’ between the two groups concerning the distribution of the different outcome variables, a finding which might be interpreted in the sense of a spectrum concept of psychotic disorders [18, 60, 69, 82]. Schizoaffective disorders are in most outcome dimensions between the both groups with a tendency to a more favourable outcome similar to the affective disorders. This might be a reason to question the category of schizoaffective disorders as a separate group [57, 61]. Interestingly, the Strauss–Carpenter scale proved its well-known prognostic value [77, 78] only in the schizophrenic spectrum group, not in the schizophrenic group, where psychopathological predictors were of greater importance. In contrast to earlier findings from our group [9], in this analysis duration of untreated psychosis (DUP) could not demonstrate prognostic relevance, which might be due to

methodological issues. Bottlender used a MANCOVA-model with several dimensional outcome variables. Apart from DUP only 'mode of onset' was included as additional independent variable in the MANCOVA-model. In our analysis, we used logistic regression analysis including several independent variables and a dichotomous outcome variable. This analysis model is less demanding regarding the independent variables in terms of normal distribution. Especially the higher number of independent variables might be the reason why DUP looses its prognostic relevance in this model.

This analysis focused only on one outcome criterion which was defined as a comprehensive criterion for a chronic course. The inclusion of other outcome criteria would definitely have involved other predictors [77, 78, 97].

It should also be considered that the reason for the fact that some variables, commonly known to have predictive power in, did not penetrate in all or some multivariate analyses models might partially be explained to be a statistical artefact. Due to the relatively high number of variables included in a multivariate model it might happen that they, although known as predictive from other studies, do in fact not appear as significant predictors in the presented analysis, because they are beaten in their prognostic relevance by other, more powerful variables. This is also the reason why in each combination of potential predictors different predictors appear as significant. The problem of 'overfitting' has to be considered as well: in a multivariate analysis a relatively high number of variables are analysed regarding their predictive power in a comparatively small sample, and the results are optimized for this special sample and need replication in another sample before final conclusions can be drawn.

Limitations of the studies are primarily resulting from the naturalistic design which is unable to consider the different interventions during the follow-up period. As to the psychopharmacological treatment of schizophrenic patients, the results primarily reflect the era of the FGAs. The sample cannot be regarded as fully representative in the epidemiological sense since our psychiatric hospitals contribute to the core of psychiatric patients in the Munich region. The comparison between first admitted schizophrenic patients and first admitted affective patients is insofar problematic as schizophrenic patients in Germany are mostly admitted without long outpatient treatment time, whereas depressive patients often have longer outpatient treatment phases. Considering this, however, the results demonstrating a much more unfavourable outcome of schizophrenic patients are even more significant, due to the fact that a higher proportion of patients with depressive disorder admitted to hospital under these conditions can be regarded as relatively therapy resistant with a relatively poor outcome to be expected. The ex post prospective design is not a fully prospective design in terms of methodological standards, but it is methodologically superior to a retrospective design. Due to the ex post prospective design, the core study is only a cross-section 3-point measurement. Of course, more consecutive assessments during the follow-up period would be preferable.

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