

## RESEARCH ARTICLE

# Problematic Substance Use in Adolescent Psychiatric Inpatients: Rates, Clinical Correlates and Effects on Therapeutic Outcomes

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**Abstract:** *Aims:* We aimed to document the clinical rates and correlates of problematic substance use among adolescent inpatients.

*Background:* Adolescents referred to psychiatric inpatient care are likely to present family and social risk factors making them at high risk of substance use disorder.

*Objective:* The objective of this study is to document the rates, clinical correlates, and effects of associated problematic substance use on therapeutic outcomes in adolescents referred to psychiatric inpatient care.

*Method:* The DEP-ADO questionnaire was used to systematically screen out problematic substance use in two 12-18 adolescent inpatient units between January 2017 to December 2018. Inpatients who were screened positively based on the DEP-ADO questionnaire and/or information gathered from repeated interviews with the youths and their families were reported to the liaison addiction unit for diagnosis. The chart-review procedure was used to document clinical correlates (*i.e.*, suicidal behavior, DSM-5 psychiatric diagnoses, the Clinical Global Impression-Severity score) and therapeutic outcomes (*i.e.*, the Clinical Global Impression-Improvement score, change in Children-Global Assessment Scale score during patients' stay and length of stay).

*Result:* Over two years, 150 adolescents completed the DEP-ADO questionnaire (Mean Age = 14.7 ± 1.7; 42% girls). Thirty percent of adolescent inpatients reported some type of problematic substance use, with a higher likelihood of daily tobacco use (*OR*=2.4), regular cannabis use (*OR*=2.3), and occasional opioid/heroin use (*OR*=9.8) compared to the general population. Adolescent inpatients who misused illegal substances prior to admission were 2.5 times more likely to report suicidal behaviors. A strong association was reported between binge drinking behavior and a discharge diagnosis of bipolar disorder (*OR*=11.0). Therapeutic outcomes were not statistically different with regards to alcohol or illicit substance use status.

*Conclusion:* Inpatient adolescents were at high risk of having associated problematic substance use. Patients with co-existing problematic substance use seem to have more severe and chronic forms of mood disturbances, although the response rate to therapeutics provided during their stay was not found to be lower compared to their counterparts without problematic substance use.

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## 1. INTRODUCTION

Adolescence is a critical lifetime period for the emergence of mental health and substance-related

problems. It is estimated that almost half of all psychiatric disorders are initiated before the age of 14 (Kessler *et al.*, 2005), and over 90% of adults with substance use disorder (SUD) begin alcohol and/or substance use during adolescence (CASA, 2011). The association with psychiatric symptoms is a norm in adolescents who abuse substances, with 61% to 88% of those with SUD

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matching criteria for at least one non-substance-related psychiatric disorder (Deas, 2006). Among the multiple reasons that could explain this coexistence, one may mention overlapping risk factors, shared developmental factors, or direct causal relationships (Lewis, 2020).

On average, youths with a characterized psychiatric disorder have an earlier initiation of substance, an independent predictor for the development of a problematic pattern of use (Vourakis, 2005). A higher likelihood of relapse after interventions for substance misuse is observed in adolescents with dual disorders than those without an associated psychiatric disorder (Armstrong & Costello, 2002; Grella, Hser, Joshi, & Rounds-Bryant, 2001). In turn, trying or regularly using alcohol or illegal substances have negative effects on the natural course of many mental health problems, with robust evidence for the links between cannabis use and psychotic disorders (Toftdahl, Nordentoft, & Hjorthøj, 2016), alcohol use and mood disorders (Brière, Fallu, Descheneaux, & Janosz, 2011; Fasteau, Mackay, Smith, & Meyer, 2017), or opioid use and borderline personality disorder or post-traumatic stress disorder (Edlund *et al.*, 2015; Subramaniam, Stitzer, Woody, Fishman, & Kolodner, 2009). Among the participants of the Treatment of Resistant Depression in Adolescents (TORDIA) study, a randomized controlled trial (RCT) comparing the effectiveness of antidepressant alone or in combination with psychotherapy for resistant depression, a greater impairment associated with substance use in participants was associated with a lower response rate to antidepressants (Asarnow *et al.*, 2009) and a lower remission rate at week 24 (Emslie *et al.*, 2010).

Findings regarding the rates and clinical correlates of adolescent psychiatric inpatients with problematic substance use are scarce (Table 1). The rate of alcohol/illegal SUD ranges from 17% to 50% in this population (Daudin *et al.*, 2010; Deas-Nesmith, Campbell, & Brady, 1998; Grilo *et al.*, 1995; Niethammer & Frank, 2007; M. F. Weaver *et al.*, 2007). As psychiatric symptoms stay in the foreground during the hospitalization, or because the adolescent may not feel

comfortable discussing substance use during interviews, or simply because the inpatient had no access to illegal substances, the clinical rate for problematic substance use may somewhat be underestimated (Niethammer & Frank, 2007). In the study conducted by M. F. Weaver *et al.* (2007), the site using a standardized screening procedure for SUD reported a prevalence twice higher than the site where a non-structured clinical interview was conducted. In practice, the lack of identification of problematic substance use represents a missed therapeutic opportunity as effective interventions for SUD do exist for adolescents (Brown *et al.*, 2015; Brown *et al.*, 2003).

Most studies have shown that hospitalized adolescents with substance misuse do not significantly differ from other inpatients in terms of psychiatric diagnosis, at the exception of a higher comorbidity rate of disruptive behavioral disorder (Daudin *et al.*, 2010; Deas-Nesmith *et al.*, 1998; Grilo *et al.*, 1995; M. F. Weaver *et al.*, 2007). Several studies have reported an association between substance use and suicidal behaviors in inpatients (Daudin *et al.*, 2010) or with borderline personality traits by definition associated with a higher propensity to engage in self-aggressive behaviors (Daudin *et al.*, 2010; Grilo *et al.*, 1995). Most authors have also noted a significant burden of psychosocial factors such as physical or sexual trauma (Daudin *et al.*, 2010; Deas-Nesmith *et al.*, 1998), sexual risky behaviors (T. Weaver *et al.*, 2003), or legal involvement (T. Weaver *et al.*, 2003) among adolescent inpatients who misuse substances.

A further important gap in the literature is whether the co-existing of substance misuse in adolescent inpatients moderates the effectiveness of the treatment provided for anxiety, depressive disorders, or suicidal behaviors during their stay. Secondary analyses of RCT showed that adolescents with associated substance use impairments had, on average, a reduced response rate to antidepressants (Asarnow *et al.*, 2009; Emslie *et al.*, 2010). However, analyses of data from clinical trials provide no clue on why these treatments are less effective in this group of patients. If the moderators of the response rate

Table 1. Previous studies measuring the rate of substance use in adolescents hospitalized for psychiatric care.

Authors	Design	Sample	Assessments	Frequencies/ Profile of Substance	Profile of Substance Users	Impact on Response to Treatment
Grilo, <i>et al.</i> [15]	Cross-sectional	N=138 University hospital (1 site) 55% male Age 15.5 ±1.4 [12-18]	SADS-SACE GAF	50% alcohol and/or illegal SUD <u>Substances:</u> NR	Positive association with DBD, borderline personality disorder. Negative association with anxiety disorder. No difference in overall functioning	NR
Deas-Nesmith, Campbell, and Brady [16]	Cross-sectional	N=100 University hospital (1 site) 45% male Age = 15.0 ±1.0 [13-17]	SCID-R PESQ, urine analysis	33% alcohol and/or illegal SUD <u>Substances:</u> Alcohol (88%), cocaine (9%), marijuana (27%), inhalants (9%), multiple (45%)	No difference in terms of Axis I or axis II diagnoses. 60% have physical or sexual trauma or family history of substance use, no difference was found	Fewer past medical hospitalizations among non-users, no difference for psychiatric hospitalization
Weaver, <i>et al.</i> [17]	Retrospective chart review	N=636 (2 sites) 49% male Age= NR [12-17] Exclusion of ID, PDD	No standardized assessment	16-39% alcohol and/or illegal SUD <u>Substances:</u> Alcohol (18%), marijuana (9%), multiple (3%)	Positive association with DBD, mood disorder (1 site). Association with age, legal involvement, sexual activity, family history of substance use	NR
Niethammer and Frank [18]	Case series	N=70 University hospital (1 site) 44% male Age [14-17] Exclusion of acute psychosis, IQ < 70, stayed in the hospital <36 h, repeated hospitalizations	Adaptation of the WHO-CIDI	37% alcohol and/or illegal SUD <u>Substances:</u> Nicotine (50%), alcohol (29%), illegal substance (26%)	Mainly diagnosed with adjustment disorder, conduct disorder, or personality disorder, but no comparison with non-users	NR

(Table 1) contd....

Authors	Design	Sample	Assessments	Frequencies/ Profile of Substance	Profile of Substance Users	Impact on Response to Treatment
Daudin, <i>et al.</i> [19]	Case-control study	N=60 (30 confirmed case vs. 30 controls) University hospital (1 site) 53% male Age= 15.82 ±1.0 [14-17]	RECAP index abDIB CGAS	Among substance users: tobacco (93%), cannabis (70%), alcohol (60%), MDMA (23%), cocaine (17%), LSD (10%), amphetamine (10%), solvents (3%)	Positive association with suicide attempts, conduct disorder, borderline personality disorder impulsivity, affect dysregulation, and interpersonal relationship. No difference in terms of other Axis I diagnose Association with maltreatment, loss of a first-degree relative, school absenteeism	No difference in terms of length of stay, functional improvement during the stay and past psychiatric hospitalization
Brown, <i>et al.</i> [21]	RCT to test the impact of 2 sessions of motivational interviewing	N=151 Private psychiatric hospital (2 sites) 35% male Age 15.85 ±4.0 [13-17]	K-SADS-PL TLFB APUS YSR	Among substance users: alcohol (73%), cannabis (95%), stimulants (19%), sedatives/anxiolytics (14%), cocaine (19%), opioid (18%), PCP (1%), hallucinogen (8%), solvents/inhalants (6%)	Mainly diagnosed with depressive disorder, conduct disorder, or PTSD, ADHD, GAD, but no comparison with non-users	NR

Note: SACE: Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic Version, GAF: Global Assessment of Functioning, NR: Not Reported, SCID-R: Structured Clinical Interview for DSM III-R, PESQ: Personal Experience Screening Questionnaire, WHO-CIDI: WHO-composite international diagnostic interview, K-SADS-PL: Kiddie Schedule for Affective Disorders and Schizophrenia-*Present and Lifetime*, TLFB: Timeline Followback, ADUS: Adolescent Problem Use Scale.

were mostly environmentally-mediated (*e.g.*, low parental support, poor observance) in adolescents with problematic substances, these factors should be at least partially controlled during a full-time hospitalization. This is therefore expected that the clinical response to the therapeutics provided during the stay of adolescent inpatients should be roughly comparable with regards to the occurrence of substance use problems. The only study comparing the therapeutic outcomes of adolescent inpatients depending on substance use problems found no difference in terms of duration of stay and improvement in overall functioning between those with or without SUD (Daudin *et al.*, 2010). If confirmed, these results would

inform discussion about the opportunity offered by full-time hospitalization in providing integrative care for adolescents suffering from dual disorders.

In the efforts to promote better integrated care for adolescent inpatients with substance-related problems, a systematic screening of substance use problems was set up at admission and during the stay of adolescent inpatients in the adolescent psychiatric units of a university hospital. The first aim of this study was to determine the clinical rates of problematic substance use in adolescents referred to two psychiatric inpatient units at a large urban university hospital. The DEP-ADO questionnaire (Germain *et al.*, 2007) was

systematically used at admission to document substance use in the last twelve months alongside routine assessment at admission. The diagnosis of SUD was confirmed after several interviews with an addiction-liaison psychologist in adolescents positively screened with the DEP-ADO or based on information provided by the main clinician. The rates of problematic substance use were compared to data from a large community-based survey EnCLASS (a French acronym for *National Study on Health behavior and Substance use in Highschool*) conducted in 2018 involving a representative sample of more than 20,000 French adolescents (Spilka *et al.*, 2019). We hypothesized that the rates of regular alcohol use, regular cannabis use, and experimentation with other illegal substances would be higher in adolescents than the general population, in line with previous findings (Brown *et al.*, 2003; Daudin *et al.*, 2010; Deas-Nesmith *et al.*, 1998; Grilo *et al.*, 1995; Niethammer & Frank, 2007; M. F. Weaver *et al.*, 2007).

The second aim of this study was to determine the correlates of problematic substance use. Correlates and outcomes were gathered from clinical management data collected from routine clinical care using chart-review procedure. To describe the features of adolescent inpatients with problematic substance use, three different subgroups were differentiated among substance users: regular alcohol use, binge drinking, and illegal substance use. We hypothesized that adolescent inpatients with substance-related problems would have distinct correlations than those without substance-related problems. In line with previous reports conducted on outpatient (Gårdvik, Rygg, Torgersen, Lydersen, & Indredavik, 2020), emergency (McDonnell, Hsiao, Russo, Pasic, & Ries, 2011), and inpatient samples (Daudin *et al.*, 2010; Deas-Nesmith *et al.*, 1998; Grilo *et al.*, 1995; Niethammer & Frank, 2007; M. F. Weaver *et al.*, 2007), we expected that substance users would differ from other patients in terms of clinical severity (lower overall functioning and higher clinical severity at baseline, more suicidal behaviors). We also expected to confirm the association between substance use and psychosocial factors such as

academic difficulties or family dysfunction (McDonnell *et al.*, 2011; Niethammer & Frank, 2007; M. F. Weaver *et al.*, 2007). Finally, we also examined how the association of substance use affects therapeutic outcomes during the hospitalizations estimated using proxy measures such as clinical improvement, changes in overall functioning, and duration of stay.

## 2. METHODS

### 2.1. Setting and Study Design

The DEP-ADO questionnaire had been included within the routine clinical assessment of all new patients referred to two adolescent inpatient units at a university hospital since January 2017. We decided to examine the rate and clinical correlates of problematic substance use between January 2017 and December 2018. In addition to the DEP-ADO questionnaire, two researchers retrospectively extracted information for all consecutive patients based on the available clinical and paramedical charts during the study period using a 66-item computerized questionnaire. The data collected encompassed (i) socio-demographic characteristics (3 items), (ii) clinical characteristics, including the discharge psychiatric diagnoses among a list of the 16 most frequently used categories (27 items), (iii) symptom severity, level of functioning, and treatment response based on the systematic use of a standardized questionnaire (described below) (9 items), (iv) developmental history and associated medical conditions (18 items), (v) school functioning and psychosocial factors (9 items). Each patient's information was cross-checked by clinicians who directly cared for the participant, and discrepancies were resolved by discussion in conjunction with the senior authors. The assessment of the inter-rater reliability was based on the analysis of ten randomly selected files (kappa = 0.87). The data extracted had been anonymized prior to statistical analysis, in line with the general ethical recommendation regarding chart review (Gearing, Mian, Barber, & Ickowicz, 2006). Only variables in line with the scope of the study are presented here. The research was funded by a competent national

authority (MILDECA project IReSP-15-Prevention-11) and received the approval of the ethics committee of the hospital. A waiver of written consent applies due to patient de-identification and the use of routine questionnaires. The French legislation regarding ethical obligations in clinical research postulates that no written consent is needed for projects involving secondary analysis of existing data previously collected for clinical purposes with the exception of genetic data (Code of public health 2016).

## 2.2. Participants

During the study period, 191 adolescents ranging from 12 to 18 years old were admitted to hospitalization. From the initial sample, data from 150 inpatients were available for analysis. In this sample, the mean age was  $14.71 \pm 0.14$  (min 10.17, max 18.14), 58% were boys, and most of them had middle or high socioeconomic status (70%). The main clinical features of this sample

are described in Table 2. Of note, this sample was particularly enriched in patients with severe treatment-refractory illness, with an average length of stay around 3 months. As the department became an expert center for the catatonic syndrome, bipolar disorder, and rare neurodevelopmental diseases with psychiatric manifestations (Consoli *et al.*, 2014; Guinchat *et al.*, 2015; Raffin *et al.*, 2015), a substantial proportion of the youths had been addressed from another hospital. For the patients who had been readmitted during the study period, only information related to the first hospitalization was analyzed (n=4).

## 2.3. Assessments

The DEP-ADO questionnaire was used to document substance use in the previous 12 months (Landry, Guyon, Bergeron, & Provost, 2002). The complete questionnaire can be seen at the website: <https://oraprdnt.uqt.quebec.ca>. The screening question was “*During the last twelve months, how often have you [has X] used one of*

**Table 2. Rates of problematic substance use among adolescent inpatients and in the 2018 French national community-based adolescent survey (EnCLASS).**

	In Clinical Sample (n=150)	By Gender		In Community-Based Sample <sup>3</sup>	Test for Independent Population	
		Male (n=88)	Female (n=64)		$\chi^2$	p
Daily tobacco use	32 (21%)	13 (15%)	19 (30%)	10%	21.09	<.001***
≥ regular alcohol use <sup>1</sup>	12 (8%)	7 (8%)	5 (8%)	10%	0.66	.415
≥ regular cannabis use <sup>1</sup>	22 (14%)	12 (13%)	10 (16%)	7%	13.34	<.001***
≥ occasional cocaine use	5 (3%)	1 (1%)	4 (6%)	2%	1.35	.245
≥ occasional inhalant/ solvent use	12 (8%)	6 (7%)	6 (9%)	9%	0.18	.669
≥ occasional hallucinogen use	5 (3%)	4 (4%)	1 (2%)	3%	0.06	.812
≥ occasional opioid/heroin use	11 (7%)	5 (6%)	6 (9%)	<1%	75.57	<.001***
≥ occasional stimulant use	9 (6%)	4 (4%)	5 (8%)	-	-	-
Binge drinking behavior <sup>2</sup>	32 (22%)	16 (18%)	16 (25%)	-	-	-
Discharge diagnostic of SUD	18 (12%)	12 (13%)	6 (10%)	-	-	-

Note. \* indicates  $p < .05$ ; \*\* indicates  $p < .01$ ; \*\*\* indicates  $p < .001$

<sup>1</sup> A regular use is defined as at least once a week.

<sup>2</sup> Binge drinking behavior was defined as at least one episode of intense alcohol intake ( $\geq 5$  drinks during the same event) in the last twelve months.

<sup>3</sup> In the EnCLASS survey, no specific question was dedicated to stimulants, and the prevalence of binge drinking behavior was examined over the last month.

the following substances: tobacco, alcohol, cannabis, cocaine, inhalant/ solvent, stimulant, hallucinogen, or heroin" (examples and trivial names were provided for each substance). For each substance, participants and their families had the options of answering: "Never," "Occasionally," "Once per month," "Once or twice per week," "More than three times per week," or "Daily." This questionnaire was self-reported, with assistance from a specially trained member of the paramedical staff if required (nurse trained in adolescent addiction). Assessments were carried out within seven days following admission and repeated if necessary (especially if the clinical condition was not compatible with self-assessment).

All youths screened positively for substance use were reported to the hospital's liaison addiction unit (ELSA, a French acronym for coordination and medical care team for addictive disorders) for proper diagnosis and care. A specific evaluation was also required for adolescents with suspected substance misuse according to repeated interviews with the youth and his/her family, even if they scored negatively to the DEP-ADO on several occasions. Urine tests were exceptionally used to document substance use, particularly for inpatients allowed to return home during the weekend. Systematic evaluation of the substance use and habits was conducted via an unstructured interview, which calculates the RECAP index, the clinician version of the DEP-ADO, and the Cannabis Use Screening Test (CAST), a self-reported scale that focuses on the use of cannabis in the previous six months. Final diagnoses of SUD were made by one of the ELSA senior psychiatrists using the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria.

Psychiatric diagnoses were based on discharge diagnoses after the assessment of all information available. The routine diagnostic work-up was based on comprehensive and repeated patient assessment and family interviews. The level of functioning was assessed using the Children-Global Assessment Scale (CGAS) (Jones, Thornicroft, Coffey, & Dunn, 1995). The CGAS was systematically measured at the first and last

week of the stay by a senior psychiatrist. Clinical improvement during the hospitalization was measured with the Clinical Global Impression – Improvement scale (CGI-I) and the severity of psychiatric symptoms with the Clinical Global Impression –Severity scale (CGI-S) (Busner & Targum, 2007). Parent-child conflict or poor parenting skills were endorsed when home educative assistance and/or prior report to child-protection agencies were reported.

## 2.4. Statistical Analysis

The first aim of this study was to determine the clinical rates of problematic substance use in this sample. Problematic substance use was defined using the threshold previously developed for the DEP-ADO questionnaire (Germain *et al.*, 2007). The use of a substance was regarded as problematic when it occurred more than once a month for alcohol and cannabis or at least occasionally for any other substance (cocaine, inhalant/ solvent, stimulant, hallucinogen, or heroin). As shown in Table 1, the previously published data showed that the rate of problematic substance use in hospitalized adolescents ranged from 17% to 50%. We fixed a mean expected rate of around 30% for our sample. The pre-determined value of maximum marginal error in estimate was fixed to  $\frac{1}{4}$  of the proportion of interest (30%) based on guidelines provided by Hajian-Tilaki (2011), *i.e.*, 7.5%. The theoretical sample size calculated was, therefore  $n = \frac{1.96^2 \times 0.30 \times 0.8}{0.075^2} = 164$

The rates of problematic substance use among inpatients were compared to findings from the 2018 version of the EnCLASS study (Spilka *et al.*, 2019). The EnCLASS study took advantage of two international surveys for adolescents conducted simultaneously: the HBSC survey (*Health Behaviour in School-aged Children*) conducted in 11-15-year-old adolescents and the ESPAD survey (*European School Project on Alcohol and other Drugs*) conducted in 15-18-year-old adolescents. For the EnClass study, all French data were extracted and pooled, leading to a representative sample of more than 20,000 French adolescents aged between 11-18 years. The

Chi-square test for independent samples was used to compare the rates of problematic substance use.

The second aim of the study was to compare the clinical features, psychosocial characteristics, and therapeutic outcomes of youths with and without problematic substance use. For alcohol use, three groups were defined: no alcohol use, regular alcohol use (defined as at least once a week alcohol intake), and pure binge drinking (not related to regular alcohol use). For continuous variables, ANOVA was performed to determine whether each variable was statistically different across the three categories. Post-hoc Scheffé tests were used for the comparisons between groups when ANOVA yielded a significant F-statistic. The non-parametric Kruskal-Wallis H test was used when the normal distribution of the variable was not confirmed. For categorical variables, Chi-square tests were performed to compare the proportions across the three groups, using the Fisher test as a non-parametric alternative. In the same way, we compared the clinical features of inpatients regarding the presence of associated illegal substance use. The same statistical analyses were performed except for the Mann-Whitney test, which was used to compare continuous variables between the two groups. A Bonferroni correction was made for multiple comparisons. List-wise deletion was used for missing values. Data were analyzed using StataIC-16 (StataCorp, 2009).

### 3. RESULTS

#### 3.1. Rates

Thirty percent of adolescent inpatients had some sort of problematic substance use (40% of girls and 22% of boys). Daily tobacco use (21%) was the most frequent problematic use, followed by regular cannabis use, regular alcohol use, and occasional inhalant/ solvent use (Table 2). In 66% of cases, the problematic substance involved several substances. Compared to adolescents from the representative sample of the EnCLASS study, adolescent inpatients were more likely to present a daily tobacco use (respectively, 21% vs. 10%, Odd-Ratio,  $OR=2.44$  [1.65-3.62]), regular cannabis use

(respectively, 7% vs. 17%,  $OR=2.28$  [1.45-3.60]), and an occasional opioid/heroin use (respectively, 0.07% vs. 7%,  $OR=9.81$  [5.21-18.48]). Twelve percent of inpatients had a confirmed diagnostic of SUD. A detailed profile of substance use is shown as Supplementary Data (Table S1).

#### 3.2. Correlates of Substance Use in Adolescent Inpatients

Regarding socio-demographic features, the gender ratio and SES did not differ across the three groups: with no use, regular alcohol use, and pure binge drinking (Table 3). Inpatients with regular alcohol use and binge drinking were statistically older than non-users (respectively, Mean Age =  $15.9 \pm 1.3$  vs. Mean Age =  $15.5 \pm 1.4$  vs. Mean Age =  $14.4 \pm 1.7$ ,  $p = .001$ ). The only clinical correlation with problematic alcohol use was a bipolar disorder that was 11 times more likely among patients who had binge drinking behavior compared to non-users ( $OR=11$  [3.07 – 39.38]). Regarding psycho-social factors, the three groups differed in terms of the history of sexual abuse and school refusal. Inpatients with regular alcohol use or binge drinking behavior were more likely to report sexual abuse than non-users. Adolescents with regular alcohol use had more frequent school refusal compared to the two other groups.

The gender ratio and SES did not differ between the adolescents with and without illegal substance use (Table 4). Inpatients with problematic illegal substance use were statistically older than non-users (respectively, Mean Age =  $15.5 \pm 1.3$  vs. Mean Age =  $14.4 \pm 1.7$ ,  $p = .004$ ). Compared to non-users, inpatients with problematic illegal substance use were more likely to report suicidal ideation ( $OR= 2.52$  [1.12 – 5.67]) and suicidal attempts ( $OR=2.61$  [1.21 – 5.65]). The two groups did not differ in terms of other clinical and psychosocial features.

#### 3.3. Therapeutic Outcomes of Substance Use in Adolescent Inpatients

The percent of patients “much improved” (CGI=1) or “very much improved” (CGI=2)

Table 3. Clinical correlates of inpatients with regards to profile of alcohol use.

Clinical features	Profiles of Alcohol Use			Statistical Tests Overall Comparisons <sup>1</sup>
	Group 1: No Use (n=115)	Group 2: Pure Binge Drinking (n=21)	Group 3: Regular Alcohol Use (n=12)	
Clinical features	-	-	-	-
Suicidal ideation (past or current)	65 (57%)	13 (62%)	10 (83%)	.192
Suicidal attempt (past or current)	32 (28%)	8 (38%)	5 (42%)	.434
Non-suicidal self-injury	32 (28%)	9 (43%)	2 (17%)	.248
Psychotic symptom	40 (35%)	6 (29%)	2 (17%)	.408
Chronic emotional dysregulation	42 (37%)	7 (33%)	3 (25%)	.151
Runaway	22 (19%)	6 (29%)	3 (25%)	.581
<b>Clinical severity and level of functioning</b>	-	-	-	-
History of admission in inpatient structure	54 (47%)	14 (67%)	7 (58%)	.216
Admission via emergency facilities	50 (43%)	12 (57%)	4 (33%)	.407
CGAS admission (mean ±SD)	36.4 ± 1.2	33.3 ± 2.5	38.7 ± 2.9	.447
CGI-S (mean ±SD)	5.1 ± 0.1	5.4 ± 0.2	4.8 ± 0.3	.377
Duration of the current symptoms, months (mean ±SD)	36.0 ± 13.8	58.8 ± 47.1	8.1 ± 1.8	.652
<b>Psychiatric diagnoses associated</b>	-	-	-	-
Anxiety disorder	53 (46%)	8 (38%)	4 (33%)	.590
Depressive disorder	50 (43%)	12 (57%)	9 (75%)	.088
Bipolar disorder	5 (4%) <sup>b</sup>	7 (33%) <sup>a</sup>	1 (8%) <sup>ab</sup>	.001***
Stress and trauma-related disorder	27 (23%)	5 (24%)	4 (33%)	.696
Disruptive behavioral disorder	32 (28%)	4 (19%)	6 (50%)	.158
Attention deficit disorder	19 (17%)	1 (5%)	3 (25%)	.251
Schizophrenia and other psychosis disorder	16 (15%)	1 (5%)	2 (17%)	.472
Intellectual disability	16 (14%)	4 (19%)	1 (8%)	.687
Autistic spectrum disorder	16 (14%)	2 (10%)	1 (8%)	.762
<b>Psychosocial features</b>	-	-	-	-
Fostered children	20 (17%)	6 (29%)	4 (33%)	.229
Parent-child conflict or poor parenting skills	52 (45%)	9 (43%)	9 (75%)	.137
Maltreatment, all types	35 (30%)	6 (29%)	3 (25%)	.919
Sexual abuse (victim or perpetrator)	11 (10%) <sup>b</sup>	8 (38%) <sup>a</sup>	4 (33%) <sup>a</sup>	.001***
Repeating grade	21 (18%)	8 (38%)	3 (25%)	.122
School refusal more than 3 months	48 (42%) <sup>b</sup>	9 (43%) <sup>b</sup>	8 (67%) <sup>a</sup>	.005**
Need of school adaptations	65 (57%)	8 (38%)	7 (58%)	.567
Need of specific educational facilities	18 (16%)	1 (5%)	1 (8%)	.594

Note. \* indicates  $p < .05$ ; \*\* indicates  $p < .01$ ; \*\*\* indicates  $p < .001$

<sup>1</sup> Fisher exact test

<sup>a-b</sup> Means in a row without a common superscript letter differ ( $p < .05$ ).

**Table 4. Clinical correlates of inpatients with regards to profile of illegal psychotropic use.**

	Profiles of Illegal Psychotropic Use		Statistical Tests Overall Comparisons <sup>1</sup>
	Group 1: No Use (n=114)	Group 2: At Least Occasional Use (n=38)	
Clinical features	-	-	-
Suicidal ideation (past or current)	60 (53%)	28 (74%)	.023*
Suicidal attempt (past or current)	27 (24%)	17 (45%)	.013*
Non-suicidal self-injury	33 (29%)	12 (32%)	.758
Psychotic symptom	35 (31%)	14 (37%)	.483
Chronic emotional dysregulation	45 (40%)	10 (26%)	.088
Runaway	23 (20%)	10 (26%)	.427
Clinical severity and level of functioning	-	-	-
History of admission in inpatient structure	53 (46%)	22 (58%)	.223
Admission <i>via</i> emergency facilities	50 (44%)	18 (47%)	.706
CGAS admission (mean ±SD)	36.5 ± 1.2	34.6 ± 1.9	.400
CGI-S (mean ±SD)	5.2 ± 0.1	5.1 ± 0.2	.796
Duration of the current symptoms, months (mean ±SD)	44.7 ± 16.3	10.7 ± 1.5	.229
Psychiatric diagnoses associated	-	-	-
Anxiety disorder	52 (46%)	15 (39%)	.509
Depressive disorder	50 (44%)	23 (61%)	.075
Bipolar disorder	7 (6%)	6 (16%)	.065
Stress and trauma-related disorder	29 (25%)	9 (24%)	.829
Disruptive behavioral disorder	33 (29%)	12 (32%)	.758
Attention deficit disorder	19 (17%)	5 (13%)	.607
Schizophrenia and other psychosis disorder	13 (7%)	6 (8%)	.479
Intellectual disability	20 (18%)	1 (3%)	.021*
Autistic spectrum disorder	16 (14%)	3 (8%)	.322
Psychosocial features	-	-	-
Fostered children	20 (18%)	12 (32%)	.066
Parent-child conflict or poor parenting skills	51 (45%)	20 (53%)	.398
Maltreatment, all types	36 (32%)	9 (24%)	.356
Sexual abuse (victim or perpetrator)	15 (13%)	9 (24%)	.123
Repeating grade	26 (23%)	5 (16%)	.358
School refusal more than 3 months	50 (44%)	17 (45%)	.216
Need of school adaptations	65 (57%)	18 (47%)	.466
Need of specific educational facilities	20 (18%)	1 (3%)	.054

Note. \* indicates  $p < .05$ ; \*\* indicates  $p < .01$ ; \*\*\* indicates  $p < .001$

<sup>1</sup> Fisher exact test

<sup>a-b</sup> Means in a row without a common superscript letter differ ( $p < .05$ ).

during their hospitalization was not significantly different across the three groups of alcohol use: 53% for “no use,” 71% for “regular alcohol use,” 72% for “pure binge-drinking,” with  $p=.196$ . The mean difference between the CGAS score at discharge and admission was not statistically different across the groups:  $M= 23.80 \pm 1.23$  for “no use,”  $M= 26.25 \pm 3.19$  for “regular alcohol use,”  $M= 26.55 \pm 3.44$  for “pure binge-drinking,” with  $p=.346$ . Finally, no difference was found in terms of duration of stays between the three groups:  $M= 104.04 \pm 10.79$  for “no use,”  $M= 99.12 \pm 22.57$  for “regular alcohol use,”  $M= 89.63 \pm 25.90$  for “pure binge-drinking,” with  $p= .960$

The percent of patients “much improved” (CGI=1) or “very much improved” (CGI=2) during their hospitalization was not significantly different between adolescents with illegal substance use (57%) and those without (58%), with  $p=.860$ . The mean difference between the CGAS score at discharge and admission was not statistically different between inpatients with illegal substance use ( $M= 25.32 \pm 2.39$ ) and those without illegal substance use ( $M= 23.86 \pm 1.18$ ), with  $p=.526$ . Finally, no difference was found in terms of duration of stays between the group with illegal substances ( $M= 92.60 \pm 15.47$ ) and those without illegal substances (use  $M= 103.21 \pm 10.84$ ), with  $p= .539$ .

## 4. DISCUSSION

### 4.1. Interpretation of the Main Findings: Rates and Clinical Correlates

This research was conducted on the grounds of previous lines of evidence supporting the vulnerability of adolescent inpatients for substance-related problems (Niethammer & Frank, 2007), the underestimation of substance misuse in inpatients when no systematic screening is applied (M. F. Weaver *et al.*, 2007), and the opportunity that represents the hospitalization to provide primary and secondary prevention programs for substance-related problems (Brown *et al.*, 2015; Brown *et al.*, 2003; Grilo *et al.*, 1995).

In the current study, 30% of the patients referred to two adolescent inpatient units had an associated problematic substance use involving multiple substances for 66% of them. Twelve percent of the participants received a diagnostic of SUD after the assessment of the liaison addiction unit. The vast majority of these patients had a “mild” or “moderate” form of SUD based on the DSM-5 classification. For example, physical symptoms of substance withdrawal (*e.g.*, shaking, sweating, nausea) infrequently occurred in the days following admission. These findings confirm the assumption that adolescent inpatients are a group at high risk of substance use-related problems. The observed rate was slightly lower than those reported in previous studies, ranging from 17% to 50% (Deas-Nesmith *et al.*, 1998; McDonnell *et al.*, 2011; M. F. Weaver *et al.*, 2007). Such discrepancy can be partly explained by using a two-step procedure to confirm the diagnostic of SUD in the current research leading to rule out adolescents with a less severe form of substance misuse, unlike other studies (Niethammer & Frank, 2007; M. F. Weaver *et al.*, 2007).

After tobacco, cannabis was the most frequent substance misused in this sample, with 14% of the adolescents having a regular use, followed by alcohol misuse (8%) and inhalant/ solvent use (8%). The rate of regular cannabis use was two times higher than in a same-age general population. The rate of opioid drug use was more than seven times higher in this sample compared to the general population. As shown in Supplementary Table S1, intravenous drug injection was exceptional. In the vast majority of cases (9/11), the adolescents used dextromethorphan-based drugs initially prescribed as an anti-cough or painkillers. An alert was published by the French national authorities of drug regulation (ANAES) in 2017 regarding the diverted uses of over-the-counter drugs in adolescents (Anaes, 2017), while the situation in France is far from the opioid crisis existing in the US.

The most frequent psychiatric diagnoses of adolescent inpatients with problematic substance use were depressive disorder, anxiety disorder, and disruptive behavioral disorder, regardless of

the profile of use. The frequencies of depressive disorder, suicidal ideation, and suicidal attempt were especially high among inpatients with regular alcohol use (respectively, 75%, 83%, and 42%). While these frequencies were higher than non-users, the differences did not reach statistical significance. These findings contradicted a large amount of literature supporting a relation between alcohol use and mood disorder in adolescence (Brière *et al.*, 2011). For example, in the retrospective review of the medical chart of 636 adolescent inpatients by M. F. Weaver *et al.* (2007), a diagnostic of mood disorder was more frequently reported among adolescents with alcohol and/or illegal SUD compared to other inpatients.

A strong relationship was found between a history of binge drinking and a diagnosis of bipolar disorder at discharge. The category of binge drinking behaviors was studied separately, as the vast majority of the adolescents involved in this pattern of use do not regularly use alcohol (Grilo *et al.*, 1995; Niethammer & Frank, 2007), and empirical evidence support distinct neurobiological correlates and clinical course (Groß *et al.*, 2014; Lees *et al.*, 2019). Among other factors, the repeated and excessive alcohol intake in binge drinking behavior could underlie the episodic course of mood symptoms (*e.g.*, elation or dysphoric mood) in bipolar disorder (Benarous, Consoli, Milhiet, & Cohen, 2016).

An illegal psychotropic use was also associated with an increased risk of reporting past or current suicidal behaviors (both suicidal ideation and attempt) among adolescent inpatients. In posthoc analysis, we found that this relationship was particularly strong for the subgroups of adolescents with anxiety disorder  $OR=12.00$  [1.47, 98.07], with  $p=.020$  and those with stress and trauma-related disorders  $OR=6.90$  [1.54-31.01]  $p=.012$ . Comparably the relation between illegal psychotropic use and suicidal behavior was particularly strong in those with anxiety disorders  $OR=6.3$  [1.82-21.81], with  $p=.004$  and those with a history of adverse childhood experience  $OR=2.81$  [1.02-7.74], with  $p=.045$ . Of note, anxiety disorders and trauma-related disorders are both risk factors for substance-related problems

and suicidal ideation in adolescents (Chan, Dennis, & Funk, 2008). The cognitive deficits observed among substance-using adolescents, such as decreased cognitive flexibility (due to pre-existing vulnerability traits or to the effects of the substance itself), could make youths with both internalized disorder and SUD more prone to commit suicide attempts when experiencing suicidal ideation compared to those without SUD (Hanson, Cummins, Tapert, & Brown, 2011). In this vein, Daudin *et al.* (2010) showed that adolescent inpatients diagnosed with SUD are more likely to present repeated suicidal attempts and borderline personality traits than their counterparts (characterized by impulsivity and chronic emotional dysregulation).

#### 4.2. Interpretation of the Main Findings: Therapeutic Outcomes

We found that clinical (CGI-I score) and functional improvements during the stay (difference between the CGAS scores at discharge and admission) were not statistically different in adolescent inpatients concerning alcohol or illegal substance use status. This finding apparently contradicts the large amount of data showing that substance misuse is associated with a lower response rate in adolescents treated for anxiety or mood disorders (Asarnow *et al.*, 2009; Deas, 2006; Emslie *et al.*, 2010; Gårdvik *et al.*, 2020). This was, however, consistent with the results of a case-control study conducted by Daudin *et al.* (2010) on hospitalized adolescents where no difference was found in terms of CGAS score improvement during the stay between a group of substance-using adolescents ( $n=30$ ) and a clinical control group ( $n=30$ ).

Expressed differently, these findings support the assumption that the substance-using adolescent inpatients do not benefit less from the treatments provided during their stay compared to their non-substance-using counterparts. The hypotheses discussed in the introduction suggest that the factors associated with a lower response rate to treatment for psychiatric disorders in substance-using adolescents can be at least partly moderated during inpatient care. This may be

explained by the fact that most of these factors are environmentally mediated (e.g., observance, exposure to ongoing stressors) and then potentially modifiable when the adolescents distance themselves from their daily environment. Brown *et al.* (2015) noted that the substance cessation inherent to full-time hospitalization is generally an opportunity in engaging the adolescents with regular substance use and their family in a more insightful discussion about risk and maintaining environmental factors.

One may argue that the comparable rates of clinical and functional improvement observed during the hospitalization between the substance-users adolescents and their counterparts result from the lack of fixed duration of stay. Therefore, inpatients were only discharged when they reached a significant level of clinical or functional improvement, which involves constructing a clinical project with the adolescent and their family. Of note, our department includes a school center, which represents a chance to get back in school and discuss academic projects. This may be particularly significant for inpatients with problematic substance use considering the high rate of school absenteeism (45% for illegal psychotropic and 67% for alcohol). This explanation has proved not to be sufficient as the mean length of stay of inpatients did not differ with regards to the profile of alcohol or illegal psychotropic use.

Finally, the lack of difference in terms of clinical and functional improvement between substance-users and non-substance-users could result from the fact that the latter were particularly enriched in adolescents with severe or refractory psychiatric problems (e.g., severe neurodevelopmental disorder) who may have lower or slower symptom reduction or functional improvement. In line with this, we found that youths with intellectual disabilities were less likely to be associated with illegal substance use problems in our study (Table 4).

### 4.3. Strengths and Limitations

This study has several limitations. The adolescents recruited had more severe clinical

features than adolescents typically referred to psychiatric inpatient facilities, as shown by the unusually long duration of stay. The overrepresentation of inpatients with severe psychiatric disorders and/or psychosocial problems can explain why some associations between substance use and clinical factors usually reported in the literature were concealed: for example, the relationships with anxiety disorder, depressive disorder (Chan *et al.*, 2008) or psychotic disorder (Volkow *et al.*, 2016).

Sampling bias may result from the analysis of only the group of participants who completed the DEP-ADO questionnaire. However, the main socio-demographic and clinical features of inpatients were roughly comparable between those who had completed the DEP-ADO questionnaire and those who had not (Table S2). Of note, this sample is likely to be free of sampling bias due to economic or patients' insurance characteristics as medical care is free of charge in France.

Measurement biases can exist even if a standardized assessment method is conducted. The DEP-ADO self-report questionnaires were completed at different times during the hospitalization. While clinical assessment commonly involved questions about substance use, this aspect was not standardized in the study. In addition, the DEP-ADO does not collect any information about the quantity of the substance consumed, which conveys information about the risk of developing psychiatric symptoms (Volkow *et al.*, 2016). The study may also be prone to measuring bias due to missing or incomplete charts.

The small sample size makes it difficult to measure the effects of confounding factors. For example, it was not possible to determine to what extent the relation between illegal psychotropic use and suicidal behaviors was accounted for a history of sexual abuse. The cross-sectional nature of this data precludes us from examining the temporal sequence between substance use and psychiatric symptoms, e.g., how stopping cannabis during hospitalization impacts psychiatric symptoms.

#### 4.4. Clinical Implications

Using a systematic screening approach, we found that 30% of adolescent inpatients had problematic substance abuse, with 12% of the total sample having a confirmed SUD. In addition, to provide individualized sessions for adolescents with SUD during their stay (such as developed in studies conducted earlier (Brown *et al.*, 2015; Brown *et al.*, 2003)), a collaboration between adolescent psychiatric staff and addiction professionals could include integrated care targeting common vulnerability factors or providing psychoeducation (*e.g.*, group sessions) on the specific risk of substance misuse in this population.

The lack of significant relations between problematic substance use and markers of clinical response to inpatient treatment should be interpreted with caution, considering the specificity of the current sample discussed above. If confirmed, this result supports the assumption that co-existing problematic substance use does not impact the response rate of therapeutics provided during the stay of adolescent inpatients. This finding should be interpreted in light of the reports showing that most therapeutics provided in outpatient facilities are less effective for youths with dual disorders compared to those without associated substance use problems (Armstrong & Costello, 2002; Bukstein & Horner, 2010; Cornelius *et al.*, 2004; Gårdvik *et al.*, 2020; Grella *et al.*, 2001).

This study adds to the limited existing evidence about the role of hospitalization in the treatment of adolescents with dual disorders. When considering the treatment plan of adolescents with the dual disorder, full-time hospitalization might be an opportunity to temporarily relieve emotional stressors associated with a harsh and insecure environment fuelling the patterns of substance use (Cohen, Hanin, & Benarous, 2021). This also allows for the possibility of more accurate identification of the underlying psychiatric disorders by putting aside the effect of the substance itself on psychiatric symptoms. The association between illegal psychotropic use and suicidal behavior reported here encourages

clinicians to pay particular attention to the assessment of substance use problems in adolescents hospitalized for complex or resistant forms of psychiatric disorders.

While full-time hospitalization is only a therapeutic option for a minority of adolescents with dual disorders, this represents for some of these patients an opportunity to better understand and take action on the interactions between an adolescent's psychiatric symptoms, suicidal behaviors, environmental backgrounds, and substance use.

#### CONCLUSION

Problematic substance use was reported in 30% of adolescents who required a full-time hospitalization for psychiatric disorders and/or severe psychosocial problems. In 66% of cases, the problematic substance involved several substances. A positive link was reported between suicidal behavior and illegal psychotropic use on the one hand; and bipolar disorder and binge drinking on the other hand. Adolescents who abused alcohol and/or illicit substance had no lower response rate to treatments provided during the hospitalization compared to other inpatients. Such findings help gain preliminary information on how hospitalization may offer an opportunity to provide integrative care for adolescents with mental health and substance-related problems.

#### LIST OF ABBREVIATIONS

ADUS	=	Adolescent Problem Use Scale
CAST	=	Cannabis Use Screening Test
CGAS	=	Children-Global Assessment Scale score
CGI-I	=	Clinical Global Impression-Improvement score
CGI-S	=	Clinical Global Impression-Severity score
DEP-ADO	=	Depistage Adolescents
DSM-5	=	Diagnostic and Statistical Manual of Mental Disorders 5 <sup>th</sup> version

- ELSA = a French acronym for coordination and medical care team for addictive disorders, hospital addiction liaison unit
- EnCLASS = a French acronym for National Study on Health behavior and Substance use in Highschool
- ESPAD survey = European School Project on Alcohol and other Drugs survey
- GAF = Global Assessment of Functioning
- HBSC survey = Health Behaviour in School-aged Children survey
- K-SADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime
- PESQ = Personal Experience Screening Questionnaire
- SACE = Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic Version
- SCID-R = Structured Clinical Interview for DSM III-R
- SUD = Substance Use Disorder
- TLFB = Timeline Followback
- WHO-CIDI = WHO-composite international diagnostic interview

**ETHICS APPROVAL AND CONSENT TO PARTICIPATE**

The study protocol was approved by the local Ethics Committee of the Amiens University Hospital, France.

**HUMAN AND ANIMAL RIGHTS**

No animals were used for studies that are the basis of this research. All the humans used were in accordance with the ethical standards of the committee responsible for human

experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013 (<http://ethics.iit.edu/ecodes/node/3931>).

**CONSENT FOR PUBLICATION**

The local Institutional Review Board deemed the study exempt from the review due to patient de-identification and the use of routine questionnaires.

**AVAILABILITY OF DATA AND MATERIALS**

The data that support the findings of this study are available on request from the corresponding author.

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**CONFLICT OF INTEREST**

The authors declare no conflict of interest, financial or otherwise.

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**SUPPLEMENTARY MATERIAL**

Supplementary material is available on the publisher's website along with the published article.

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