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Differences between first episode schizophrenia and schizoaffective disorder

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ABSTRACT

Background: The diagnostic and clinical overlap between schizophrenia and schizoaffective disorder is an important nosological issue in psychiatry that is yet to be resolved. The aim of this study was to compare the clinical and functional characteristics of an epidemiological treated cohort of first episode patients with an 18-month discharge diagnosis of schizophrenia (FES) or schizoaffective disorder (FESA).
Methods: This study was part of the larger First Episode Psychosis Outcome Study (FEPOS) which involved a medical file audit study of all 786 patients treated at the Early Psychosis Prevention and Intervention Centre between 1998 and 2000. Of this cohort, 283 patients had an 18-month discharge diagnosis of FES and 64 had a diagnosis of FESA. DSM-IV diagnoses and clinical and functional ratings were derived and validated by two consultant psychiatrists.
Results: Compared to FES patients, those with FESA were significantly more likely to have a later age of onset ($p = .004$), longer prodrome ($p = .020$), and a longer duration of untreated psychosis ($p < .001$). At service entry, FESA patients presented with a higher illness severity ($p = .020$), largely due to the presence of more severe manic symptoms ($p < .001$). FESA patients also had a greater number of subsequent inpatient admissions ($p = .017$), had more severe depressive symptoms ($p = .011$), and higher levels of functioning at discharge.
Discussion: The findings support the notion that these might be considered two discernable disorders; however, further research is required to ascertain the ways and extent to which these disorders are discriminable at presentation and over time.

1. Introduction

The term schizoaffective disorder (SAD) was first coined in the 1930s to capture those patients presenting with characteristics of both schizophrenia and affective disturbance (Kasanin, 1933). SAD comprises bipolar or depressive subtypes. There has been much contention as to whether SAD can be considered a distinct and valid nosological entity. On the one hand, it has been argued that SAD is a mood disorder with psychotic features, and as such, should be excluded as a diagnostic category from the 5th edition of Diagnostic and Statistical Manual for Mental Disorders (DSM-5) (Lake and Hurwitz, 2008). On the other hand, as at 30 April 2012, the current DSM-5 proposal is for SAD to be categorised as a schizophrenia spectrum disorder. In order to support this proposal, it is important to delineate the extent of the similarities and differences between SAD and schizophrenia.

There is much contention regarding the extent of difference between SAD and schizophrenia. Some studies have found that patients with SAD are more likely to be female (Cheniaux et al., 2008; Saracco-Alvarez et al., 2009; Bredicean et al., 2011), have a later age of onset (Averill et al., 2004; Cheniaux et al., 2008; Saracco-Alvarez et al., 2009), have better premorbid adjustment (Bottlender et al., 2002; Norman et al., 2005; Saracco-Alvarez et al., 2009), a longer duration of untreated psychosis (DUP) (Sim et al., 2007), higher vocational

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and social functioning (Benabarre et al., 2001; Cheniaux et al., 2008; Bottlender et al., 2010; Bredicean et al., 2011), greater drug and alcohol problems (Nardi et al., 2005), and less severe negative symptoms (Saracco-Alvarez et al., 2009). Some have also reported that the outcomes of SAD are better than those for schizophrenia (Harrow et al., 2000; Tohen et al., 2000; Abrams et al., 2008; Jäger et al., 2011). There are however, other studies reporting no differences in gender ratio (Frazier et al., 2007; Sim et al., 2007; Kao and Liu, 2010), age of onset of illness (Benabarre et al., 2001; Jäger et al., 2004; Nardi et al., 2005; Sim et al., 2007; Kao and Liu, 2010), and long-term symptom and functional outcomes (Tsuang and Coryell, 1993; Lay et al., 1997; Harrow et al., 2000).

An array of methodological issues contributes to the heterogeneity of findings. First, there have been problems associated with definition of SAD (Murru et al., 2011). For example, the ICD-10 criteria for SAD are broader than the DSM-IV-TR criteria (Vollmmer-Larsen et al., 2006; Malhi et al., 2008). Although both diagnostic systems require the combination of a full affective syndrome (either manic or depressive symptoms) in addition to schizophrenic symptoms, DSM-IV-TR additionally requires a 2 week period of prominent schizophrenic symptoms without the presence of affective symptoms (Vollmmer-Larsen et al., 2006; Malhi et al., 2008). In ICD-10 SAD is viewed as episodic in nature whereas DSM-IV-TR conceptualises SAD as uninterrupted illness with schizophrenic symptoms being concurrent to depressive, manic or mixed episodes (Malhi et al., 2008). Consequently, ICD-10 SAD is a more heterogeneous entity.

Second, the timing of the diagnosis can also affect study outcomes. Many studies have erroneously used diagnosis at illness onset (Harrow and Grossman, 1984). The diagnostic stability of SAD is poor (Schwartz et al., 2000; Abrams et al., 2008); patients initially diagnosed as having SAD often later meet diagnostic criteria for schizophrenia, bipolar disorder, or mood disorder with psychotic features. Further, the diagnosis at first presentation cannot be considered definitive, as longitudinal context is required to gauge the temporal overlap between psychotic and affective symptoms (Ledda et al., 2009). There have been other studies that have not specified the timing of diagnosis in relation to illness course; thus, it is difficult to ascertain the validity of the diagnostic categories (Harrow and Grossman, 1984).

A third issue relates to the phase and severity of psychotic illness. During phases of acute versus stabilised symptoms, the degree of difference between schizophrenia and schizoaffective disorder may fluctuate. Use of chronic inpatient populations treated with neuroleptics and longstanding illness may also confound group differences. Using patients at their index inpatient admission (e.g., Bottlender et al., 2002; Jäger et al., 2004; Bredicean et al., 2011) could also be considered problematic; such studies exclude patients at the less severe spectrum of illness and chronicity of illness is not necessarily controlled with some patients already developing a deteriorating illness course (Harrow and Grossman, 1984).

Finally, in many studies, the two diagnoses are often combined for statistical analyses and there is no consideration of differences between groups (Ledda et al., 2009). On the basis of these methodological issues, research findings depicting any group differences (or the lack of such differences) are inconclusive; they may apply to only ill-defined sub-populations.

The nature of the differences between these diagnostic groups in the early phase of illness is particularly unclear. However, studying clinical and functional differences between these two diagnostic groups in the early stages of illness avoids confounds such as duration of illness, relapses and medications (Conus et al., 2007).

Understanding differences in patients with these disorders in the first episode is also an important strategy to facilitate early differential diagnosis (Benabarre et al., 2001). Accurate diagnosis is important for the provision of targeted interventions; the psychopharmacological and psychosocial interventions that maximise outcomes for patients with schizophrenia and SAD might differ (Murru et al., 2011).

Thus, the aim of this study was to compare, within a treated epidemiological cohort of FEP patients, the clinical characteristics of patients with schizophrenia (FES) or schizoaffective disorder (FESA).

2. Material and methods

2.1. Sample and setting

The sample was part of a larger file audit study (the First Episode Outcome Study, FEPOS) of a treated epidemiological cohort of 786 patients with FEP (Conus et al., 2007). Patients were treated for their first episode of psychosis at the Early Psychosis Prevention and Intervention Centre (EPPIC), Melbourne, Australia between 1998 and 2000. At the time of the study, EPPIC served a catchment area of approximately 880,000. This catchment area covered the north-west and western suburbs of Melbourne. There was an absence of other treatment facilities for the target population and a virtual absence of private psychiatrists in the area. There was little, if any leakage to private facilities outside the catchment area. Thus, this was a truly epidemiological cohort (Conus et al., 2007). For this study, the sample comprised 283 patients with a discharge diagnosis of FES and 64 patients with FESA.

2.2. Materials and procedure

To systematically assess consecutive medical files we used the Early Psychosis File Questionnaire (EPFQ, see Conus et al., 2007 for a full description). This questionnaire was a specifically designed file audit tool and included questions derived from the following assessment tools and scales: the Royal Park Multi-diagnostic Instrument for Psychosis (RP-MIP, McGorry et al., 1990a,b); the Drug and Alcohol Assessment Schedule (DAAS, McGorry et al., 1990a,b); the Duration of Untreated Psychosis Scale (McGorry et al., 1996); the Clinical Global Impressions-Severity of Illness Scale (CGI-S, Guy, 1976); the Clinical Global Impressions-Severity of Illness Scale-Bipolar Illness (CGI-BP, Spearing et al., 1997); the Global Assessment of Functioning Scale (GAF); the Modified Vocational Status Index (MVSI, Tohen et al., 2000); and the Modified Location Code Index (MLCI, Tohen et al., 2000). More specific details follow.

2.3. Diagnosis

Diagnosis was based on DSM-IV-TR criteria. For FESA, patients needed to satisfy Criterion A for schizophrenia (e.g. delusions and hallucinations) as well as the criterion that there was a period of at least two weeks of psychotic symptoms after remission of mood symptoms.

Clinical diagnoses at EPPIC are derived by consensus, following an intensive diagnostic and treatment process over the first 6 weeks of admission, conducted by well-trained clinicians working in a specialised assessment and crisis intervention team (Conus et al., 2007). Eighteen-month discharge clinical diagnoses are based on an iterative process involving clinical assessments performed by a treating team that includes a case manager, psychiatric trainee, and consultant psychiatrist. This team is likely to have on average 94 treatment contacts with the patient and/or family over 18 months (Schimmelmann et al., 2005).

Two research psychiatrists (ML and PC) assessed all information available in medical records with respect to baseline and 18 month diagnoses. This is based on all elements contained in the file over the entire span of treatment. In the event of disagreement with clinical diagnoses, a consensus rating between both research psychiatrists and the case manager was performed. For a subset of 115 randomly selected patients, SCID-I/P diagnoses were available and were used to determine the validity of FEPOS discharge diagnoses (see Conus et al., 2007). There was good concordance for both psychotic ($\kappa = 0.80$) and substance use ($\kappa = 0.74$) diagnoses (Conus et al., 2007).

Because of the known issue of initial instability of diagnosis in the early stage of illness (Schimmelmann et al., 2005), a final 18-month discharge diagnosis was used to define these FES and FESA diagnostic groups and was used as a criterion variable in the statistical analyses.

2.4. Pre-treatment characteristics

Pre-treatment characteristics assessed included: past history of DSM-IV psychiatric disorder; substance use; past suicide attempts (classified based on ICD-10 criteria); family history; premorbid adjustment; duration of prodrome; age of onset; and duration of untreated illness. GAF was used to assess premorbid functioning (best level of functioning in the year preceding illness onset).

2.5. Service entry

Diagnoses at service entry were ascertained according to DSM-IV criteria. Illness severity was assessed according to scores on the CGI-S and the CGI-BP. Insight was coded on a three-point scale (0 'absence of insight'; 1 'partial insight — perception of being ill but persistence of illogical or irrational explanations'; and 2 'full insight'). Functioning was assessed using the GAF and the Modified Vocational Status Index (MVSI) (Tohen et al., 2000).

2.6. Treatment and service discharge characteristics

Treatment information included: newly developed co-morbid DSM-IV diagnoses; suicide attempts; inpatient admissions (both number of and duration); medication non-compliance (≥1 week without taking medication whilst being a registered at EPPIC patient); and level of service engagement. At service discharge, final diagnoses and substance use were documented. Symptom severity was determined using CGI-S, CGI-BP, and the insight scale. The GAF and MVSI were used to assess discharge functional status.

2.7. Reliability and validity

Estimates obtained for inter-rater reliability for the CGI, CGI-BP, GAF, and insight for 40 files were good (range: $ICC_{2,1} = 0.87$ for CGI-S to $ICC_{2,1} = 0.89$ for insight score) (Conus et al., 2007).

2.8. Data analysis

IBM SPSS Statistics Version 20.0 (IBM Corp., 2011) was used for the proceeding analyses. A series of logistic regressions were conducted with discharge diagnosis as the dependent variable (schizophrenia as the reference category), and the individual premorbid and service entry variables as predictors. From these analyses, odds ratios (ORs) and the 95% confidence intervals (CI) of the ORs were derived. The Wald statistic (z) was used to determine significance of predictors. For the treatment and discharge variables, adjusted ORs and 95% CI of the adjusted ORs were reported, controlling for entry characteristics and time in service (e.g., for GAF at discharge, the covariates were time in service and GAF at entry).

3. Results

3.1. Diagnostic stability

There were 64 patients who had a discharge diagnosis of FESA. Of these patients, 54.7% had received a diagnosis of FESA at baseline. The remaining patients had the following diagnoses at baseline: 23.4% ($n = 15$) with bipolar disorder; 12.5% ($n = 8$) with schizophreniform disorder; 4.7% ($n = 3$) with schizophrenia; 3.1% ($n = 2$) with MDE with psychotic features; and 1.5% ($n = 1$) with a diagnosis of other psychoses. Of the 283 patients with a discharge diagnosis of FES, 50.2% ($n = 142$) had an initial diagnosis of FES, 43.8% ($n = 124$) had schizophreniform disorder, 1.8% ($n = 5$) had FESA, 0.7% ($n = 2$) had bipolar disorder, 0.4% ($n = 1$) had MDE with psychotic features, and 2.3% ($n = 9$) had other psychoses. We have previously reported the positive consistency (positive predictive value or the proportion of patients in a category at baseline who retained the same diagnosis at discharge) and retrospective consistency (sensitivity or the proportion of patients with a specific discharge diagnosis who received the same diagnosis at service entry) (Schimmelmann et al., 2005). For schizophrenia, the prospective consistency was 97.3% and retrospective consistency was 50.2%. For schizoaffective disorder, the prospective consistency was 94.1% and retrospective consistency was 57.1% (Schimmelmann et al., 2005). This supports not only the notion that a longitudinal diagnostic process is required (Schimmelmann et al., 2005) but also the validity of using a diagnostic variable that is based on 18-months of assessment.

3.2. Univariate associations

Patients with a discharge diagnosis of FESA were significantly more likely to have a shorter prodrome (OR = 0.72, $p = .020$), a shorter DUP (OR = 0.57 $p < .001$), and a later age of onset (OR = 1.12, $p = .004$) as compared to the FES group (see Table 1).

At service entry, FESA patients had a higher illness severity (CGI-S, OR = 1.55, $p = .020$); which related to more severe manic symptoms (OR = 3.28, $p < .001$) than the FES group. Conversely, the FES group had significantly higher levels of depressive symptoms than the FESA group (OR = 0.20, $p = .043$).

The FESA group had more inpatient admissions than the FES group (OR = 2.88, $p = .017$) during the 18-month treatment period. Those with FESA were more likely to decrease or cease their substance use during treatment compared to FES (OR = 2.19, $p = .003$) (see Table 2). At discharge, those with FESA were more likely to have more severe depressive symptoms (CGI-BP depression, OR = 1.48, $p = .008$) and slightly higher functioning as measured by the GAF (OR = 1.02, $p = .043$).

Notably, there were no significant differences between the two groups with respect to gender, premorbid functioning, past history of psychiatric illness, years of education, family history of psychiatric disorder, insight at service entry and discharge, and compliance with treatment.

4. Discussion

This is the first study to compare these diagnostic groups at the point of first contact with services, as well as at 18-months post service discharge. Other strengths of this study include the epidemiological representativeness of the treated sample and the use of 18-month diagnosis rather than initial diagnosis, ensuring greater diagnostic reliability. Important differences between these two diagnostic categories were found with respect to illness onset, psychopathology at entry, treatment characteristics, severity of affective symptoms at discharge, and discharge functioning.

Univariate analyses indicated that the path to illness onset was different in the two groups, with FESA patients having a shorter prodrome, a later age of onset, and shorter DUP compared to FES patients. Shorter prodrome in FESA might be due to a more abrupt onset of mood symptoms, in addition to positive psychotic symptoms (Abrams et al., 2008), whereas the prodrome of schizophrenia is often more insidious (Beiser et al., 1993). The combination of psychotic and manic symptoms might also result in patients with FESA receiving earlier treatment than patients with FES. It is unclear, however, as to whether this earlier identification of FESA may alter the early illness course and potentially confound differences observed between FESA and FES.

Existence of differences in the age of onset of illness between schizophrenia and SAD is somewhat controversial, with a diverse range of findings noted. It has been argued that conceptually there

Table 1
The associations (odds ratios, ORs; 95% confidence intervals of the ORs) between pre-treatment and service entry characteristics and a discharge diagnosis of FES or FESA.

Variable		First episode		OR[a]	95% CI		*p* value
		Schizophrenia ($n = 283$)	Schizoaffective disorder ($n = 64$)		LCI	UCI	
Pre-treatment variables							
Gender %Male	% (*n*)	70.3 (199)	64.1 (41)	0.75	0.43	1.33	.329
Years in school	M (SD)	10.3 (1.5)	10.6 (1.5)	1.16	0.96	1.40	.133
Pre-morbid GAF	M (SD)	67.1 (10.1)	69.7 (9.4)	1.03	0.99	1.06	.063
Duration of prodrome (in days)[b]	M (SD)	464.7 (556.2)	345.6 (612.5)	0.72	0.55	0.95	.020
Duration of untreated psychosis (in days)[b]	M (SD)	433.1 (716.0)	153.1 (220.1)	0.57	0.43	0.77	<.001
Age at onset (years)	M (SD)	20.4 (3.6)	21.9 (3.7)	1.12	1.04	1.22	.004
Past history of suicide attempt (%Yes)	% (*n*)	18.9 (53)	12.9 (8)	0.63	0.28	1.41	.265
Family history of psychiatric disorder	% (*n*)	56.7 (157)	54.1 (33)	0.90	0.52	1.57	.713
Diagnostic variables							
Past history							
Psychiatric disorder %Yes	% (*n*)	47.0 (133)	40.6 (26)	0.77	0.44	1.34	.356
Major depressive disorder (MDD) (%Yes)	% (*n*)	23.0 (65)	21.9 (14)	0.94	0.49	1.81	.851
Substance use disorder (SUD) (%Yes)	% (*n*)	75.6 (214)	84.4 (54)	1.74	0.84	3.60	.135
At service entry							
Comorbid psychiatric disorder (%Yes)	% (*n*)	21.9 (62)	10.9 (7)	0.44	0.19	1.01	.052
Comorbid MDD (%Yes)	% (*n*)	9.9 (28)	3.1 (2)	0.29	0.07	1.27	.100
Substance use disorder (SUD) (%Yes)	% (*n*)	62.9 (178)	68.8 (44)	1.30	0.73	2.32	.379
Baseline variables							
Age at service entry	M (SD)	21.7 (3.3)	22.4 (3.6)	1.07	0.99	1.16	.106
Severity of symptoms at entry							
CGI-S severity score	M (SD)	5.6 (0.8)	5.9 (0.7)	1.55	1.07	2.24	.020
CGI-BP depression[b]	M (SD)	2.1 (1.6)	1.8 (1.7)	0.20	0.04	0.95	.043
CGI-BP mania	M (SD)	1.1 (0.5)	3.4 (2.1)	3.28	2.46	4.36	<.001
Functional level at entry							
Employment/occupation (%Yes)	% (n)	38.8 (109)	51.6 (33)	1.68	0.97	2.90	.063
GAF	M (SD)	30.9 (9.1)	29.3 (8.6)	0.98	0.95	1.01	.228
Insight at entry (%No)	% (*n*)	62.9 (178)	67.7 (42)	1.24	0.69	2.22	.473

Note: OR — odds ratio; LCI — lower confidence interval; UCI — upper confidence interval; GAF — Global Assessment of Functioning; CGI-S — Clinical Global Impression Scale-Severity; CGI-BP — Clinical Global Impressions-Severity of Illness Scale-Bipolar Illness.
[a] Odds ratio based on schizophrenia as reference category.
[b] Raw data are presented, however the test statistics were based on log10 (+constant) transformed data because of extreme positive skewness.

should be no difference in age of onset of these two disorders (Abrams et al., 2008). Specifically, the symptoms of delusions, hallucinations, disorganised speech, abnormal psychomotor behaviour, and negative symptoms (or DSM-IV Criterion A) should emerge around the same age in both disorders; that is, late teens to early twenties. There have been some studies that support this contention (Benabarre et al., 2001; Jäger et al., 2004; Nardi et al., 2005). We, however, found an earlier age of onset in FES, which is supported by other studies (Averill et al., 2004; Saracco-Alvarez et al., 2009). Importantly, an earlier age of onset of psychosis and a longer DUP have been associated with poor long-term outcomes and a more severe illness course in FES (Schimmelmann et al., 2007, 2008). Such features have been considered characteristic of schizophrenia and/or a neuroprogressive process (Berk et al., 2011) and might be one reason why patients with FES had lower global functioning at service discharge. Although the age of onset of patients with FES was statistically younger than patients with FESA, the actual difference in the mean age between the diagnostic groups was less than two years. The developmental and clinical importance of this difference in age of onset is open to debate.

Patients with FESA had a greater number of inpatient admissions compared with those patients with FES; a finding commensurate with previous studies (Averill et al., 2004; Cheniaux et al., 2008; Bredicean et al., 2011). This may relate to their greater severity of illness at service entry, which was largely driven by manic symptoms. Patients with SAD also have a more episodic illness course than schizophrenia (episodes including depression, hypomania, and mania) (Benabarre et al., 2001; Cheniaux et al., 2008); and thus require more frequent inpatient admissions.

Interestingly, the course of depressive symptoms differed between FES and FESA patients. We have previously reported that approximately 25% of patients with FES have moderate to severe depressive symptoms during their first acute psychotic episode (Cotton et al., 2012), whereas during the first psychotic episode, SAD is more likely to be characterised by manic symptoms (Benabarre et al., 2001). At discharge, depressive symptoms were more prominent in the FESA group. The exact mechanisms underlying depressive pathology in FES and FESA are unclear, and given the differences in timing of presentation of such symptoms, may indicate that the aetiology of depressive symptoms differs across the two disorders. This highlights the importance of mapping the trajectory of depressive and manic symptoms in early illness course of psychotic disorders.

The FESA diagnostic group were more likely to decrease or cease substance use during treatment than FES patients. Whilst this finding is new, it is consistent with existing evidence of an association between substance use and negative affect (Blanchard et al., 1999), indicating that it may be important to map the trajectory of substance use as well as depressive and manic symptoms in future studies to increase understanding of FESA.

The main limitation of this study is the use of a retrospective medical file audit. Possible problems with this approach include: (i) potential poor quality of documented information; (ii) reliance on clinical experience of raters; (iii) lack of inter-rater reliability; and (iv) questionable data validity. File audits can also restrict the richness of clinical and functional data collected. For example, we were unable to collect more precise information regarding positive and negative psychotic symptoms. Negative symptoms have been noted to be more prominent in inpatients with schizophrenia than those with a diagnosis of SAD; conversely, the disorders might not differ with respect to hallucinations and delusions (Pini et al., 2004). This issue has yet to be examined in a first episode cohort.

Importantly, in the current study we adopted strategies to minimise the impact of most of these limitations including: (i) medical files at

Table 2
The associations (odds ratios, ORs; 95% confidence intervals of the ORs) between pre-treatment and discharge characteristics and a discharge diagnosis of FES or FESA.

Variable		First episode diagnosis		OR	95% CI		*p* value
		Schizophrenia ($n = 283$)	Schizoaffective disorder ($n = 64$)		LCI	UCI	
Treatment variables							
Length of time in service (in weeks)	M (SD)	68.8 (32.8)	71.4 (29.7)	1.00	0.99	1.01	.562
Admitted to hospital (%Yes)[a]	% (n)	70.7 (200)	87.5 (56)	2.88	1.31	6.31	.008
Number of admissions[a]	M (SD)	1.6 (1.7)	2.2 (1.8)	1.19	1.03	1.38	.017
Compliance with treatment (%Yes)[a]	% (n)	65.8 (183)	67.7 (42)	1.09	0.61	1.97	.765
Substance use disorder (SUD)[a, b]							
No SUD	% (n)	32.2 (91)	23.4 (15)	na			
Remitted SUD (decreased or stopped)	% (n)	34.3 (97)	54.7 (35)	2.19	1.12	4.27	.022
Persistent SUD (increased or no change)	% (n)	33.6 (95)	21.9 (14)	0.90	0.41	1.99	.795
Suicide attempt in treatment (%Yes)[a]	% (n)	8.8 (25)	13.1 (8)	1.53	0.65	3.58	.329
Insight at discharge (%No)[c]	% (n)	22.7 (64)	17.2 (11)	0.71	0.33	1.49	.358
Severity of symptoms at discharge							
CGI-S severity score[d]	M (SD)	3.5 (1.2)	3.2 (1.3)	0.81	0.65	1.03	.084
CGI-BP depression score[e]	M (SD)	1.4 (0.9)	1.7 (1.2)	1.48	1.10	1.97	.008
CGI-BP mania score[f]	M (SD)	1.0 (0.1)	1.3 (0.9)	2.25	0.81	6.24	.121
Functional level at discharge							
Employment/occupation (%Yes)[g]	% (n)	34.3 (84)	30.0 (15)	0.61	0.30	1.23	.167
GAF[h]	M (SD)	56.6 (13.4)	60.6 (13.9)	1.02	1.01	1.04	.043

[a] Covariate was time in service.
[b] Based on multinomial logistic regression with 'no substance use' as the reference category for the dependent variable.
[c] Covariates were time in service and insight at service entry.
[d] Covariates were time in service and CGI-S at entry, unadjusted means and standard deviations are reported.
[e] Covariates were time in service and CGI-BP depression (logarithmic transformed) at entry, unadjusted means and standard deviations are reported.
[f] Covariates were time in service and CGI-BP mania at entry, unadjusted means and standard deviations are reported.
[g] Covariates were time in service and employment status at entry.
[h] Covariates were time in service and GAF score at entry.

EPPIC were systematised according to FEP guidelines (Early Psychosis Prevention and Intervention Centre (EPPIC), 2010); (ii) medical files were rated by two consultant psychiatrists with expert knowledge of EPPIC and the treatment of FEP; (iii) sound inter-rater reliability was determined for clinical and functioning measures(Conus et al., 2007); and (iv) concurrent validity of psychoses and baseline SUD was established for a sub-sample of patients (Conus et al., 2007). File audit methodologies have commonly been adopted in psychiatric research (Norman et al., 1996; Sernyak et al., 2003). Data sourced through file audits has been considered comparable to data collected prospectively (Norman et al., 1996). It has also been argued that 'best-estimate diagnosis' which is based on information from the patient, family members and medical files, is the most valid method for diagnosing psychiatric disorders (Leckman et al., 1982). File audits also minimise sample biases due to informed consent procedures and thus patients across the severity spectrum can be included in a study. This allows for a highly representative sample of FEP patients (Conus et al., 2007).

A further limitation was the absence of data on medications prescribed. It is plausible to hypothesise that the two groups may have differed on the pharmacology used to manage symptoms. We expect that patients with FESA would have been more likely to be treated with mood stabilisers during the course of treatment, given the severity of symptoms of mania at presentation.

In summary, SAD has been considered a diagnosis of dubious validity and credibility (Abrams et al., 2008) and there have been moves to remove it from DSM-V (Malhi et al., 2008; Korver-Nieberg et al., 2011). In the current study, we addressed methodological confounds of previous studies, and differences were found between patients with FES and FESA with respect to severity of illness at entry, affective symptoms at entry and discharge, functioning at discharge, and the increased need for inpatient admissions. The affective symptoms that characterise the presentation and clinical course of patients with schizoaffective disorder are features that most distinguish FESA from FES. However, there is substantial overlap suggesting that the two diagnostic entities share some features. Longer term follow-up will be required to ascertain whether differences in illness course persist, which would, in turn, inform whether schizophrenia and SAD are better described as a single syndrome or alternatively considered as distinct diagnostic entities.

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Contributors

Prof. Lambert, Prof. Conus, and Prof. McGorry designed the First Episode Outcome Study (FEPOS). Prof. Lambert and Prof. Conus collected the data and also provided feedback on drafts of the manuscript. A/Prof. Cotton analysed and interpreted the data and wrote the first draft of this manuscript. The other authors all provided feedback and comments on the various versions of the manuscript. All authors have contributed to and have approved the final manuscript.

Conflict of interest

Prof. Lambert, Prof. Conus, Prof. Schimmelmann, and Prof. McGorry have served on the speakers' board of Eli Lily. Prof. Berk has served on advisory boards and received funds and/or honoraria from Astra Zeneca, Eli Lilly, Janssen Cilag, Lundbeck, Servier, Glaxo Smith Kline, Organon, Novartis, Pfizer, Bristol Myers Squibb, Sanofi Synthelabo and Solvay.

There are no other relevant disclosures.

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