Impact of Severity of Substance Use Disorder on Symptomatic and Functional Outcome in Young Individuals With First-Episode Psychosis

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Objective: To investigate whether severity of substance use disorder is independently associated with 15-month symptomatic or functional outcome in young individuals with first-episode psychosis.

Method: Ninety-two individuals aged 15 to 30 years with first-episode psychosis participated in a 15-month prospective follow-up study. DSM-IV criteria were used to diagnose psychotic disorders, and DSM-III-R criteria were used to diagnose substance use disorder (abuse or dependence). Measures of outcome included severity of positive and negative symptoms, quality of life, and level of social functioning. Data were collected between March and July 2001 at a specialist first-episode psychosis service and between January and December 1997 at 2 generic mental health services.

Results: Multiple linear regression showed that heavy substance use disorder was significantly associated with more severe positive symptoms at 15 months after controlling for the effects of gender, duration of untreated psychosis, and medication adherence (vs. no substance use disorder, p = .006; vs. mild substance use disorder, p = .023). Heavy substance use disorder was also significantly associated with poorer social functioning at 15 months after controlling for the effects of gender, duration of untreated psychosis, medication adherence, and positive symptoms (vs. no substance use disorder, p = .025; vs. mild substance use disorder, p = .047). Heavy substance use disorder was not associated with negative symptoms or quality of life after controlling for the effects of potential confounding variables.

Conclusion: Heavy but not mild substance use disorder appears to be independently associated with poorer symptomatic and functional outcome in young patients with first-episode psychosis.

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Longitudinal studies are needed to better understand the effects of substance use disorder (SUD) on clinical and functional outcome of psychotic disorders.[1] Few longitudinal studies of at least 6 months' duration have examined whether SUD is associated with positive symptoms, negative symptoms, or social functioning in patients with psychotic disorders. Most relevant studies have reported that SUD is associated with longer time to remission of positive symptoms in first-episode psychosis[2] and shorter time to relapse and/or increased risk of relapse of positive symptoms in first-episode psychosis[3,4] and chronic psychosis.[5,6] Two studies that reported a lack of association between SUD and positive symptoms in first-episode psychosis assessed SUD at initial presentation rather than during the follow-up period.[7,8] Longitudinal studies of SUD in first-episode psychosis have found no clear evidence of an association between SUD and the severity of negative symptoms.[3,8,9] Substance use disorder has been linked with poorer social functioning in nonaffective first-episode psychosis[8] and chronic psychosis,[10] although other studies have not found an association between SUD and social functioning in first-episode[4,9] or more chronic psychosis.[11] Inadequate statistical power may have contributed to a lack of

association between SUD and social functioning in some studies.[9,11]

Relatively little information is available about whether the *severity* of SUD is associated with outcome of psychotic disorders. Linszen et al.[3] reported that patients with heavy cannabis abuse (more than once per day) were particularly prone to earlier and more frequent relapse during 12-month follow-up in 93 patients with recent-onset schizophrenia or related psychotic disorders. Further studies are required to examine the potential impact of SUD severity on symptomatic and functional outcome of recent-onset psychosis. The results of these studies are likely to assist with the development and targeting of secondary prevention efforts during the early course of psychosis.[12]

The aim of this study was to examine whether SUD severity in young patients with first-episode psychosis is independently associated with symptomatic or functional outcome at 15-month follow-up after controlling for potential confounding variables. Based on findings of previous studies, our hypotheses were that heavy SUD compared with mild and no SUD would be associated with more severe positive symptoms but not negative symptoms at 15 months.

METHOD

Participants

We have previously reported details of the study design and entry criteria as well as findings regarding the course of SUD and daily tobacco use[13] and the impact of SUD on inpatient admission and the course of positive symptoms in this sample.[14] Consecutive inpatient and outpatient admissions of individuals with first-episode psychosis were screened for the study at 3 mental health services in Melbourne, Australia. The services were the Central East Area Mental Health Service (CEAMHS), the Northern Area Mental Health Service (NAMHS), and the Early Psychosis Prevention and Intervention Centre (EPPIC). The CEAMHS and the NAMHS are generic mental health services for adults with serious mental illnesses, while EPPIC is a specialist mental health service for youth with first-episode psychosis. The services provide comprehensive services within defined catchment areas and are funded by the state government. The inclusion criteria for the study were age of 15 to 30 years, fluency in English, ability to give informed consent, and clear evidence of psychosis with a diagnosis of DSM-IV[15] schizophrenia or schizophreniform, schizoaffective, delusional, bipolar, or major depressive disorder; substance-induced or brief psychotic disorder; or psychotic disorder not otherwise specified. The exclusion criteria were psychotic disorder due to a general medical condition, severe intellectual impairment, history of brain damage or epilepsy, and more than 6 months of prior treatment for a psychotic disorder. The research and ethics committees of the North-Western Mental Health Program approved the study. Data were collected between March and July 2001 at EPPIC and between January and December 1997 at the CEAMHS and the NAMHS.

One hundred twenty-six patients (EPPIC, N = 71; CEAMHS, N = 32; NAMHS, N = 23) were recruited to the study. One hundred three (81.7%) of the 126 patients had known SUD status (yes/no) during follow-up; the remaining 23 patients had missing data due to not being contactable at 9 and/or 15 months. Ninety-two (89.3%) of the 103 patients with known SUD status (yes/no) had complete clinical ratings at baseline and 3 and 15 months and an estimate of medication adherence during follow-up. These 92 subjects comprised the study sample on which the current analyses were based.

Measures

An updated version of the Royal Park Multidiagnostic Instrument for Psychoses[16] was used to diagnose DSM-IV[15] psychotic disorders and to estimate the duration of untreated psychosis (DUP) in days, defined as the time from onset of psychotic symptoms to service entry. The Chemical Use, Abuse, and Dependence Scale (CUAD)[17] was used to diagnose DSM-III-R[18] SUD (criteria met for abuse or dependence). An advantage of this measure is that it also provides an estimate of an individual's overall severity of substance use. The CUAD is a reliable and valid measure of SUD and severity of substance use among individuals with serious mental illness.[17,19] Other measures used were the Brief Psychiatric Rating Scale (BPRS),[20] the Scale for the Assessment of Negative Symptoms (SANS),[21] the Quality of Life Scale (QLS),[22] the Social and Occupational Functioning Assessment Scale (SOFAS),[23] and a 4-point scale to rate medication adherence: 1 for 0%–24% adherence (no or irregular adherence), 2 for 25%–49% adherence (rather irregular adherence), 3 for 50%–74% adherence (rather regular adherence), and 4 for 75%–100% adherence (regular adherence).

Procedure

A baseline assessment was completed at entry to treatment, and follow-up assessments were undertaken at 3, 9, and 15 months following the initial assessment. Semistructured interviews using the Royal Park Multidiagnostic Instrument for Psychoses were completed at baseline and 3 months. Psychotic disorder diagnoses were subsequently categorized as schizophrenia-spectrum psychosis (schizophrenia or schizophreniform, schizoaffective, or delusional disorder) or other psychosis (bipolar, major depressive disorder, not otherwise specified, substance-induced, or brief).

The CUAD was administered at 9 months (for the interval between baseline and 9 months) and 15 months (for the interval between 9 and 15 months) to assess for

the presence of SUD (abuse or dependence) during the 15-month follow-up period. Substances assessed included alcohol, amphetamine, benzodiazepine, cannabis, cocaine, hallucinogen, inhalant, opioid, and phencyclidine (PCP). Diagnoses of SUD are based on 17 items rated true or false for each substance. Each item corresponds to a criterion of DSM-III-R substance abuse or dependence. Individual substance use severity scores are based on weighted scores from 1 to 4 for the items rated true for each substance. For example, item 1 assesses whether the individual often takes the substance in larger amounts or more often than intended. A rating of true for this item receives a score of 1. Item 16 assesses whether the individual experiences characteristic physical or psychological withdrawal symptoms. A rating of true for this item receives a score of 4. The sum of individual substance use severity scores provides a total substance use severity score for all substances used. The higher total substance use severity score at the 9- or 15-month time-point was used to calculate the total substance use severity score during the follow-up period. Substance use disorder severity during 15-month follow-up was categorized as heavy, mild, or no SUD. The distinction between heavy versus mild SUD was based on a median split of CUAD total substance use severity scores for the 55 (of 103) patients with SUD during follow-up; 48 of the 55 patients had complete clinical ratings and an estimate of medication adherence and comprised the patients with SUD included in the main analyses.

The BPRS, SANS, and SOFAS were administered at baseline and 3, 9, and 15 months. The sum of the BPRS psychotic subscale items (hallucinations, conceptual disorganization, unusual thought content, and suspiciousness) measured the severity of positive psychotic symptoms. The sum of the 5 SANS global severity items measured the severity of negative psychotic symptoms. The QLS was administered at 3, 9, and 15 months. Medication adherence was assessed at 3 months (for the interval between baseline and 3 months), 9 months (for the interval between 3 months and 9 months), and 15 months (for the interval between 9 and 15 months). Medication adherence ratings were subsequently recoded to denote adherence (a score of 4; 75%–100% adherence) or nonadherence (a score of 3 or less; 0%–74% adherence). Medication nonadherence during follow-up was defined as the presence of a score less than 4 at 3, 9, or 15 months. All diagnostic and clinical assessments were based on patient interviews supplemented by information derived from informants (family members and/or clinicians) and a review of medical records.

Experienced raters received training in administering the assessment instruments by senior research assistants prior to commencement of the study. We have previously reported excellent agreement between research and file-based diagnoses for patients involved in this study.[24] Interrater agreement on the 4 BPRS psychotic subscale items, 5 SANS global severity items, and the SOFAS was assessed by comparing ratings made by the first author (D.W.) and a second rater on 5 cases. Agreement was defined as the percentage of items that were rated within 1 point by both raters on the 4 BPRS psychotic subscale items and 5 SANS global severity items and the percentage of ratings within 10 points by both raters on the SOFAS. A minimum of 92% agreement was achieved on the 4 BPRS psychotic subscale items (95.0%; 19/20), 5 SANS global severity items (92.00%; 23/25), and the SOFAS (100%; 5/5).

Data Analyses

Assessment of differences at baseline between patients with heavy SUD, mild SUD, and no SUD on nominally measured variables was undertaken by cross-tabulating the data and performing Pearson χ^2 tests of independence, with exact tests used where appropriate. Group differences on continuous variables were assessed using independent samples t tests, and for more than 2 groups, 1-way analysis of variance was performed. The Tukey honestly significant difference post hoc test was used to isolate specific group differences when a statistically significant omnibus F test was obtained. The nonparametric Mann-Whitney U test or the Kruskal-Wallis test for multiple groups was employed for data that were substantially positively skewed. A series of multiple linear regression analyses were performed to examine predictors of BPRS-PS, SANS total, QLS total, and SOFAS at 15 months. Substance use disorder severity was coded into 3 dummy variables representing heavy SUD, mild SUD, and no SUD, with no SUD specified as the reference category. Demographic and clinical variables associated with SUD severity in univariate analyses at a significance level at or below the .10 probability level were also entered into each regression model simultaneously. All statistical tests were 2-tailed and results regarded as statistically significant at or below the .05 probability level. Analyses were undertaken using SPSS for Windows (version 12.0.2).

RESULTS

Sample

The mean age of the 92 patients was 21.5 (SD = 3.4) years. The patients were predominantly male (70.7%) and single (90.2%), and approximately one third (32.6%) of the patients had completed secondary school. The majority of patients were diagnosed with schizophrenia-spectrum psychoses (75.0%). Patients were grouped on the basis of SUD severity during follow-up as follows: heavy SUD (N = 21), mild SUD (N = 27), and no SUD (N = 44).

Comparisons were undertaken between patients included in the current analyses (N = 92) and those with

Table 1. Ratings of BPRS-PS, SANS Total, QLS Total, SOFAS, and Medication Adherence at Baseline and During Follow-Up for Patients With Heavy, Mild, and No Substance Use Disorder (SUD)

	Heavy SUD (N = 21)			Mild SUD (N = 27)			No SUD (N = 44)			
Rating	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	p
BPRS-PS										
Baseline	17.9	4.9	19.0	16.9	3.9	16.0	16.8	3.8	16.0	.580
3 mo	7.8	4.6	6.0	7.4	4.4	7.0	6.1	2.6	5.0	.417[a]
15 mo	8.6	5.1	7.0	5.7	3.0	4.0	5.0	2.2	4.0	.001[a,b]
SANS total										
Baseline	10.3	5.2	11.0	8.9	4.1	8.0	9.9	4.8	10.0	.512
3 mo	9.0	4.7	8.0	7.8	3.8	8.0	8.0	5.3	8.0	.639
15 mo	7.7	4.6	7.0	3.7	3.9	2.0	4.5	5.1	3.0	.005[a,c]
QLS total										
3 mo	66.6	22.2	67.0	69.9	21.7	68.0	72.8	26.4	73.3	.618
15 mo	72.1	22.8	72.0	90.1	23.3	92.0	92.1	25.7	97.0	.008[d]
SOFAS										
Baseline	43.4	14.2	45.0	44.6	9.0	45.0	40.0	13.2	35.0	.281
3 mo	55.1	10.4	55.0	59.3	12.2	60.0	60.8	14.1	60.0	.253
15 mo	54.4	15.8	50.0	69.2	14.0	70.0	73.9	15.3	77.5	< .001[e]
	%	N		%	N		%	N		
Medication nonadherence[f]	76.2	16		81.5	22		43.2	19		.002

[a]Kruskal-Wallis test.
[b]Mann-Whitney U test post hoc comparisons between patient groups on BPRS-PS scores at 15 months: heavy SUD versus mild SUD (p = .020); heavy SUD versus no SUD (p < .001); mild SUD versus no SUD (p = .160).
[c]Mann-Whitney U test post hoc comparisons between patient groups on SANS total scores at 15 months: heavy SUD versus mild SUD (p = .002); heavy SUD versus no SUD (p = .006); mild SUD versus no SUD (p = .962).
[d]Tukey honestly significant difference (HSD) test post hoc comparisons between patient groups on QLS total scores at 15 months: heavy SUD versus mild SUD (p = .034); heavy SUD versus no SUD (p = .007); mild SUD versus no SUD (p = .940).
[e]Tukey HSD test post hoc comparisons between patient groups on SOFAS scores at 15 months: heavy SUD versus mild SUD (p = .003); heavy SUD versus no SUD (p < .001); mild SUD versus no SUD (p = .402).
[f]Medication nonadherence was defined as the presence of less than regular adherence (a score less than 4) at any time during follow-up.
Abbreviations: BPRS-PS = Brief Psychiatric Rating Scale psychotic subscale, QLS = Quality of Life Scale, SANS = Scale for the Assessment of Negative Symptoms, SOFAS = Social and Occupational Functioning Assessment Scale.

missing outcome or SUD data (N = 34) on demographic and clinical variables at baseline. No significant between-group differences were found on gender, age, marital status, education level, employment status, psychotic disorder diagnosis, DUP, any lifetime SUD at baseline, or mental health service (CEAMHS, NAMHS, or EPPIC). Moreover, no significant between-group differences were found on BPRS-PS, SANS total, or SOFAS scores at baseline.

Heavy Versus Mild Substance Use Disorder During Follow-Up

The mean CUAD total substance use severity score for patients with heavy SUD was 20.2 (SD = 4.3; median = 20.0; range, 14–29) compared to 6.7 (SD = 4.0; median = 6.0; range, 1–13) for patients with mild SUD ($t = -11.30$, $df = 46$, $p < .001$). Patients with heavy SUD compared to patients with mild SUD were significantly more likely to meet criteria for cannabis use disorder (95.2% [20/21] vs. 63.0% [17/27]; exact p = .013) and polysubstance use disorder (76.2% [16/21] vs. 38.5% [10/26]; $\chi^2 = 6.69$, $df = 1$, $p = .010$). The majority (N = 23; 88.5%) of the 26 patients with polysubstance use disorder met criteria for cannabis use disorder (15/16 patients with heavy SUD and 8/10 patients with mild SUD). No between-group differences were found for alcohol use disorder (57.1% [12/21] vs. 57.7% [15/26]; p = .970) or other SUD (40.0% [8/20] vs. 23.1% [6/26]; p = .216). The varying number of patients with SUD for these analyses (N = 46–48) was due to missing data on individual SUDs.

Baseline Demographic and Clinical Correlates of Substance Use Disorder Severity

Patients with heavy, mild, and no SUD were compared on a range of demographic and clinical characteristics at baseline. Substance use disorder severity was significantly associated with gender ($\chi^2 = 14.38$, $df = 2$, $p = .001$); patients with heavy SUD were more likely to be male (100%) compared to patients with no SUD (54.5%). No significant associations were found between SUD severity and age (p = .361), marital status (p = .165), education level (p = .197), employment status (p = .374), psychotic disorder diagnosis (p = .609), DUP (p = .054), BPRS-PS (p = .580), SANS total (p = .512), or SOFAS (p = .281).

Clinical Correlates of Substance Use Disorder Severity at Baseline and 3 and 15 Months

Comparisons were undertaken between patients with heavy SUD, mild SUD, and no SUD on the following measures: BPRS-PS, SANS total, and SOFAS at baseline, 3 months, and 15 months; QLS total at 3 and 15 months; and a rating of medication adherence during follow-up (Table 1). Patients with heavy SUD had significantly more severe positive symptoms (higher BPRS-PS scores) and

Table 2. Summary of Regression Models for Predictors of BPRS-PS, SANS Total, QLS Total, and SOFAS at 15-Month Follow-Up (N = 92)

Dependent Variable	Independent Variables	B	β	p	Adjusted R^2
BPRS-PS[a,b]	No SUD[c]	–0.131	–0.351	.006	
	Mild SUD[c]	–0.110	–0.266	.023	
	Male gender	0.047	0.114	.234	
	DUP[a]	0.106	0.400	< .001	
	Nonadherent with medication	0.028	0.074	.433	0.320
SANS total	No SUD[c]	–1.195	–0.124	.379	
	Mild SUD[c]	–2.842	–0.268	.041	
	Male gender	2.396	0.226	.035	
	DUP[a]	1.256	0.187	.066	
	Nonadherent with medication	1.403	0.141	.180	0.151
QLS total	No SUD[c]	10.043	0.198	.161	
	Mild SUD[c]	12.798	0.230	.079	
	Male gender	–10.449	–0.189	.078	
	DUP[a]	–6.126	–0.174	.088	
	Nonadherent with medication	–9.316	–0.178	.092	0.149
SOFAS	No SUD[c]	14.382	0.431	.002	
	Mild SUD[c]	12.016	0.328	.010	
	Male gender	–6.258	–0.171	.095	
	DUP[a]	–2.614	–0.113	.245	
	Nonadherent with medication	–4.028	–0.117	.244	0.221

[a]Log-transformed due to positive skewness.
[b]N = 91 due to 1 case excluded as an outlier.
[c]Reference group is heavy SUD.
Abbreviations: BPRS-PS = Brief Psychiatric Rating Scale psychotic subscale, DUP = duration of untreated psychosis, QLS = Quality of Life Scale, SANS = Scale for the Assessment of Negative Symptoms, SOFAS = Social and Occupational Functioning Assessment Scale, SUD = substance use disorder.

negative symptoms (higher SANS total scores) and also significantly poorer quality of life (lower QLS total scores) and social functioning (lower SOFAS scores) at 15 months compared to patients with mild SUD and no SUD. Substance use disorder severity was significantly associated with medication adherence ($\chi^2 = 12.75$, df = 2, p = .002); patients with mild SUD were more likely to be noncompliant with medication (81.5%) compared to patients with no SUD (43.2%). No other significant between-group differences were identified.

A series of multiple regression analyses were undertaken to assess whether heavy SUD was significantly associated with 15-month outcome after controlling for the effects of gender, DUP, and medication adherence (Table 2). Heavy SUD remained significantly associated with more severe positive symptoms and poorer social functioning compared with mild SUD and no SUD after adjusting for the effects of these potential confounding variables. Heavy SUD remained significantly associated with more severe negative symptoms compared with mild SUD, although heavy SUD was not significantly associated with negative symptoms compared with no SUD. Heavy SUD was not significantly associated with quality of life compared with mild SUD and no SUD. Regarding the effects of the other predictors of outcome, longer DUP was significantly associated with more severe positive symptoms and male gender was significantly associated with more severe negative symptoms at 15 months.

To exclude the possibility that the associations between heavy SUD and negative symptoms and social functioning were confounded by positive symptoms, secondary analyses were undertaken to assess whether heavy SUD was associated with SANS total and SOFAS at 15 months after controlling for the effects of 15-month BPRS-PS in addition to gender, DUP, and medication adherence. Heavy SUD was no longer significantly associated with 15-month SANS total compared with mild SUD (B = –2.224, β = –0.220, p = .086) and was not significantly associated with 15-month SANS total compared with no SUD (B = –0.506, β = –0.055, p = .697; N = 91 due to exclusion of 1 case as an outlier). Heavy SUD remained significantly associated with 15-month SOFAS compared with mild SUD (B = 8.932, β = 0.244, p = .047) and no SUD (B = 10.199, β = 0.305, p = .025). The unstandardized β coefficients (B) indicate that on average patients with heavy SUD had a SOFAS score that was almost 9 points lower than patients with mild SUD and 10 points lower than patients with no SUD after adjusting for the effects of 15-month BPRS-PS, gender, DUP, and medication adherence. Regarding the effects of 15-month BPRS-PS, more severe positive symptoms were significantly associated with 15-month SANS total (p = .004) and SOFAS (p = .003).

To determine whether the associations between heavy SUD and 15-month outcome variables held true for only patients with schizophrenia-spectrum disorders, the

multiple regression analyses undertaken were repeated for this diagnostic group. Patients with schizophrenia-spectrum disorders (N = 69) were grouped as follows: heavy (N = 17), mild (N = 21), and no SUD (N = 31). After adjusting for the effects of gender, age, DUP, and medication adherence, the pattern of associations between heavy SUD and BPRS-PS, SANS total, QLS total, and SOFAS was similar to the previous findings for all patients (N = 92) except that the association between heavy SUD and positive symptoms compared with mild SUD was no longer statistically significant (B = –0.110, β = –0.243, p = .085). After adjusting for the effects of gender, age, DUP, medication adherence, and 15-month BPRS-PS, the only difference in the pattern of associations between heavy SUD and SANS total and SOFAS was that the association between heavy SUD and social functioning compared with no SUD was no longer statistically significant (B = 9.091, β = 0.263, p = .091). These nonsignificant findings were probably due to inadequate statistical power given that the unstandardized β coefficients are similar in size to those found when all patients were included in the analyses.

The use of a median split to collapse a continuous variable into groups is potentially problematic. To address this issue, the original multiple regression analyses were repeated using the upper and lower quartiles (rather than a median split) of the total substance use severity scores to form the heavy SUD (N = 11) and mild SUD (N = 15) groups. The 44 subjects with no SUD remained the same, leaving 70 patients included in the analyses. The use of quartiles to form the heavy and mild SUD groups had little effect on the results of multiple regression analyses despite inclusion of fewer patients and reduced statistical power. After adjusting for the effects of gender, age, DUP, and medication adherence, the pattern of associations between heavy SUD and BPRS-PS, SANS total, QLS total, and SOFAS was similar to the original results except that the association between heavy SUD and negative symptoms compared with mild SUD was no longer statistically significant (B = –2.572, β = –0.217, p = .187). After adjusting for the effects of gender, age, DUP, medication adherence, and 15-month BPRS-PS, the only difference in the pattern of associations between heavy SUD and SANS total and SOFAS was that the association between heavy SUD and social functioning compared with mild SUD just failed to reach statistical significance (B = 12.066, β = 0.303, p = .051). These results are consistent with the original findings and support the robustness of those findings.

DISCUSSION

The aim of this study was to examine whether SUD severity in patients with first-episode psychosis is independently associated with symptomatic or functional outcome at 15-month follow-up. Multivariate analyses showed that heavy SUD was independently associated with positive symptoms and social functioning but not negative symptoms or quality of life at 15 months after controlling for potential confounding variables. The findings support the hypotheses that heavy SUD compared with mild and no SUD is associated with more severe positive symptoms but not negative symptoms at 15 months.

The finding that heavy SUD was independently associated with more severe positive symptoms at 15 months is consistent with a previous study that reported that patients with more than daily cannabis use and recent-onset psychosis were more prone to relapse of positive symptoms.[3] The finding also provides further evidence for a link between SUD and positive symptoms in patients with psychotic disorders.[2–6] The association between SUD and positive symptoms may be due to neurobiological effects of substance use on dopaminergic mechanisms,[25] although other explanations are possible. First, patients may engage in substance abuse to cope with distressing positive symptoms. However, the onset of substance use precedes the onset of positive symptoms in most relevant cases,[26] which tends not to support the self-medication hypothesis for positive symptoms. Second, a common factor such as personality traits or life stressors may be associated with both SUD and more severe positive symptoms.

The finding of an independent association between heavy SUD and poorer social functioning at 15 months extends previous reports from longitudinal studies of an association between SUD and social functioning in patients with psychotic disorders.[8,10] The association between heavy but not mild SUD and poorer social functioning may help to explain inconsistent findings of previous studies that have examined SUD and social functioning. That is, categorizing patients as "substance abusers" irrespective of the severity of SUD may reduce the likelihood of identifying a link between SUD and social functioning. However, other methodological factors may also be relevant. For example, the use of categorical measures of social functioning such as independent living and regular employment[4] may not be sufficiently sensitive to the range of interpersonal and social problems associated with comorbid SUD and psychotic disorders.[27]

Patients with heavy SUD also had more severe negative symptoms and poorer quality of life at 15 months compared to patients with mild SUD and no SUD. However, heavy SUD was not associated with negative symptoms or quality of life after the effects of potential confounding variables were taken into account. The lack of an independent association between SUD and negative symptoms is consistent with other prospective studies that have found no clear association between SUD and

negative symptoms in first-episode or recent-onset psychosis.[3,9,11] The similar pattern of findings between SUD and both negative symptoms and quality of life probably reflects the sensitivity of the QLS to deficit or enduring negative symptoms of schizophrenia.[22]

By definition, patients with mild SUD had substance-related problems. However, mild SUD did not appear to be associated with symptomatic or functional outcome of first-episode psychosis. The findings suggest that patients with mild SUD are less likely to experience adverse effects of substance use on symptomatic or functional outcome compared to patients with heavy SUD. Similarly, a previous study of recent-onset psychosis found that patients with mild cannabis abuse were less prone to relapse compared to patients with heavy cannabis abuse.[3] These findings provide indirect support for therapeutic interventions that promote harm-minimization in patients with comorbid SUD and recent-onset psychosis,[28] although further controlled trials of treatment interventions are necessary to examine potential benefits of reductions in the severity of SUD in first-episode psychosis.

The study has several limitations. First, complete follow-up data for the current analyses were only available for 92 (73.0%) of the 126 patients recruited to the study. Hence, sample bias may have affected the results despite the finding that patients included and not included in the current analyses had similar baseline demographic and clinical characteristics. Second, analysis of the independent effects of different types of SUD on outcome was not possible given that most patients with heavy SUD engaged in abuse of cannabis as well as alcohol and/or other substances. Nevertheless, it seems reasonable to conclude that cannabis is implicated in the adverse effects of heavy SUD given that (1) almost all (20/21) patients with heavy SUD met criteria for cannabis use disorder, (2) patients with heavy SUD had a higher rate of cannabis use disorder than patients with mild SUD, and (3) other studies[3,5] have also demonstrated a link between cannabis use and poor clinical outcome. Third, it would have been desirable to have undertaken urine drug screens or other biomedical tests to confirm substance use. Fourth, it was not possible to use intraclass correlation coefficients to establish interrater agreement because of the small sample size (N = 5) of interrater reliability data.

There were a number of strengths of the study. First, the study analyzed the effects of SUD present during the follow-up period rather than at initial presentation. Second, SUD was assessed using a structured instrument combined with data collection from multiple sources. Third, standardized instruments were used to assess symptomatic and functional outcome. Fourth, multivariate analyses were used to examine whether SUD severity was independently associated with 15-month outcome.

In conclusion, heavy but not mild SUD is independently associated with poorer symptomatic and functional outcome for patients treated for first-episode psychosis. Patients with more severe SUD during treatment for first-episode psychosis appear to be most in need of therapeutic interventions that seek to reduce the adverse impact of comorbid SUD and psychosis.

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Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Childhood and Adolescent Mental Health section. Please contact Melissa P. DelBello, M.D., at delbelmp@email.uc.edu.