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Original article

Rates and predictors of 18-months remission in an epidemiological cohort of 661 patients with first-episode psychosis

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ABSTRACT

Objectives: Most first episode psychosis (FEP) outcome studies are based on patient samples enrolled through an informed consent procedure, which may induce important biases. Our aim was to study the 18-month outcome of FEP in an epidemiological sample of patients treated at the Early Psychosis Prevention and Intervention Centre (EPPIC).

Methods: The files of 661 FEP patients treated for up to 18 months between 1998 and 2000 were assessed. Symptomatic remission was defined as receiving a score ≤ 3 on the Clinical Global Impressions (CGI) scales, and functional remission as concurrent fulfillment of occupation/employment and independent living. Predictors were analyzed using stepwise logistic regression models.

Results: At endpoint, 63% of FEP patients had reached symptomatic remission and 44% functional remission. Duration of untreated psychosis, baseline symptom intensity, time in service and decrease or remission of substance use, predicted both symptomatic and functional outcome. A history of suicide attempt or non-adherence to medication was linked to lower likelihood to reach symptomatic remission while pre-morbid GAF and employment at baseline were linked to functional outcome.

Conclusions: The development of early intervention strategies should be pursued, in order both to provide treatment before symptoms reach a high intensity and to maintain social integration. Specific strategies need to promote engagement, facilitate adherence to medication and to create a framework where key issues such as substance abuse co-morbidity can be addressed.

Key words: First episode psychosis, outcome, functioning, symptoms, predictors, schizophrenia

1. INTRODUCTION

While outcome studies conducted in the 80's[1-3] contradicted the idea that schizophrenia would inevitably lead to profound deterioration, this disorder is still considered with pessimism, on the basis of more recent studies published in the nineties which have shown that, whilst a minority of patients may experience recovery, a majority will display repeated relapses and progressive impairment[4,5]. These disillusioning results were largely based on samples selecting hospitalized, chronic or treatment non-responsive patients and therefore may not reflect the entire span of outcome for these disorders[6,7]. Research based on first episode psychosis (FEP) samples offer the possibility to study a wider range of patients, including those who do not relapse after recovery from the initial psychotic episode and may lead to the identification of factors linked to poorer outcome that may be influenced by treatment adaptations.

In the first decade of 2000, six "population-based" FEP short term outcome studies have been published[6-11] and later reviewed by DeMaio et al[12]. Their results suggest that after one to two years of treatment, rates of symptomatic remission range from 36% to 74%[6-11] and rates of functional remission from 26% to 51%[7,9,10] and rates of combined symptomatic and functional remission from 17% to 19%[9,10]. Male gender, living in a developed country, family history of schizophrenia, poor premorbid functioning, lower education level, earlier age of onset, insidious onset, longer duration of prodromal phase (DPP), longer duration of untreated psychosis (DUP), higher degree of negative symptoms at baseline, comorbidity of substance use disorder (SUD), diagnosis of schizophrenia and treatment with conventional antipsychotics were all identified as significant predictors of poor outcome in one or more of these studies.

A later wave of similar studies have either compared the impact of specialized programs with standard treatment[13] or compared subgroup of patients on the basis of characteristics of interest such as substance abuse[14] or cognition[15] for example. Finally, more recent studies have focused on longer term outcome and on the maintenance of the impact of early intervention programs[16], showing that unless specialized treatment is continued, their short term benefits could be lost after a few years[17].

However, despite being referred to as "population-based", most of these studies still suffer, to a variable degree, from an important selection bias, patients being enrolled through an informed consent procedure. Reported refusal rates, ranging from 24%[6] to 42%[9] suggesting that results of such research may not be relevant to the most challenging FEP patients, who are unlikely to accept prospective assessment, such as those with

highest illness severity, highest rate of SUD and poorer engagement in treatment. This assumption is supported by Menezes et al.'s [18] literature review on outcome in FEP. Worse outcome was mainly linked to the epidemiological representativeness of the cohort, and there were major differences between epidemiologically-based and selected FEP samples in terms of readmission rate (56.1% vs. 33.2%), employment rate (24.2% vs. 49.9%), global functional outcome (mean Global Assessment of Functioning (GAF[19]); 48.6 vs. 60.1) and overall favorable outcome (35.6% vs. 50.3%). In addition, representativeness of a FEP sample is improved if it stems from a center with a treatment mandate in a catchment area where an early psychosis community awareness campaign has been conducted, which leads to a higher FEP recognition rate[20] and where there are no financial barriers for access to care.

The First Episode Psychosis Outcome Study (FEPOS) cohort fulfills these conditions and is based on an audit of the files of all patients who were treated at the Early Psychosis Prevention and Intervention Centre (EPPIC) between 1998 and 2000[21,]. Considering the limitations of previous studies mentioned above and in the frame of conducting a long term outcome study of the FEPOS sample, we wanted to answer the following questions regarding short term outcome in this unique clinical sample: (i) What are the rates of symptomatic remission and functional recovery in an epidemiological cohort treated in a specialized FEP service?; and (ii) What are the key pre-morbid, baseline, and treatment predictors of poor outcome in such patients?

2. METHODS

2.1. Patients sample

Details of study methodology and context have been published previously[21,22]. The initial sample comprised a population-based cohort of 786 FEP patients consecutively admitted to EPPIC in Melbourne between 1998 and 2000[21,22]. At the time of the study, EPPIC was mandated to treat all FEP patients aged 15-29 in the catchment area with little if any leakage to private psychiatrists; as such, the study sample represents a treated epidemiological cohort. The files of 82 patients (10%) had been sent to other services at time of discharge and were not available for the study; these patients did not differ regarding diagnostic distribution and available demographic characteristics. Among 704 available files, 43 were excluded because of a non-psychotic diagnosis at endpoint. Data on 661 patients were analyzed. The local ethics committee granted approval for this study. The data result from extraction of information from the files on the basis of a file audit per-

formed between 2001 and 2002 by two experienced psychiatrists (ML and PC) assessed patients' medical files using a specifically designed file-audit tool (Early Psychosis File Questionnaire; EPFQ[21]). The EPFQ is a form where data extracted from the files can be recorded. It contains the following domains of assessment: demographic data, forensic history, past history of suicide attempts, family history of mental illness, past psychiatric history, exposure to traumatic and life events, drug and alcohol assessment schedule (type of substance, age of onset, current use or not), premorbid level of functioning, age at onset of prodrome and first psychotic episode, intensity of symptoms and functional level at baseline and at the time of discharge or disengagement on the basis of scales described below.

2.2. Diagnostic assessment

Clinical diagnoses at EPPIC are the consensus result of an intensive diagnostic and treatment process, first within the initial 6 weeks of admission by well-trained clinicians working in a specialized assessment and crisis assertive community treatment team, and then throughout the entire duration of treatment. Diagnoses for FEPOS were derived according to Diagnostic and Statistical Manual of Mental Disorder, 4th edition (DSM-IV criteria)[23] on the basis of information gathered from the medical file and their validity has been established as detailed elsewhere[21].

2.3. Pre-treatment, baseline and outcome characteristics

(i) Pre-treatment characteristics: Premorbid functioning was assessed with the Global Assessment of Functioning Scale (GAF), as recommended by the Early Psychosis Association for the definition of prodromal patients at high risk for transition to psychosis[24]. Duration of untreated psychosis (DUP) was assessed by means of the DUP-scale[25,26]. Age at onset was defined as the age when first sustained positive psychotic symptoms occurred, according to the DUP-scale[25,26], on the basis of a procedure detailed elsewhere[27]. Past psychiatric diagnoses were also assessed according to DSM-IV criteria and past suicide attempts according to ICD-10 classification[28]. (ii) *Baseline and outcome characteristics:* Patients were assessed on the basis of file data collected at baseline and at the time of discharge (either at the end of 18 months of treatment or on the basis of the last file-entry if patients moved out of catchment area, disengaged or had died). Severity of illness at baseline and discharge was assessed with the Clinical Global Im-

pressions-Severity of Illness scale (CGI-S[29]) and the CGI-BP mania and CGI-BP depression (CGI-BP[30]). CGI scales are based on global assessment of illness severity rated from 1to 7. CGI-S scores the global severity of the illness, taking all elements into account while CGI-BP allows the scoring of the mania and depression dimensions separately. Level of functioning was rated on the GAF. Insight into illness was assessed on the basis of one item with three anchors ranging from absent to partial and full insight[21,22]. Patients were rated as "working at entry" (having employment/occupation at entry) on the basis of the Modified Vocational Status Index (MVSI[31]) if they fulfilled following criteria: having a job (full-time or part-time) or being a student at school or university for at least the previous 4 weeks. Patients were rated as "living independently" on the basis of the Modified Location Code Index (MLCI[31]) if they fulfilled the following criteria: being head of household, living alone or with peers or living with family under minimal supervision. "Medication non-adherence" was defined as failure to take medication for 1 week or longer over the entire treatment period at EPPIC in accordance with Robinson et al [32]. Patients were also classified within 3 groups according to the evolution of SUD during treatment period in the following three groups: (i) absence of SUD; (ii) decrease or stopping of SUD over treatment period; and (iii) persistence, increase or commencement of SUD over period[22]. Inter-rater reliability (between ML and PC) was established for CGI-S ($ICC_{2,1}$=0.87), GAF ($ICC_{2,1}$=0.88), and insight score ($ICC_{2,1}$=0.89).

2.4. Outcome definitions

Symptom remission was defined as a score ≤ 3 on all three of the discharge CGI rating scales (CGI-S, CGI-BP mania, and CGI-BP depression), similar to Lambert et al[33]. *Functional recovery* was defined as concurrent fulfillment of: (1) occupational/vocational status as measured by the MVSI (i.e., paid or unpaid full- or part-time employment, being an active student in school or university, or head of household with employed partner (homemaker), or full- or part-time volunteer); and (2) independent living according to the MLCI (i.e., head of household, living alone, with partner, or with peers, and living with family with minimal supervision).

2.5. Data analysis

Descriptive statistics were used to describe the pre-treatment, service entry, and treatment characteristics of the entire cohort. For scale data not conforming to the normal Gaussian distribution, logarithmic transformations (plus a constant such as one where 0

was observed in the data) were employed. Untransformed data are used to describe sample characteristics whereas transformed data were used in the proceeding analyses.

Preliminary analyses focused on determining which pre-treatment, service entry, and treatment variables were related to symptom remission and functional recovery. A series of sequential logistic regression models were conducted with remission or recovery (poor outcome as the reference category) serving as the dependent variable and the predictor of interest (e.g., gender or substance use) the independent variable in the model. As length of time in service varied from less than one week to 208 weeks, time in service was entered into the first step of the model. For symptom remission, it was also important to control for baseline symptoms, so CGI-S and CGI-BP scores at service entry were also included in the first step. For functional recovery, vocational/occupational and independent living statuses at service entry were also included in the first step. The predictor of interest was entered into the second step of the model. From these logistic regression analyses, adjusted odds ratios (OR; adjusting for time in service and baseline characteristics), the 95% of confidence intervals (CI) of the adjusted ORs, and the *p* values for Wald statistics (*z*), are reported. A variety of contrasts were used to derive OR for categorical variables (i.e., gender, diagnosis, insight at entry) including indicator and deviation contrasts.

Variables identified in these preliminary analyses to be significant predictors of remission or recovery (at the $p<.10$ level) were entered into two separate stepwise logistic regression models with each of the outcome measures serving at the dependent variable. The purpose of these models was to determine whether there were different predictors of symptomatic remission and functional recovery. ORs, 95% CI of the OR, and the *p* values derived from the Wald statistics were reported for the significant predictors of remission or remission included in the final step of the models.

We were also interested to determine a series of cut-off scores that would best demarcate the number of risk factors associated with poor symptom remission or poor functional recovery. For each outcome type, the risk factors associated with outcome were identified from the stepwise logistic models. A total risk score was then derived. Receiver operator curves (ROCs) were then used to determine the appropriate cut-off scores. Youden's J statistic was used to determine the performance of the cut-off scores. Area under the curve (AUC) values of ≥0.90 were considered excellent, 0.80-0.90 good, 0.70-0.80 fair, and <0.70 poor.

3. RESULTS

3.1 Sample Characteristics

Patients' average age was 22.0 years and the majority was male, with a history of exposure to traumatic events and SUD co-morbidity (see Table 1); 14.3% had a history of suicide attempt, baseline CGI-S score revealed a marked severity of illness and insight at entry was poor. On average, time in contact with the service lasted 63.3 weeks. Nearly two thirds of patients were not fully adherent to medication and persistent SUD was common, observed in 61% of patients.

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3.2 Remission and recovery Rates

Data on symptomatic remission at discharge was available in 655 patients. The mean CGI-S score at discharge for the total cohort was 3.0 (*SD*=1.3), 1.1 (*SD*=0.53) for CGI-BP mania and 1.4 (*SD*=1.0) for CGI-BP depression. Data found in the file on functional recovery was considered reliable in only 556 patients. On the MVSI, 44.7% (*n*=255, *N*=571) were engaged in meaningful employment. On the MLCI, 83.0% (*n*=463, *N*=558*)* were living independently with minimal supervision. Using the remission and recovery criteria specified earlier, there were 62.9% (*n*=412, *N*=655) patients who had achieved symptom remission and 44.2% (*n*=246, *N*=556) who had achieved functional recovery at discharge. These percentages were determined for symptom and functioning as discrete variables. Just over a third of patients had achieved combined remission at discharge (37.6%, *n*=209, *N*=556).

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3.3 Predictors of outcome

A number of variables were associated with the various aspects of outcome, while controlling for time in service and baseline characteristics (see Table 2). Among pre-treatment variables, number of years in school, premorbid functioning, and DUP were associated with both symptomatic remission and functional recovery. In addition, age of onset and history of suicide attempts were related to symptomatic remission. Regarding

baseline variables, global CGI-S of symptoms and employment status were associated with both symptomatic remission and functional recovery. A diagnosis of bipolar I disorder or schizophreniform disorder was associated with better symptomatic remission as compared to a diagnosis of schizophrenia. In addition, severity of depression and mania on CGI-BP scales and SUD status were associated with symptomatic remission. Global functional and insight levels at baseline were associated with functional recovery. Finally, duration of time in service, adherence to treatment and evolution of SUD over the treatment period were associated with both symptom remission and functional recovery.

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The above variables as well as those associated with the outcomes at a $p<.10$ level were included in two stepwise logistic regression models to determine, which variables best predicted symptomatic remission and functional recovery (see Table 3). Forward method using Wald criteria was used to determine the selection of variables in the model. Four variables were significantly associated with both symptoms remission and functional recovery: DUP, Intensity of symptoms at baseline (CGI-S), time in service and SUD profile. Regarding the latter, decrease or interruption of SUD was associated with better outcome and maintenance or increase of SUD with poorer outcome. Additionally, symptom remission was associated with the absence of a past history of suicide attempt and adherence to medication during treatment, while functional recovery was associated with pre-morbid GAF and employment status at baseline.

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A risk score for poor symptomatic outcome was derived on the basis of DUP, past history of suicide attempt, CGI-S at entry, adherence to treatment and SUD profile during treatment. In order to dichotomise DUP, we chose, on the basis of earlier work[27], a cut-off at 30 days. CGI-S score were collapsed into 2 categories (score of 5 or below and score of 6 or 7). Thus, on the basis of these variables, an individual could obtain a total symptomatic risk score ranging from 0 to 5, with 5 depicting greater number of risk factors. Figure **1** depicts the ROC curve for the symptom risk score against not achieving

symptomatic remission. The AUC was 0.76 (95% CI 0.71-0.79) indicating fair discrimination. On the basis of Youden's J index, a cut off of greater than or equal to 3 on the risk score was chosen. The sensitivity for the cut-off score was 0.66, specificity 0.75, positive predictive value (PPV) of 0.61 and negative predictive value (NPV) of 0.79.
For functional outcome, a risk score was based on premorbid GAF, DUP, CGI-S, employment at service entry and SUD profile over treatment period. Premorbid GAF was dichotomised into <70 and ≥70. An individual could receive a risk score for functioning out of 5. The AUC was 0.73 (95% CI 0.68-0.76) which is considered fair. On the basis of Youden's J, a cut off of greater than or equal to 3 on the risk score was chosen. The sensitivity of the cutoff was 0.58, specificity 0.76, PPV was 0.76 and NPV of 0.59.

4. DISCUSSION

This study is one of the largest FEP outcome studies, and one of the very few based on a true epidemiological sample of patients treated in a specialized early psychosis service where operationalized criteria were applied to define symptomatic and functional outcome. Considering FEPOS allowed the assessment of all patients treated at EPPIC over a defined period of time, including those who would be likely to refuse to participate in prospective studies, our results are likely to be representative of the outcome of FEP patients treated in a specialized centre embedded in the public system of similar socio-economic level.

4.1. Key findings

Our data showed that after a period of up to 18 months of treatment, 63% of FEP patients had reached symptomatic remission and 44% functional recovery. These findings confirm that, in the early phase of psychosis, outcome is better than previously thought.
Compared to other studies, rate of symptomatic remission in our sample is similar to findings from the TIPPS project[6], but relatively higher than rates observed after 2 years by Petersen et al[9] and Wundering et al[10]. Likewise, rate of functional remission was also higher in our sample than both Petersen et al[9] and Wunderink et al[10] reported. This may be due to various factors. First, contrary to these two studies, FEPOS includes bipolar I disorders and other affective psychoses besides schizophrenia, a sub-group of patients who had a better outcome. Second, outcome criteria applied in these studies may have been more restrictive. Finally, better outcome in our sample could also reflect the effect of treatment at a centre that has been specialised in early intervention for many years. In

addition, these outcome figures confirm the marked discrepancy between symptomatic and functional outcome[7,31], and highlight the importance to address this issue in the early phase of psychoses. Data from a recent randomized controlled trial showed that vocational intervention adapted to FEP patients have a significant impact on likelihood to return to work[34]; this confirms pilot data from Killackey et al[35] and suggests more effort should be made in this direction.

While a number of variables were associated with the aspects of outcome we explored, a stepwise logistic regression procedure identified those with the most robust predictive validity. Four elements appear to determine both symptomatic and functional outcome: treatment delay, intensity of symptoms at baseline, evolution of co-morbid substance use over the treatment period and time in treatment. Despite convincing evidence of an association between longer DUP and poorer outcome[27,36] , this issue is still a matter of controversy; in keeping with the litterature[6,9,10,11], our results support to the idea that reduction of DUP may improve outcome and should therefore be a priority in early intervention programs. Higher intensity of symptoms at baseline was linked to poorer outcome, which is congruent with findings from Menzes et al[7] and suggests that symptom reduction in the early recovery phase may be a pre-requisite for patient to benefit from other aspects of treatment. Repeated assessment of symptomatic remission should therefore be conducted regularly and specific approach be applied when symptoms persist[37]. Expanding on previous results[22], we found that patients who decreased or interrupted SUD during the treatment period were significantly more likely to reach both symptomatic and functional remission, even when compared to patients who did not present this comorbidity at baseline. This latter observation, discussed in a previous paper[22] suggests that patients using substances may have better premorbid social competence and a form of illness where SUD may play a potentiating role; this confirms this potential for recovery should not be neglected and confirms the importance to address this issue in early psychosis patients. Finally, a longer engagement with the service was linked to a better outcome. Engagement and therapeutic alliance are closely interconnected, and there is now compelling evidence showing that the therapeutic relationship is a significant predictor of clinical outcome across a number of disorders[38-41]. A shorter duration of treatment is likely to prevent such a relationship to establish, and to deprive patients from exposure to psychotherapeutic aspects of the treatment. Our results emphasize the importance to identify such patients early and to use an adapted approach, in order to facilitate their engagement[41-43] and increase their chances of func-

tional remission. Finally, these results are in line with more recent outcome studies suggesting that treatment should be pursued for sufficient time if short term benefits are to be maintained over time[16,17].

Symptom remission was predicted by two additional factors. First, in keeping with Malla et al[44] and Petersen et al[9], patients who were adherent to treatment were twice more likely to display symptom remission after 18 months. Second, patients who had suicide history of suicide attempts in the past were less likely to achieve symptoms remission; while this needs further exploration, our hypothesis is that occurrence of previous suicide attempt may be linked to other characteristics such as exposure to sexual abuse or comorbid borderline personality traits, which may explain persistence of symptoms that are globally assessed by the CGI-S scale.

Finally, patients with a higher premorbid functional level and those who were employed or had a meaningful activity at baseline had a better functional outcome at the end of the treatment period. This confirms data from previous studies[6,8,9] and suggests the effort to develop early intervention strategies that may prevent or delay development of psychosis should be pursued, considering they may offer an opportunity to mitigate premorbid decline in functioning and risk of social marginalization.

Globally, it is interesting to note that our study replicated the various outcome predictors that have been identified in previous studies that were based on informed consent procedure; although this would need to be replicated, it suggests that the informed consent procedure may not induce a major bias in study samples, which is reassuring.

In an attempt to provide clinicians with elements predicting individual trajectories, we attempted to define cut-off scores that would best demarcate the number of risk factors associated with poor outcome. This analysis showed that symptom remission is unlikely to occur if a patient displays 3 or more of the following factors: DUP longer that 30 days, past history of suicide attempt, CGI≥6, poor adherence to treatment and increase or persistence of SUD over the treatment period. Similarly, functional recovery is unlikely if a patient displays 3 or more of the following factors: DUP longer than 30 days, unemployment at baseline, pre-morbid GAF<70, CGI≥6 and increase or persistence of SUD over

the treatment period. The validity of these predictive profiles need, however, to be validated prospectively.

4.2 Limitations

Some limitations should be kept in mind when interpreting the results. (1) Data was gathered retrospectively, and are based on case notes written by numerous clinicians whose inter-rater reliability could not be evaluated. Elements of patients' past history as well as their symptoms may be under-reported by patients, unnoticed by clinicians or not transcribed in the files. Other factors that usually limit the validity of data extracted from medical record comprise: a lack of information due to multiplicity of treatment sites and multiplicity of files for a single patient; file assessment by raters lacking clinical experience; absence of strategies to limit inconsistencies between raters in data collection; or absence of strategies to assess validity of the data collected from the files. However, in the present study, files were assessed exclusively by two senior clinicians (PC & ML) who have extensive experience in treatment of early psychosis and have a thorough knowledge of the single site EPPIC program. Additionally, validity of the data as well as inter-rater reliability were assessed and proven satisfactory, as highlighted in the methods section. (2) The fact that 10% of the files were not available du to the fact that they had been sent to other services where patients continued to receive treatment after discharge from EPPIC is also a limitation to the representativeness of the sample. (3) Unfortunately, data on functional outcome (location and vocation) was reliably recorded in the file for only 71% of the initial cohort, which limits the value of the results. It should also be mentioned that functional recovery was broadly defined, including for example part time unpaid job or living with friends. This definition may be considered over inclusive, but the aim was to capture return to activity and ability to live in an environment not specifically designed for the care of psychiatric patients and is in line with the recovery concept where the definition of a fulfilling life doesn't forcibly include paid job. (4) As mentioned in the methods section, outcome was based on file entries at 18 months or on the last file entry in case of disengagement or movement outside of catchment area, which explains the variability in treatment duration. While duration of treatment was taken into account in data analysis, this is likely to have nevertheless biased the results. (5) Finally, due to the retrospective nature of this study, ratings of symptom remission are based on CGI-S score, which only provides a very global reflection of symptom levels; specifically, this scale doesn't allow the distinction between positive and negative

symptoms while the latter are an important driver of unfavorable trajectory. Assessment of symptom remission could not be done on the basis criteria published in the literature[45]; however, such criteria have been developed for schizophrenia and would not necessarily be adapted to patients with affective psychosis.

4.3. Clinical implications and future research directions

Considering these strengths and limitations, this study provides important information regarding outcome characteristics of a large epidemiological sample of FEP patients, and shows that while two thirds are in symptom remission after 18 months of treatment, 60% fail to reach functional recovery. We suggest that various strategies may contribute to improve these figures. First, the development of early intervention strategies should be pursued, not only in order to shorten DUP and to provide treatment before symptoms reach a high intensity, but also with the aim to maintain social and functional integration. Second, a good knowledge of the specific approaches that may promote engagement[45] is necessary when treating FEP patients, in order not only to facilitate their adherence to medication but also to allow sufficient time in treatment, in order to address key issues such as substance abuse co-morbidity. This study allowed us to examine the potentially modifiable risk factors that impact on the short-term outcomes of FEP patients. Importantly, a study mapping the longer term illness trajectories and outcomes (over 15 years) of this cohort is currently being undertaken and we will be able to determine whether the risk factors that influence short-term outcomes also impact on long-term illness course.

Conflict of interest: There is no conflict of interest for any of the authrs regarding the content of this publication

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Table 1

Description of patients' demographic, premorbid, service entry, and treatment characteristics for 661 patients with first episode psychosis

Predictor variables	Statistic	Value for Total sample[a]
Pre-treatment variables		
Age (years)	M (SD)	22.0 (3.4)
Sex (% Male)	% (n)	65.8 (435)
Years in school	M (SD)	10.5 (1.5)
Pre-morbid GAF	M (SD)	69.4 (10.6)
Duration of untreated psychosis (in weeks)	M (SD)	36.4 (77.7)
	Mdn	8.7
Age at onset (years)	M (SD)	21.3 (3.6)
Exposure to traumatic event (% Yes)	% (n)	82.7 (544)
Past history of suicide attempt (% Yes)	% (n)	14.3 (93)
Past substance use disorder (%Yes)	% (n)	74.1 (490)
Forensic history (%Yes)	% (n)	28.9 (187)
Baseline variables		
Diagnosis at entry (%Yes)		
Schizophrenia	% (n)	22.0 (145)
Schizophreniform disorder	% (n)	39.1 (258)
Schizoaffective disorder	% (n)	6.1 (40)
Bipolar I disorder	% (n)	18.9 (125)
Other psychosis	% (n)	14.0 (92)
Severity of symptoms at entry		
CGI-S severity score	M (SD)	5.5 (0.8)
CGI-BP depression score	M (SD)	2.0 (1.6)
CGI-BP mania score	M (SD)	2.0 (1.8)
Functional level at entry (%Yes)		
Employment/occupation	% (n)	48.0 (316)
Independent living	% (n)	74.5 (487)
Substance use disorder (SUD) (% Yes)	% (n)	61.4 (406)
Insight at entry (%No)	% (n)	62.4 (410)
Treatment variables		
Length of time in service (in weeks)	M (SD)	63.3 (34.2)
Compliance with treatment (%No)	% (n)	60.6 (379)
Substance use disorder (SUD) (% Yes)		
No SUD	% (n)	34.6 (229)
Remitted SUD (decreased or stopped)	% (n)	25.3 (167)
Persistent SUD (increased or no change)	% (n)	40.1 (265)

[a] Percentages were based on non-missing observations.

Table 2: *Adjusted odds ratios from preliminary analyses depicting the relationships between pre-treatment, service entry and treatment characteristics and remission*

	Symptomatic remission				Functional remission			
Predictor	OR [a]	95% CI		p-value	OR [b]	95% CI		p-value
Pre-treatment variables								
Age (years)	1.03	0.98	1.08	.237	0.99	0.94	1.04	.728
Sex (male)	0.81	0.57	1.16	.251	0.79	0.54	1.15	.218
Years in school	**1.14**	**1.02**	**1.28**	**.022**	**1.18**	**1.04**	**1.35**	**.013**
Pre-morbid GAF	**1.04**	**1.02**	**1.06**	**<.001**	**1.04**	**1.02**	**1.06**	**<.001**
Duration of untreated psychosis (in weeks) [d]	**0.51**	**0.39**	**0.66**	**<.001**	**0.56**	**0.43**	**0.74**	**<.001**
Age at onset (years)	**1.06**	**1.02**	**1.11**	**.010**	1.01	0.96	1.07	.638
Exposure to traumatic event (%Yes)	0.97	0.62	1.50	.875	0.95	0.60	1.52	.832
Past history of suicide attempt (%Yes)	**0.43**	**0.27**	**0.70**	**.001**	0.93	0.55	1.57	.771
Past substance use disorder (%Yes)	0.72	0.48	1.07	.099	0.88	0.59	1.31	.521
Forensic history (%Yes)	0.70	0.49	1.00	.052	0.75	0.49	0.14	.181
Baseline variables								
Diagnosis at entry								
Schizophrenia	Reference category				Reference category			
Schizophreniform disorder	**1.57**	**1.09**	**2.24**	**.015**	1.23	0.87	1.72	.238
Schizoaffective disorder	0.77	0.42	1.4	.389	0.52	0.26	1.00	.051
Bipolar I disorder	**2.13**	**1.17**	**3.86**	**.013**	1.45	0.96	2.21	.080
MDD with psychotic features	0.78	0.33	1.85	.328	1.61	0.72	3.59	.246
Other psychosis	1.01	0.62	1.65	.966	1.13	0.68	1.89	.635
Severity of symptoms at entry								
CGI-S severity score	**0.66**	**0.53**	**0.83**	**<.001**	**0.68**	**0.54**	**0.85**	**.001**
CGI-BP depression score	**1.12**	**1.01**	**1.25**	**.037**	1.09	0.97	1.22	.148
CGI-BP mania score	**1.26**	**1.14**	**1.40**	**<.001**	1.01	0.91	1.12	.872
Functional level at entry								
Employment/occupation (%Yes)	**1.82**	**1.29**	**2.55**	**.001**	**3.99**	**2.77**	**5.75**	**<.001**
Independent living (%Yes)	1.26	0.87	1.84	.224	1.43	0.95	2.17	.090
GAF	1.01	0.98	1.03	.701	**1.03**	**1.01**	**1.05**	**.004**
Substance use at entry (%Yes)	**0.69**	**0.49**	**0.98**	**.039**	0.79	0.54	1.13	.197
Insight at entry (%No)	0.85	0.58	1.25	.393	**0.63**	**0.43**	**0.91**	**.015**
Treatment variables								
Length of time in service	**1.01**	**1.01**	**1.02**	**<.001**	**1.01**	**1.01**	**1.01**	**.014**
Compliance with treatment (%Yes)	**3.37**	**2.29**	**4.94**	**<.001**	**1.51**	**1.03**	**2.22**	**.034**
Substance use disorder (SUD)								
No SUD	Reference category				Reference category			
Remitted SUD (decreased or stopped)	**2.51**	**1.93**	**3.25**	**<.001**	**1.65**	**1.27**	**2.14**	**<.001**
Persistent SUD (increased or no change)	**0.24**	**0.18**	**0.32**	**<.001**	**0.44**	**0.32**	**0.60**	**<.001**

[a] Adjusted odds ratio controlling for time in service, and CGI-S and CGI-BP service entry scores

[b] Adjusted odds ratio controlling for time in service, and working/studying and independent living status at service entry

[c] Adjusted odds ratio controlling for time in service, and service entry symptom and functioning variables

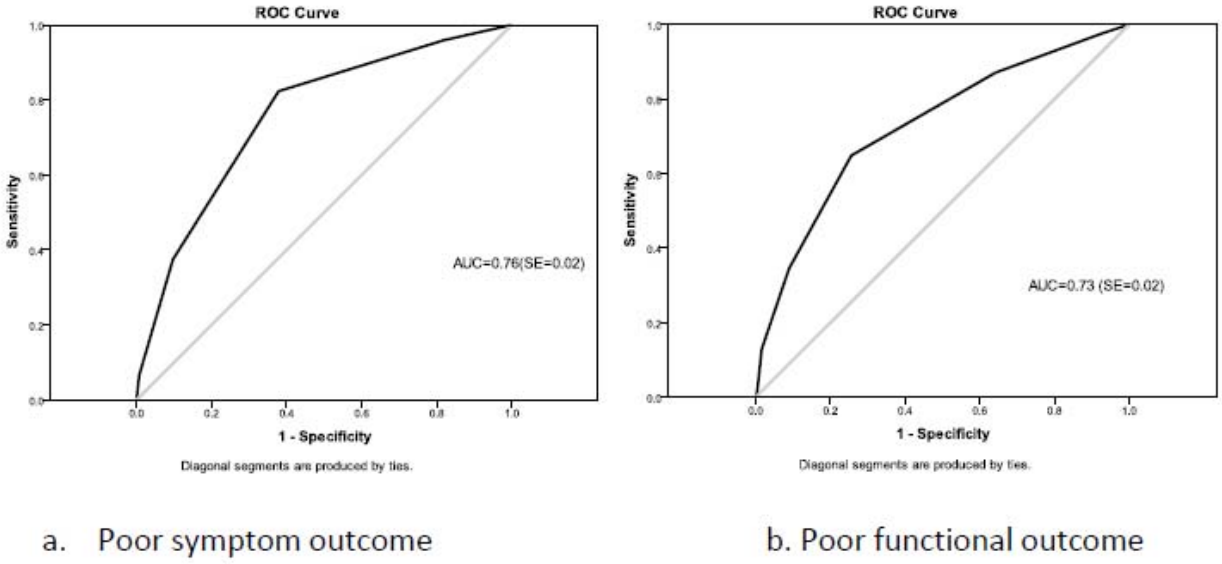
[d] Logarithmic transformation (plus constant) was applied to the variable due to extreme skewnesss

Table 3: Results (OR, 95% CI OR, and p value from Wald statistics) from two stepwise logistic regression (based on forward Wald criteria for selection of variables) models depicting the best predictors of symptomatic andfunctional ombined remission.

	Symptomatic remission (n=528)				Functional remission (n=459)			
Predictor	OR	95% CI		p-value	OR	95% CI		p-value
Pre-treatment variables								
Years in school								
Pre-morbid GAF					1.02	1.01	1.05	.041
Duration of untreated psychosis (in days) [d]	0.51	0.38	0.69	<.001	0.53	0.39	0.72	<.001
Age at onset (years)								
Past history of suicide attempt (%Yes)	0.52	0.30	0.90	.020				
Baseline variables								
Diagnosis at entry								
Schizophrenia								
Schizophreniform disorder								
Schizoaffective disorder								
Bipolar I disorder								
MDD with psychotic features								
Other psychosis								
Severity of symptoms at entry								
CGI-S severity score	0.72	0.55	0.94	.016	0.63	0.48	0.82	.001
CGI-BP depression score								
CGI-BP mania score								
Functional level at entry								
Employment/occupation (%Yes)					2.92	1.93	4.43	<.001
GAF								
Substance use at entry (%Yes)								
Insight at entry (%No)								
Treatment variables								
Length of time in service	1.01	1.01	1.02	.015	1.01	1.01	1.02	.004
Adherence with treatment (%Yes)	0.42	0.27	0.65	<.001				
Substance use disorder (SUD)				<.001				<.001
No SUD	Reference category							
Remitted SUD (decreased or stopped)	2.37	1.79	3.14	<.001	1.63	1.23	2.17	.001
Persistent SUD (increased or no change)	0.27	0.20	0.37	<.001	0.53	0.38	0.75	<.001

[a] Logarithmic transformation (plus constant) was applied to the variable due to extreme skew-nesss

Abbreviations: CGI-S = Clinical Global Impressions-Severity of Illness scale, GAF - Global Assessment of Functioning, SUD = substance use disorder



a. Poor symptom outcome

b. Poor functional outcome

Figure 1. *Receiver operating curve (ROC) for poor symptomatic and poor functional outcomes (based on DUP, past history of suicide attempt, CGI-S at entry, adherence to treatment and SUD profile during treatment).*