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Demographic and clinical correlates of substance use disorders in first episode psychosis

Mary F. Brunette [a,b,*], Kim T. Mueser [c], Steven Babbin [d], Piper Meyer-Kalos [e], Robert Rosenheck [f], Christoph U. Correll [g,h,i,j], Corrine Cather [s], Delbert G. Robinson [g,h,i,j], Nina R. Schooler [g,k], David L. Penn [l,m], Jean Addington [n], Sue E. Estroff [o], Jennifer Gottlieb [c], Shirley M. Glynn [p], Patricia Marcy [q], James Robinson [r], John M. Kane [g,h,i,j]

[a] Geisel School of Medicine at Dartmouth, Lebanon, NH, USA
[b] Bureau of Mental Health Services, Department of Health and Human Services, Concord, NH, USA
[c] Center for Psychiatric Rehabilitation, Departments of Occupational Therapy, Psychiatry, and Psychology, Boston University, Boston, MA, USA
[d] University of Massachusetts, Boston, MA, USA
[e] Minnesota Center for Chemical and Mental Health, University of Minnesota, School of Social Work, St. Paul, MN, USA
[f] Yale Medical School, New Haven, CT, USA
[g] Zucker Hillside Hospital, Psychiatry Research, North Shore - Long Island Jewis Glen Oaks, NY, USA
[h] The Feinstein Institute for Medical Research, Manhasset, NY, USA
[i] Hofstra North Shore LIJ School of Medicine, Departments of Psychiatry and Molecular Medicine, Hempstead, NY, USA
[j] Albert Einstein College of Medicine, Department of Psychiatry and Behavioral Sciences, Bronx, NY, USA
[k] SUNY Downstate Medical Center, Department of Psychiatry, Brooklyn, NY, USA
[l] University of North Carolina-Chapel Hill, Department of Psychology, Chapel Hill, NC, USA
[m] Australian Catholic University, School of Psychology, Melbourne, VIC, Australia
[n] Hotchkiss Brain Institute, Department of Psychiatry, University of Calgary, Calgary, Canada
[o] Department of Social Medicine, University of North Carolina, Chapel Hill, NC, USA
[p] Semel Institute of Neuroscience and Human Behavior, University of California, Los Angeles, CA, USA
[q] Vanguard Research Group, NY, USA
[r] Nathan Kline Institute, Orangeburg, NY, USA
[s] Massachusetts General Hospital, Boston, MA, USA

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ABSTRACT

Background: We assessed the prevalence and correlates of lifetime substance use disorders in people with first episode psychosis using the baseline data from the Recovery After an Initial Schizophrenia Episode (RAISE) Early Treatment Program study.
Methods: Research staff assessed 404 first episode patients at 34 community mental health centers across the United States with the Structured Clinical Interview for DSM-IV for diagnoses of psychotic and substance use disorders. Logistic regression was used to evaluate the relationships between participant characteristics and lifetime substance use disorders, followed with generalized linear mixed-effects regression models to identify unique predictors of lifetime substance use disorders.
Results: Approximately one-third of participants reported recent alcohol use (36.6%) and cannabis use (30.7%), and one half (51.7%) met criteria for any lifetime alcohol or drug use disorder. Lifetime substance use disorders were associated with male gender, White race, higher excited (hyperactivity, mood lability, impulsivity, hostility, and uncooperativeness), psychotic and depressive symptoms, less impaired cognition, and greater perceived stigma. Gender, race, and excited symptoms were the most consistent unique predictors of lifetime substance use disorders found in multivariate analyses.
Conclusions: Half of first episode psychosis patients have co-occurring substance use disorders, which are associated with both more severe symptoms and greater perceptions of stigma. Programs aiming to serve these patients must have the skills and clinical strategies to help people with these unique characteristics.

1. Introduction

Approximately 50% of people with schizophrenia have a lifetime history of substance use disorder (SUD), a rate at least three times higher

* Corresponding author at: Geisel School of Medicine at Dartmouth, Lebanon, NH, USA.
E-mail address: mary.f.brunette@dartmouth.edu (M.F. Brunette).

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than that in the general population (Degenhardt and Hall, 2001; Regier et al., 1990; Sara et al., 2014). Alcohol is the most commonly reported substance of abuse in this group, followed by cannabis and stimulants. Male gender, younger age, and lower educational attainment have been associated with higher rates of substance use disorder comorbidity (for a review, see (Brunette et al., 2016)). Findings for race and ethnicity have varied, presumably reflecting variation in access to different substances across communities. Patients with schizophrenia and co-occurring SUD tend to have lower adherence to treatment and a poorer long-term course than those without such disorders, including higher rates of hospitalization, and increased likelihood of violence, victimization, homelessness, infectious disease, and premature mortality (Brunette et al., 2016).

Less is known about SUD among people at the time of their first episode of psychosis (FEP). Reports mostly from the U.S., Canada, Western Europe, and Australia have indicated that 24–74% of this group has a lifetime SUD (e.g., Addington, 1999; Addington and Addington, 2007; Barnett et al., 2007; Kavanagh et al., 2004; Kovasznay et al., 1997; Lambert et al., 2005; Mauri et al., 2006; Rabinowitz et al., 1998; Sara et al., 2013; Van Mastrigt et al., 2004; Wade et al., 2005), with rates of cannabis use slightly higher and alcohol use slightly lower than in multi-episode samples (Koskinen et al., 2010). Being male has been consistently associated with co-occurring substance use and SUD in FEP. Younger age, less education, and unemployment are less consistently associated with co-occurring SUD in FEP (Addington and Addington, 2007; Kavanagh et al., 2004; Larsen et al., 2006; Patel et al., 2016; Sara et al., 2013; Van Mastrigt et al., 2004; Wade et al., 2005). Some studies have reported higher levels of psychotic symptoms (Addington and Addington, 2007; Baeza et al., 2009; Green et al., 2004; Kamali et al., 2009; Mauri et al., 2006; Sevy et al., 2010) and suicidal ideation (Togay et al., 2015; Verdoux et al., 1999, 2001), and lower levels of negative symptoms (Baeza et al., 2009; Green et al., 2004; Larsen et al., 2006) in patients with co-occurring FEP and SUD. These clinical characteristics are generally similar to those in multi-episode patients.

More comprehensive information about the prevalence and correlates of SUD in patients with FEP is needed in order to inform treatment development. This report focuses on the prevalence and the demographic and clinical correlates of SUD from baseline data collected within the National Institute of Mental Health Recovery After an Initial Schizophrenia Episode (RAISE) Early Treatment Program (ETP) study, which is the largest treatment study of people with FEP conducted to date in the U.S. (Kane et al., 2015).

2. Methods

2.1. Overview

In the RAISE-ETP study, 34 community mental health centers were randomly assigned to deliver the NAVIGATE program, a coordinated specialty care intervention for FEP (Heinssen et al., 2014), or usual community care. Eligible participants were assessed in person at baseline and every 6 months, as well as by phone monthly, for two years. This study focuses on the baseline assessments only.

2.2. Participants

Participants (N = 404) were recruited from 34 community mental health centers located in 21 states between 2010 and 2012. Inclusion/exclusion criteria for the study were: 1) between 15 and 40 years of age; 2) DSM-IV diagnoses of schizophrenia, schizoaffective disorder, schizophreniform disorder, brief psychotic disorder, or psychotic disorder not otherwise specified; 3) no history of clinically significant head trauma, or other serious medical conditions; 4) first episode of psychosis, regardless of duration since onset of symptoms; and 5) antipsychotic medication taken ≤6 months over the person's lifetime.

Written informed consent was obtained from adult participants age 18 and older. Youth under age 18 provided written assent and their legal guardians provided written informed consent. The study was approved by the institutional review board of the coordinating center, as well as by the boards of many of the study sites as required. The NIMH Data and Safety Monitoring Board provided study oversight.

2.3. Assessment strategy and measures

Site research staff collected demographic information. Additional trained and blinded research staff used secure, live, two-way video conferencing to perform diagnostic interviews and assessments of symptoms and quality of life, a method that has been shown to have comparable acceptability and reliability to in-person assessment (Zarate et al., 1997).

The Structured Clinical Interview for DSM-IV (SCID) was used to evaluate diagnoses of psychotic and SUD diagnoses (current and lifetime) (First et al., 1996). Four variables representing different domains of lifetime SUD at baseline were created and utilized as dependent variables: alcohol abuse or dependence, cannabis abuse or dependence, other drug abuse or dependence, and summed lifetime number of SUDs (no lifetime SUD, one lifetime SUD, two or more lifetime SUDs).

Data collected during the SCID interview were also used to assess duration of untreated psychosis, which was defined as the period between the onset of the first psychotic symptom and initial treatment with antipsychotic medications (Addington et al., 2015). Symptoms were assessed using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987); we calculated PANSS subscales for positive, negative, disorganized, excited, and depressive symptoms with a five factor model (Wallwork et al., 2012). Depression was assessed using the Calgary Depression Scale for Schizophrenia (CDSS) (Addington et al., 1993). The Heinrichs-Carpenter Quality of Life Scale (QLS) (Heinrichs et al., 1984), a semi-structured interview, was used to gather information for 21 items that cover four domains: interpersonal relations, instrumental role functioning, intrapsychic foundations (e.g., sense of purpose, motivation), and common objects and activities. Cognition was evaluated with the Brief Assessment of Cognition in Schizophrenia (BACS) (Keefe et al., 2004), a brief assessment of domains commonly impaired in schizophrenia.

Using a standard phone interview at baseline and monthly (McLellan et al., 1992; Rosenheck et al., 2003; Rosenheck et al., 2006), site research staff also assessed self-reported substance use (Desmarais et al., 2013). Participants reported number of days of use of alcohol, cannabis, other drugs (including all street drugs and medications that were not prescribed for the person) as well as tobacco, which will be described in a separate report. The questions were framed as follows: "*In the past 30 days, on how many days did you <drink alcohol>?*" (McLellan et al., 1992).

Patient perception of stigma was assessed with seven items from the Stigma Scale (King et al., 2007). The original Stigma Scale includes 28 items corresponding to three factors; four items were drawn from the discrimination factor, two from the disclosure factor, and one from the positive aspects factor. We used mean total scores. The coefficient alpha for these items was 0.60. Perceived well-being was assessed with a subset of 18 items from the Perceived Well-being Scale (Ryff, 1989). Attitudes about medication adherence were measured with a subset of 4 items from the Brief Evaluation of Medication Influences and Beliefs (Dolder et al., 2004). The 6-item Autonomy Support Scale, a short version of the Health Care Climate Questionnaire (Williams et al., 1998), reflected perceptions of support for autonomy from treatment providers. An abbreviated version of the Mental Health Recovery Measure (Young and Bullock, 2003) was used to assess participants' perceptions of their recovery from mental illness. Participants rated their overall level of functioning with the Patient Self-rated Global Functioning Scale that corresponds to the global assessment item in the Quality of Life Interview (Lehman, 1988).

2.4. Data analysis

Associations among baseline SUD indicators and correlates were tested in three steps. First, potentially correlated variables were tested in a series of bivariate chi-square and *t*-tests (for alcohol, cannabis, and all other substance disorders combined) and one-way ANOVAs (for lifetime number of SUDs). In this step we examined both total PANSS scale scores and factor scores. Second, statistically significant ($p < 0.05$) variables were entered into stepwise logistic regressions for each SUD variable. We utilized only PANSS scale scores to avoid collinearity. Backward elimination was utilized for each model. Variables that were associated with a SUD at $p < 0.1$ in the bivariate analyses were entered into the model, but were kept in the model only if they remained uniquely predictive of SUD at $p < 0.05$. Then, variables that were statistically significant in the logistic regression models were included in generalized linear mixed-effects regression models with a random effect (intercept) for site to evaluate their relationships accounting for site variation. This step was necessary to adjust the standard errors for the clustered nature of these data within the sites and served to further test the significant associations that emerged in the stepwise models. Alcohol, cannabis, and other SUDs were specified to have a binary distribution (present or absent), and lifetime number of SUDs was specified to have a multinomial distribution (absent, one disorder present, or two or more disorders present).

3. Results

Participant characteristics are shown in Tables 1a and 1b. They were 23.1 years old on average. About half were White, the majority were male, and most lived with family. About 20% were in school and 14.3% were working at the time of study enrollment. Participants were moderately symptomatic.

About one-third (36.6%) of participants reported past 30-day alcohol use and 30.7% reported cannabis use (Table 2). Very few reported recently using other drugs. Among participants who had used substances in the past month, cannabis was used on twice as many days as alcohol, on average (9.9 vs. 5.0 days per month, respectively).

While 13.6% of the sample had a current SUD, over one half (51.7%) met criteria for a lifetime SUD, with alcohol use disorder most common (36.4%), closely followed by cannabis use disorder (34.7%), and then other drug use disorders (16.3%). Additionally, almost one-third of the group (30.2%) had experienced two or more lifetime SUDs (e.g., alcohol and cannabis). Having a lifetime alcohol use disorder and having more than one SUD were significantly correlated with having all of the other SUDs (all p values ≤ 0.001).

Many subjects had recently been hospitalized immediately before enrollment in the study. Since being in the hospital can reduce opportunity to use substances, and reports of recent substance use are often minimized in psychiatric inpatients (Drake et al., 1996), regression analyses were conducted on lifetime SUDs as the primary diagnoses of interest. As shown in Tables 1a, 1b, 3a and 3b, several participant characteristics were associated with lifetime SUD in bivariate analyses. Male gender and White race were associated with any SUD. Younger age was associated with cannabis disorder, whereas older age was associated with alcohol and multiple SUDs.

The results of the bivariate analyses indicated that symptoms were associated with lifetime SUD in several ways (Tables 3a and 3b). First, participants with any SUD had more severe symptoms on the PANSS excited subscale than those with no SUD. Second, participants with a drug use disorder other than cannabis, and those with multiple SUDs, had more severe psychotic and depressed symptoms (and total scores) on the PANSS, and more severe depression on the CDSS than others. Additionally, participants with any SUD, alcohol use disorders and multiple SUDs had less severe cognitive impairment. Duration of untreated psychosis was longer for participants with drug use disorders other than cannabis, but there were not any relationships between the age of onset of psychosis symptoms and lifetime SUD. There was also a pattern of associations between higher perceived stigma scores and lifetime SUDs.

The generalized mixed effects linear regression analyses accounting for site variation, with subject characteristics entered into the models, showed independent associations between lifetime SUDs and male gender, younger age, White race, higher PANSS excited factor, longer DUP, and higher levels of perceived stigma (see Table 4).

4. Discussion

About one-half of this large U.S. sample of young people with FEP met criteria for a lifetime SUD. The prevalence of different lifetime SUDs was in the middle of the 24–74% range reported in previously published FEP studies (Bühler et al., 2002; Lambert et al., 2005; Myles et al., 2016). Additionally, lifetime drug use disorders in these study participants with FEP were more common than in general population studies of young adults for: cannabis use disorders, 34.7 vs. 11.0% (Hasin et al., 2016); cocaine, stimulant and PCP use disorders, 4–5 vs. 2.8% (Compton et al., 2007); and opiate use disorders, 4.5 vs. approximately

Table 1a
Sociodemographic characteristics of 404 study participants by presence of any substance use disorder.

	Total study group N = 404	Any lifetime alcohol or drug disorder		
		Absent	One or more	Two or more
		N = 195 (48.3%)	N = 209 (51.7%)	N = 122 (30.2%)
Number male (%)	293 (72.5%)	127 (65.1%)	166 (79.4%)**	97 (79.5%)**
Mean age (SD)	23.1 (5.1)	22.9 (5.3)	23.3 (4.8)	24.1 (5.0)*
Number living with family (parents, grandparents, siblings) (%)	320 (79.2%)	189 (96.9%)	131 (62.7%)	87 (71.3%)
Number never married (%)	358 (88.6%)	177 (90.8%)	181 (86.6%)	104 (85.2%)
Race[a]				
Number White (%)	218 (54.0%)	93 (47.7%)	125 (59.8%)[a]	77 (63.1%)[a]
Number African American (%)	152 (37.6%)	87 (44.6%)	65 (31.1%)	33 (27.0%)
Number other (%)	34 (8.4%)	15 (7.7%)	19 (9.1%)	12 (9.8%)
Number Hispanic (%)	73 (18.1%)	37 (19.0%)	36 (17.2%)	22 (18.0%)
Patient's education				
Number some college or higher (%)	145 (35.9%)	69 (35.4%)	76 (36.5%)	40 (33.1%)
Number completed high school (%)	133 (32.9%)	66 (33.8%)	67 (32.2%)	42 (34.7%)
Number some high school (%)	125 (30.9%)	60 (30.8%)	65 (31.3%)	39 (32.2%)
Number current student (%)	82 (20.3%)	47 (24.1%)	35 (20.3%)	20 (16.4%)
Number currently working (%)	58 (14.4%)	29 (14.9%)	29 (13.9%)	16 (13.1%)

*p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001; Significant in bivariate tests.
Group with substance use disorder is significantly different from those without the substance use disorder.
[a] Chi-square tests comparing Whites vs. African Americans were significant p ≤ 0.01 for any lifetime alcohol or drug and lifetime multiple alcohol and drug disorders.

Table 1b
Sociodemographic characteristics of 404 study participants by presence of alcohol, cannabis or other drug disorder.

	Total study group N = 404	Lifetime alcohol disorder		Lifetime cannabis disorder		Lifetime other drug disorder	
		Absent	Present	Absent	Present	Absent	Present
		N = 257 (63.6%)	N = 147 (36.4%)	N = 264 (65.3%)	N = 140 (34.7%)	N = 338 (83.7%)	N = 66 (16.3%)
Number male (%)	293 (72.5%)	178 (69.3%)	115 (78.2%)*	177 (67.0%)	116 (82.9%)***	247 (73.1%)	46 (69.7%)
Mean age (SD)	23.1 (5.1)	22.8 (5.2)	23.8 (4.9)*	23.4 (5.4)	22.7 (4.4)*	22.8 (4.9)	24.9 (5.5)
Number living with family (parents, grandparents, siblings) (%)	320 (79.2%)	215 (85.7%)	105 (75.5%)	218 (84.5%)	102 (77.3%)	271 (82.9%)	49 (77.8%)
Number never married (%)	358 (88.6%)	232 (90.3%)	126 (85.7%)	233 (88.3%)	125 (89.3%)	305 (90.2%)	53 (80.3%)*
Race[a]							
Number White (%)	218 (54.0%)	125 (48.6%)	93 (63.3%)*a	143 (54.2%)	75 (53.6%)	172 (50.9%)	46 (69.7%)[a]
Number African American (%)	152 (37.6%)	111 (43.2%)	41 (27.9%)*	101 (38.3%)	51 (36.4%)	137 (40.5%)	15 (22.7%)
Number other (%)	34 (8.4%)	21 (8.2%)	13 (8.8%)	20 (7.6%)	14 (9.9%)	29 (8.6%)	5 (7.6%)
Number Hispanic (%)	73 (18.1%)	47 (18.3%)	26 (17.7%)	47 (17.8%)	26 (18.6%)	63 (18.6%)	10 (15.2%)
Patient's education							
Number some college or higher (%)	145 (35.9%)	95 (37.1%)	50 (34%)	97 (36.7%)	48 (34.5%)	118 (34.9%)	27 (41.5%)
Number completed high school (%)	133 (32.9%)	87 (34%)	46 (31.3%)	84 (31.8%)	49 (35.3%)	113 (33.4%)	20 (30.8%)
Number some high school (%)	125 (30.9%)	65 (27.3%)	50 (34%)	83 (31.4%)	42 (30.2%)	107 (31.7%)	18 (27.7%)
Number current student (%)	82 (20.3%)	56 (21.8%)	26 (17.7%)	60 (22.7%)	22 (15.7%)	71 (21%)	11 (16.7%)
Number currently working (%)	58 (14.4%)	36 (14%)	22 (15.0%)	41 (15.5%)	17 (12.1%)	50 (14.8%)	8 (12.1%)

*p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001; Group with substance use disorder is significantly different from those without the substance use disorder in bivariate tests.
[a] Chi-square tests comparing Whites vs. African Americans were significant p ≤ 0.01 for lifetime alcohol and lifetime other drug disorders

3% (Kerridge et al., 2015). In contrast, the rate of lifetime alcohol disorder in this sample was similar to that found in general population young adults (34.7 vs. 37.0%) (Grant et al., 2015). The relative consistency of SUD prevalence rates in FEP across the developed world suggests that the increased risk for SUD in schizophrenia is a characteristic of the illness in societies where there is ready access to substances and most treatment is provided in the community.

Consistent with previous research in FEP (e.g., Sara et al., 2013) and in the general population (Grant et al., 2015; Hasin et al., 2016), male participants were more likely to have an SUD, White participants were more likely to have alcohol and drug use disorders than Blacks (Compton et al., 2007; Grant et al., 2015), whereas lifetime cannabis use disorder diagnosis did not differ by race (Hasin et al., 2016). The age-related patterns are also consistent with previous work in FEP (Sara et al., 2013) and the general population (Wagner and Anthony, 2002), in which age of developing cannabis use disorders is younger than the age of developing alcohol, other drug or multiple drug disorders. This likely also reflects a common pattern in drug addiction in which people start with cannabis before progressing to other drugs (Secades-Villa et al., 2015), and onset of alcohol use disorder is delayed by age limits on sales (DeJong and Blanchette, 2014). Although having psychosis predisposes people to develop substance use disorders in general, the predominating demographic patterns of substance use in American culture are apparent in this group of people with FEP.

The relationships between drug use disorders and more severe psychotic symptoms found here are consistent with prior FEP studies using cross-sectional (Baeza et al., 2009; Kamali et al., 2009; Rabinowitz et al., 1998) and longitudinal study designs (e.g., Addington and Addington, 2007; Foti et al., 2010; Grech et al., 2005; Harrison et al., 2008; Hides et al., 2006; Hinton et al., 2007; Seddon et al., 2016; Sorbara et al., 2003; Turkington et al., 2009; van der Meer et al., 2015; Wade et al., 2006; Wade et al., 2007). The associations between SUDs and severity of depression are also consistent with prior longitudinal studies (Addington and Addington, 2007; Barrowclough et al., 2015; Harrison et al., 2008; Seddon et al., 2016; Turkington et al., 2009; van der Meer et al., 2015; Wade et al., 2006).

The most consistent relationship between SUDs and symptoms was with the excited factor of the PANSS, which includes five specific items: hyperactivity, mood lability, impulsivity, hostility, and uncooperativeness. These symptoms overlap with antisocial personality disorder and its precursor, conduct disorder, which have a very high co-occurrence with SUDs in the general population and in people with schizophrenia (Moran and Hodgins, 2004; Mueser et al., 1999). Furthermore, antisocial personality disorder is associated with more severe substance use and functioning problems among both patients with a primary SUD (Cacciola et al., 2001; Ford et al., 2009), as well as among those with co-occurring substance use and severe psychiatric disorders (Huber et al., 2016; Mueser et al., 2006; Mueser et al., 1997). In line with this interpretation, a recent report indicated that higher PANSS excited scores were associated with an earlier age at onset of psychosis, antisocial personality disorder, and substance use disorders (Huber et al., 2016).

In the bivariate analyses, participants with SUDs tended to have less impaired cognitive functioning than those without these disorders, although these relationships were not independent predictors of SUD in the mixed effects multiple logistic regression models with gender, race, symptoms, and perceived stigma. Similar associations between

Table 2
Baseline substance use and disorder diagnoses among study participants with first episode psychosis.

Type of substance	Past month use	Past month abuse or dependence	Lifetime abuse	Lifetime dependence	Lifetime abuse or dependence
Any: alcohol or drug, N (%)	197 (48.8%)	55 (13.6%)	99 (24.5%)	145 (35.9%)	209 (51.7%)
Alcohol, N (%)	148 (36.6%)	18 (4.5%)	52 (12.9%)	95 (23.5%)	147 (36.4%)
Cannabis, N (%)	124 (30.7%)	43 (10.6%)	57 (14.1%)	83 (20.5%)	140 (34.7%)
Other substances, N (%)	12 (3.0%)	–	–	–	–
Cocaine, N (%)	–	2 (0.5%)	5 (1.2%)	16 (4.0%)	21 (5.2%)
Opioids, N (%)	–	1 (0.2%)	6 (1.5%)	12 (3.0%)	18 (4.5%)
PCP, N (%)	–	0	10 (2.5%)	8 (2.0%)	18 (4.5%)
Stimulants, N (%)	–	1 (0.2%)	5 (1.2%)	12 (3.0%)	17 (4.2%)
Sedatives, N (%)	–	0	1 (0.2%)	2 (0.5%)	3 (0.7%)
Other, N (%)	–	0	0	2 (0.5%)	2 (0.5%)
Poly-substance, N (%)	–	0	0	4 (1.0%)	4 (1.0%)

Dep = dependence.

Table 3a
Clinical characteristics of study participants with first episode psychosis and lifetime substance use disorders.

	Total study group	Any lifetime alcohol or drug disorder		
		Absent	One or more	Two or more
	N = 404	N = 195 (48.3%)	N = 209 (51.7%)	N = 122 (30.2%)
Symptoms				
Total (PANSS) score (30−210)	76.6 (15.0)	75.4 (16.0)	77.8 (13.9)	80.2 (13.3)**
PANSS positive factor (4–28)	12.2 (3.8)	11.8 (3.9)	12.6 (3.7)*	13.2 (3.5)**
PANSS negative factor (7–42)	16.7 (5.2)	16.9 (5.4)	16.5 (5.0)	16.8 (5.1)
PANSS disorganized/concrete factor (3−21)	7.8 (2.8)	7.8 (3.0)	7.8 (2.5)	7.8 (2.5)
PANSS excited factor (4–28)	6.8 (2.8)	6.4 (2.5)	7.1 (3.0)**	7.7 (3.1)***
PANSS depressed factor (3–21)	8.1 (3.3)	7.8 (3.2)	8.3 (3.4)	8.7 (3.4)*
Calgary Depression Scale for Schizophrenia (0–27)	4.7 (4.3)	4.3 (4.0)	4.9 (4.5)	5.5 (4.8)*
Cognition				
BACS composite Z score	−2.1 (1.6)	−2.3 (1.7)	−1.9 (1.5)**	−1.9 (1.5)*
Timing of symptoms and illness				
Duration untreated psychosis (weeks)	193.5 (262.2)	171.7 (235.0)	213.8 (284.2)	235.9 (304.5)
Age first psychiatric illness	16.5 (6.3)	16.9 (6.4)	16.1 (6.3)	15.8 (6.4)
Age first psychotic symptoms	19.2 (6.1)	19.5 (6.4)	18.8 (5.8)	19.2 (5.8)
Psychosocial function				
Quality of life total scale score (0–126)	52.6 (18.8)	53.0 (21.2)	52.3 (16.2)	51.5 (16.3)
QLS interpersonal relations (0–48)	19.8 (8.7)	19.8 (9.1)	19.7 (8.3)	19.5 (8.2)
QLS instrumental role (0–24)	5.6 (6.5)	6.1 (6.6)	5.0 (6.4)	4.5 (6.0)
QLS intrapsychic foundations (0–42)	20.8 (7.0)	20.7 (7.9)	20.9 (6.0)	20.7 (6.3)
QLS common objects and activities (0−12)	6.5 (2.3)	6.4 (2.5)	6.6 (2.1)	6.7 (2.3)
Subjective appraisals				
Mean Stigma scale score (1–7)	4.0 (1.2)	3.9 (1.2)	4.1 (1.1)*	4.2 (1.1)*
Well-being Scale mean score (1–6)	4.0 (0.8)	4.0 (0.8)	4.0 (0.8)	3.9 (0.8)
Autonomy support scale mean score (1–7)	5.5 (1.2)	5.6 (1.3)	5.5 (1.1)	5.5 (1.1)
Medication influences and beliefs scale mean score (1–7)	4.9 (1.0)	5.0 (1.0)	4.8 (1.0)	5.0 (1.0)*
Mental health recovery measure mean score (1–7)	4.9 (1.2)	4.9 (1.3)	4.9 (1.2)	4.9 (1.2)
Global state of mental health (1−100)	62.1 (23.6)	63.1 (23.5)	61.3 (23.8)	59.3 (23.6)
Global feelings about life as a whole (1–7)	4.4 (1.4)	4.4 (1.4)	4.3 (1.5)	4.2 (1.4)

Bivariate analyses indicate that group with SUD is significantly different from those without that specific SUD.
SUD = substance use disorder; PANSS = Positive and Negative Symptom Scale; BACS = Brief Assessment of Cognition in Schizophrenia
* $p \le 0.05$.
** $p \le 0.01$.
*** $p \le 0.001$.

SUD and higher levels of cognitive functioning among FEP patients have previously been reported for cannabis use disorder or mixed samples of disorders (de la Serna et al., 2010; Leeson et al., 2012; McCleery et al., 2006; Sevy et al., 2001; Stirling et al., 2005), but not specifically for alcohol use disorder. More preserved cognitive function may lead to increased exposure to licit and illicit substances through social connections, thereby increasing vulnerability to developing a use disorder. Although others have found higher social functioning (Leeson et al., 2012) or more contact with friends (Larsen et al., 2006) in FEP patients with SUDs than those without, our analysis did not find this association. However, due to the fact that many participants had been recently hospitalized, the assessment of social functioning at baseline may have not accurately reflected more stable levels of social functioning that could influence substance use behavior.

Higher levels of perceived stigma were uniquely associated with lifetime alcohol use disorders in this sample of FEP patients, suggesting the possible importance of motives for substance use that requires further exploration. Specific motives and expectancies regarding the effects of substances may play a role in the development and persistence of SUDs in this population (Childs et al., 2011; Lobbana et al., 2010; Mueser et al., 1995). Qualitative research suggests that people with FEP are aware of the stigma of their mental illness and have personal experiences of discrimination (Lasalvia et al., 2014). It is possible that recognition of psychiatric symptoms and either awareness or endorsement of stigmatizing attitudes towards mental illness during the early phases of developing a psychosis may have contributed to participants' substance use with peers as a "normalizing" activity or to gain social acceptance (Childs et al., 2011; Lobbana et al., 2010). The portrayal of people with mental illness who have achieved recovery with treatment is associated with reduced stigma (McGinty et al., 2015). Thus, facilitating contact of FEP patients with peers in recovery may be an important strategy for reducing stigma in treatment programs (Estroff et al., 2004). Further longitudinal research is required to better understand the role of stigma in substance use behavior among people with FEP.

In our sample, people with drug use disorders other than cannabis had longer DUP. Problematic use of substances such as cocaine, amphetamines, or opioids could pose a particular challenge to families' and clinicians' ability to recognize and diagnose psychotic symptoms, resulting in delay of needed treatment. The lower prevalence of these drug use disorders in the general population (as well as in people with FEP) may contribute to a "diagnostic overshadowing" effect (Reiss et al., 1982) in which the presence of one disorder (non-cannabis drug use disorder) obscures the recognition of the other disorder (FEP).

We did not find a relationship between substance use disorders and age of onset of psychosis, whereas many previous studies from Australia (e.g. Leeson et al., 2012; Power et al., 2013; Stefanis et al., 2014) Western Europe (e.g. Dekker et al., 2012; Helle et al., 2016; Tosato et al., 2013), and Canada (e.g. Addington and Addington, 2007) have found that cannabis use was associated with earlier age of onset, and also identified a cumulative relationship (more substances) with earlier age onset (Power et al., 2013; Stefanis et al., 2014). Our study is similar to previous U.S. studies (Compton et al., 2009; Green et al., 2004; Kamali et al., 2009), in which this relationship was not present, although one study found that people whose cannabis use progressed to daily use immediately prior to onset had a younger age of onset (Compton et al., 2009), and one study from the 1990s found a relationship between SUD and age of onset only in women with mixed diagnoses including depression and bipolar disorder (Rabinowitz et al., 1998).

Table 3b
Clinical characteristics of study participants with first episode psychosis and lifetime substance use disorders.

	Total study group	Lifetime alcohol disorder		Lifetime cannabis disorder		Lifetime other drug disorder	
		Absent	Present	Absent	Present	Absent	Present
	N = 404	N = 257 (63.6%)	N = 147 (36.4%)	N = 264 (65.3%)	N = 140 (34.7%)	N = 338 (83.7%)	N = 66 (16.3%)
Symptoms							
Total (PANSS) score (30–210)	76.6 (15.0)	76.0 (15.4)	77.7 (14.2)	75.3 (16.0%)	79.0 (12.7)*	75.7 (15.0)	81.4 (14.1)**
PANSS positive factor (4–28)	12.2 (3.8)	12.0 (3.9)	12.6 (3.8)	11.9 (4.0)	12.9 (3.5)*	12.0 (3.8)	13.6 (3.8)**
PANSS negative factor (7–42)	16.7 (5.2)	16.9 (5.1)	16.3 (5.3)	16.6 (5.4)	16.9 (4.7)	16.8 (5.2)	16.4 (4.9)
PANSS disorganized/concrete factor (3–21)	7.8 (2.8)	7.8 (2.9)	7.8 (2.5)	7.7 (2.9)	8.0 (2.4)	7.8 (2.8)	7.8 (2.7)
PANSS excited factor (4–28)	6.8 (2.8)	6.45 (2.6)	7.3 (3.0)**	6.4 (2.5)	7.4 (3.1)**	6.5 (2.7)	7.8 (3.0)**
PANSS depressed factor (3–21)	8.1 (3.3)	7.8 (3.2)	8.5 (3.5)	8.0 (3.3)	8.2 (3.4)	7.90 (3.3)	8.8 (3.5)*
Calgary Depression Scale for Schizophrenia (0–27)	4.7 (4.3)	4.3 (3.9)	5.3 (4.8)*	4.6 (4.2)	4.8 (4.4)	4.5 (4.1)	5.7 (4.8)*
Cognition							
BACS composite Z score	−2.1 (1.6)	−2.3 (1.6)	−1.8 (1.6)**	−2.2 (1.6)	−1.9 (1.5)	−2.1 (1.6)	−1.9 (1.4)
Timing of symptoms and illness							
Duration untreated psychosis (weeks)	193.5 (262.2)	175.2 (244.5)	225.4 (288.6)	196.0 (260.4)	188.8 (266.4)	168.5 (237.2)	321.1 (338.4)**
Age first psychiatric illness	16.5 (6.3)	17.0 (6.3)	15.7 (6.3)	16.7 (6.4)	16.2 (6.1)	16.8 (6.2)	15.1 (6.7)*
Age first psychotic symptoms	19.2 (6.1)	19.2 (6.3)	19.06 (5.8)	19.4 (6.3)	18.6 (5.7)	19.3 (6.1)	18.5 (6.2)
Psychosocial function							
Quality of life total scale score (0–126)	52.6 (18.8)	52.3 (19.8)	53.2 (17.0)	53.4 (20.2)	51.1 (15.6)	53.0 (19.3)	51.0 (16.0)
QLS interpersonal relations (0–48)	19.8 (8.7)	19.5 (8.8)	20.2 (8.5)	20.0 (8.9)	19.3 (8.2)	19.9 (8.9)	19.1 (7.5)
QLS instrumental role (0–24)	5.6 (6.5)	5.8 (6.5)	5.1 (6.6)	6.1 (6.7)	4.5 (6.0)	5.7 (6.6)	5.0 (6.3)
QLS intrapsychic foundations (0–42)	20.8 (7.0)	20.7 (7.4)	21.1 (6.2)	20.8 (7.4)	20.8 (6.2)*	21 (7.1)	20.2 (6.5)
QLS common objects and activities (0–12)	6.5 (2.3)	6.3 (2.4)	6.8 (2.1)*	6.5 (2.3)	6.5 (2.3)	6.4 (2.3)	6.7 (2.2)
Subjective appraisals							
Mean stigma scale score (1–7)	4.0 (1.2)	3.9 (1.2)	4.2 (1.1)**	4.0 (1.2)	4.0 (1.1)	3.9 (1.2)	4.3 (1.0)**
Well-being scale mean score (1–6)	4.0 (0.8)	4.0 (0.8)	3.9 (0.8)	3.9 (0.8)	4.1 (0.8)*	4.0 (0.8)	3.9 (0.8)
Autonomy support scale mean score (1–7)	5.5 (1.2)	5.6 (1.3)	5.5 (1.1)	5.5 (1.3)	5.6 (1.1)	5.6 (1.2)	5.4 (1.2)
Medication influences and beliefs scale mean score (1–7)	4.9 (1.0)	5.0 (1.0)	4.8 (1.0)	4.9 (1.1)	4.9 (1.0)	4.9 (1.0)	4.8 (1.0)
Mental health recovery measure mean score (1–7)	4.9 (1.2)	4.9 (1.2)	4.8 (1.2)	4.8 (1.3)	5.1 (1.1)*	5.0 (1.2)	4.6 (1.3)
Global state of mental health (1–100)	62.1 (23.6)	63.9 (22.8)	59.0 (24.8)	60.7 (24.9)	64.8 (21.0)	63.2 (23.0)	56.4 (26.1)*
Global feelings about life as a whole (1–7)	4.4 (1.4)	4.5 (1.4)	4.2 (1.4)	4.3 (1.4)	4.5 (1.4)	4.4 (1.4)	4.0 (3.7)*

*p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001 Bivariate analyses indicate that group with SUD is significantly different from those without that specific SUD.
SUD = substance use disorder; PANSS = Positive and Negative Symptom Scale; BACS = Brief Assessment of Cognition in Schizophrenia.

We can speculate about several possible reasons for the different relationships found in different countries. Much of this research and discussion about whether substance use may "bring out" schizophrenia has focused on cannabis as a risk factor for earlier onset, or for developing schizophrenia outright (Evins et al., 2012). Although use of other substances in combination with cannabis has also been associated with earlier age of onset (Power et al., 2013; Stefanis et al., 2014), here we will focus on cannabis. First, it is possible that regional differences in the strength or type of available cannabis, with varying levels of THC and cannabidiol, may explain the different findings (Bhattacharyya et al., 2010; Colizzi and Bhattacharyya, 2017; Iseger and Bossong, 2015; Silva et al., 2015). Strains of cannabis available in the U.S. during the study period may have been less potent or had higher ratios of cannabidiol to THC than commonly available cannabis in Western Europe and Australia, although this is unknown. Second, early age of cannabis use and heavier use seems to contribute to onset of psychosis in vulnerable people (Di Forti et al., 2014). In cultures where cannabis use generally occurs later in adolescence, this relationship may not exist, as there is less opportunity for cannabis use to influence age of onset in vulnerable people. Lastly, methodological differences may contribute to different findings. This

Table 4
Predictors of lifetime substance use disorders (odds ratios) from generalized linear mixed models with site-level random effects.

	Alcohol abuse or dependence[a]		Cannabis abuse or dependence[a]		Other drug abuse or dependence[a]		Lifetime number of substance use disorders (0, 1, or 2+)[b]	
	OR (95% CI)	*t*	OR (95% CI)	*t*	OR (95% CI)	*t*	OR (95% CI)[c]	*t*
Female	0.53 (0.31, 0.91)	−2.33*	0.41 (0.25, 0.70)	−3.35***			0.50 (0.27, 0.91)	−2.27*
Age	1.06 (1.01, 1.11)	2.52*					1.06 (1.01, 1.12)	2.33*
White	1.31 (1.08, 1.73)	2.62**			1.82 (1.29, 2.58)	3.43***	1.50 (1.15, 1.97)	2.97**
Duration untreated psychosis[d]					2.56 (1.37, 4.77)	2.96**		
PANSS – excited factor	1.09 (1.00, 1.18)	2.01*	1.14 (1.06, 1.23)	3.42***	1.12 (1.01, 1.24)	2.23*	1.20 (1.09, 1.32)	3.84***
PANSS – positive factor					1.10 (1.02, 1.20)	2.33*		
Stigma scale	1.25 (1.03, 1.53)	2.21*						

PANSS = Positive and Negative Syndrome Scale score.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.
[a] Binary distribution.
[b] Multinomial (nominal) distribution.
[c] ORs represent > 1 substance use disorder group compared to 0 substance use disorder group in multinomial analysis.
[d] Duration in weeks using median.

American study examined the relationship using *lifetime substance use disorder as assessed by the SCID*, whereas many other studies examined the relationship using assessments of *any substance use*. This study was not designed to carefully examine past substance use over time.

Given the high prevalence of SUD in FEP, it is clear that FEP treatment programs must be prepared to address co-occurring substance use disorders in addition to psychosis. Research to date suggests that many patients with co-occurring substance use problems improve with comprehensive FEP treatment, including education about substance abuse and advice to avoid use (for review, see Wisdom et al., 2011). A small number of studies have reported mixed findings for more intensive SUD treatment in FEP (Wisdom et al., 2011).

Several study limitations and strengths warrant mention. We did not obtain a detailed lifetime history of the timing of substance use and SUD onset. We were therefore not able to examine the relationship between onset of substance use and onset of psychotic symptoms. The strengths of our study include the large, geographically diverse, national sample and the use of trained, blinded, and professional raters who implemented the gold standard SCID for SUD assessments. Given the size of the study group and the quality of the assessments, this study provides the best U. S. estimate for SUD prevalence with demographic and clinical correlates in first episode psychosis to date.

5. Conclusions

This large U.S. FEP study confirms previous findings of high SUD comorbidity, and also indicates that excitatory symptoms and mental illness stigma are important characteristics of this population that warrant attention. Clinical programs for people with FEP must be prepared to treat people not just with psychosis, depression, and cognitive deficits, but also with substance use disorders and associated PANSS excited factor symptoms (hyperactivity, mood lability, impulsivity, hostility, and uncooperativeness), as well as important concerns about stigma.

Author disclosures

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Author contributions

Kane, Addington, Brunette, Correll, Estroff, Klein, Penn, Robinson, Robinson, Rosenheck and Schooler contributed to the study design and study protocol.

Brunette and Mueser designed the secondary analysis.

Brunette and Mueser managed the literature searches.

Mueser, Rosenheck and Babbin managed the statistical approach.

Babbin conducted the statistical analyses.

Brunette wrote the first draft of the manuscript.

Brunette, Mueser, Meyer-Kalos, Cather, and Rosenheck completed the discussion section.

All authors contributed to and have approved the final manuscript.

Author conflicts of interest

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Executive Committee: John M. Kane, M.D., Delbert G. Robinson, M.D., Nina R. Schooler, Ph.D., Kim T. Mueser, Ph.D., David L. Penn, Ph.D., Robert A. Rosenheck, M.D., Jean Addington, Ph.D., Mary F. Brunette, M.D., Christoph U. Correll, M,D., Sue E. Estroff, Ph.D., Patricia Marcy, B.S.N., James Robinson, M.Ed.

NIMH Collaborators: Robert K. Heinssen, Ph.D., ABPP, Joanne B. Severe, M.S., Susan T. Azrin, Ph.D., Amy B. Goldstein, Ph.D.

Additional contributors to design and implementation of NAVIGATE: Susan Gingerich, M.S.W., Shirley M. Glynn, Ph.D., Jennifer D. Gottlieb, Ph.D., Benji T. Kurian, M.D., M.P.H.,

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