

Illness characteristics and symptoms in an Irish early intervention for psychosis service

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Objectives. Study of illness characteristics and symptoms in a young population with psychosis can assist for understanding of their needs, and can inform service planning strategies. The aims of the current study were to describe illness characteristics and symptoms of a first episode psychosis (FEP) sample aged 25 years and under, and compare with a sample aged over 25 years.

Methods. Interviews were conducted for 437 individuals aged 16–65 years presenting with suspected psychosis between 2005 and 2012 in a defined catchment area (population of 390 000) using the Structured Clinical Interview for DSM IV to determine the presence of a psychosis diagnosis. Individuals with confirmed psychosis were assessed using standardised instruments to determine illness characteristics at first presentation.

Results. Among the 25 years, and under FEP sample, 23.9% had their first onset of symptoms (prodromal or psychotic) before 18 years of age. After controlling for confounders, the sample aged 25 years and under had a significantly shorter log transformed duration of untreated psychosis ($p = 0.002$), more negative symptoms ($p = 0.045$) and greater frequency of comorbid cannabis abuse diagnosis ($p = 0.027$).

Conclusions. Symptom onset in a youth FEP sample frequently occurs before age 18 years. Certain illness characteristics differed across the age categories, such as greater negative symptoms and cannabis abuse in the youth sample. Overall, the findings support the provision of adequate strategies for management of negative symptom deficits and substance abuse across all ages in FEP.

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Introduction

Schizophrenia can be a devastating illness, which is associated with huge disability across society (Murray & Lopez, 1996; World Health Organisation, 2001). This disorder can be associated with poor long-term outcomes (Lang *et al.* 2013), reduced life expectancy (Saha *et al.* 2007) and imposes a major financial cost to society, estimated at 460 million euros/annum in Ireland alone (Behan *et al.* 2008).

Epidemiology aims to describe illness characteristics, such as demographics and risk factors of disease, with the ultimate aim of intervening to reduce morbidity and mortality (Gordis, 2009). The epidemiology of schizophrenia has been previously described in several international studies. Age of onset usually occurs

during late adolescence or early adulthood (Owens *et al.* 2005; Jones, 2013), with an earlier mean age of onset in males (Angermeyer & Kuhn, 1988). The peak age of onset distribution occurs between 18 and 30 years for males and females, and there is a second peak later in life for females (American Psychiatric Association, 2000; Kirkbride *et al.* 2012). This age of onset distribution suggests that adequate resources should be provided for identifying and treating individuals presenting with psychosis at this young age.

Momentum for delivery of specialised first episode psychosis (FEP) services has increased over the last few decades (McGorry, 2013). FEP services have been introduced in Ireland, and are established in several other countries such as United Kingdom, Australia and Canada. Concurrently, services that specialise in youth mental health have been growing internationally (Birchwood & Singh, 2013). This has provided focus for intervention in the young with a view to improving lifelong mental health.

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Given that FEP and youth mental health have been identified as an important target for mental health research, the current epidemiological study investigates early psychosis in a youth population. To our knowledge, no previous Irish study has compared characteristics and symptoms between a youth population and an older FEP population. The aim of this exploratory study was to describe characteristics and symptoms in a youth FEP sample, and compare with a sample aged over 25 years. We chose 25 years as a cutoff, as this age has been used for delivery of youth mental health services both in Ireland and internationally (McGorry *et al.* 2013). This research is part of a larger project investigating symptomatology, specifically negative symptoms and FEP outcomes (Lyne *et al.* 2014).

Methods

Study setting and participants

The study was based in the Dublin and East Treatment and Early Care Team (DETECT), an Irish early intervention in psychosis service, located in South Dublin and County Wicklow between February 2005 and January 2012. DETECT receives referrals for all inpatient and outpatient cases of suspected FEP aged 16–65 years within a defined catchment area. The catchment area comprises three geographically defined mental health services serving a population of 390 000. DETECT also receives referrals from St. John of God Hospital, a private inpatient psychiatric facility located within the catchment area, which receives referrals from both within the catchment area and nationally. Proactive efforts are made to identify cases of suspected psychosis within the DETECT catchment area.

Following referral to the service, a Structured Clinical Interview for DSM IV (SCID) assessment was conducted to determine the presence or absence of a psychosis diagnosis (First *et al.* 1995). All individuals satisfying criteria for a psychosis diagnosis and with <30 days antipsychotic treatment were eligible for study inclusion. Individuals with learning disability and with psychotic disorder owing to a general medical condition were excluded from the study. In the entire study sample of 437 individuals, 158 (36.2%) individuals were aged 25 years and under, whereas 279 (63.8%) individuals were aged over 25 years. The 25 years and under sample will be referred to as the youth sample for the rest of the manuscript. Informed consent was obtained from all study participants and ethics approval was obtained before commencing the study.

Measures

A comprehensive assessment was conducted at first presentation for all study participants. Demographic

information was collected, including age, gender, marital status, living status, socioeconomic group, country of birth and working status. SCID assessment also determined the presence or absence of a lifetime diagnosis of substance abuse/dependence, including for alcohol and cannabis abuse. The term substance abuse diagnosis is used throughout the manuscript to refer to individuals with a lifetime substance abuse/dependence diagnosis.

Negative symptoms were measured with the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1984a), which has been recommended for use in negative symptom research (Kirkpatrick *et al.* 2006). Positive symptoms were measured using the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984b). Standardised remission criteria were used to determine the presence of positive and negative symptoms in the sample (Andreasen *et al.* 2005). The Calgary Depression Scale for Schizophrenia was used to measure depressive symptoms, for which a cutoff score of 7 or greater was used to determine the presence or absence of depressive symptoms (Addington *et al.* 1993).

The Beiser Scale was used to determine the first onset of the psychosis prodrome and the first onset of psychosis, in order to determine duration of untreated psychosis (DUP), duration of psychosis prodrome (DP) and duration of untreated illness (DUI) (Beiser *et al.* 1993). DUP was recorded in months as the duration between first onset of prominent psychotic symptoms and the date of first presentation for treatment. DP was recorded in months as the duration between onset of first noticeable signs and first onset of prominent psychotic symptoms. DUI was recorded in months as the sum of the DP and DUP.

Premorbid adjustment was measured by summing all items of the Premorbid Adjustment Scale (PAS) and dividing by the total possible score for these items (Cannon-Spoor *et al.* 1982; van Mastrigt & Addington, 2002). Higher scores on PAS represent poorer premorbid adjustment. Items from age groups that overlapped with or occurred subsequent to psychosis prodrome onset were excluded to ensure PAS scores were not influenced by psychosis prodrome symptoms.

Inter-rater reliability was conducted for each of the 17 data collectors in the study. Intraclass correlation coefficients (ICC) for SANS global total ranged between 0.67 and 0.99 for SANS (median 0.86, 16 out of 17 raters had ICC of >0.7), between 0.82 and 1.00 for SAPS (median 0.91) and between 0.78 and 1.00 for DUP, DP and DUI (median 0.99). Concordance of SCID diagnosis across raters was >0.82 for all assessors.

Statistical analysis

For the purposes of this study, data were anonymised and SPSS statistical software was used to conduct analyses.

Significance level for statistical testing was set at 0.05, and all statistical tests were two-tailed. The Beiser Scale was used to determine first symptom onset (either prodromal or psychosis) by subtracting DUI from age at first presentation. Where DUI data was unavailable ($n = 17$), DUP was used to calculate first symptom onset.

Logarithmic transformations were used to normalise the positively skewed distributions for DP, DUP and DUI for statistical tests. χ^2 test was used to compare categorical characteristics across relevant categories, whereas independent samples t -test was used to compare continuous variables across relevant categories. Variables significantly associated with age category were included as explanatory variables in a binary logistic regression model to assess for confounding. Age category was the binary dependent variable in the model. The variation in the model explained by the dependent variable was ascertained using the Cox and Snell R^2 and the Nagelkerke R^2 .

Results

Sample description and first symptom onset

The mean age of the entire sample was 32 years (s.d. = 11.6). In all, 40% of the sample was female, 65% were inpatient at first assessment, median DUP was 3 months and median DUI was 12 months.

First symptom onset occurred at age 25 years and under for 46.7% of the entire sample aged 16–65 years. Onset of first symptoms occurred before age 18 years for 9.3% of the entire sample. Of the youth sample, 23.4% experienced first symptoms before the age of 18 years. Figure 1 shows the age at first symptom onset and age at first presentation for the youth sample.

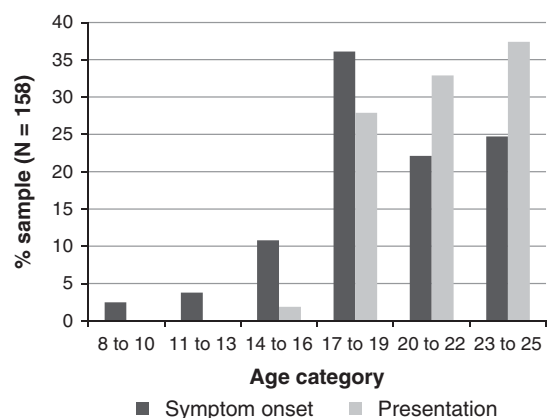


Fig. 1. Age at first symptom onset (prodrome or psychosis) and age at first presentation for treatment in the 25 years and under sample.

Highest percentage of first symptom onset in this age category was in the 17–19 years age category (36.1%).

Comparison of characteristics across age categories

Comparison of all diagnoses between the youth sample and the over 25 years sample suggested a significant difference ($\chi^2 = 22.81$, $p = 0.004$). When individual diagnoses were considered, the youth sample had significantly fewer cases of delusional disorder and significantly more cases of substance-induced psychosis (Table 1). In Table 1, the schizophrenia spectrum group included schizophrenia ($n = 142$), schizophreniform disorder ($n = 43$) and schizoaffective disorder ($n = 6$). The substance-induced psychosis group included individuals with substance-induced psychotic disorder ($n = 50$) and substance-induced mood disorder with psychotic features ($n = 9$).

Significant differences in the characteristics of the youth sample included fewer living alone, fewer married, more diagnoses of cannabis abuse, more negative symptoms and shorter DUP (Table 2). Of note, median DUP was 3 months in both the youth sample and the over 25 years sample. In the youth male sample, 28.0% had a diagnosis of cannabis abuse and 35.5% had a diagnosis of any substance abuse.

The five significantly different characteristics in the youth sample were included as explanatory variables in a binary logistic regression model, with age category as the binary dependent variable. Explanatory variable data was missing for 14 cases leaving 423 cases for the regression analysis. The variation in the model explained by the dependent variable (R^2) was between 23% and 31%. Omnibus test of model coefficients was significant ($p < 0.001$) for the regression model (p -values of < 0.05 suggest good model fit). The significance level for the Hosmer–Lemeshow Goodness of Fit Test ($p = 0.947$) was > 0.05 (Field, 2005). Each of the explanatory variables remained significant predictors of age category in the regression analysis (Table 3). When we repeated the regression analysis as a linear regression analysis with the same explanatory variables and with age as a continuous dependent variable, each of the explanatory variables remained significant except for negative symptoms ($\beta = 0.75$, 95% CI -0.20 – 3.73 , $p = 0.078$).

Subanalysis of youth sample

Given the relatively higher prevalence of negative symptoms in the youth sample, we conducted a subanalysis comparing characteristics in a negative symptom ($n = 78$) and no negative symptom group ($n = 80$) in the youth sample. The significant differences in the negative symptom group included fewer working (20.5% v. 46.2%), more with a schizophrenia spectrum diagnosis (70.5% v. 23.8%), poorer premorbid

Table 1. Sample diagnoses

| | ≤ 25 years (n = 158) | | > 25 years (n = 279) | | χ^2 |
|--|----------------------|------|----------------------|------|----------|
| | n | % | n | % | |
| Schizophrenia spectrum | 74 | 46.8 | 117 | 41.9 | 0.98 |
| Bipolar disorder with psychotic symptoms | 21 | 13.3 | 28 | 10.1 | 1.07 |
| Major depression with psychotic symptoms | 11 | 7.0 | 34 | 12.2 | 2.98 |
| Delusional disorder | 5 | 3.2 | 38 | 13.6 | 12.43** |
| Brief psychotic disorder | 9 | 5.7 | 23 | 8.2 | 0.97 |
| Psychotic disorder NOS | 6 | 3.8 | 12 | 4.3 | 0.07 |
| Substance-induced psychosis | 32 | 20.3 | 27 | 9.7 | 9.66** |

NOS, not otherwise specified.

**Significance level of $p < 0.01$ comparing ≤ 25 years and > 25 years.

Table 2. Comparison of categorical and continuous characteristics at first presentation across age categories

| Characteristic | ≤ 25 years (n = 158) | | > 25 years (n = 279) | | χ^2 |
|--|----------------------|-------------|----------------------|-------------|----------|
| | n | % | n | % | |
| <i>A: Categorical</i> | | | | | |
| Female sex | 51 | 32.3 | 124 | 44.4 | 6.22 |
| No post-high school education | 79 | 50.0 | 122 | 43.9 | 0.23 |
| Living alone | 14 | 9.4 | 68 | 24.8 | 14.69** |
| Never married | 151 | 95.6 | 166 | 59.5 | 65.89** |
| Upper socioeconomic class (Class 1–3) | 68 | 57.6 | 105 | 54.7 | 0.26 |
| Inpatient | 95 | 60.5 | 187 | 67.5 | 2.16 |
| Currently working | 53 | 33.5 | 112 | 40.1 | 1.87 |
| Lifetime cannabis abuse diagnosis | 34 | 21.5 | 32 | 11.5 | 7.95** |
| Lifetime alcohol abuse diagnosis | 19 | 12.0 | 49 | 17.6 | 2.35 |
| Lifetime any substance abuse diagnosis | 45 | 28.5 | 80 | 28.7 | 0.01 |
| Birth abroad | 31 | 20.5 | 51 | 18.7 | 0.21 |
| Positive symptoms present | 126 | 79.1 | 239 | 86.0 | 2.86 |
| Negative symptoms present | 78 | 49.4 | 109 | 39.1 | 4.37* |
| Depressive symptoms present | 46 | 29.5 | 75 | 27.1 | 0.29 |
| | n | M (s.d.) | n | M (s.d.) | T |
| <i>B: Continuous</i> | | | | | |
| PAS total | 119 | 0.19 (0.14) | 160 | 0.22 (0.15) | 1.95 |
| Log DUP (months) | 158 | 0.64 (0.57) | 279 | 0.81 (0.71) | 2.76** |
| Log DP (months) | 139 | 0.78 (0.63) | 238 | 0.74 (0.69) | 0.54 |
| Log DUI (months) | 139 | 1.07 (0.59) | 238 | 1.11 (0.71) | 0.64 |

PAS, Premorbid Adjustment Scale; DUP, duration of untreated psychosis; DP, duration of psychosis prodrome; DUI, duration of untreated illness.

Data excluded from table where missing.

*Significance level of $0.05 > p > 0.01$ comparing ≤ 25 years and > 25 years.

**Significance level of $p < 0.01$ comparing ≤ 25 years and > 25 years.

adjustment (mean 0.23 *v.* 0.16), longer log DUP (mean 0.82 *v.* 0.46) and longer log DUI (mean 1.29 *v.* 0.85).

Given the relatively higher prevalence of cannabis abuse diagnosis in the youth sample, we conducted a subanalysis comparing characteristics among individuals with ($n = 34$) and without ($n = 124$) cannabis abuse

diagnosis in the youth sample. This subanalysis aimed to determine whether characteristics of youth individuals with cannabis abuse differed from the rest of the youth sample. Significant differences were noted for the cannabis abuse group including more males (88.2% *v.* 62.1%) and more alcohol abuse diagnoses (32.4% *v.* 6.5%).

Table 3. Logistic regression model with age category as the binary dependent variable ($n = 423$)

| | Wald | OR | 95% CI | <i>p</i> |
|--------------------------|-------|------|----------|----------|
| Living status | 13.65 | 3.42 | 1.8–6.6 | <0.001 |
| Marital status | 42.88 | 15.2 | 6.7–34.3 | <0.001 |
| Cannabis abuse diagnosis | 4.88 | 2.0 | 1.1–3.6 | 0.027 |
| Negative symptoms | 4.02 | 1.6 | 1.0–2.7 | 0.045 |
| Log DUP | 9.56 | 1.81 | 1.2–2.7 | 0.002 |

OR, odds ratio; DUP, duration of untreated psychosis.

Given that not all individuals with comorbid cannabis abuse diagnosis had a primary diagnosis of substance-induced psychosis (15 out of 34 individuals with cannabis abuse diagnosis had a primary diagnosis of substance-induced psychosis), we conducted a further analysis comparing individuals in the sample with substance-induced psychosis diagnosis ($n = 32$) with the rest of the youth sample ($n = 126$). This sub-analysis only showed significantly more cannabis abuse diagnoses (46.9% *v.* 15.1%) and more alcohol abuse diagnoses (25.0% *v.* 8.7%) in the substance-induced psychosis sample. When this analysis was repeated excluding affective psychosis ($n = 32$), the substance-induced psychosis sample had significantly fewer negative symptoms (34.4% *v.* 66.0%), shorter log DUP (mean 0.50 *v.* 0.77), more cannabis abuse diagnoses (46.9% *v.* 16.0%) and more alcohol abuse diagnoses (25.0% *v.* 9.6%).

Discussion

This study described characteristics and symptoms in an FEP sample, comparing a youth sample with a cohort aged over 25 years. Within the youth sample, first onset of symptoms commonly occurred before age 18 years. The youth sample had more substance-induced psychosis diagnoses, more cannabis abuse diagnoses and more negative symptoms at first presentation. The over 25 years sample had more delusional disorder diagnosis, longer DUP, were more likely to be married and more likely to be living alone. Individuals with negative symptoms in the youth sample were less likely to be working, had poorer premorbid adjustment and longer delays to treatment. Individuals with cannabis abuse diagnosis in the youth sample were predominantly male; those with substance-induced psychosis were more likely to have shorter DUP and fewer negative symptoms than the non-affective FEP sample.

The findings of lower likelihood of living alone and being married in the youth sample are intuitive and consistent with previous studies (Subramaniam *et al.* in press). The finding in relation to marital status likely

reflects the age demographic during which marriage occurs, whereas the living status finding could be explained by the younger sample commonly residing with their parents, although we cannot definitively conclude this from our data.

Negative symptoms

Overall, the sample had a high prevalence of negative symptoms, and the youth sample had greater negative symptoms than the over 25 years sample at first presentation. Of note, when the regression analysis was repeated with age as a continuous variable, the relationship between age and negative symptoms was no longer significant. The finding of greater negative symptoms among those with younger age of onset has been reported previously (Clarke *et al.* 2006); however, the finding requires further study and the reasons for this finding are not fully clear. Those with negative symptoms in the youth sample had poorer premorbid adjustment and longer delays to treatment, both of which could be a contributing factor to negative symptoms (MacBeth & Gumley, 2008; Boonstra *et al.* 2012); these individuals were also less likely to be working, which could have impact on their recovery and quality of life (Turner *et al.* 2009).

The high prevalence of negative symptoms across all age categories suggests the need for a more intensive approach to treating these symptoms following FEP presentation. This approach could consist of a 'second wave' of intervention delivered during the medium term after initial presentation to prevent the progression of negative/cognitive deficits and functional disability (Alvarez-Jimenez *et al.* 2012). Possible interventions include cognitive behavioural therapy, cognitive remediation therapy, supported employment and family education, as well as a detailed review of the need for pharmacotherapy strategies such as clozapine.

Substance use and other characteristics

Given the high prevalence of cannabis and other substance use diagnoses in the youth sample, services treating young individuals with FEP, particularly young males, need to be adequately resourced to cater for these needs. The finding of greater cannabis use in those with presentation in youth is consistent with a previous meta-analysis, which suggested a relationship between cannabis use and earlier onset of psychosis (Large *et al.* 2011). It should be noted that this relationship could have several explanations, such as a generally higher rate of cannabis use in young populations, rather than greater cannabis having a causal relationship with younger onset of psychosis. Interpretation of this relationship is further complicated by the possibility that substance-induced psychosis

could be a different condition to schizophrenia. This would be supported by our finding of significant differences between the youth sample with substance-induced psychosis and the rest of the youth sample with non-affective psychoses. Ongoing research relating to this should focus on the age of cannabis use onset and the trajectory of psychotic symptoms (Stefanis *et al.* 2013).

The substance-induced psychosis youth sample had fewer negative symptoms than the non-affective FEP youth sample, which is consistent with a previous study reporting fewer negative symptoms among individuals with schizophrenia and comorbid substance use disorder (Potvin *et al.* 2006). The finding of shorter DUP in the substance-induced psychosis sample could be explained by a more acute presentation following the onset of psychosis owing to substance misuse when compared with the insidious illness onset sometimes associated with schizophrenia.

The finding that not all individuals with cannabis abuse diagnosis had a substance-induced psychosis diagnosis suggests that when considered clinically, cannabis abuse is common among individuals whose psychotic symptoms do not present as being directly related to cannabis abuse. All SCID diagnoses in this study were discussed at consensus clinical meetings attended by a senior psychiatrist. In spite of previous advances in clinical descriptions of illness, the boundaries between some early psychosis diagnoses such as substance-induced psychosis and schizophrenia remain blurred, which is supported by previous findings that up to half of individuals with substance-induced psychosis may eventually develop schizophrenia (Whitty *et al.* 2005; Bromet *et al.* 2011). Future research should aim to improve our understanding diagnostic boundaries in psychosis (Carpenter, 2014).

Overall, substance abuse did not differ between the youth sample and the over 25 years sample, which may be partly explained by a non-significantly higher alcohol abuse diagnosis in the over 25 years sample. This finding highlights the importance of managing comorbid substance use conditions across all age categories in FEP presentations.

It is estimated that ~40% of people with psychosis will abuse substances at some point in their lifetime (National Institute for Health and Care Excellence, 2011), and our findings suggest that almost 30% satisfy a substance abuse diagnosis at first presentation with psychosis. Comorbid substance abuse can complicate management of FEP for several reasons: substance use can result in psychosis relapse and can increase the challenge for engaging individuals with mental health services. Implementation of guidelines and intensive early management of dual diagnosis presentations may be necessary for management of these complex needs (NICE, 2011).

Onset of FEP symptoms

Major mental disorders commonly have onset in adolescence and early adulthood (Jones, 2013), and this study supports that young individuals presenting with FEP commonly have onset of first symptoms before the age of 18 years. In our sample, prodromal and psychotic symptoms were present before age 18 years in 23.4% of the youth sample. This suggests that symptoms are commonly present during the transition from adolescence to adulthood, which needs consideration when delivering services to young individuals with FEP.

Strengths and limitations

Some of the variables collected, such as delays to treatment and premorbid adjustment, may have been subject to recall bias owing to the retrospective nature of their data collection. Multiple raters collected data for the study, which may have introduced measurement bias, although comprehensive training was given to all data collectors before commencement, and median inter-rater reliability was good for all scales. Inter-rater reliability for the SANS was good for most raters, although of note ICC was <0.7 for one rater.

Strengths of the study are that to our knowledge this is the largest epidemiological description of FEP in a youth population in Ireland to date. Validated and reliable scales such as the SCID were used for all participants. The use of face-to-face interview for consecutive inpatient and outpatient FEP presentations is a further study strength.

Conclusions

This description of characteristics and symptoms in a young Irish FEP sample is important, given the lack of previous epidemiological studies conducted on youth samples in Ireland to date (Lynch *et al.* 2006). The findings can inform the ongoing development of services for young people in Ireland. Early intervention strategies play an important role for management of FEP (McGorry, 2013), and our findings suggest the need for adequate resources for management of negative symptoms and substance abuse in early psychosis. It is essential that we continue to evaluate how our services cater for young people with the aim of providing high-quality care for serious mental illness in youth (McNamara *et al.* 2014).

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Conflicts of Interest

The authors declare they have no conflicts of interest.

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