

A 24-Month Prospective Outcome Study of First-Episode Schizophrenia and Schizoaffective Disorder Within an Early Psychosis Intervention Program

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Background: Within the schizophrenia spectrum disorders, schizoaffective disorder is conventionally considered to have a better prognosis compared to schizophrenia. We tested the hypothesis that patients with first-episode schizoaffective disorder had better clinical and functional outcomes compared to patients with first-episode schizophrenia.

Method: The study population consisted of consecutive subjects with first-episode schizophrenia or first-episode schizoaffective disorder (diagnosed according to DSM-IV criteria) enrolled in the national Early Psychosis Intervention Program at the Institute of Mental Health/Woodbridge Hospital in Singapore from March 2001 to March 2003. The subjects' level of psychopathology, insight, socio-occupational functioning, and quality of life were assessed using the Positive and Negative Syndrome Scale (PANSS), the Scale to Assess Unawareness of Mental Disorder, the Global Assessment of Functioning scale, and the World Health Organization Quality of Life-BREF scale, respectively, at baseline and at 6, 12, 18, and 24 months.

Results: At baseline, patients with schizoaffective disorder ($N = 24$) were more likely to be employed ($OR = 3.38$, $95\% CI = 1.27$ to 9.02 , $p < .05$), had a shorter duration of untreated psychosis ($z = -3.30$, $p < .005$), but had greater general psychopathology subscale scores on PANSS ($z = -2.69$, $p < .01$) compared to patients with schizophrenia ($N = 254$). Patients with schizophrenia had better insight into their psychiatric illness ($z = -3.93$, $p < .001$) at 6 months and expressed a better level of quality of life in the psychological health domain ($z = -3.83$, $p < .001$) at 12 months compared to patients with schizoaffective disorder. At 18 months, patients with schizoaffective disorder continued to have higher general psychopathology subscale scores on PANSS ($z = -3.89$, $p < .001$) compared to patients with schizophrenia.

Conclusion: Patients with first-episode schizoaffective disorder do not necessarily have less severe psychopathology or better longitudinal outcomes compared to patients with first-episode schizophrenia, a finding that warrants attention in the clinical management of these patients.

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Since the coining of the term *schizoaffective disorder* by Kasanin in 1933,¹ there has been unabated and continued interest into the nosologic features, subtyping, and significance of this condition.^{2–4} Several schools of thought have emerged in the quest to understand this nosologic and diagnostic entity.⁵ Essentially, the methods used to conceptualize schizoaffective disorder can be summed up as categorical, dimensional, or mixed approaches. In the categorical group, schizoaffective disorder is seen as either schizophrenia with incidental affective features^{6,7} or manic depressive disorder with incidental schizophrenia-like symptoms.^{8,9} It is also seen as an intermediate entity between schizophrenia and affective disorders.^{10,11} Additionally, it has been seen as a completely new and third psychotic disorder that is unrelated to the Kraepelinian dichotomy of schizophrenia or manic depressive disorder.¹² In the dimensional group, schizoaffective disorder is thought to exist along a continuous spectrum of psychotic disorders with schizophrenia at one end and manic depressive disorder at the other.¹³ Schizoaffective disorder may also represent genuine, heterogeneous interforms reflecting unknown etiologic interactions between schizophrenia and manic

depressive disorder.^{14,15} In the mixed approach, schizoaffective disorder is thought to result from a mixture of the aforementioned processes in the categorical as well as the dimensional groups.¹⁶

Studies of the longitudinal course and outcome of schizoaffective disorder, especially in different populations of patients, are important for several reasons. First, they help to increase our understanding of the natural history of the illness, and findings from such studies allow for clearer discussion with patients and their families about the course and management of the condition. Second, they may allow a better appreciation of the prognosis, with the possibility of identifying predictive variables. Third, these studies may help to initiate further studies to elucidate underlying etiologic factors with treatment implications. Last, but not least, longitudinal data, including treatment response and prognostic information, can be used to clarify diagnostic heterogeneity and stability, as well as to validate diagnostic concepts. For example, longitudinal studies of individuals with first-episode psychosis have revealed relative diagnostic stability for schizophrenia, bipolar disorder, and schizoaffective disorder, but less so for schizophreniform disorder and psychotic disorder not otherwise specified.^{17,18} Earlier longitudinal studies of patients with schizoaffective disorder also revealed heterogeneous outcomes favoring nosologic typing toward schizophrenia, affective disorders, or both. Welner et al.,¹⁹ in their prospective study of 114 patients with schizoaffective disorder, found that more than two thirds had a chronic, deteriorating course of illness, hence resembling schizophrenia more than affective disorders. This finding is in support of the notion that schizoaffective disorder is a variant of schizophrenia with incidental affective colorings. On the other hand, Möller et al.²⁰ compared the longitudinal outcomes of 183 patients with functional psychoses and found that schizoaffective and affective psychoses demonstrated favorable prognoses compared to schizophrenia, thus lending support to the notion of schizoaffective disorder as an affective disorder with schizophrenia-like symptoms. Marneros et al.²¹ followed up 101 patients with schizoaffective disorder over a mean duration of 25.5 years and found that the development of persisting psychosocial alteration was associated with the absence of melancholic episodes, the presence of first-rank symptoms, and higher number of episodes, while the development of a negative social outcome was associated with low-self-confident, premorbid personality. The authors concluded that there were only partial similarities between schizoaffective disorder and affective disorder or schizophrenia, implying that schizoaffective disorder may be an intermediate entity between the 2 groups of conditions.²¹

Furthermore, previous studies of patients with schizoaffective disorders were conducted mostly in patients with chronic illnesses. Studies of chronic patients are

often confounded by the prevailing effects of psychotropic medications and their interactions with the disease process. Hence, in this study, we sought to examine the differences in sociodemographic and clinical correlates between patients with first-episode schizoaffective disorder and first-episode schizophrenia. Based on extant literature, we tested the hypothesis that patients with schizoaffective disorder had less severity of illness and better longitudinal outcomes compared to patients with schizophrenia.

METHOD

Study Design and Participants

The study population consisted of consecutive subjects with first-episode schizophrenia or first-episode schizoaffective disorder enrolled in the national Early Psychosis Intervention Program at the Institute of Mental Health/Woodbridge Hospital in Singapore from March 2001 to March 2003. The subjects fulfilled the following criteria: (1) age between 18 and 40 years, (2) English-speaking, and (3) presented with a first-episode schizoaffective disorder or schizophrenia and had no previous psychiatric hospitalization or antipsychotic treatment. The Institute of Mental Health/Woodbridge Hospital is the only state psychiatric hospital in the country, and it serves as a principal treatment and follow-up facility for patients suffering from severe psychotic illnesses such as the schizophrenia spectrum disorders. The subjects were excluded from this study if the psychotic symptoms (1) were secondary to acute intoxication or withdrawal from alcohol or other psychoactive substances or (2) resulted entirely from a medical illness as determined by a comprehensive medical and neurologic evaluation. The study had the approval of the hospital ethics committee, and all participants provided written, informed consent after a full explanation of the nature of the study.

All new psychiatric admissions were reviewed daily, and out of 360 potential study participants, 278 subjects (77.2%; 24 patients with schizoaffective disorders and 254 patients with schizophrenia) provided written informed consent, completed the 24-month protocol, and are the subjects of this report. There were no significant differences in the basic demographic variables (age and sex) of patients who were willing or not willing to participate in the study.

Diagnostic Assessment

Axis I psychiatric diagnoses were assessed by psychiatrists at the index hospitalization and at 24 months by means of the Structured Clinical Interview for DSM-IV Axis I Disorders, Patient Edition (SCID-P).²² In completing the SCID-P, combined symptom information was obtained from various sources, including clinical interviews with the subjects as well as significant others,

medical records, and the records of other primary treating clinicians whenever necessary.

Symptom Assessment

The Positive and Negative Syndrome Scale (PANSS),²³ the Scale to Assess Unawareness of Mental Disorders (SUMD),²⁴ and the Global Assessment of Functioning (GAF)²⁵ scale (SCID Axis V) were used to assess the severity of psychopathology, level of insight, and psychosocial functioning, respectively. Interrater reliability was obtained by rating 8 subjects by 2 raters with an intraclass correlation coefficient above 0.80 for all the observer-rated scales.

The subjective quality of life (QOL) at baseline was assessed using the 26-item World Health Organization Quality of Life-BREF (WHOQOL-BREF) scale, an abbreviated version of the WHOQOL-100 assessment instrument.²⁶ It is a valid and reliable self-rated instrument that is sensitive to the health-related QOL in subjects with psychotic illnesses²⁷ and has been well validated in Asian subjects.^{28,29} The 26 items produce scores for 4 domains related to QOL, namely physical health (activities of daily living, dependence on medical treatment, energy and fatigue, mobility, pain and discomfort, sleep, work capacity), psychological health (bodily image and appearance, negative feelings, positive feelings, self-esteem, spirituality, concentration), social relationships (personal relationships, social support, sexual activity), and environment (finances, physical safety, access to health services, home environment, opportunities to acquire new information, leisure activities, physical environment, transport). In addition, it also includes 1 item each on overall QOL and general health.

The duration of untreated psychosis (DUP) was defined as the duration between the onset of psychotic symptoms (such as hallucinations, delusions, disorganization of thought) and the time that treatment was initiated.³⁰ Basic sociodemographic data were also collected.

Outcome Assessment

Follow-up assessments were scheduled for 6, 12, 18, and 24 months after each patient's index hospitalization. Interviews were conducted with the patient, and information from the informant and medical records were also reviewed at periodic intervals after the index hospitalization. Clinical and symptomatic outcomes were evaluated using PANSS, SUMD, and other data including total duration of rehospitalization following the index hospitalization and the medication dosage in daily chlorpromazine equivalents.^{31,32} Functional outcome was assessed from the GAF and WHOQOL-BREF scores. To improve the validity of the diagnosis and clinical measures, "best-estimate" meetings were held after the completion of the 24-month follow-up visit³³ and involved the review of all assessments and diagnoses from the index hospitalization, follow-up evaluations, and available clinical records.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS), Windows version 11.0 (SPSS, Inc., Chicago, Ill.). Normality of quantitative data was checked using the Kolmogorov-Smirnov 1-sample test. Differences between groups were tested by the Student *t* test and Mann-Whitney *U* test for normal and nonnormal continuous variables, respectively, and the χ^2 test or Fisher exact test for categorical variables whenever appropriate. Correlations for normally distributed data were made with linear regression (Pearson r_p), and nonnormally distributed data were correlated with a rank method (Spearman *r*).

The respective rating scores assessed over time were subjected to repeated-measure analysis of variance, using diagnosis (schizoaffective disorder vs. schizophrenia) as the between-group factor and the different rating scores over time as the within-group factors. Significant interactions (group vs. time) were then explored with post hoc change-score analyses. A *p* value of < .05 (2-tailed) was taken to indicate statistical significance.

RESULTS

Demographic and Clinical Characteristics

Table 1 compares the basic demographic and clinical characteristics of patients with first-episode schizoaffective disorder or first-episode schizophrenia. Patients with schizoaffective disorders were more educated (mean $\pm$ SD years, 12.63 $\pm$ 3.70 vs. 10.64 $\pm$ 3.36, $z = -2.15$, $p = .032$), were more likely to be employed (OR = 3.38, 95% CI = 1.27 to 9.02, $p = .019$), and had a shorter duration of untreated psychosis (mean $\pm$ SD months, 11.44 $\pm$ 14.13 vs. 28.09 $\pm$ 36.43, $z = -3.30$, $p = .001$) compared to patients with first-episode schizophrenia. There were no significant baseline differences in terms of age at onset of illness, gender, marital status, living arrangements, or family history of mental illness.

At baseline, patients with first-episode schizoaffective disorder had higher general psychopathology subscale scores on the PANSS ($z = -2.69$, $p = .007$) compared to patients with schizophrenia (Table 2). Patients with schizoaffective disorder did not differ significantly from patients with first-episode schizophrenia in the other baseline subscale scores of PANSS or in the SUMD or GAF scores (Table 2). Within the PANSS general psychopathology subscale at baseline, patients with schizoaffective disorder scored higher on the guilt feelings (mean $\pm$ SD, 1.67 $\pm$ 1.27 vs. 1.19 $\pm$ 0.68, $p = .007$), depression (3.04 $\pm$ 1.89 vs. 1.56 $\pm$ 1.03, $p < .001$), and poor attention (1.95 $\pm$ 1.22 vs. 1.46 $\pm$ 0.98, $p = .012$) items compared to patients with schizophrenia. Table 3 compares baseline QOL between the 2 groups, with lower scores indicating poorer QOL, and includes scores for overall QOL, general health, and 4 other QOL subdomains.

Table 1. Demographic and Clinical Features of Patients With Schizoaffective Disorder or Schizophrenia

Characteristic	Schizoaffective Disorder (N = 24)		Schizophrenia (N = 254)		p Value	z Statistic ^a
	Mean	SD	Mean	SD		
Age at onset of illness, y	27.35	5.23	28.75	6.53	.33	-0.98
Years of schooling	12.63	3.70	10.64	3.36	.03	-2.15
Duration of untreated psychosis, mo	11.44	14.13	28.09	36.43	.001	-3.30
	N	%	N	%	p Value	χ^2 Statistic
Gender					.83	0.089
Male	13	54.2	140	55.1		
Female	11	45.8	114	44.9		
Marital status					.75	0.428
Married	2	8.3	36	14.2		
Not married	22	91.7	218	85.8		
Employment status					.019	6.538
Employed	7	29.2	31	12.2		
Unemployed	17	70.8	223	87.8		
Living arrangements					.69	0.015
Self	1	4.2	13	5.1		
Living with others	23	95.8	241	94.9		
Family history of mental illness					.47	0.586
Yes	8	33.3	71	28.0		
No	16	66.7	183	72.0		

^aMann-Whitney U test.**Table 2. Baseline PANSS, SUMD, and GAF Scores in Patients With Schizoaffective Disorder or Schizophrenia**

Scale	Schizoaffective Disorder (N = 24)		Schizophrenia (N = 254)		p Value	z Statistic ^a
	Mean	SD	Mean	SD		
PANSS scores						
Total	67.29	12.38	62.72	14.87	.12	-1.56
Positive subscale	19.84	5.39	18.94	5.49	.46	-0.74
Negative subscale	11.24	5.92	12.82	7.51	.66	-0.44
General psychopathology subscale	35.87	7.49	31.08	7.93	.007	-2.69
SUMD scores (current awareness) ^b						
Mental disorder	2.38	0.64	2.41	0.67	.57	-0.56
Social consequences	2.33	0.64	2.40	0.68	.65	-0.46
Medication effects	2.08	0.72	2.04	0.87	.90	-0.12
Hallucinations	2.13	0.87	1.95	0.99	.60	-0.53
Delusions	2.08	1.18	2.01	1.13	.63	-0.49
Thought disorder	1.54	1.38	1.40	1.35	.49	-0.70
Flat affect	1.38	1.35	1.29	1.33	.69	-0.40
Anhedonia	1.29	1.08	1.38	1.21	.62	-0.49
Asociality	1.38	1.06	1.66	1.17	.17	-0.14
GAF score	41.08	13.29	37.86	15.45	.22	-1.22

^aMann-Whitney U test.^bHigher scores indicate lower level of insight.

Abbreviations: GAF = Global Assessment of Functioning scale, PANSS = Positive and Negative Syndrome Scale, SUMD = Scale to Assess Unawareness of Mental Disorder.

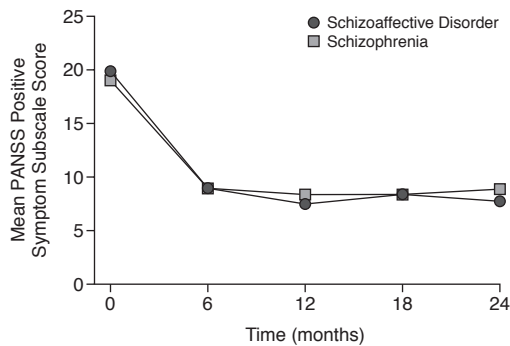
Table 3. Baseline WHOQOL-BREF Scores in Patients With Schizoaffective Disorder or Schizophrenia

WHOQOL-BREF Domains	Schizoaffective Disorder (N = 24)		Schizophrenia (N = 254)		p Value	z Statistic ^a
	Mean	SD	Mean	SD		
Overall quality of life	3.25	1.29	3.26	1.03	.78	-0.28
General health	3.38	1.26	3.39	1.12	.97	-0.03
Physical health	14.08	3.17	13.83	2.74	.81	-0.16
Psychological health	13.14	2.93	12.65	2.81	.70	-0.39
Social relationships	13.14	3.77	12.84	3.39	.98	-0.02
Environment	13.25	2.46	12.97	2.73	.67	-0.43

^aMann-Whitney U test.

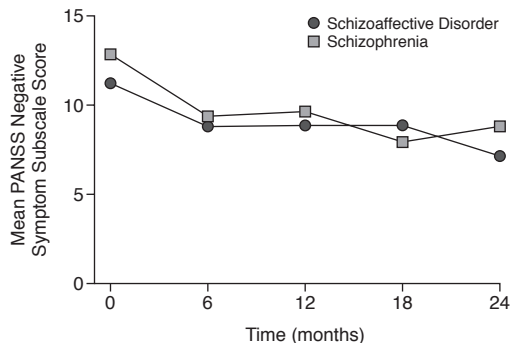
Abbreviation: WHOQOL-BREF = World Health Organization Quality of Life-BREF scale.

Figure 1. Mean PANSS Positive Symptom Subscale Scores Between the 2 Groups Over 24 Months



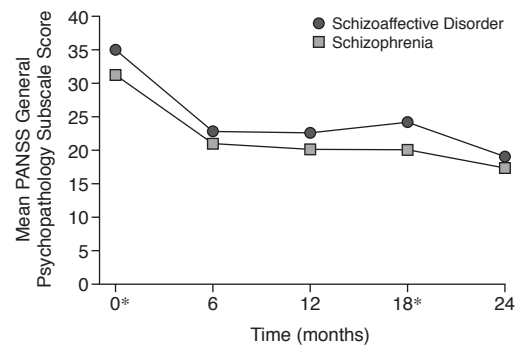
Abbreviation: PANSS = Positive and Negative Syndrome Scale.

Figure 2. Mean PANSS Negative Symptom Subscale Scores Between the 2 Groups Over 24 Months



Abbreviation: PANSS = Positive and Negative Syndrome Scale.

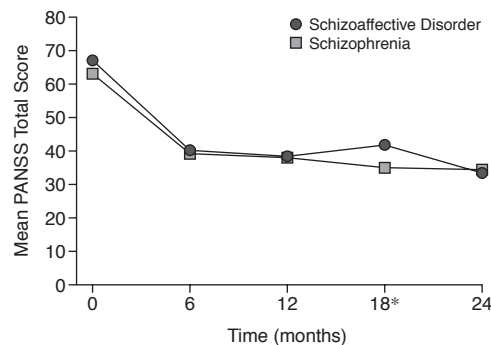
Figure 3. Mean PANSS General Psychopathology Subscale Scores Between the 2 Groups Over 24 Months



* $p < .05$.

Abbreviation: PANSS = Positive and Negative Syndrome Scale.

Figure 4. Mean PANSS Total Scores Between the 2 Groups Over 24 Months



* $p < .05$.

Abbreviation: PANSS = Positive and Negative Syndrome Scale.

Prospective Clinical and Functional Outcomes

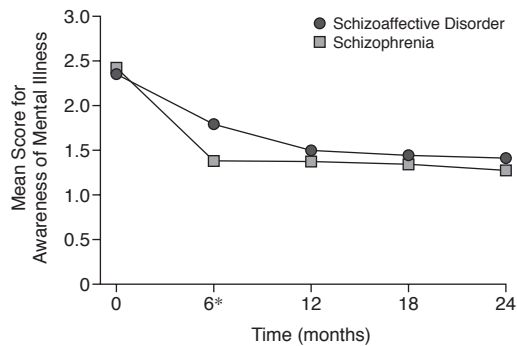
Longitudinally, significant differences between the 2 groups of patients (schizoaffective disorder and schizophrenia) were demonstrated in PANSS total ($F = 10.86$, $df = 1,277$; $p = .001$) and general psychopathology subscale ($F = 6.54$, $df = 1,277$; $p = .01$) scores, awareness of psychiatric illness ($F = 5.35$, $df = 1,277$; $p = .02$), and WHOQOL-BREF scores in the psychological health subdomain ($F = 4.08$, $df = 1,277$; $p = .04$). There were no differences in rating scores across time between the 2 groups in PANSS positive and negative subscale scores, GAF scores, or medication doses in daily chlorpromazine equivalents (Figures 1–8).

Patients with schizophrenia had better insight into their psychiatric illness (mean $\pm$ SD SUMD score, 1.38 ± 0.52 vs. 1.78 ± 0.72 , $z = -3.93$, $p < .001$) at 6 months and expressed a better QOL in the psychological health domain of the WHOQOL-BREF (mean $\pm$ SD score, 13.73 ± 1.96 vs. 12.01 ± 1.44 , $z = -3.83$, $p < .001$) at 12 months compared to patients with schizoaffective

disorder. At 18 months, patients with schizoaffective disorder had higher PANSS total (mean $\pm$ SD, 42.02 ± 12.68 vs. 35.05 ± 8.43 , $z = -3.62$, $p < .001$) and general psychopathology subscale (24.00 ± 2.89 vs. 19.83 ± 4.29 , $z = -3.89$, $p < .001$) scores compared to patients with schizophrenia.

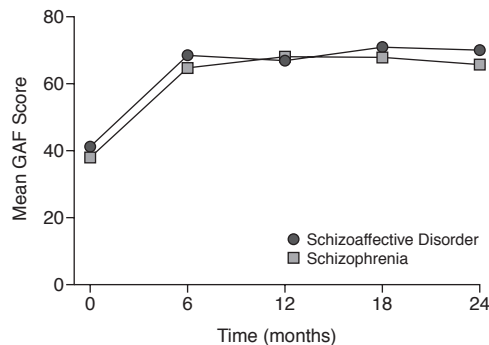
There was no difference in the total length of hospitalization between the 2 groups of patients with schizoaffective disorder or schizophrenia (mean $\pm$ SD days, 29.71 ± 20.70 vs. 26.95 ± 26.93 , $z = -1.11$, $p = .27$). In terms of correlations, within the group of patients with schizoaffective disorder, age was correlated with GAF score at 2 years ($r = -0.90$, $p < .01$); years of schooling were correlated with baseline PANSS positive symptom subscale score ($r = -0.50$, $p < .01$); and DUP was significantly correlated with baseline WHOQOL-BREF psychological health subdomain score ($r = -0.58$, $p < .01$). Within the group of patients with schizophrenia, age was correlated with baseline GAF score ($r = -0.22$, $p < .01$); years of schooling were correlated with DUP ($r = -0.23$,

Figure 5. Mean Scores for Awareness of Mental Illness Between the 2 Groups Over 24 Months



* $p < .05$.

Figure 6. Mean GAF Scores Between the 2 Groups Over 24 Months



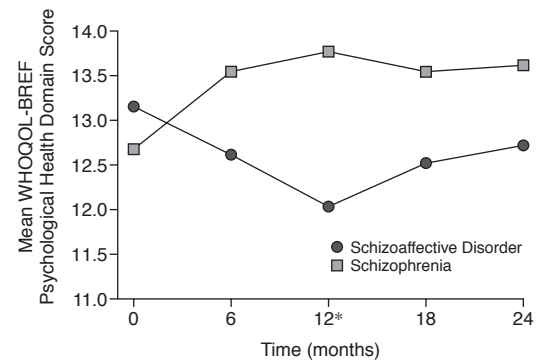
Abbreviation: GAF = Global Assessment of Functioning scale.

$p < .01$); and DUP was significantly correlated with baseline PANSS total ($r = 0.14$, $p < .01$) and negative symptom subscale ($r = 0.16$, $p < .01$) scores and GAF score ($r = -0.17$, $p < .01$).

DISCUSSION

This study yielded a few main findings: first, schizoaffective disorder was associated with better patient employment status, a shorter DUP, and better patient education, but higher general psychopathology scores on PANSS, compared to the findings in patients with schizophrenia at baseline. Second, the greater psychopathology on PANSS in patients with schizoaffective disorder persisted over time. Third, patients with schizoaffective disorder had poorer insight into their psychiatric illness at 6 months and a poorer QOL, especially in the psychological health subdomain of the WHOQOL-BREF at 1 year, compared to patients with schizophrenia. These findings refuted our hypothesis that patients with schizoaffective disorder necessarily had less severity of illness and better

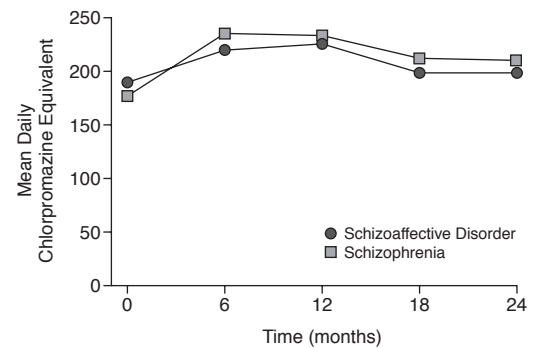
Figure 7. Mean WHOQOL-BREF Psychological Health Domain Scores Between the 2 Groups Over 24 Months



* $p < .05$.

Abbreviation: WHOQOL-BREF = World Health Organization Quality of Life-BREF scale.

Figure 8. Mean Daily Chlorpromazine Equivalents Between the 2 Groups Over 24 Months



prospective clinical and functional outcomes compared to patients with schizophrenia.

Schizoaffective disorder was more likely to be associated with patient employment compared to the findings in patients with schizophrenia, indicating a more favorable level of social functioning in schizoaffective disorder at baseline, and this result is in agreement with the findings of earlier studies.^{34,35} Grossman et al.³⁴ studied 39 patients with schizoaffective disorder, 47 patients with schizophrenia, and 81 subjects with affective disorder and found that patients with schizoaffective disorder had better work performance compared with patients with schizophrenia. Jäger et al.,³⁵ comparing their cohort of 30 patients with schizoaffective disorder with 64 patients with schizophrenia, also found that regular employment rates were higher in schizoaffective disorder (73.3%) compared with schizophrenia (46.9%).³⁵

Duration of untreated psychosis was shorter in patients with schizoaffective disorder, and this result was corre-

lated with better QOL, especially in the domain of psychological health at baseline. Malla et al.,³⁶ in their study to evaluate the determinants of QOL in patients with first-episode psychosis, similarly reported that DUP was inversely related to the social relationship domain using the Wisconsin Quality of Life scale. In our study, within the cohort of patients with schizophrenia, an increased DUP was further correlated with greater severity of PANSS total and negative subscale scores as well as lower GAF scores, which is consistent with the findings of previous studies.^{37,38} Melle et al.³⁷ found that DUP was associated with 3-month global symptom severity and global functional outcomes using a modified GAF. In a meta-analytic study, Perkins et al.³⁸ found that greater severity of negative symptoms at first treatment contact was significantly associated with longer DUP. The length of DUP may be a marker of the severity of the psychotic illness, and the relationship between DUP and outcome may reflect an underlying, progressive pathophysiologic process associated with postulated neural network dysregulation,³⁹ changes in synaptic plasticity,⁴⁰ or an acceleration of normal synaptic pruning or apoptotic processes.⁴¹ This notion lends further support for early intervention that seeks to reduce DUP, a potentially malleable and modifiable clinical factor, and affect the symptomatologic and functional domains of individuals suffering from psychotic illness.

Better education, in terms of more years of schooling, was found in patients with schizoaffective disorder compared to patients with schizophrenia, and this result is in agreement with the findings of other investigators. Marneros et al.¹⁰ found a significantly higher educational level in their cohort of subjects with schizoaffective disorder compared to subjects with schizophrenia but not when compared to patients with pure affective disorder. In addition, more years of schooling were correlated with decreased PANSS positive subscale scores in patients with schizoaffective disorder and shorter DUP in patients with first-episode schizophrenia.¹⁰ It is interesting to postulate that education may exert its protective effects through greater awareness of the mental condition and illness, earlier access to treatment, shorter DUP, and less severe psychopathology.

Of note, schizoaffective disorder was associated with greater severity of psychopathology, especially in the general psychopathology subscale of PANSS at baseline, with several implications. This result may reflect a higher level of affective symptoms in these individuals and could be attributed to the presentation of the illness or related to other associated psychiatric syndromes. Earlier studies have found substantial prevalence rates of psychiatric comorbidities in patients with first-episode psychosis including schizophrenia spectrum disorders.^{42,43} Furthermore, a separate analysis of the baseline psychopathology subscale scores revealed that patients with

schizoaffective disorder scored higher on the guilt feelings, depression, and poor attention items. The greater severity of psychopathology in the presence, or otherwise, of other concurrent psychiatric symptoms or syndromes may impact negatively on longitudinal outcomes such as QOL within these individuals.

With regard to gender, a female preponderance within patients with schizoaffective disorder had been found in previous studies but not in this study. For example, Marneros et al.¹⁰ found that females constituted 63% of their patients with schizoaffective disorder. In a prospective analysis of antecedent psychopathologic features and sociodemographic risk factors in schizophrenia spectrum disorders with data from 5 community sites in the National Institute of Mental Health Epidemiologic Catchment Area Program, Tien and Eaton⁴⁴ found that the relative risk for developing a psychotic disorder with affective features (including schizoaffective disorder) was 6.8 in females compared to males. However, this gender difference was not found in all studies; for example, Kitamura and Suga⁴⁵ reported no gender differences in terms of preponderance in both schizo-depressive and schizo-manic syndromes.

Age at onset was previously noted to be younger in patients with schizoaffective disorder, but this association was not found in our study. Marneros et al.¹⁰ investigated 106 affective, 101 schizoaffective, and 148 schizophrenic disorders after a long-term course of illness and found that the median age at onset of illness for schizoaffective disorder was younger than that for affective disorder but older than that for schizophrenia. However, Tsuang et al.⁴⁶ did not find any difference in their study cohort, although they found that the mean age at onset of illness was significantly younger in schizoaffective disorder when compared to affective disorders using the Washington University criteria. However, in both groups of patients, age at onset was correlated with a lower level of psychosocial functioning,^{10,46} and this finding underscores the need for early identification of these individuals for more intensive management including psychoeducation and timely enrollment in rehabilitation programs.

At 6 months, patients with schizoaffective disorder tended to have poorer insight into their illness compared to patients with schizophrenia. At 12 months, these patients expressed a lower level of QOL, especially in the psychological health domain. Furthermore, the higher baseline PANSS general psychopathology subscale score persisted over time, especially at 18 months, suggesting that schizoaffective disorder may not be associated with better prospective clinical outcomes. A few reasons may be posited. First, the lower level of insight may be related to the greater severity of psychopathology, which may also affect negatively their own evaluation of a sense of well-being. Second, these individuals may be more willing to express their feelings and emotional state and

hence were rated higher on the PANSS general psychopathology subscale. Third, patients with schizoaffective disorders may have inherently poorer-quality lives and thus rated their health-related QOL according to their internal feeling state. Fourth, affective symptoms in schizoaffective disorder may independently affect QOL.⁴⁷ Fifth, greater cognitive deficits may underlie the poor insight and also have an impact on the degree of psychopathology in these individuals.^{48,49}

There were several limitations in this study. First, the sample size for patients with schizoaffective disorder was small, hence disallowing unjustifiable subgrouping of these patients for further analysis of associated outcome predictors. Second, the patients were followed up for only 24 months. It remains unknown whether other differences in clinical and functional outcome variables may unfold over a longer period of study. Third, we did not compare schizoaffective disorder with affective disorders; thus, we are not able to make comments regarding the prospective outcomes between the 2 groups or implications regarding nosologic validity of schizoaffective disorder in relation to affective disorders.

In conclusion, our findings refuted the notion that patients with schizoaffective disorder necessarily have better prospective outcomes compared to patients with schizophrenia. This result should raise awareness in the treatment and management of these patients with a potentially crippling psychiatric illness.

REFERENCES

- Kasanin J. The acute schizoaffective psychoses: 1933. *Am J Psychiatry* 1994;151(suppl 6):144-154
- Harrow M, Grossman LS. Outcome in schizoaffective disorders: a critical review and reevaluation of the literature. *Schizophr Bull* 1984; 10:87-108
- Lapensee MA. A review of schizoaffective disorder, I: current concepts. *Can J Psychiatry* 1992;37:335-346
- Maj M, Perris C. An approach to the diagnosis and classification of schizoaffective disorders for research purposes. *Acta Psychiatr Scand* 1985;72:405-413
- Kendell RE. The relationship of schizoaffective illness to schizophrenic and affective disorders. In: Marneros A, Tsuang MT, eds. *Schizoaffective Psychoses*. Berlin, Germany: Springer-Verlag; 1986:18-30
- Evans JD, Heaton RK, Paulsen JS, et al. Schizoaffective disorder: a form of schizophrenia or affective disorder? *J Clin Psychiatry* 1999;60: 874-882
- Himmelhoeh JM, Fuchs CZ, May SJ, et al. When a schizoaffective diagnosis has meaning. *J Nerv Ment Dis* 1981;169:277-282
- Pope HG Jr, Lipinski JF Jr. Diagnosis in schizophrenia and manic-depressive illness: a reassessment of the specificity of "schizophrenic" symptoms in the light of current research. *Arch Gen Psychiatry* 1978;35: 811-828
- Pope HG Jr, Lipinski JF, Cohen BM, et al. "Schizoaffective disorder": an invalid diagnosis? a comparison of schizoaffective disorder, schizophrenia, and affective disorder. *Am J Psychiatry* 1980;137:921-927
- Marneros A, Deister A, Rohde A. Psychopathological and social status of patients with affective, schizophrenic and schizoaffective disorders after long-term course. *Acta Psychiatr Scand* 1990;82:352-358
- Tsuang MT, Dempsey GM. Long-term outcome of major psychoses, 2: schizoaffective disorder compared with schizophrenia, affective disorders, and a surgical control group. *Arch Gen Psychiatry* 1979;36: 1302-1304
- Perris C. A study of cycloid psychoses. *Acta Psychiatr Scand Suppl* 1974;253:1-77
- Angst J, Scharfetter C, Stassen HH. Classification of schizo-affective patients by multidimensional scaling and cluster analysis. *Psychiatr Clin (Basel)* 1983;16:254-264
- Berg E, Lindelius R, Petterson U, et al. Schizoaffective psychoses: a long-term follow-up. *Acta Psychiatr Scand* 1983;67:389-398
- Levitt JJ, Tsuang MT. The heterogeneity of schizoaffective disorder: implications for treatment. *Am J Psychiatry* 1988;145:926-936
- Brockington IF, Kendell RE, Wainwright S. Depressed patients with schizophrenic or paranoid symptoms. *Psychol Med* 1980;10:665-675
- Addington J, Chaves A, Addington D. Diagnostic stability over one year in first-episode psychosis. *Schizophr Res* 2006;86:71-75
- Schimmelmann BG, Conus P, Edwards J, et al. Diagnostic stability 18 months after treatment initiation for first-episode psychosis. *J Clin Psychiatry* 2005;66:1239-1246
- Welner A, Croughan J, Fishman R, et al. The group of schizoaffective and related psychoses: a follow-up study. *Compr Psychiatry* 1977;18: 413-422
- Möller HJ, Hohe-Schramm M, Cording-Tommel C, et al. The classification of functional psychoses and its implications for prognosis. *Br J Psychiatry* 1989;154:467-472
- Marneros A, Rohde A, Deister A. Factors influencing the long-term outcome of schizoaffective disorders. *Psychopathology* 1993;26: 215-224
- First MB, Spitzer RL, Gibbon M, et al. *Structured Clinical Interview for DSM IV Axis I Disorders, Patient Edition (SCID-P)*, version 2. New York, NY: New York State Psychiatric Institute, Biometrics Research; 1994
- Kay SR, Fiszbein A, Opler LA. The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophr Bull* 1987;13:261-276
- Amador XF, Flaum M, Andreasen NC, et al. Awareness of illness in schizophrenia and schizoaffective and mood disorders. *Arch Gen Psychiatry* 1994;51:826-836
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Washington, DC: American Psychiatric Association; 1994:32
- The WHOQOL Group. Development of the World Health Organization WHOQOL-BREF quality of life assessment. *Psychol Med* 1998;28: 551-558
- Herrman H, Hawthorne G, Thomas R. Quality of life assessment in people living with psychosis. *Soc Psychiatry Psychiatr Epidemiol* 2002; 37:510-518
- Saxena S, Carlson D, Billington R, et al. The WHO quality of life assessment instrument (WHOQOL-BREF): the importance of its items for cross-cultural research. *Qual Life Res* 2001;10:711-721
- Yao G, Chung CW, Yu CF, et al. Development and verification of validity and reliability of the WHOQOL-BREF Taiwan version. *J Formos Med Assoc* 2002;101:342-351
- McGlashan TH. Duration of untreated psychosis in first-episode schizophrenia: marker or determinant of course? *Biol Psychiatry* 1999;46: 899-907
- American Psychiatric Association. *Practice Guideline for the Treatment of Patients With Schizophrenia*. *Am J Psychiatry* 1997;154(suppl 4):1-63
- Woods SW. Chlorpromazine equivalent doses for the newer atypical antipsychotics. *J Clin Psychiatry* 2003;64:663-667
- Leckman JF, Sholomskas D, Thompson WD, et al. Best estimate of lifetime psychiatric diagnosis: a methodological study. *Arch Gen Psychiatry* 1982;39:879-883
- Grossman LS, Harrow M, Fudala JL, et al. The longitudinal course of schizoaffective disorders: a prospective follow-up study. *J Nerv Ment Dis* 1984;172:140-149
- Jäger M, Bottlender R, Strauss A, et al. Fifteen-year follow-up of ICD-10 schizoaffective disorders compared with schizophrenia and affective disorders. *Acta Psychiatr Scand* 2004;109:30-37
- Malla AK, Norman RM, McLean TS, et al. Determinants of quality of life in first-episode psychosis. *Acta Psychiatr Scand* 2004;109:46-54
- Melle I, Larsen TK, Haahr U, et al. Reducing the duration of untreated first-episode psychosis: effects on clinical presentation. *Arch Gen Psychiatry* 2004;61:143-150
- Perkins DO, Gu H, Boteva K, et al. Relationship between duration of untreated psychosis and outcome in first-episode schizophrenia: a critical review and meta-analysis. *Am J Psychiatry* 2005;162:1785-1804

39. Lieberman JA. Is schizophrenia a neurodegenerative disorder? a clinical and neurobiological perspective. *Biol Psychiatry* 1999;46:729–739
40. McGlashan TH. Is active psychosis neurotoxic? *Schizophr Bull* 2006; 32:609–613
41. Margolis RL, Chuang DM, Post RM. Programmed cell death: implications for neuropsychiatric disorders. *Biol Psychiatry* 1994;35:946–956
42. Sim K, Mahendran R, Chong SA. Health-related quality of life and psychiatric comorbidity in first episode psychosis. *Compr Psychiatry* 2005;46:278–283
43. Sim K, Swapna V, Mythily S, et al. Psychiatric comorbidity in first episode psychosis: the Early Psychosis Intervention Program (EPIP) experience. *Acta Psychiatr Scand* 2004;109:23–29
44. Tien AY, Eaton WW. Psychopathologic precursors and sociodemographic risk factors for the schizophrenia syndrome. *Arch Gen Psychiatry* 1992;49:37–46
45. Kitamura T, Suga R. Depressive and negative symptoms in major psychiatric disorders. *Compr Psychiatry* 1991;32:88–94
46. Tsuang MT, Simpson JC, Fleming JA. Diagnostic criteria for subtyping schizoaffective disorder. In: Marneros A, Tsuang MT, eds. *Schizoaffective Psychoses*. Berlin, Germany: Springer-Verlag; 1986:50–62
47. Tollefson GD, Andersen SW. Should we consider mood disturbance in schizophrenia as an important determinant of quality of life? *J Clin Psychiatry* 1999;60(suppl 5):23–29
48. Drake RJ, Lewis SW. Insight and neurocognition in schizophrenia. *Schizophr Res* 2003;62:165–173
49. Robinson DG, Woerner MG, McMeniman M, et al. Symptomatic and functional recovery from a first episode of schizophrenia or schizoaffective disorder. *Am J Psychiatry* 2004;161:473–479