Short-term outcome of first episode delusional disorder in an early intervention population

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Abstract

Background: Previous evidence suggests that delusional disorder has a later onset and better functional outcomes compared to schizophrenia. However, studies have not examined longitudinal outcomes in a first episode population, where confounding factors may be adjusted for.

Methods: A nested case control study was designed within the National EDEN study; a cohort of 1027 first episode psychosis patients. Patients with a baseline diagnosis of delusional disorder (n=48) were compared with schizophrenia (n=262) at 6 and 12 months with respect to symptomatic and functional outcomes. Regression analysis was used to adjust for possible confounders.

Results: Delusional disorder patients had a shorter duration of untreated psychosis compared to schizophrenia but were similar in other baseline characteristics. At baseline, delusional disorder patients had lower symptom scores but higher function scores compared to those with schizophrenia. At 12 months the differences persisted for symptoms scores but not overall function scores. After adjusting for baseline score, age and duration of untreated psychosis, differences between the groups remained significant only for Positive and Negative Syndrome Scale (PANNS) negative, general and total scores and recovery rates. There were no differences in changes in outcomes scores.

Conclusions: Delusional disorder in a first episode psychosis population presents with less severe symptoms, higher recovery rates and better functioning than schizophrenia, but at 12 months differences are ameliorated when adjusting for baseline differences.

Keywords: Delusional disorder; Schizophrenia; First episode psychoses; Early intervention; Outcome.

1. Introduction

The validity of delusional disorder as a diagnostic entity separate from schizophrenia continues to be debated (Hui et al., 2015; Marneros et al., 2012). Winokur initially refined the description of Kraeplin's 'paranoia' to describe 'delusional disorder' (Winokur, 1977), and in current diagnostic classifications it occurs as delusional disorder in DSM-V and persistent delusional disorder in ICD-10. Delusional disorder has an estimated prevalence of around 0.18% in the general population and between 1-4% of psychiatric inpatient admissions (Kendler, 1982; Perala et al., 2007), although the true prevalence is likely to be higher as lack of insight prevents help seeking and recognition of the illness (Perala et al., 2007).

Despite this, delusional disorder is widely assumed to have favourable functional outcomes when compared to schizophrenia, despite ongoing delusional symptoms which can be resistant to treatment (Marneros et al., 2012; Opjordsmoen, 1988). This often leads to different treatment pathways within psychiatric services, such as differential prescribing of antipsychotic medication (Marneros et al., 2012) and service provision (Drake et al., 2000), while noncompliance and disengagement with services has a detrimental impact on treatment outcomes (Munro and Mok, 1995). This is further compounded by the limited high-quality evidence for the effectiveness of treatments for delusional disorder (Gonzalez-Rodriguez et al., 2016; Manschreck and Khan, 2006; Skelton et al., 2015).

However, outcomes in delusional disorder have not been extensively investigated in a first episode population where differences in symptomatology and functioning have been more difficult to illicit (Hui et al., 2015). Extant follow-up studies have either been limited by small samples or not considered other possible confounders in the relationship between diagnosis and outcome. However, the diagnosis of delusional disorder does appear to have some stability (Fusar-Poli et al., 2016; Kulkarni et al., 2016; Marneros et al., 2012) although others continue to question the distinction between delusional disorder and paranoid schizophrenia (Hui et al., 2015).

The National Eden Study is a database of over 1000 patients admitted to Early Intervention (EI) services in the UK and provides an excellent opportunity to investigate the outcome of first episode psychotic disorders in a larger sample with the ability to adjust for a number of potential confounders in the relationship between diagnosis and outcome. This study aimed to investigate 6 and 12-month functional and symptomatic outcomes of first episode psychosis patients who present with a delusional disorder compared to those presenting with schizophrenia, in order to test the hypothesis that a diagnosis of delusional disorder leads to improved functional outcomes.

2. Materials and Methods

2.1 Setting

The current study was designed as a nested case-control within the National EDEN database. The National EDEN study is a longitudinal cohort study including 1027 first episode psychosis cases admitted to Early Intervention (EI)

services between August 2005 to April 2009 from in five geographical sites across England: Birmingham, Cornwall, Cambridge, Norwich and Lancashire (Birchwood et al., 2014). It aimed to evaluate the implementation and outcomes of EI services across England. Ethical approval for the cohort study was given by Suffolk Local Research Ethics Committee, UK. This study investigated those who received an initial diagnosis of delusional disorder at baseline and compared them to those with a diagnosis of schizophrenia.

2.2 Participants

The National EDEN study approached all patients referred to EI services in participating centres between August 2005 and April 2009 for inclusion in the study. Inclusion criteria were the same as criteria for acceptance into EI services according to The Department of Health, which is 'first presentation of psychotic symptoms between the ages of 14 and 35 years'. The study excluded those with 'ultra-high risk' symptoms as they do not meet the criteria for psychosis. Of the 2097 patients that were eligible for inclusion 1027 consented to participate and were entered into the National EDEN study (49%). 825 patients completed the 6 month follow up and 791 completed 12 month follow up.

Diagnosis was established at baseline entry to the study using the OPCRIT diagnostic tool (operationalised criteria computerized diagnostic system)(McGuffin et al., 1991) which generates ICD10 and DSM IV diagnoses based on analysis of case notes, and has shown good validity and inter-rate reliability in establishing psychiatric diagnoses (Williams et al., 1996). This study included those with diagnoses of delusional disorder (n=48) and schizophrenia (n=262) according to DSM IV made using OPCRIT criteria.

2.3 Assessments

A number of symptom and functional outcomes were available at 6 and 12-month follow-up in the National EDEN study. This study utilised assessments of; Positive and Negative Syndrome Scale (PANNS) total, general psychopathology, negative and positive symptoms (Kay et al., 1987), Young Mania Rating Scale (YMRS) total score (Young et al., 1978), Calgary Depression Scale for Schizophrenia total score (Addington et al., 1993), EQ-5D measurement of health-related quality of life (Brooks, 1996), Global Assessment of Functioning (GAF) (Jones et al., 1995) symptom, disability and total score. Each of these scales are frequently used in psychosis research and have well established validity and reliability (Addington et al., 1992; Brooks, 1996; Jones et al., 1995; Kay et al., 1989; Young et al., 1978).

Duration of untreated psychosis (DUP) was recorded at baseline along with other demographic characteristics. DUP was defined as the delay between the onset of psychosis and the onset of criteria for treatment and was calculated using a combination of retrospective PANSS assessment, a semi-structured interview and patient notes (Birchwood et al., 2014). The onset of psychosis was considered to have occurred when participants scored 4 or above for one symptom from the positive scale of the retrospective PANSS, or a cluster of symptoms including delusions, hallucinations or conceptual disorganisation which reached a total of 7 or more in the positive subscale. Additionally, these symptoms had to present for at least 2 weeks.

Relapse and recovery were assessed using the Bebbington *et al* method (Bebbington et al., 2006), which involved a combination of clinical interviews

and extracting information from case notes to determine changes in symptoms. Using these criteria, remission can be classified as either full, partial or absent. If there is no remission, then relapse is recorded as 'not recovered'. Relapse can be a type 1 (full), type 2 (exacerbation) or non-recovery.

2.4 Reliability across sites

Research associates were trained in the use of scales such as PANSS, GAF, YMRS, Calgary Depression Scale, relapse and recovery and DUP assessment. All staff were required to attend a training programme and new staff were required to achieve concordance rate of kappa r>0.75 compared to trainers when assessing tapes of previous interviews. Additionally, every 12 months five DUP assessments and five relapse and recovery assessments from all sites were independently assessed for concordance, with kappa r>0.75 required. Every 20th PANSS assessment was observed by an experienced interviewer for site specific monitoring, and PANSS reliability was also assessed using a trained rater from each main site. The average intraclass correlation was 0.90 for positive scale, 0.89 for negative scale and 0.91 for general psychopathology scale. The overall agreement in relapse categories was 73% (kappa 0.62) with an intraclass correlation of 0.77 for time to relapse.

2.5 Analysis strategy

All statistical analyses were conducted in IBM SPSS version 24. The delusional disorder and schizophrenia groups were compared with respect to baseline demographics including age, gender, ethnicity, DUP, education level, living circumstances and occupation. The groups were also compared with respect to

PANSS, YMRS and Calgary Depression Scale at baseline, 6 months and 12 months, and EQ-5D health thermometer and GAF scores at baseline and at 12 months. Differences between the groups were assessed using the independent samples t-test for continuous variables and χ^2 test for categorical variables. The level of significance for all testing was set at $p<0.05$ for all statistical tests.

Regression models were created for each individual outcome of interest as the independent variable and diagnostic group as the dependent variable. Covariates included age and DUP, as well as the baseline score for the independent variable being investigated.

The change in each outcome was also compared between delusional disorder and schizophrenia groups, using a regression model with change scores as the independent variable, with diagnostic group as the dependent variable and age and DUP as covariates. Due to the relatively small number of delusional disorder patients, ethnicity and gender were not used as covariates in the models due to over-fitting, (Harrell et al., 1996) and the evidence relating ethnicity to outcome in psychosis is inconsistent (Chorlton et al., 2012). Regression models were created for change in PANSS, YMRS and Calgary Depression Scale at 6 and 12 months, and for EQ-5D health thermometer and GAF at 12 months follow up.

3. Results

3.1 Sample information

Of the 815 patients with diagnostic information, a total of 48 patients with a diagnosis of delusional disorder and 262 patients with a diagnosis of schizophrenia according to DSM IV were included in this study. However, the

number of patients that provided information for each assessment varied, and the specific numbers of participants in each analysis are shown in tables 1, 2 and 3.

3.2 Baseline demographics

The were no differences in age of onset, gender or ethnicity between patients with delusional disorder and schizophrenia (table 1). There were no overall differences in educational level, living circumstances or occupational circumstances between the groups, although when examined on a pairwise basis a significantly larger proportion of those with delusional disorder were in paid employment (29.8%) compared to those with schizophrenia (13%) p=0.004. Mean DUP was also significantly shorter in delusional disorder (135.8 days, 95% CI 66.5-205.1) compared to schizophrenia (330.2 days, 95% CI 248.8-411.7) p<0.001. There was no difference in lifetime history of substance misuse between the groups (table 2).

3.3 Baseline symptoms and function

Baseline PANSS, YMRS, Calgary Depression Scale, EQ-5D and GAF scores for each group are shown in table 2. The delusional disorder group had significantly better functioning at baseline in terms of GAF total (delusional disorder mean 52.88 95% CI 47.31-58.45, schizophrenia mean 46.89 95% CI 44.77-49.01, p=0.036), GAF symptom (delusional disorder mean 55.47 95% CI 50.02-60.91, schizophrenia mean 48.85 95% CI 46.71-50.98, p=0.02) and GAF disability scores (delusional disorder mean 58.61 95% CI 53.58-63.64, schizophrenia mean 48.7 95% CI 46.75-50.68, p<0.001) compared to the schizophrenia group.

PANSS mean scores were also significantly lower for the delusional disorder group compared to schizophrenia, in positive (delusional disorder 14.44 95% CI 12.70-16.19, schizophrenia 16.75 95% CI 15.96-17.55, p=0.023), negative (delusional disorder 13.26 95% CI 11.26-15.25, schizophrenia 16.09 95% CI 15.28-16.9, p=0.008), general psychopathology (delusional disorder 30.62 95% CI 27.5-33.75, schizophrenia 34.01 95% CI 32.68-35.35, p=0.049) and total (delusional disorder 58.14 95% CI 51.9-64.38, schizophrenia 66.23 95% CI 63.88-68.58, p=0.009) subsection mean scores. There were no differences in YMRS, Calgary depression or EQ-5D health thermometer mean scores between the two groups.

3.4 6 and 12 months follow up symptoms and functioning

As shown in table 3, at 6 months the delusional disorder group has significantly lower PANSS mean scores than the schizophrenia group in positive (delusional disorder 9.92 95% CI 8.88-10.96, schizophrenia 12.65 95% CI 11.94-13.36, p<0.001), negative (delusional disorder 10.95 95% CI 9.70-12.20, schizophrenia 14.44 95% CI 13.62-15.26, p<0.001), general (delusional disorder 24.66 95% CI 22.40-26.92, schizophrenia 28.12 95% CI 26.95-29.28, p=0.017) and total (delusional disorder 45.53 95% CI 41.66-49.39, schizophrenia 55.01 95% CI 52.75-57.27, p<0.001) subsection mean scores. Additionally, delusional disorder patients had significantly lower YMRS mean scores (delusional disorder 2.0 95% CI 1.07-2.93, schizophrenia 4.15 95% CI 3.39-4.90, p=0.001), although Calgary Depression Scale mean scores were not different between the groups.

As shown in table 3, at 12 months the delusional disorder group continued to have lower PANSS mean scores than the schizophrenia group in positive

(delusional disorder 10.26 95% CI 9.07-11.44, schizophrenia 12.07 95% CI 11.38-12.77, p=0.01), negative (delusional disorder 10.69 95% CI 9.56-11.83, schizophrenia 13.39 95% CI 12.57-14.21, p<0.001), general (delusional disorder 23.11 95% CI 20.97-25.24, schizophrenia 26.82 95% CI 25.60-28.04, p=0.014) and total (delusional disorder 44.13 95% CI 40.29-47.97, schizophrenia 52.24 95% CI 49.84-54.64, p=0.001) subsection mean scores. Baseline, 6 and 12 month PANSS subsection mean scores are shown in figure 1. Additionally, patients with delusional disorder continued to have significantly better functioning in terms of GAF symptoms (delusional disorder mean 67.79 95% CI 63.18-72.40 schizophrenia mean 61.56 95% CI 59.16-63.96, p=0.042) and disability scores (delusional disorder mean 68.24 95% CI 62.91-73.56, schizophrenia mean 59.29 95% CI 56.93-61.66, p=0.004), although the difference in GAF total score failed to reach significance at the 0.05 level (delusional disorder mean 66.53 95% CI 61.01-72.04, schizophrenia mean 60.43 95% CI 57.93-62.93, p=0.056). Baseline, 6 and 12 month GAF mean scores are shown in figure 2. There was no difference at 12 months between the groups in YMRS, Calgary Depression Scale or EQ-5D health thermometer mean scores. There was also no difference in the number of patients who received antipsychotic treatment at 12 months. Relapse rates did not differ between the groups, although a significant difference was seen in recovery rates with 72.3% of those with delusional disorder achieving full recovery compared to 47.9% with schizophrenia, and only 2.1% of those with delusional disorder failing to achieve recovery compared to 14% with schizophrenia (p=0.004).

At 12 months the delusional disorder group continued to have a significantly larger proportion paid employment (27.1%) compared to those with schizophrenia (12.6%) p=0.009.

3.5 *Adjusted analysis at 6 and 12 months*

Due to evidence of skew with data, 6 and 12 month outcomes underwent log transformation prior to adjustment using regression models. The adjusted analysis with each of the assessment outcomes as the independent variable is shown in table 3.

Once adjusted for the corresponding baseline score, DUP and age the delusional disorder group still had significantly lower PANSS positive (p=0.022) negative (p=0.011), and total (p=0.022) scores compared to the schizophrenia group at 6 months. There was no significant difference between the groups for PANSS general scores, YMRS or Calgary Depression Scale at 6 months follow up.

At 12 months follow up the delusional disorder group had significantly lower PANSS negative (p=0.045), general (p=0.032) and total (p=0.040) scores compared to the schizophrenia group when adjusted for baseline score, DUP and age. In the adjusted analysis there was no significant difference between the groups for PANSS positive scores, YMRS, Calgary Depression Scale, EQ-5D health thermometer or any subsection of GAF scores. Once adjusted for age and DUP the delusional disorder group continued to have significantly higher rates of recovery (p=0.002), but there was no difference between the groups for relapse at 12 months.

3.6 Analysis of change scores

The delusional disorder and schizophrenia groups were also compared with respect to the change in each outcome from baseline to the 6 and12 month assessment (table 3). There were no significant differences between the groups in the mean change in each outcome from baseline to either 6 or 12 months (data not shown). Once adjusted using a regression model with DUP and age of onset entered as covariates, there remained no significant differences in the change scores for any outcome between the groups at either 6 or 12 months follow up.

4. Discussion

4.1 Summary and interpretation of the results

This nested case control used data from The National EDEN study to compare patients with a diagnosis of delusional disorder to those with schizophrenia and assess differences in outcomes at 6 and 12 months. This is the first study that the authors are aware of to compare outcomes of first episode delusional disorder and schizophrenia patients in a longitudinal follow up study.

This study found that patients with a diagnosis of delusional disorder have better functioning and less severe symptomatology at initial presentation, which mostly persisted at 6 and 12 months follow up. After adjusting for age and DUP, patients with delusional disorder did not demonstrate any differences in functioning scores compared to the schizophrenia diagnosis group. This may suggest that factors such as age of onset and DUP are the determinants of functional outcome, rather than the diagnosis of delusional disorder itself.

At 6 month follow up less severe positive and negative symptoms were independently related to a diagnosis of delusional disorder, although the

difference in positive symptoms scores did not persist at 12 months, possibly as the schizophrenia group continued to improve in this domain from 6 to 12 months. The only 12 month outcomes that appeared to be independently related to a diagnosis of delusional disorder were negative and general psychopathology and total PANSS score. This contrasts with some previous studies of patients with delusional disorder, which have generally found that they have improved functional outcomes compared to schizophrenia patients (Opjordsmoen, 1988), as well as less severe psychopathology (Marneros et al., 2012). However, this study did find that those with delusional disorder had significantly higher rates of recovery than those with schizophrenia, which remained significant after adjusting for baseline characteristics. As the definition of recovery is based on symptoms and correlates well with PANSS scores (Bebbington et al., 2006), this likely reflects the less severe psychopathology in the delusional disorder group.

There were no differences between schizophrenia and delusional disorder when looking at changes in the outcome scores, although both groups improved over 12 months on both symptom and function scores. This appears to suggest that while patients with delusional disorder may present with a less severe illness form, both groups showed similar symptomatic and functional improvement in the short term.

Another interesting finding was the significantly shorter DUP in patients with delusional disorder compared to schizophrenia. This is contrary to what has been previously been suggested for delusional disorder, as it is often thought that due to less severe illness, better functioning and poor insight patients frequently delay help seeking (or others seek help for them) and therefore have

longer DUP (Ibanez-Casas and Cervilla, 2012). Notwithstanding this, other studies have shown similar (González-Rodríguez et al., 2015) or slightly shorter DUP in patients with delusional disorder (Hui et al., 2015). The shorter DUP in the delusional disorder patients in this cohort may explain the improved functioning found in the unadjusted 12 month outcomes shown above.

The use of a cohort of first episode psychosis patients may explain some of the differences compared with previous studies into delusional disorder. Previous studies investigating delusional disorder patients have found an older age of onset compared to schizophrenia (Marneros et al., 2012; Opjordsmoen, 1988), and may present more frequently around middle age (Manschreck and Khan, 2006). The mean age of onset in this study was almost identical for both groups (21.3 and 21.7 years for schizophrenia and delusional disorder respectively) and considerably younger than previously reported for delusional disorder. All patients in this study were referred to EI services, which at this time in the UK treated patients aged 18-35 years, and therefore a significantly older age group was de facto excluded. Patients in this study also showed a significant male predominance, and while this has been reported previously (Opjordsmoen, 1988; Opjordsmoen and Retterstol, 1991; Winokur, 1977), the proportion of 81% male is particularly high. Therefore, it may be that early onset delusional disorder patients have a different demographics, poorer functioning and worse prognosis to the 'traditional' later onset delusional disorder, and instead present more similarly to schizophrenia, albeit with a milder illness form. On the other hand, the presentation of delusional disorder at an earlier stage may have a significant effect on social integration, education and occupational activities, and

therefore these patients end up with poorer functioning as a result of the earlier presentation.

4.2 Strengths and Limitations

This study included a large cohort of patients with first episode delusional disorder and schizophrenia patients, with systematic, reliable assessments of diagnosis, symptomatology and functioning, and naturalistic 12 month follow up. This allowed for adjustment in a number of confounding factors when investigating outcomes. Despite these strengths, there are a number of limitations that need to be considered when interpreting the findings. At present the follow up data for the National EDEN study is only available up to 12 months, and short-term outcome measurements may not be sufficient to detect any divergence in the illness course of delusional disorder from schizophrenia which has been shown previously (Marneros et al., 2012; Opjordsmoen, 1988). There were some missing data and 6 and 12 month follow up points for both groups and the specific numbers for each outcome are detailed in table 3, but these were relatively modest and therefore missing data analysis was not performed.

Furthermore, diagnosis was assessed using OPCRIT diagnostic tool, which is not a gold standard structured clinical interview. This diagnosis was not reassessed at the 12 month follow up point, and therefore it is not possible to tell if there was some diagnostic shift between groups. Notwithstanding, a diagnosis of delusional disorder at first presentation has been shown to have diagnostic stability over time (Fusar-Poli et al., 2016; Marneros et al., 2012). Previous studies have also found differences in the nature of delusions experienced between delusional disorder and schizophrenia, and while detailed information

was available for PANSS scores, details on specific psychotic symptoms, such as first rank symptoms and the nature of delusions were not assessed in this cohort.

Another possible explanation for the differences between this cohort and previous studies investigating later onset delusional disorder is that many patients with less severe symptoms who function well in the community may not may never be referred to EI services. Such patients may only come to attention of mental health teams when there is an issue of risk or life stressors affect their ability to function, and may therefore present later in life. This may contribute to the relatively small number of delusional disorder patients in this cohort, which also limits the generalisability of the findings.

While DUP was carefully defined and calculated from historical information, accurate measurement remains difficult, especially so in delusional disorder (Compton et al., 2007). Finally, while every effort was made to adjust for confounding factors that are known to influence outcome and prognosis in psychotic illnesses, there may be further unknown factors which affect outcome which we have not adjusted for.

4.3 Clinical Implications

This study suggests that patients presenting with a first episode delusional disorder have less severe symptomatology and better functioning at baseline compared to patients presenting with first episode schizophrenia. The majority of these differences persisted at 12 months follow up, although after adjusting for confounding factors only PANSS negative and general scores were significantly lower in the delusional disorder group, while schizophrenia

patients had lower rates of recovery. However, it could be considered that baseline differences in the two groups such as age of onset and DUP are inherent characteristics of the diagnostic group rather than confounders. Therefore, the unadjusted scores presented here should be considered as relevant to the prognosis of delusional disorder in first episode patients. Nonetheless, the differences in the adjusted scores demonstrates that early age of onset and longer DUP still act as negative prognostic factors for those with delusional disorder, leading to poorer functioning.

There were no differences in the change in outcome scores between the groups, which suggests that both groups appeared to improve to a similar degree over 12 month follow up.

There has been much debate in literature as to the existence of delusional disorder as a separate diagnostic entity that is different to schizophrenia (Hui et al., 2015; Marneros et al., 2012; Opjordsmoen and Retterstol, 1991). This study adds a unique insight into this debate by reporting on a cohort of first episode delusional disorder patients with a younger age of onset. Previous studies of delusional disorder reporting improved functional outcomes have suggested that delusional disorder has an older age of onset than schizophrenia (Kendler, 1982; Manschreck and Khan, 2006; Marneros et al., 2012; Winokur, 1977). This may not be directly comparable to the younger onset delusional disorder patients described here, who appear to present with a shorter DUP, better baseline functioning and fewer symptoms than patients with schizophrenia, and similar improvements over 12 months. Further studies are required to determine if

there are differences in functional outcomes between early and late onset delusional disorder.

Recent studies have suggested a dimensional concept of psychoses, and that delusional disorder could be viewed as a 'partial psychoses', with fewer negative symptoms than schizophrenia and fewer affective symptoms than schizoaffective disorder (Munoz-Negro et al., 2015; Opjordsmoen, 2014). This study may support this approach. Clinically this suggests that although delusional disorder patients present with less severe illness than schizophrenia, EI services should treat these patients similarly, as current evidence suggests they do respond to antipsychotic treatment (Gonzalez-Rodriguez et al., 2016; Manschreck and Khan, 2006) and patients demonstrate improvement similar to that seen in schizophrenia. Further follow up studies are required to determine whether younger onset delusional disorder patients retain their diagnosis over time, and whether illness courses diverge from schizophrenia in the longer term.

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Figure Legends

Figure 1: Mean PANSS positive, negative, general and total scores at baseline, 6 months and 12 months for delusional disorder and schizophrenia groups.

Figure 2: Mean GAF total, symptom and disability scores at baseline and 12 months for delusional disorder and schizophrenia groups.

Table 1: Baseline demographics and substance use of the sample by diagnostic group

	Schizophrenia*	Delusional disorder *	Total*	P value
Age at onset N total	 252	 47	 299	0.607

Mean (SD) 95% CI	21.28 (4.95) (20.66, 21.89)	21.68 (4.86) (20.26, 23.11)	21.34 (20.78, 21.9)	
Gender N total Male (%)	 262 191 (72.9)	 48 39 (81.3)	 310 230 (74.2)	0.224
DUP N total Mean (SD) 95% CI	 258 330.26 (664.4) (248.81, 411.72)	 47 135.79 (236.1) (66.46, 205.12)	 305 300.3 (621.8) (230.24, 370.35)	**<0.001**
Educational level/Qualifications N total (%) None Basic (GCSE/NVQ ½) Advanced (A level/BTEC/NVQ3) Degree/HND/NVQ 4+ Special needs educational qualifications	 257 71 (27.6%) 111 (43.2%) 58 (22.6%) 16 (6.2%) 1 (0.4%)	 47 7 (14.9%) 23 (48.9%) 11 (23.4%) 5 (10.6%) 1 (2.1%)	 304 78 (25.7%) 134 (44.1%) 69 (22.7%) 21 (6.9%) 2 (0.7%)	0.217
Ethnicity N total Asian Black Caucasian Mixed Other	 262 49 (18.7%) 23 (8.8%) 172 (65.6%) 15 (5.7%) 3 (1.1%)	 48 3 (6.3%) 5 (10.4%) 36 (75%) 4 (8.3%) 0 (0%)	 310 52 (16.8%) 28 (9%) 208 (67.1%) 19 (6.1%) 3 (1%)	0.249
Living circumstances N total Alone With parents/guardians With partner Other	 260 39 (15%) 171 (65.8%) 16 (6.2%) 34 (13.1%)	 48 10 (20.8%) 26 (54.2%) 4 (8.3%) 8 (16.7%)	 308 49 (15.9%) 197 (64.0%) 20 (6.5%) 42 (13.6%)	0.494
Occupational circumstances N total Working (paid) Working (voluntary) Unemployed Homemaker Student Other	 261 34 (13%) 4 (1.5%) 178 (68.2%) 6 (2.3%) 37 (14.2%) 2 (0.8%)	 47 14 (29.8%) 0 (0%) 28 (59.6%) 1 (2.1%) 4 (8.5%) 0 (0%)	 308 48 (15.6%) 4 (1.3%) 206 (66.9%) 7 (2.3%) 41 (13.3%) 2 (0.6%)	0.085

DUP, duration of untreated psychosis; GCSE, General Certificate of Secondary Education; NVQ, National Vocational Qualification; BTEC, Business and Technology Educational Council; HND, Higher National Diploma.

P-values in bold indicate significance at the <0.05 level.

Table 2: Baseline symptoms and functioning scores by diagnostic group

		Schizophrenia*	Delusional disorder*	Total*	Mean difference	P value
PANSS positive	N Mean score (SD) 95% CI	244 16.75 (6.32) (15.96, 17.55)	45 14.44 (5.81) (12.70, 16.19)	289 16.39 (6.29) (15.67, 17.12)	2.31 (0.31, 4.31)	**0.023**
PANSS negative	N Mean score (SD) 95% CI	241 16.09 (6.38) (15.28, 16.9)	43 13.26 (6.5) (11.26, 15.25)	284 15.66 (6.46) (14.91, 16.42)	2.84 (0.75, 4.92)	**0.008**
PANSS general	N Mean score (SD) 95% CI	244 34.01 (10.58) (32.68, 35.35)	45 30.62 (10.41) (27.5, 33.75)	289 33.48 (10.61) (32.26, 34.71)	3.39 (0.02, 6.76)	**0.049**

PANSS total	N Mean score (SD) 95% CI	237 66.23 (18.38) (63.88, 68.58)	43 58.14 (20.28) (51.9, 64.38)	280 64.99 (18.87) (62.77, 67.21)	8.09 (1.99, 14.18)	**0.009**
Calgary Depression Scale	N Mean score (SD) 95% CI	245 5.46 (5.17) (4.81, 6.11)	44 5.95 (5.4) (4.31, 7.6)	289 5.54 (5.20) (4.93, 6.14)	-0.49 (-2.17, 1.18)	0.563
YMRS	N Mean score (SD) 95% CI	244 6.78 (7.30) (5.86, 7.7)	42 5.36 (8.0) (2.88, 7.84)	286 6.57 (7.40) (5.71, 7.44)	1.43 (-1.01, 3.86)	0.250
GAF total	N Mean score (SD) 95% CI	248 46.89 (16.96) (44.77, 49.01)	42 52.88 (17.88) (47.31, 58.45)	290 47.76 (17.20) (45.77, 49.74)	-5.99 (-11.61, -0.38)	**0.036**
GAF symptoms	N Mean score (SD) 95% CI	246 48.85 (17.00) (46.71, 50.98)	43 55.47 (17.70) (50.02, 60.91)	289 49.83 (17.24) (47.83, 51.83)	-6.62 (-12.18, -1.06)	**0.020**
GAF disability	N Mean score (SD) 95% CI	247 48.70 (15.70) (46.75, 50.68)	41 58.61 (15.90) (53.58, 63.64)	288 50.13 (16.08) (48.26, 51.99)	-9.89 (-15.11, -4.67)	**<0.001**
EQ-5D health thermometer	N Mean score (SD) 95% CI	227 61.63 (22.36) (58.70, 64.55)	36 60.00 (24.11) (51.84, 68.16)	263 61.40 (58.66, 64.14)	1.63 (-6.36, 9.61)	0.689
Lifetime substance use (n=297)	Yes No	176 74	32 15	208 89		0.751

*overall N for Delusional Disorder = 48, for schizophrenia = 262 and total = 310, number vary slightly by individual symptom outcome

Footnote: GAF= Global Assessment of Functioning scale; YMRS= Young Mania Rating Scale; PANSS= Positive and Negative Syndrome Scale; EQ= EuroQol

P-values in bold indicate significance at the <0.05 level.

Table 3: 6 and 12 month symptom and functional outcomes for Delusional Disorder and Schizophrenia unadjusted and adjusted for baseline score, DUP and age after natural log transformation

		Unadjusted 6 month outcomes			Adjusted 6 month outcomes*		6 month change scores		Unadjusted 12 month outcomes			Adjusted 12 month outcomes*		12 month change score	
		Schizophrenia	**Delusional disorder**	**P value**	**P value**	**Beta**	**P value**	**Beta**	**Schizophrenia**	**Delusional disorder**	**P value**	**P value**	**Beta**	**P value**	**Beta**
PANSS positive	N Mean 95% CI	201 12.65 (11.94, 13.36)	38 9.92 (8.88, 10.96)	**<0.001**	**0.022**	-0.142	0.389	-0.060	205 12.07 (11.38, 12.77)	39 10.26 (9.07, 11.44)	**0.010**	0.127	-0.099	0.859	0.012
PANSS negative	N Mean 95% CI	199 14.44 (13.62, 15.26)	38 10.95 (9.70, 12.20)	**<0.001**	**0.011**	-0.147	0.371	-0.063	203 13.39 (12.57, 14.21)	39 10.69 (9.56, 11.83)	**<0.001**	**0.045**	-0.132	0.784	-0.019
PANSS general	N Mean 95% CI	200 28.12 (26.95, 29.28)	38 24.66 (22.40, 26.92)	**0.017**	0.161	-0.090	0.689	-0.028	205 26.82 (25.60, 28.04)	38 23.11 (20.97, 25.24)	**0.014**	**0.032**	-0.138	0.466	-0.049
PANSS total	N Mean 95% CI	198 55.01 (52.75, 57.27)	38 45.53 (41.66, 49.39)	**<0.001**	**0.022**	-0.139	0.442	-0.054	203 52.24 (49.84, 54.64)	38 44.13 (40.29, 47.97)	**0.001**	**0.040**	-0.134	0.766	-0.021
Calgary Depression Scale	N Mean 95% CI	208 3.80 (3.19, 4.42)	38 3.79 (2.38, 5.19)	0.986	0.462	0.056	0.767	-0.027	204 3.11 (2.56, 3.67)	38 2.21 (0.94, 3.49)	0.202	0.701	-0.032	0.134	-0.137
YMRS	N Mean 95% CI	211 4.15 (3.39, 4.90)	37 2.00 (1.07, 2.93)	**0.010**	0.528	-0.020			206 3.79 (3.07, 4.50)	39 2.95 (1.39, 4.51)	0.351	0.979	0.002	0.572	0.057
GAF total	N Mean 95% CI								217 60.43 (57.93, 62.93)	40 66.53 (61.01, 72.04)	0.056	0.179	0.085	0.906	0.008

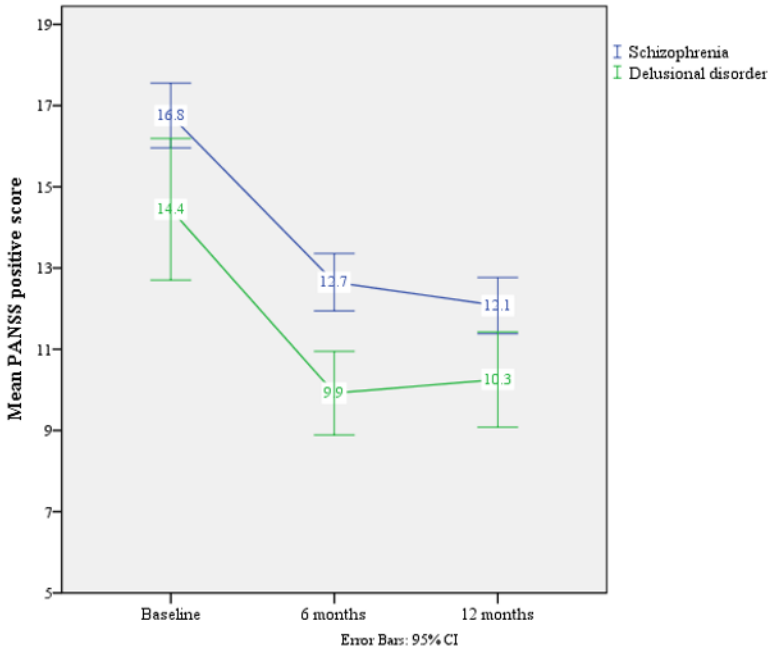
GAF symptoms	N Mean 95% CI								214 61.56 (59.16, 63.96)	38 67.79 (63.18, 72.40)	**0.042**	0.070	0.112	0.826	0.015
GAF disability	N Mean 95% CI								214 59.29 (56.93, 61.66)	38 68.24 (62.91, 73.56)	**0.004**	0.083	0.111	0.821	-0.015
EQ5D health thermometer	N Mean 95% CI								182 66.03 (62.81, 69.25)	34 68.79 (60.78, 76.81)	0.505	0.301	0.074	0.285	0.081
Relapse (%) None Type 2 exacerbation Type 1 true									145 (66.5%) 47 (21.6%) 26 (11.9%)	34 (77.3%) 8 (18.2%) 2 (4.5%)	0.261	0.106			
Recovery (%) None Partial Full									36 (14.0%) 98 (38.1%) 123 (47.9%)	1 (2.1%) 12 (25.5%) 34 (72.3%)	**0.004**	**0.002**			
Antipsychotic treatment (%) N=310									34 (13%)	9 (18.8%)	0.287				

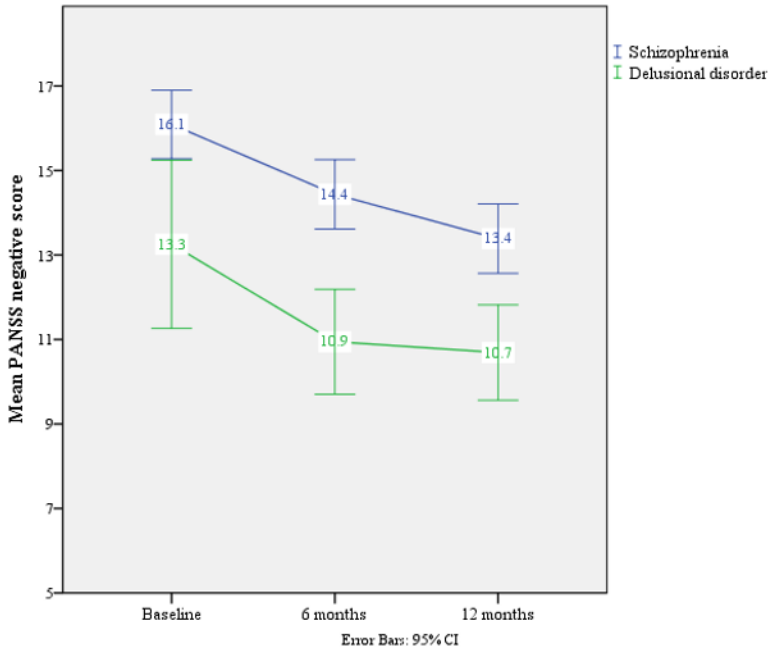
*adjusted analysis with DUP (Duration of Untreated Psychosis), age and baseline scores as covariates, apart from the analyses for relapse and recovery when baseline scores were not a covariate

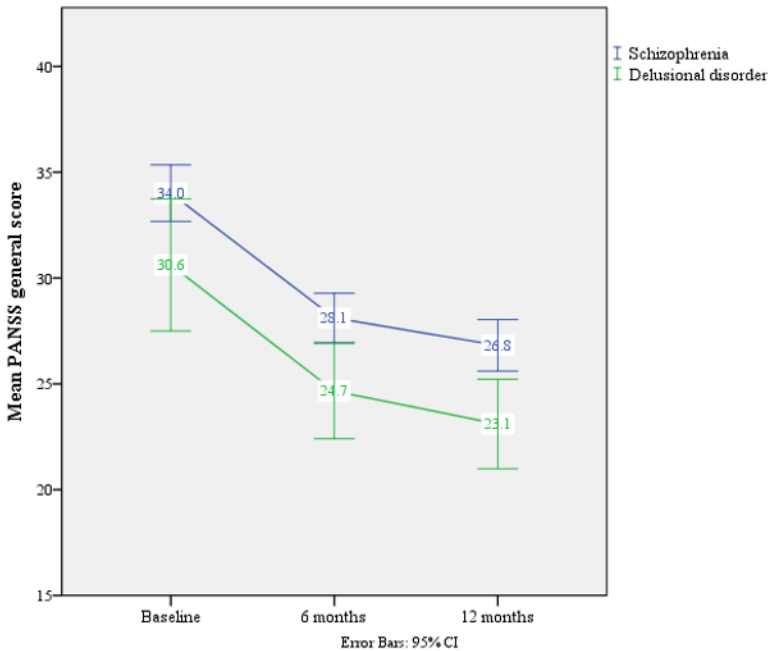
Footnote: GAF= Global Assessment of Functioning scale; YMRS= Young Mania Rating Scale; PANSS= Positive and Negative Syndrome Scale; EQ= EuroQol

P-values in bold indicate significance at the <0.05 level.

Figure 1


Mean PANSS positive score
19
17
15
13
11
9
7
5
16.8
14.4
12.7
9.9
12.1
10.3
Baseline
6 months
12 months
Error Bars: 95% CI
Schizophrenia
Delusional disorder


Mean PANSS negative score
17
15
13
11
9
7
5
16.1
13.3
14.4
10.9
13.4
10.7
Baseline
6 months
12 months
Error Bars: 95% CI
Schizophrenia
Delusional disorder


Mean PANSS general score
40
35
30
25
20
15
34.0
30.6
28.1
24.7
26.8
23.1
Baseline
6 months
12 months
Error Bars: 95% CI
Schizophrenia
Delusional disorder

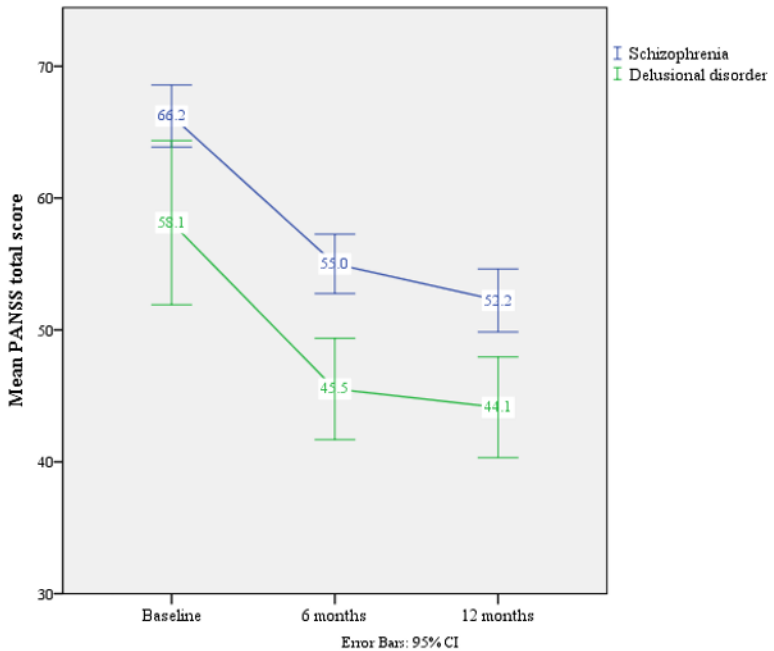
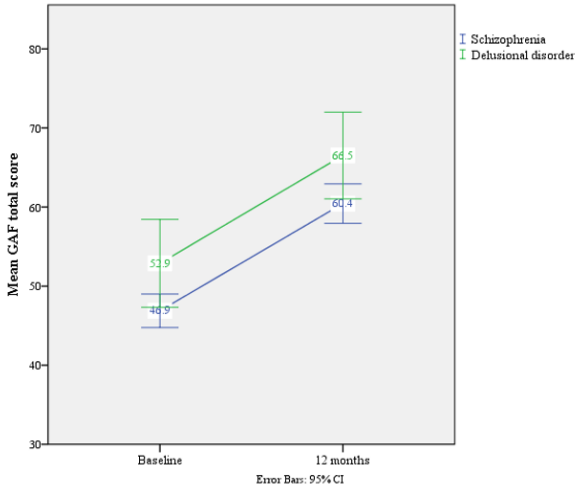

Mean PANSS total score
70
60
50
40
30
66.2
58.1
55.0
45.5
52.2
44.1
Baseline
6 months
12 months
Error Bars: 95% CI
Schizophrenia
Delusional disorder

Figure 2


Schizophrenia
Delusional disorder
Mean GAF total score
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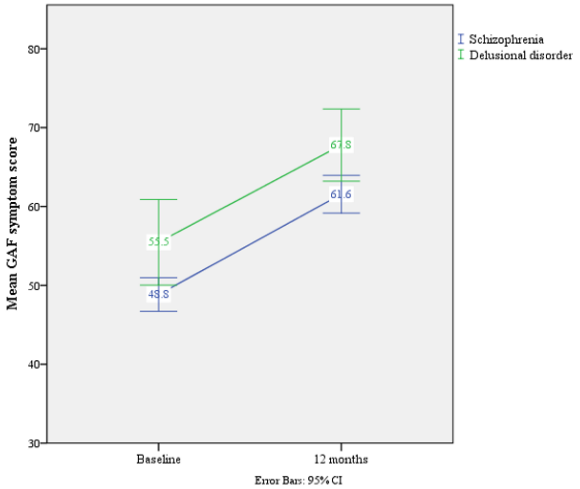
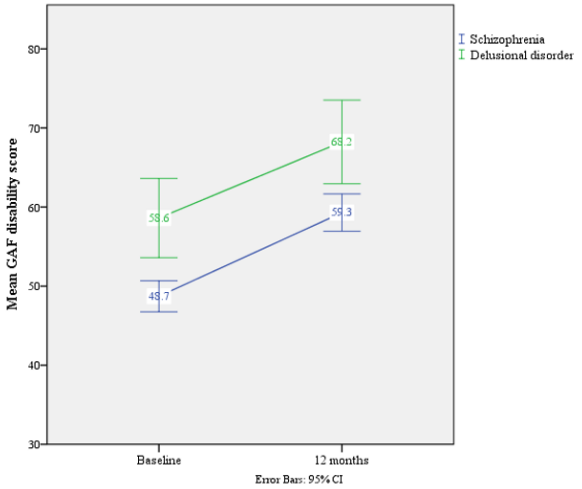
70
60
50
40
30
52.9
66.5
46.9
60.4
Baseline
12 months
Error Bars: 95% CI


Schizophrenia
Delusional disorder
Mean GAF symptom score
80
70
60
50
40
30
55.5
67.8
48.8
61.6
Baseline
12 months
Error Bars: 95% CI


Schizophrenia
Delusional disorder
Mean GAF disability score
80
70
60
50
40
30
58.6
68.2
48.7
59.3
Baseline
12 months
Error Bars: 95% CI