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

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4

1 **Abstract**

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

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

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

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

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

3 **1. Introduction**

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

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

1 However, outcomes in delusional disorder have not been extensively
2 investigated in a first episode population where differences in symptomatology
3 and functioning have been more difficult to illicit (Hui et al., 2015). Extant follow-
4 up studies have either been limited by small samples or not considered other
5 possible confounders in the relationship between diagnosis and outcome.

6 However, the diagnosis of delusional disorder does appear to have some stability
7 (Fusar-Poli et al., 2016; Kulkarni et al., 2016; Marneros et al., 2012) although
8 others continue to question the distinction between delusional disorder and
9 paranoid schizophrenia (Hui et al., 2015).

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

19 **2. Materials and Methods**

20 *2.1 Setting*

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

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

8 *2.2 Participants*

9 The National EDEN study approached all patients referred to EI services in
10 participating centres between August 2005 and April 2009 for inclusion in the
11 study. Inclusion criteria were the same as criteria for acceptance into EI services
12 according to The Department of Health, which is 'first presentation of psychotic
13 symptoms between the ages of 14 and 35 years'. The study excluded those with
14 'ultra-high risk' symptoms as they do not meet the criteria for psychosis. Of the
15 2097 patients that were eligible for inclusion 1027 consented to participate and
16 were entered into the National EDEN study (49%). 825 patients completed the 6
17 month follow up and 791 completed 12 month follow up.

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

1 2.3 Assessments

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

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

23 Additionally, relapse and recovery were assessed using the Bebbington *et al*
24 method (Bebbington et al., 2006), which involved a combination of clinical

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

5 *2.4 Reliability across sites*

6 Research associates were trained in the use of scales such as PANSS, GAF, YMRS,
7 Calgary Depression Scale, relapse and recovery and DUP assessment. All staff
8 were required to attend a training programme and new staff were required to
9 achieve concordance rate of kappa $r > 0.75$ compared to trainers when assessing
10 tapes of previous interviews. Additionally, every 12 months five DUP
11 assessments and five relapse and recovery assessments from all sites were
12 independently assessed for concordance, with kappa $r > 0.75$ required. Every 20th
13 PANSS assessment was observed by an experienced interviewer for site specific
14 monitoring, and PANSS reliability was also assessed using a trained rater from
15 each main site. The average intraclass correlation was 0.90 for positive scale,
16 0.89 for negative scale and 0.91 for general psychopathology scale. The overall
17 agreement in relapse categories was 73% (kappa 0.62) with an intraclass
18 correlation of 0.77 for time to relapse.

19 *2.5 Analysis strategy*

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

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

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

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

19 **3. Results**

20 *3.1 Sample information*

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

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

4 *3.2 Baseline demographics*

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

15 *3.3 Baseline symptoms and function*

16 Baseline PANSS, YMRS, Calgary Depression Scale, EQ-5D and GAF scores for each
17 group are shown in table 2. The delusional disorder group had significantly
18 better functioning at baseline in terms of GAF total (delusional disorder mean
19 52.88 95% CI 47.31-58.45, schizophrenia mean 46.89 95% CI 44.77-49.01,
20 $p=0.036$), GAF symptom (delusional disorder mean 55.47 95% CI 50.02-60.91,
21 schizophrenia mean 48.85 95% CI 46.71-50.98, $p=0.02$) and GAF disability
22 scores (delusional disorder mean 58.61 95% CI 53.58-63.64, schizophrenia
23 mean 48.7 95% CI 46.75-50.68, $p<0.001$) compared to the schizophrenia group.

1 PANSS mean scores were also significantly lower for the delusional disorder
2 group compared to schizophrenia, in positive (delusional disorder 14.44 95% CI
3 12.70-16.19, schizophrenia 16.75 95% CI 15.96-17.55, $p=0.023$), negative
4 (delusional disorder 13.26 95% CI 11.26-15.25, schizophrenia 16.09 95% CI
5 15.28-16.9, $p=0.008$), general psychopathology (delusional disorder 30.62 95%
6 CI 27.5-33.75, schizophrenia 34.01 95% CI 32.68-35.35, $p=0.049$) and total
7 (delusional disorder 58.14 95% CI 51.9-64.38, schizophrenia 66.23 95% CI
8 63.88-68.58, $p=0.009$) subsection mean scores. There were no differences in
9 YMRS, Calgary depression or EQ-5D health thermometer mean scores between
10 the two groups.

11 *3.4 6 and 12 months follow up symptoms and functioning*

12 As shown in table 3, at 6 months the delusional disorder group has significantly
13 lower PANSS mean scores than the schizophrenia group in positive (delusional
14 disorder 9.92 95% CI 8.88-10.96, schizophrenia 12.65 95% CI 11.94-13.36,
15 $p<0.001$), negative (delusional disorder 10.95 95% CI 9.70-12.20, schizophrenia
16 14.44 95% CI 13.62-15.26, $p<0.001$), general (delusional disorder 24.66 95% CI
17 22.40-26.92, schizophrenia 28.12 95% CI 26.95-29.28, $p=0.017$) and total
18 (delusional disorder 45.53 95% CI 41.66-49.39, schizophrenia 55.01 95% CI
19 52.75-57.27, $p<0.001$) subsection mean scores. Additionally, delusional disorder
20 patients had significantly lower YMRS mean scores (delusional disorder 2.0 95%
21 CI 1.07-2.93, schizophrenia 4.15 95% CI 3.39-4.90, $p=0.001$), although Calgary
22 Depression Scale mean scores were not different between the groups.

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

1 (delusional disorder 10.26 95% CI 9.07-11.44, schizophrenia 12.07 95% CI
2 11.38-12.77, $p=0.01$), negative (delusional disorder 10.69 95% CI 9.56-11.83,
3 schizophrenia 13.39 95% CI 12.57-14.21, $p<0.001$), general (delusional disorder
4 23.11 95% CI 20.97-25.24, schizophrenia 26.82 95% CI 25.60-28.04, $p=0.014$)
5 and total (delusional disorder 44.13 95% CI 40.29-47.97, schizophrenia 52.24
6 95% CI 49.84-54.64, $p=0.001$) subsection mean scores. Baseline, 6 and 12 month
7 PANSS subsection mean scores are shown in figure 1. Additionally, patients with
8 delusional disorder continued to have significantly better functioning in terms of
9 GAF symptoms (delusional disorder mean 67.79 95% CI 63.18-72.40
10 schizophrenia mean 61.56 95% CI 59.16-63.96, $p=0.042$) and disability scores
11 (delusional disorder mean 68.24 95% CI 62.91-73.56, schizophrenia mean 59.29
12 95% CI 56.93-61.66, $p=0.004$), although the difference in GAF total score failed
13 to reach significance at the 0.05 level (delusional disorder mean 66.53 95% CI
14 61.01-72.04, schizophrenia mean 60.43 95% CI 57.93-62.93, $p=0.056$). Baseline,
15 6 and 12 month GAF mean scores are shown in figure 2. There was no difference
16 at 12 months between the groups in YMRS, Calgary Depression Scale or EQ-5D
17 health thermometer mean scores. There was also no difference in the number of
18 patients who received antipsychotic treatment at 12 months. Relapse rates did
19 not differ between the groups, although a significant difference was seen in
20 recovery rates with 72.3% of those with delusional disorder achieving full
21 recovery compared to 47.9% with schizophrenia, and only 2.1% of those with
22 delusional disorder failing to achieve recovery compared to 14% with
23 schizophrenia ($p=0.004$).

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

4 *3.5 Adjusted analysis at 6 and 12 months*

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

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

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

23 *3.6 Analysis of change scores*

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

8 **4. Discussion**

9 *4.1 Summary and interpretation of the results*

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

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

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

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

14 There were no differences between schizophrenia and delusional disorder when
15 looking at changes in the outcome scores, although both groups improved over
16 12 months on both symptom and function scores. This appears to suggest that
17 while patients with delusional disorder may present with a less severe illness
18 form, both groups showed similar symptomatic and functional improvement in
19 the short term.

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

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

6 The use of a cohort of first episode psychosis patients may explain some of the
7 differences compared with previous studies into delusional disorder. Previous
8 studies investigating delusional disorder patients have found an older age of
9 onset compared to schizophrenia (Marneros et al., 2012; Opjordsmoen, 1988),
10 and may present more frequently around middle age (Manschreck and Khan,
11 2006). The mean age of onset in this study was almost identical for both groups
12 (21.3 and 21.7 years for schizophrenia and delusional disorder respectively) and
13 considerably younger than previously reported for delusional disorder. All
14 patients in this study were referred to EI services, which at this time in the UK
15 treated patients aged 18-35 years, and therefore a significantly older age group
16 was de facto excluded. Patients in this study also showed a significant male
17 predominance, and while this has been reported previously (Opjordsmoen,
18 1988; Opjordsmoen and Retterstol, 1991; Winokur, 1977), the proportion of
19 81% male is particularly high. Therefore, it may be that early onset delusional
20 disorder patients have a different demographics, poorer functioning and worse
21 prognosis to the 'traditional' later onset delusional disorder, and instead present
22 more similarly to schizophrenia, albeit with a milder illness form. On the other
23 hand, the presentation of delusional disorder at an earlier stage may have a
24 significant effect on social integration, education and occupational activities, and

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

3 *4.2 Strengths and Limitations*

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

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

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

3 Another possible explanation for the differences between this cohort and
4 previous studies investigating later onset delusional disorder is that many
5 patients with less severe symptoms who function well in the community may not
6 may never be referred to EI services. Such patients may only come to attention of
7 mental health teams when there is an issue of risk or life stressors affect their
8 ability to function, and may therefore present later in life.

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

15 *4.3 Clinical Implications*

16 This study suggests that patients presenting with a first episode delusional
17 disorder have less severe symptomatology and better functioning at baseline
18 compared to patients presenting with first episode schizophrenia. The majority
19 of these differences persisted at 12 months follow up, although after adjusting
20 for confounding factors only PANSS negative and general scores were
21 significantly lower in the delusional disorder group, while schizophrenia
22 patients had lower rates of recovery. However, it could be considered that
23 baseline differences in the two groups such as age of onset and DUP are inherent

1 characteristics of the diagnostic group rather than confounders. Therefore, the
2 unadjusted scores presented here should be considered as relevant to the
3 prognosis of delusional disorder in first episode patients. Nonetheless, the
4 differences in the adjusted scores demonstrates that early age of onset and
5 longer DUP still act as negative prognostic factors for those with delusional
6 disorder, leading to poorer functioning.

7 There were no differences in the change in outcome scores between the groups,
8 which suggests that both groups appeared to improve to a similar degree over
9 12 month follow up.

10 There has been much debate in literature as to the existence of delusional
11 disorder as a separate diagnostic entity that is different to schizophrenia (Hui et
12 al., 2015; Marneros et al., 2012; Opjordsmoen and Retterstol, 1991). This study
13 adds a unique insight into this debate by reporting on a cohort of first episode
14 delusional disorder patients with a younger age of onset. Previous studies of
15 delusional disorder reporting improved functional outcomes have suggested that
16 delusional disorder has an older age of onset than schizophrenia (Kendler, 1982;
17 Manschreck and Khan, 2006; Marneros et al., 2012; Winokur, 1977). This may
18 not be directly comparable to the younger onset delusional disorder patients
19 described here, who appear to present with a shorter DUP, better baseline
20 functioning and fewer symptoms than patients with schizophrenia, but little
21 difference in the course of the illness over 12 months. Further studies are
22 required to determine if there are differences in functional outcomes between
23 early and late onset delusional disorder.

1 Recent studies have suggested a dimensional concept of psychoses, and that
2 delusional disorder could be viewed as a 'partial psychoses', with fewer negative
3 symptoms than schizophrenia and fewer affective symptoms than schizoaffective
4 disorder (Munoz-Negro et al., 2015; Opjordsmoen, 2014). This study may
5 support this approach. Clinically this suggests that although delusional disorder
6 patients present with less severe illness than schizophrenia, EI services should
7 treat these patients similarly, as current evidence suggests they do respond to
8 antipsychotic treatment (Gonzalez-Rodriguez et al., 2016; Manschreck and Khan,
9 2006) and patients demonstrate improvement similar to that seen in
10 schizophrenia. Further follow up studies are required to determine whether
11 younger onset delusional disorder patients retain their diagnosis over time, and
12 whether illness courses diverge from schizophrenia in the longer term.

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12 **Figure Legends**

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

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

17

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

	Schizophrenia*	Delusional disorder *	Total*	P value
Age at onset				
N total	252	47	299	0.607
Mean (SD)	21.28 (4.95)	21.68 (4.86)	21.34	
95% CI	(20.66, 21.89)	(20.26, 23.11)	(20.78, 21.9)	
Gender				
N total	262	48	310	0.224
Male (%)	191 (72.9)	39 (81.3)	230 (74.2)	

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

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

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

5

6 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

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

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

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

6

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.