



Characteristics and outcomes of young people with substance induced psychotic disorder

Jessica O'Connell^{a,b,c}, Monica Sunwoo^c, Patrick McGorry^{a,b}, Brian O'Donoghue^{a,b,c,*}

^a Orygen, the National Centre of Excellence in Youth Mental Health, Melbourne, Australia

^b Centre for Youth Mental Health, University of Melbourne, Australia

^c Orygen Youth Health, 35 Poplar Rd, Parkville, VIC 3025, Australia

ARTICLE INFO

Article history:

Received 29 July 2018

Received in revised form 6 November 2018

Accepted 6 November 2018

Available online 22 November 2018

Keywords:

Substance induced psychotic disorder

First episode psychosis

Early intervention

Schizophrenia

Cannabis

ABSTRACT

Background: Substance induced psychotic disorders (SIPD) have been historically considered as associated with better clinical and functional outcomes than other psychotic diagnoses. As a result, treatments for those with SIPD are often considerably less intensive, yet this is not based on evidence. The present study aimed to examine whether differences exist between those with SIPD and other first episode psychosis (FEP) diagnoses in regards to demographic and clinical factors, and to determine the symptomatic, clinical and functional outcomes in those with SIPD.

Methods: This study included all young people aged 15–24 who presented with a FEP to the Early Psychosis Prevention and Intervention Centre between 01/01/2011 and 31/12/2013. Group differences were analysed with independent samples *t*-tests and chi-square analyses and equivalent non-parametric tests as appropriate. Where applicable, odds ratios were calculated.

Results: 544 young people presented with a FEP and 10.3% ($N = 56$) were diagnosed with SIPD. Individuals with SIPD were more likely to be male, unemployed, and have a comorbid substance use disorder. There were no significant differences between groups regarding duration of untreated psychosis, severity of psychotic symptoms, time to remission, or rates of relapse. Those with SIPD were less likely to be employed or engaged in study at discharge and 35.7% of those with SIPD had a change of diagnosis to a schizophrenia spectrum or bipolar disorder after a median of 84 weeks.

Conclusion: Young people diagnosed with SIPD should be an important focus of early intervention services and receive comparable treatment to those with other psychotic diagnoses.

© 2018 Elsevier B.V. All rights reserved.

1. Introduction

A small but significant proportion of individuals presenting with a first episode of psychosis (FEP) will receive a diagnosis of substance induced psychotic disorder (SIPD). This diagnosis has attracted criticism, as a large proportion of individuals with a psychotic disorder will also have a concurrent substance abuse disorder (Jablensky et al., 2000; Wilson et al., 2017) and thus accurate diagnosis can be difficult (Mathias et al., 2008). Despite this, individuals with a diagnosis of SIPD are often excluded from research studies (Jorgensen et al., 2000), have shorter periods of clinical care (National Institute for Mental Health in England, 2008), and have longer delays to care post first referral to services (Kirkbride et al., 2017). This practice is however counter-intuitive, considering that SIPD is a psychotic disorder which warrants

appropriate treatment, and that the diagnosis is associated with a high risk of subsequently developing schizophrenia. Specifically, between 25 and 46% of individuals with SIPD transition to a schizophrenia spectrum disorder, often within three years of first service presentation (Arendt et al., 2005; Caton et al., 2007; Crebbin et al., 2009; Niemi-Pynttari et al., 2013).

In addition to this, individuals with SIPD present with more severe depressive symptoms and suicidal ideation (Caton et al., 2005; Nunez and Gurpegui, 2002), and similar levels of positive symptoms, quality of life, functioning and relapse rates compared to individuals with other psychotic disorders (Thompson et al., 2016), though are more likely to lose contact with mental health services (Crebbin et al., 2009). Further, individuals with a concurrent psychotic disorder and cannabis abuse disorder are more likely to present at a younger age (Large et al., 2011; O'Donoghue et al., 2015) and any substance misuse has been associated with increased risk of inpatient admission and earlier relapse of symptoms for those with FEP (Wade et al., 2006). All of these clinical factors provide a strong justification for a need for care

* Corresponding author at: Orygen, The National Centre of Excellence in Youth Mental Health, 35 Poplar Road, Parkville, VIC 3052, Australia.

E-mail address: brian.odonoghue@orygen.org.au (B. O'Donoghue).

within this FEP sub-group, however contention still exists about where those diagnosed with SIPD should receive treatment, what treatments they should receive, and for how long.

This study aims to add to the current literature with an epidemiological longitudinal examination of those presenting to an early intervention service with a SIPD compared to those with other affective or non-affective first episodes of psychosis. Specifically, the study aims to determine:

- (i) the proportion of young people presenting with a SIPD
- (ii) whether demographic and clinical characteristics are associated with a diagnosis of a substance induced psychosis
- (iii) rates of remission and relapse in the SIPD group compared to other FEP diagnoses
- (iv) functional outcomes, in regards to education and employment, in the SIPD group
- (v) the proportion of those who have a diagnosis of SIPD at presentation and who later fulfil criteria for a different psychotic disorder

2. Methodology

2.1. Participants

This study included an epidemiological cohort of 544 young people with a diagnosis of a first episode of psychosis (FEP) who received treatment at the Early Psychosis Prevention and Intervention Centre (EPPIC).

2.2. Setting

EPPIC is a comprehensive treatment program within Orygen Youth Health (OYH) for young people aged 15 to 25 years with a FEP in the north-western regions of Melbourne, Australia. This catchment area covers more than one million people and EPPIC provides services to approximately 400 people at any one time, with over 200 new referrals per annum. As such, the EPPIC service comprises a treated epidemiological cohort of young people with FEP. Average treatment duration at EPPIC is eighteen months and a maximum of twenty-four months (except for those under the age of 18, who can continue to receive service beyond two years until their 18th birthday). Regardless of psychosis diagnosis, young people in the EPPIC program all receive cognitive-behavioural case management and psychiatric care. All participants also have access to drug and alcohol support, a psychosocial group program, family support, and physical health interventions such as dietetics and exercise physiology.

2.3. Case identification and eligibility criteria

Individuals included in this study were assessed over the period from 1st January 2011 to 31st December 2013 inclusive. In this study period, a total of 555 young people attended the EPPIC service. Criteria for inclusion for the present study were a DSM-IV-TR diagnosis of a FEP (American Psychiatric Association [APA], 2000). Individuals with comorbid personality disorders, intellectual disability, and substance misuse or dependence were included. Six individuals were excluded due to a non-psychotic diagnosis at service discharge and five files were unavailable. Data was thus collected for the remaining 544 eligible individuals.

2.4. Data sources, measures and definitions

2.4.1. Medical records

Clinical notes were documented by the case-manager, psychiatric registrar, or consultant psychiatrist. For each individual, information collected during their episode of care was recorded and stored in a single medical file. Individuals obtaining treatment through EPPIC received

outpatient services and were eligible for inpatient admissions as clinically indicated. Individuals were typically seen weekly during the first three months of service engagement. Appointments were then usually extended to fortnightly, or more frequently where clinically indicated. An instrument was developed to facilitate extraction of quantitative data concerning pre-treatment and baseline characteristics, as well as treatment course and outcome measures. Case files were analysed from the time of first registration with OYH. The follow up period was until discharge from EPPIC.

2.4.2. Demographic variables

Demographic variables analysed at service entry were gender, age, employment status, marital status, history of a psychotic disorder in a first degree relative, and migrant status.

2.4.3. Outcome variables

2.4.3.1. Diagnoses. Diagnoses of psychotic disorders and comorbidities, including substance abuse, were made by the treating consultant psychiatrist at three months after service entry and were reviewed at discharge according to the DSM-IV-TR (APA, 2000) criteria. Some individuals disengaged from the service before a longitudinal assessment could be conducted for diagnostic purposes and were given a generic diagnosis of FEP.

2.4.3.2. Symptom measurement. The severity of psychotic symptoms was assessed and rated at baseline, and at three monthly intervals thereafter. The short form Scale for the Assessment of Positive Symptoms (SAPS) was used to rate positive symptoms of psychosis by clinicians and researchers. The short form SAPS is divided into four symptom domains and the presence of symptoms are rated on a scale from absent (0) to severe (5). The short-form SAPS has shown good internal consistency ($\alpha = 0.78$; Alonso et al., 2008). Routinely, case managers and psychiatrists conducted and documented mental state examinations in the clinical notes. These were used as the basis from which to assess and rate psychotic symptoms using the SAPS criteria.

2.4.3.3. Remission and relapse. Remission was defined as positive psychotic symptoms of severity less than or equal to two on the short form SAPS for a period of at least twelve weeks. Relapse was defined as the return of positive symptoms of severity greater than a rating of two on the short form SAPS for a period of at least one week.

2.4.3.4. Functional outcomes. The Health of the Nation Outcome Scale (HoNOS) was used to determine functional outcomes. This questionnaire was completed at baseline and discharge for all participants. Functional information pertaining to education and employment was also drawn from the clinical notes.

2.5. Statistical analysis

Data was analysed using the Statistical Package for the Social Sciences (SPSS) version 22. Group differences between those with SIPD and other psychotic diagnoses were analysed using independent samples *t*-tests for continuous variables and chi-squared analyses for categorical variables. Where applicable, odds ratios were also calculated for categorical variables. The Kruskal-Wallis non-parametric test was utilised where data was not normally distributed and the Mann-Whitney test was used to determine whether there was a difference in medians. Cox regression analysis was used to determine if there was a difference in relapse rates between groups, as it was a time-dependent variable. Binary logistic regression was used to determine whether a diagnosis of SIPD was associated with functional outcomes when potential confounders were controlled for. The dependent variable in the model was 'working or studying at the time of discharge' and potential confounders of age, sex, and concurrent cannabis or

amphetamine abuse were entered in the model. The level of significance was set at $p < 0.05$. Bonferonni corrections were however applied when multiple testing occurred.

2.6. Ethics approval

This study received ethical approval from the Royal Melbourne Human Research Ethics Committee. In order to ensure all data from the retrospective file audit was obtained for this epidemiological cohort, ethics approval was granted to waive informed consent.

3. Results

3.1. Demographic characteristics of cohort

The cohort consisted of 544 individuals, 325 of whom were male (59.7%). At service entry, the mean age of the cohort was 19.5 years (sd ± 2.9). The median length of time in service was 84 weeks (I.Q.R. 53, 101). Table 1 details the demographic and clinical characteristics of the cohort.

3.2. Diagnosis and duration of untreated psychosis (DUP)

Fifty-six individuals in the cohort had a diagnosis of a SIPD (10.3%) at three months of service engagement. A complete list of diagnoses is detailed in Table 1. The mean DUP in the cohort was 25.4 weeks (sd ± 47.2) and the median DUP was 6.5 weeks (I.Q.R. 2, 24). A total of 40.7% (N = 197) had a DUP of <4 weeks, 34.5% (N = 167) had a DUP

of between 4 and 26 weeks and 24.8% (N = 120) had a DUP of >26 weeks.

3.3. Demographic characteristics associated with SIPD

Males were more likely than females to have a diagnosis of SIPD (OR = 4.57, 95% C.I. 2.12–9.87, $\chi^2 = 17.5$, df = 1, $p < 0.001$), as were those who were not in education or employment (OR = 2.09, 95% C.I. 1.19–3.64, $\chi^2 = 6.88$, df = 1, $p = 0.009$). Individuals with a diagnosis of SIPD were more likely to present at an older age compared to those with other FEP diagnoses (20.3 yrs. vs 19.4 yrs., $t = 2.21$, $p = 0.027$). There were no differences between those with a SIPD compared to those with other psychotic disorders in regards to marital status at service entry ($\chi^2 = 1.5$, df = 4, $p > 0.05$), family history of a psychotic disorder in a first degree relative ($\chi^2 = 0.3$, df = 1, $p > 0.05$), or migrant status ($\chi^2 = 0.1$, df = 1, $p > 0.05$).

3.4. Clinical characteristics associated with SIPD

Individuals with a diagnosis of SIPD were 1.77 times more likely to have a co-morbid substance use disorder compared to individuals with other psychotic disorders (96.4% vs. 54.6%, $\chi^2 = 36.2$, df = 1, $p < 0.001$) (OR = 1.77, 95% C.I. 1.60–1.94). Table 1 details the types of substance use disorders present for those with a diagnosis of SIPD and other psychotic disorders. The median DUP in those with a SIPD was 7 weeks (I.Q.R. 2–18) and the median DUP in other psychotic disorders was 6 weeks (I.Q.R. 2, 26) and this difference was not statistically significant (Z = -0.60, $p = 0.55$). There was no difference in the DUP between groups when the DUP was examined as a categorical variable

Table 1
Demographic and clinical characteristics of cohort.

	Total cohort		SIPD		Other FEP		Statistical test
Sex	n	%	n	%	N	%	χ^2
Males	325	59.7	48	85.7	277	56.8	4.57**
Females	219	40.3	8	14.3	211	43.2	
Age at presentation, years	19.5		20.3		19.4		t-test 2.21*
Employment at baseline							
In education or employment	331	60.8	25	44.6	306	62.7	6.88*
Not in education or employment	213	39.2	31	55.4	182	37.2	
Migrant status							χ^2
Born in Australia	407	74.8	43	76.8	364	74.6	0.13
First generation migrant	137	25.2	13	23.2	124	25.4	
Duration of untreated psychosis, weeks	Median	IQR	Median	IQR	Median	IQR	Mann-Whitney, Z
	6.5	2,24	7.0	2,18	6.0	2,26	-0.60
Diagnosis	n	%					
Schizophrenia	70	12.9					
Schizophreniform disorder	137	25.2					
Substance-induced psychotic disorder	56	10.3					
Psychosis NOS	69	12.7					
Brief psychotic disorder	16	2.9					
Delusional disorder	5	0.9					
Schizoaffective disorder	24	4.4					
Bipolar affective disorder	102	18.8					
Depression with psychosis	52	9.6					
Unspecified (FEP)	13	2.4					
Concurrent substance abuse disorders	n	%	n	%	n	%	χ^2
Any concurrent substance abuse	319	59	54	96.4	265	54.6	36.2**
Alcohol abuse	104	19.1	17	30.4	87	17.8	5.1*
Cannabis abuse	282	25.4	47	83.9	253	51.8	25.75**
Amphetamine abuse	138	25.4	38	67.9	100	20.5	59.53**
Hallucinogen abuse	25	4.6	5	8.9	20	4.1	2.67
Cocaine abuse	11	2.0	4	7.1	7	1.4	8.26*
Heroin abuse	12	2.2	2	3.6	10	2.0	0.54

* $p < 0.05$.

** $p < 0.001$.

(<4 weeks, 4–26 weeks and >26 weeks) ($\chi^2 = 1.84$, $df = 2$, $p = 0.40$). There was also no difference in the severity of positive symptoms at the time of first presentation in those with a diagnosis of a SIPD compared to other psychotic disorders ($t = -0.21$, $df = 520$, $p = 0.84$). Table 2 details mean scores for each of the four items on the SAPS for those with SIPD and those with other psychotic diagnoses. As four analyses were completed, a Bonferroni correction was applied and thus the level of significance was set at <0.0125.

3.5. Outcomes

3.5.1. Remission

A total of 90.1% ($N = 490$) of young people with FEP achieved remission of positive psychotic symptoms during their treatment period at EPPIC and there was no difference in the proportion who achieved symptomatic remission according to SIPD compared to other disorders (92.9% vs 89.9%, $\chi^2 = 0.61$, $df = 1$, $p = 0.44$). There was also no significant difference between groups on the time to achieve remission ($\chi^2 = 0.22$, $df = 1$, $p = 0.64$). Table 3 details the percentage of individuals in each group that achieved remission after specific time points.

3.5.2. Relapses

Relapse occurred for 41.2% of the total cohort throughout an episode of care. In the sub-group with a diagnosis of SIPD, 40.7% ($N = 22$) experienced a relapse compared to 41.3% ($N = 192$) of the other FEP diagnoses. There was no significant difference in rates of relapse between those with SIPD and those with other psychotic diagnoses ($HR = 1.1$, 95% C.I. = 0.69–1.74, $p = 0.69$).

3.5.3. Functional outcomes in the SIPD group

At the time of discharge or transfer to another service, young people with a diagnosis of SIPD were less likely to be in employment or education compared to those with a diagnosis of another psychotic disorder ($OR = 0.48$, 95% C.I. 0.27–0.86, 35.7% vs 53.6%, $\chi^2 = 6.43$, $df = 1$, $p = 0.01$).

When controlled for potential confounders, the association between the diagnosis of SIPD and functional outcomes became non-significant. Results are presented in Table 4. Cannabis abuse remained significant, indicating that this was likely a confounder in the relationship between the diagnosis of SIPD and functional outcomes. Individuals with a diagnosis of a psychotic disorder with concurrent cannabis abuse were more likely to be unemployed or not studying at discharge ($aOR = 1.50$, 95% C.I. 1.02–2.19, $p = 0.04$), when controlled for age, sex and amphetamine abuse.

3.5.4. Diagnosis at discharge

Of those in the SIPD group, 35.7% ($n = 20$) no longer had a diagnosis of SIPD at discharge from service. Nine individuals (16.1%) were diagnosed with schizophrenia, four with bipolar affective disorder with psychotic features (7.1%), three with psychosis not otherwise specified (5.4%), two with schizophreniform disorder (3.6%), one with schizoaffective disorder (1.8%), and one with delusional disorder (1.8%).

Table 2
Mean SAPS scores for SIPD and other FEP diagnoses.

	SIPD	Other FEP	<i>t</i>	<i>P</i> value
	Mean (SD)	Mean (SD)		
SAPS				
Hallucinations	1.8 (1.8)	2.4 (2.0)	−2.4	0.03
Delusions	3.1 (1.6)	2.9 (2.0)	1.0	0.33
Bizarre behaviour	1.1 (1.7)	1.3 (1.9)	−0.9	0.36
Positive formal thought disorder	1.1 (1.5)	1.3 (1.9)	−0.7	0.51

4. Discussion

There are a number of important findings from this study. First, there were minimal differences in the clinical characteristics and outcomes of those with a SIPD compared to other psychotic disorders. As would be expected, those with a SIPD were more likely to have a concurrent substance abuse disorder, but notably, there was no difference in regards to psychotic symptom severity, remission and relapse rates, and DUP. In the only difference between groups, the SIPD group fared worse in regard to occupational outcomes, though this was explained by substance abuse. Finally, over one third of young people who had a SIPD at the time of service entry subsequently fulfilled criteria for a diagnosis of a schizophrenia spectrum or bipolar affective disorder. All of these results indicate that this is a group who requires intensive interventions and the validity of a specific diagnosis of substance induced psychotic disorder is called into question.

4.1. Comparison to previous literature

Past research has attempted to identify demographic and clinical differences to distinguish SIPD from other psychotic diagnoses. A family history of psychotic disorders (Fraser et al., 2012) and more severe psychotic symptoms (Caton et al., 2005) have been identified as associated with schizophrenia spectrum disorders when compared to SIPD. This was however not supported in results of the current study. Clinical results were notably similar to those of Thompson et al. (2016) who found no difference between those with SIPD and other FEP diagnoses with respect to psychotic symptoms, and rates of recovery and relapse in an epidemiological cohort at an early intervention service.

Rates of diagnostic transition to a schizophrenia spectrum or bipolar disorder at service discharge were also comparable to the extant literature (Arendt et al., 2005; Caton et al., 2007; Crebbin et al., 2009; Niemi-Pynttari et al., 2013). Of note, past research has suggested cannabis induced psychosis poses a particularly high risk for the later development of schizophrenia (Arendt et al., 2005; Niemi-Pynttari et al., 2013) and is associated with a family history of psychosis (Wilson et al., 2017). Cannabis was the most commonly used substance in the present cohort and this may explain our findings.

Whilst it was identified those with SIPD had poorer functional outcomes, when controlling for a number of potential confounders the relationship between diagnosis and functioning was not significant. Rather, cannabis abuse in particular was associated with a 50% reduction in the likelihood of engagement in employment or study for all participants. Other recent research has reported no difference in functioning between those with SIPD and other FEP diagnoses (Thompson et al., 2016), and those with psychotic disorders and concurrent substance abuse (Wilson et al., 2017). It is however important to note the present study reported results pertaining to vocational functioning only, rather than vocational and social functioning.

4.2. Validity and utility of the diagnosis of substance induced psychotic disorder

Of particular importance, results of the current study do not support the notion that the diagnostic category of SIPD can be differentiated from a primary psychotic disorder with respect to clinical and functional characteristics and outcomes. Both the validity and utility of the diagnosis of SIPD are thus called into question. Whilst the DSM 5 suggests these diagnostic groups can be distinguished by ascertaining whether psychotic symptoms occurred prior to first substance use, or during periods of abstinence (APA, 2013), this assessment is understandably fraught when working with a FEP cohort. Of note, a recent longitudinal study found those diagnosed with substance induced psychosis at baseline did not show improvements to psychotic symptomatology at follow-up, despite periods of abstinence (Mauri et al., 2017). Further, DSM markers for differentiation may be entirely arbitrary, as the significant

Table 3
Percentage of group who achieved remission by time.

Time to remission	SIPD	Cumulative	Other FEP	Cumulative	Total	Cumulative
	N (%)	N(%)	N (%)	N(%)	N (%)	N(%)
12 weeks	37 (71.2)	37 (66.1)	294 (67.1)	294 (60.2)	331 (67.6)	331 (60.8)
24 weeks	7 (13.5)	44 (78.6)	75 (17.1)	369 (75.6)	82 (16.7)	413 (75.9)
36 weeks	4 (7.7)	48 (85.7)	34 (7.8)	403 (82.6)	38 (7.8)	451 (82.9)
48 weeks	0 (0)	48 (85.7)	12 (2.7)	415 (85.0)	12 (2.4)	463 (85.1)
60 weeks	2 (3.8)	50 (89.3)	12 (2.7)	427 (87.5)	14 (2.9)	477 (87.7)
72 weeks	0 (0)	50 (89.3)	1 (0.2)	428 (87.7)	1 (0.2)	478 (87.9)
84 weeks	1 (1.9)	51 (91.1)	4 (0.9)	432 (88.5)	5 (1.0)	483 (88.8)
96 weeks	1 (1.9)	52 (92.9)	5 (1.1)	437 (89.5)	6 (1.2)	489 (89.9)
108 weeks	0 (0)	52 (92.9)	1 (0.2)	438 (89.8)	1 (0.2)	490 (90.1)

transition rates to schizophrenia spectrum disorders do not support the premise that SIPD is a distinct clinical entity. This is consistent with theory that cannabis induced psychosis in particular may be an early sign of schizophrenia rather than a separate diagnostic event (Arendt et al., 2008).

Outside of psychosis secondary to a medical condition, SIPD is the only diagnosis that prescribes causality to presenting symptoms. This practice however, appears in contrast to the atheoretical, phenomenological framework of the key diagnostic texts. Whilst this has been the focus of previous debate (see Mathias et al., 2008), no meaningful nosological change has occurred to date. Extensive literature has however addressed the varied and complex aetiologies of psychotic disorders that cover biological, psychological, and social domains (see Jackson and McGorry, 2009). Consistent with previous work (Wade, 2005), we thus argue that the often proximal relationship between substance use and symptoms of psychosis in young people should not be confused for causality, independent of a plethora of other known predisposing and precipitating factors impacting the onset of psychotic disorders.

Finally, significant research and clinical attention has been rightly paid to those at ultra-high risk (UHR) for the development of psychotic disorders (Nelson et al., 2013) and specific interventions have been developed to prevent transition to schizophrenia spectrum disorders (McGorry et al., 2009). Results of the present study and other recent research strongly suggest that such an approach is now required for those presenting to services with substance induced psychoses, a group at significantly high risk for the development of schizophrenia. Whilst past intervention studies have targeted cannabis use in FEP cohorts (Edwards et al., 2006), and have noted significant reductions in rates of substance use disorder diagnoses throughout an episode of care with early intervention services (Lambert et al., 2005), no specific interventions known to the authors have been developed or researched for those with SIPD to reduce rates of transition to schizophrenia in this group.

4.3. Limitations

The results of this study need to be considered within its limitations. The present study relied on accurate diagnosis of the participants' psychotic disorders by the treating team at three months in service. Whilst treating psychiatrists utilised DSM-IV-TR criteria for diagnosis, not all diagnoses would have been made following a structured clinical interview and can be influenced by clinician experiences and biases. Biases

may have impacted rates of diagnosis of SIPD in males compared to females in particular. Diagnosis can also be impacted by the unstable nature of symptoms and presentations in a FEP cohort. This however, adds to our argument that the groups are clinically indistinct in early intervention settings. Whilst this is an epidemiological cohort that included consecutive cases, it only included treated cases of FEP and it is possible that a number of young people who were experiencing a first episode of psychosis did not present to mental health services.

4.4. Future directions

Future research should include examination of predictors of those who experience diagnostic change from SIPD to a schizophrenia spectrum or bipolar disorder throughout a period of psychiatric care. Research is also needed regarding current treatment differences in clinical services for those diagnosed with SIPD as opposed to other FEP diagnoses.

5. Conclusion

Young people with SIPD experience similar severity of psychotic symptoms and rates of relapse and remission to those with other FEP diagnoses, though experience poorer vocational outcomes as explained by cannabis use. This study does not lend evidence to the widely held view that less intensive treatments are required for those with SIPD and suggests such individuals should be an important focus of engagement and treatment within early intervention for psychosis services. Continued review of diagnostic criteria for SIPD and a model that suggests association with substance use as opposed to causation is recommended.

Conflict of interest

All authors declare that they have no conflicts of interest.

Contributors

Jessica O'Connell conducted literature searches and wrote the first draft of the manuscript. Monica Sunwoo and Patrick McGorry assisted literature searches and contributed to the writing of the introduction and discussion. Brian O'Donoghue designed the study, wrote the protocol, and conducted data analysis. All authors contributed to and have approved the final manuscript.

Role of the funding bodies

Dr. Brian O'Donoghue is a recipient of a NHMRC Early Career Fellowship.

Acknowledgments

We thank Meghan Bowtell, Scott Eaton, Melissa Bardell-Williams, Linglee Downey, and Kristen Thien who completed data collection for this study.

References

- Alonso, J., Ciudad, A., Casado, A., Gilaberte, I., 2008. Measuring schizophrenia remission in clinical practice. *Can. J. Psychiatr.* 53 (3), 202–206. <https://doi.org/10.1177/070674370805300311>.
- American Psychiatric Association, 2000. *Diagnostic and Statistical Manual of Mental Disorders*. (4th ed., text rev.). Author, Washington, DC.

Table 4
Binary logistic regression for potential confounders of functional outcomes.

	B	SE β	Wald χ^2	p	OR	95%CI OR
SIPD diagnosis	−0.36	0.32	1.26	0.26	0.70	[0.90, 1.01]
Age	−0.50	0.03	2.52	0.11	0.95	[0.82, 1.70]
Sex	0.17	0.19	0.79	0.38	1.20	[0.38, 1.30]
Cannabis abuse	0.40	0.20	4.25	0.04	1.50	[1.02, 2.19]
Amphetamine abuse	0.32	0.23	1.99	0.16	1.38	[0.88, 2.17]

- Arendt, M., Rosenberg, R., Foldager, L., Perto, G., Munk-Jorgensen, P., 2005. Cannabis-induced psychosis and subsequent schizophrenia-spectrum disorders: follow-up study of 535 incident cases. *Br. J. Psychiatry* 187, 510–515. <https://doi.org/10.1192/bjp.187.6.510>.
- Arendt, M., Mortensen, P.B., Rosenberg, R., Pedersen, C.B., Waltoft, B.L., 2008. Familial predisposition for psychiatric disorder: comparison of subjects treated for cannabis-induced psychosis and schizophrenia. *Arch. Gen. Psychiatry* 65 (11), 1269–1274. <https://doi.org/10.1001/archpsyc.65.11.1269>.
- Caton, C.L., Drake, R.E., Hasin, D.S., Dominguez, B., Shrout, P.E., Samet, S., Schanzer, B., 2005. Differences between early-phase primary psychotic disorders with concurrent substance use and substance-induced psychoses. *Arch. Gen. Psychiatry* 62 (2), 137–145. <https://doi.org/10.1001/archpsyc.62.2.137>.
- Caton, C.L., Hasin, D.S., Shrout, P.E., Drake, R.E., Dominguez, B., First, M.B., et al., Schanzer, B., 2007. Stability of early-phase primary psychotic disorders with concurrent substance use and substance-induced psychosis. *Br. J. Psychiatry* 190, 105–111. <https://doi.org/10.1192/bjp.bp.105.015784>.
- Crebbin, K., Mitford, E., Paxton, R., Turkington, D., 2009. First-episode drug-induced psychosis: a medium term follow up study reveals a high-risk group. *Soc. Psychiatry Psychiatr. Epidemiol.* 44 (9), 710–715. <https://doi.org/10.1007/s00127-008-0490-2>.
- Edwards, J., Elkins, K., Hinton, M., Harrigan, S.M., Donovan, K., Athanasopoulos, O., McGorry, P.D., 2006. Randomized controlled trial of a cannabis-focused intervention for young people with first-episode psychosis. *Acta Psychiatr. Scand.* 114 (2), 109–117. <https://doi.org/10.1111/j.1600-0447.2006.00783.x>.
- Fraser, S., Hides, L., Phillips, L., Proctor, D., Lubman, D.I., 2012. Differentiating first episode substance induced and primary psychotic disorders with concurrent substance use in young people. *Schizophr. Res.* 136 (1–3), 110–115. <https://doi.org/10.1016/j.schres.2012.01.022>.
- Jablensky, A., McGrath, J., Herrman, H., Castle, D., Gureje, O., Evans, M., et al., Harvey, C., 2000. Psychotic disorders in urban areas: an overview of the study on low prevalence disorders. *Aust. N. Z. J. Psychiatry* 34 (2), 221–236. <https://doi.org/10.1080/j.1440-1614.2000.00728.x>.
- Jackson, H.J., McGorry, P.D., 2009. *The Recognition and Management of Early Psychosis: a Preventive Approach*. 2nd ed. Cambridge University Press, Cambridge, UK; New York.
- Jorgensen, P., Nordentoft, M., Abel, M.B., Gouliava, G., Jeppesen, P., Kassow, P., 2000. Early detection and assertive community treatment of young psychotics: the opus study rationale and design of the trial. *Soc. Psychiatry Psychiatr. Epidemiol.* 35 (7), 283–287.
- Kirkbride, J.B., Hameed, Y., Wright, L., Russell, K., Knight, C., Perez, J., Jones, P.B., 2017. Waiting time variation in early intervention psychosis services: longitudinal evidence from the SEPEA naturalistic cohort study. *Soc. Psychiatry Psychiatr. Epidemiol.* 52 (5), 563–574. <https://doi.org/10.1007/s00127-017-1343-7>.
- Lambert, M., Conus, P., Lubman, D.I., Wade, D., Yuen, H., Moritz, S., et al., Schimmelmann, B.G., 2005. The impact of substance use disorders on clinical outcome in 643 patients with first-episode psychosis. *Acta Psychiatr. Scand.* 112 (2), 141–148. <https://doi.org/10.1111/j.1600-0447.2005.00554.x>.
- Large, M., Sharma, S., Compton, M.T., Slade, T., Nielsen, O., 2011. Cannabis use and earlier onset of psychosis: a systematic meta-analysis. *Arch. Gen. Psychiatry* 68 (6), 555–561. <https://doi.org/10.1001/archgenpsychiatry.2011.5>.
- Mathias, S., Lubman, D.I., Hides, L., 2008. Substance-induced psychosis: a diagnostic conundrum. *J. Clin. Psychiatry* 69 (3), 358–367.
- Mauri, M.C., Di Pace, C., Reggiori, A., Paletta, S., Colasanti, A., 2017. Primary psychosis with comorbid drug abuse and drug-induced psychosis: diagnostic and clinical evaluation at follow up. *Asian J. Psychiatr.* 29, 117–122. <https://doi.org/10.1016/j.ajp.2017.04.014>.
- McGorry, P.D., Nelson, B., Amminger, G.P., Bechdolf, A., Francey, S.M., Berger, G., et al., Yung, A.R., 2009. Intervention in individuals at ultra-high risk for psychosis: a review and future directions. *J. Clin. Psychiatry* 70 (9), 1206–1212. <https://doi.org/10.4088/JCP.08r04472>.
- National Institute for Mental Health in England, 2008. *National Early Intervention Programme. Early Intervention (EI) Acceptance Criteria Guidelines*. NIMHE, London.
- Nelson, B., Yuen, H.P., Wood, S.J., Lin, A., Spiliotacopoulos, D., Bruxner, A., et al., Yung, A.R., 2013. Long-term follow-up of a group at ultra high risk ("prodromal") for psychosis: the PACE 400 study. *JAMA Psychiatr.* 70 (8), 793–802. <https://doi.org/10.1001/jamapsychiatry.2013.1270>.
- Niemi-Pynttari, J.A., Sund, R., Putkonen, H., Vormaa, H., Wahlbeck, K., Pirkola, S.P., 2013. Substance-induced psychoses converting into schizophrenia: a register-based study of 18,478 Finnish inpatient cases. *J. Clin. Psychiatry* 74 (1), e94–e99. <https://doi.org/10.4088/JCP.12m07822>.
- Nunez, L.A., Gurpegui, M., 2002. Cannabis-induced psychosis: a cross-sectional comparison with acute schizophrenia. *Acta Psychiatr. Scand.* 105 (3), 173–178.
- O'Donoghue, B., Lyne, J., Madigan, K., Lane, A., Turner, N., O'Callaghan, E., Clarke, M., 2015. Environmental factors and the age at onset in first episode psychosis. *Schizophr. Res.* 168 (1–2), 106–112. <https://doi.org/10.1016/j.schres.2015.07.004>.
- Thompson, A., Marwaha, S., Winsper, C., Everard, L., Jones, P.B., Fowler, D., et al., Birchwood, M., 2016. Short-term outcome of substance-induced psychotic disorder in a large UK first episode psychosis cohort. *Acta Psychiatr. Scand.* 134 (4), 321–328. <https://doi.org/10.1111/acps.12623>.
- Wade, D., 2005. Cannabis use and schizophrenia. *Am. J. Psychiatry* 162 (2), 401 author reply 402. <https://doi.org/10.1176/appi.ajp.162.2.401>.
- Wade, D., Harrigan, S., Edwards, J., Burgess, P.M., Whelan, G., McGorry, P.D., 2006. Substance misuse in first-episode psychosis: 15-month prospective follow-up study. *Br. J. Psychiatry* 189, 229–234. <https://doi.org/10.1192/bjp.bp.105.017236>.
- Wilson, L., Szigeti, A., Kearney, A., Clarke, M., 2017. Clinical characteristics of primary psychotic disorders with concurrent substance abuse and substance-induced psychotic disorders: a systematic review. *Schizophr. Res.* <https://doi.org/10.1016/j.schres.2017.11.001>.