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Polydrug use disorders in individuals with opioid use disorder

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ABSTRACT

Background: Understanding the association of polydrug use disorders (PUD) with psychosocial and clinical factors is essential for the treatment of individuals with opioid use disorder (OUD). The aim of this study is to examine whether there is an association between childhood maltreatment, mood disorders, anxiety disorders, personality disorders, or posttraumatic stress disorder (PTSD) and PUD in individuals with OUD.

Methods: We used data from 356 individuals with OUD in the past 12 months from a nationally representative database in the United States. PUD patients were classified into two groups: a group with additional one substance disorder (OUD + 1) and that with two or more additional substance disorders (OUD + 2). We conducted multivariate logistic regression to predict the PUD status, after adjustment for confounders including childhood maltreatment.

Results: Among all individuals, 57.3% were polydrug users (n = 204) and 42.7% were not (n = 152). There was a high prevalence of childhood maltreatment in both groups, ranging from 16.1% to 59.5%, but the difference was not statistically significant. After adjustment for confounders, we found an association between past-year PTSD and OUD + 2 (odds ratio: 3.98; 95% confidence interval: 1.15–13.72; p = 0.03) but not with OUD + 1.

Conclusion: PTSD is highly prevalent in individuals with OUD using multiple substances and could influence PUD. We recommend screening for PTSD in cases of PUD. Future studies should evaluate the effect of PTSD treatment on PUD.

1. Introduction

The rate of polydrug use disorders (multiple simultaneous drug use disorders) has been significantly increasing over the past two decades (Zambon et al., 2017). Epidemiological studies have indicated a high prevalence of polydrug use (30–49.7%), particularly among individuals with opioid use disorder (OUD), in the United States (Jarlenski et al., 2017; Wu et al., 2010). Rates of polydrug use remained high (65%) in OUD patients receiving treatment (i.e., methadone or buprenorphine), which is of concern due to the potential complications (Heikman et al., 2017).

Polydrug use compromises the outcome of drug treatment and increases the risk of relapse (Wang et al., 2017; Wasserman et al., 1998). The use of multiple substances at the same time is associated with suicidal ideations, suicidal attempts, and several types of aggressive behavior (Hakansson et al., 2011; Martinotti et al., 2009a; Steele and Peralta, 2017). In a cohort study, polydrug users had more than 10 times the risk of premature mortality, drug overdose being the most common cause of death (Gjersing and Bretteville-Jensen, 2018). Data from a prospective study showed that over one-third of young individuals (age: 12–18 years) transitioned from single or two substance use to polysubstance use over a 10-year period (Merrin et al., 2018). Youth who were polysubstance users were the most resistant to change over time, and the authors proposed that this unchanged pattern of polysubstance use could indicate underlying social or individual contributing factors (Merrin et al., 2018).

Polydrug use was associated with certain demographic features such as male sex, white ethnicity, less education, and unemployment (John et al., 2018). Polysubstance users with psychiatry comorbidities had high frequency of use of opioid and cannabis, which may indicate self-selection for analgesic agents in this population (Anderson et al., 2018).

Understanding the association of polydrug use with psychosocial problems and clinical presentations can help customize the treatment options for this population. Childhood maltreatment has a powerful

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association with substance use. Various types of childhood maltreatment increase the risk of initiating substance use with an early onset during adolescence (Afifi et al., 2012a; Hussey et al., 2006; Shin et al., 2009). The association between childhood maltreatment and a pattern of polysubstance use has been repeatedly reported, but in varying degrees. Two studies reported the association of polydrug use with child sexual abuse in adolescent females only, and with physical abuse in males (Armour et al., 2014; Shin et al., 2010). Another study reported the association between polydrug use and childhood emotional and physical neglect in treatment-seeking Italian adults (Martinotti et al., 2009b). A study by Alvarez-Alonso et al. reported that all types of childhood maltreatment increased the odds of polydrug use in a Mediterranean adolescent sample with primary alcohol use disorder (Alvarez-Alonso et al., 2016). A study from a nationally representative sample indicated that exposure to different types of childhood maltreatment increased the risk of polydrug use more in men than in women (Evans et al., 2017).

Despite these results, the association of polydrug use disorders with social and clinical presentation is scarcely known in individuals with OUD. Given the recent opioid crisis and the related increase in mortality rate, the characteristics of the polydrug users require special attention (Gomes et al., 2014; UNODC, 2013). Furthermore, the strong association of psychiatric disorders in adults, and posttraumatic stress disorder (PTSD) in particular, with childhood maltreatment requires further evaluation, because not all childhood maltreatment victims develop PTSD.

A recent study by Yang et al. evaluated polydrug use in heroin users in the Chinese population and reported an association between polydrug use and major depression, dysthymia, and antisocial personality disorder, but not with PTSD (Yang et al., 2018a). The authors evaluated the association of polydrug use with lifetime PTSD diagnosis, rather than with PTSD diagnosed during the time of polydrug use. Therefore, periods of polydrug use might not have included active PTSD symptoms. Also, the authors evaluated drug use only, and not the consequent drug use disorder. The aim of this study is to compare the severity and prevalence of childhood maltreatment in individuals with OUD, with and without polydrug use disorders. We also compared the prevalence of psychiatric disorders between these groups.

2. Methods

2.1. Participants

We used cross-sectional data from the third wave of the National Epidemiologic Survey on Alcohol and Related Disorders (NESARC-III, n = 36,309), conducted by the National Institute on Alcohol Abuse and Alcoholism (NIAAA). A detailed description of the data is presented elsewhere (Grant et al., 2015). The NESARC data include American noninstitutionalized adult civilians, aged 18 years and older, in the United States. The population was randomly selected using multistage probability.

In this study, we included all individuals diagnosed with OUD, including prescription painkillers and/or heroin, in the year before the survey (n = 356).

2.2. Measures

The clinical diagnosis of OUD, other clinical diagnoses, and demographics were collected with a semi-structured interview, using the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-5). The reliability of the substance use disorder diagnosis was good to excellent, and the reliability of PTSD and mood and anxiety disorder diagnosis was fair to good (Grant et al., 2015). Nineteen questions measured the five types of childhood maltreatment (emotional abuse, emotional neglect, physical abuse, physical neglect, and sexual abuse). These questions were adapted from two validated Likert scales: The Conflict Tactics Scale (Straus, 1979) and the Childhood Trauma Questionnaire (Bernstein et al., 1994). The questions related to each type of childhood maltreatment have been reported elsewhere (Keyes et al., 2012). The reliability of these questions was evaluated to be good to excellent (Ruan et al., 2008). We used the binary classification of each childhood maltreatment as defined by Afifi et al. (Afifi et al., 2012b). We also represented each trauma as a continuous variable, in which the higher the number the more severe the trauma. The total childhood trauma score was given by the sum of all types of trauma, indicating the severity of childhood adversities.

Polydrug use disorder patients were divided into two groups, one including individuals with OUD and one additional substance use disorder (OUD + 1), and the other individuals with OUD with two or more additional substance use disorders (OUD + 2). This latter group has been defined by other researchers (Connor et al., 2014; Martinotti et al., 2009b), as the diagnosis of at least three classes of substance use disorders during the same 12-month period, excluding caffeine and tobacco. Finally, we considered the group of patients with OUD only, without additional substance use disorder (OUD only). We defined polydrug use as the use of any listed substance, excluding caffeine and tobacco, whether or not meeting the substance use disorder diagnostic criteria. Alcohol use was defined as the consumption of at least 12 alcoholic drinks in the past year, as described by other researchers (Saha et al., 2007). All substance use disorders, PTSD, mood disorders (major depressive disorder, bipolar I, bipolar II, or dysthymia) and anxiety disorders (generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, or specific phobia), and eating disorders (anorexia nervosa, bulimia nervosa, binge-eating disorder) were limited to those reported to be active in the past 12 months. Personality disorders included antisocial personality disorder, borderline personality disorder, and schizotypal personality disorders.

2.3. Statistical analyses

To account for the complexity of the NESARC data survey, the entire analysis was performed with the Software for Survey Data Analysis (SUDAAN), version 11, which uses Taylor series linearization. We set the level of significance at $p < 0.05$, two-sided. We compared the two groups (polydrug use disorder group and control group) on demographics, clinical features, familial history, and childhood maltreatment, using weighted chi squared or two-sample *t*-tests as appropriate. To clarify the relationship between childhood maltreatment and OUD, we conducted a *t*-test comparing the severity of the reported childhood maltreatment between individuals with and without past-year OUD.

We performed binary logistic regression with the OUD + 2 group or OUD + 1 group as dependent variable and PTSD/mood disorders/anxiety disorders/personality disorders as independent variables, while controlling for confounders in different models. We controlled for variables that were different in the two groups or had been reported to be risk factors for polydrug use disorder in the previous literature, including age (Martinotti et al., 2009b), sex, ethnicity (Jarlenski et al., 2017), marital status (Martinotti et al., 2009b), employment status (Martinotti et al., 2009b), age of onset of opioid use (Yang et al., 2018b), past-year axis I disorders, mood disorders, personality disorders (McCabe and West, 2017), family history of drug use, and childhood maltreatment.

3. Results

Three hundred thirty-two individuals with OUD (93.3%) used two or more substances, in addition to opioids, in the past year. Table 1 describes the prevalence of the various substances used in the past 12 months among the individuals with OUD. Alcohol was the most used substance followed by cannabis, sedatives, stimulants and cocaine, in decreasing order.

Ninety-three (26.1%) individuals with OUD had two or more

Table 1
Prevalence of the most common substance used in the past 12 months in individuals diagnosed with opioid use disorder in the same period.

Past-year use of substances in individuals with opioid use disorder	% (SE)
Alcohol consumption	68.4 (5.9)
Cannabis use	50.94 (6.87)
Sedative use	41.08 (6.78)
Stimulant use	15.92 (5.36)
Cocaine use	15.18 (6.01)
Hallucinogens use	8.83 (4.99)
Inhalants use	3.16 (4.31)
Club drug use	8.84 (4.51)
Other drug use	3.04 (2.44)

Table 2
Demographic, familial, and clinical information about polydrug group and the control group.

	OUD only n = 152	OUD + 1 n = 111	OUD + 2 n = 93
Age: mean (SE)	47.23 (1.78)	38.76 (1.61)***	32.61(1.16)***
Gender: female % (SE)	53.82 (4.77)	47.34 (5.15)	37.31 (6.33)*
Marital status: % (SE)			
Married	48.90 (4.95)	22.16 (3.87)***	7.57 (2.62)***
Living with someone as if married	10.37 (3.60)	19.74 (5.02)	15.72 (5.42)
Widowed	5.17 (1.96)	1.32 (0.95)	4.19 (2.92)
Divorced	13.21 (3.13)	23.22 (4.83)	12.34 (3.49)
Separated	2.85 (1.10)	5.87 (2.03)	14.20 (5.12)
Never married	19.50 (3.70)	27.69 (5.67)	45.99 (6.41)
Unemployed % (SE)	12.75 (3.51)	7.43 (2.59)	20.97 (5.67)
Education % (SE)			
Completed grade 5 or 6	0.37 (0.37)	0.33 (0.33)	0 (0.0)
Completed grade 7	0 (0.0)	1.00 (0.99)	0.92 (0.66)
Completed grade 8	5.09 (2.19)	0.57 (0.56)	4.3 (2.37)
Some high school	16.69 (4.06)	25.92 (5.67)	17.19 (4.81)
Completed high school	25.70 (4.79)	30.58 (4.91)	26.13 (5.96)
Graduate equivalency degree	12.36 (3.45)	6.03 (2.56)	14.32 (4.85)
Some college	31.93 (4.74)	27.50 (5.52)	29.19 (6.64)
Completed associate or other technical 2-year degree	7.86 (2.95)	10.06 (3.45)	7.95 (3.17)
Race % (SE)			
White	67.11 (3.93)	70.83 (4.94)	80.29 (4.11)
Black	13.04 (2.84)	15.73 (4.29)	11.58 (2.78)
American Indian/Alaska Native	3.48 (1.97)	2.78 (1.62)	0.61 (0.61)
Asian/Native Hawaiian/other Pacific Islander	1.69 (1.27)	0.00 (0.00)	0.73 (0.73)
Hispanic, any race	14.68 (2.90)	10.66 (2.58)	6.80 (2.80)
Personality disorders % (SE)	46.85 (4.24)	60.43 (5.80)	66.41 (5.80)**
Family history of alcohol use disorder % (SE)	65.77 (4.77)	62.95 (6.21)	72.89 (6.01)
Family history of drug use disorder % (SE)	42.25 (4.50)	52.58 (6.00)	61.12 (6.28)*
Past-year mood disorders % (SE)	39.63 (4.40)	51.89 (5.94)	63.99 (6.44)**
Past-year anxiety disorders % (SE)	38.95 (4.81)	35.14 (4.94)	41.62 (7.05)
Past-year PTSD % (SE)	16.48 (3.64)	19.61 (4.31)	34.17 (6.80)*
Past-year eating disorders % (SE)	1.22 (0.82)	3.17 (1.55)	5.04 (2.72)
Age of onset of opioid use mean (SE)	34.30 (2.83)	31.93 (2.52)	26.10 (2.09)*
Age of onset of heroin use mean (SE)	21.38 (0.68)	21.07 (1.86)	21.52 (1.04

Past-year mood disorders: major depressive disorder, bipolar I, bipolar II or dysthymia. Past-year anxiety disorders: generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, or specific phobia. Past-year eating disorders: anorexia nervosa, bulimia nervosa, or binge-eating disorder.
* < 0.05; ** < 0.01; *** < 0.001.

substance use disorders (OUD + 2), 111 (31.2%) had only one additional substance disorder (OUD + 1) and 152 (42.7%) did not have any additional substance use disorder (OUD only). Table 2 describes the demographics, familial history, and clinical diagnoses of the three groups. Individuals in the OUD + 2 group were younger and showed a significantly earlier age of onset of opioid use compared with the OUD only group. The OUD + 2 group also had a higher prevalence of men, singles, unemployment, personality disorders, family history of drug use, and past-year mood-disorder than the OUD only group. There was no significant difference in the rates of higher education achieved, ethnicity, family history of alcohol use, or past-year anxiety disorders between the two groups. There were no significant differences between the OUD + 1 and OUD only groups, except in age and marital status (Table 2).

Similar to the ranking of used substances in the individuals with OUD, the most common drug use disorders in the OUD + 2 group, in addition to opioids, was alcohol use disorder, followed by cannabis use disorder, sedatives use disorder, stimulants use disorder, and cocaine use disorder, in decreasing order. There was a similar pattern in the OUD + 1 group, alcohol use disorder being the most prevalent, followed by sedative, cannabis, stimulant, and cocaine use disorders. The prevalence of each drug disorder and the corresponding 95% confidence standard error are presented in Table 3.

The total childhood maltreatment severity was 33.64 ± 0.85 (mean ± standard error) in individuals with past-year OUD, and 26.23 ± 0.09 in those without past-year OUD ($p < 0.001$). Within individuals with past-year OUD, the OUD + 2 group showed a total childhood maltreatment severity of 35.05 ± 1.93, compared with 32.55 ± 1.21 for the OUD only group ($p = 0.28$). There was no significant difference between the OUD + 2 group and the OUD only group in any of the trauma subtype mean scores: Emotional abuse (mean 6.83 and 6.09, respectively for OUD + 2 and OUD only), physical abuse (4.30 and 3.90), sexual abuse (5.79 and 5.11), physical neglect (8.21 and 7.95), and emotional neglect (9.92 and 9.50). Similarly, there were no significant differences in total childhood maltreatment total score or any specific trauma type score between the OUD + 1 and the OUD only group. The prevalence of each trauma type is presented in Table 4.

In the OUD + 2 group, 34.2% had a diagnosis of PTSD in the past year and active symptoms, compared with 16.5% of the OUD only group and 19.6% of the OUD + 1 group. Similarly, the prevalence of past-year mood disorders and personality disorders was 64% and 66.4% in OUD + 2 group, respectively, compared with 51.9% and 60.4% in the OUD + 1, and 39.6% and 46.9% in the OUD only group. There was no significant difference between the prevalence of past-year anxiety disorders in the OUD + 2 (41.6%), OUD + 1 (35.1%), and OUD only group (39%).

Table 5 shows the association between childhood maltreatment, personality disorders, past-year mood disorder, past-year anxiety

Table 3
Prevalence of the most common substance use disorder between both groups.

Past-year prevalence of substance use disorder	OUD + 2 % (SE)	OUD + 1 % (SE)
Alcohol use disorder	85.13 (5.43)	66.43 (4.58)
Cannabis use disorder	71.89 (5.48)	12.37 (3.81)
Sedative use disorder	48.37 (6.34)	24.74 (3.31)
Stimulant use disorder	31.59 (6.73)	3.27 (2.13)
Cocaine use disorder	27.83 (6.72)	1.64 (1.02)
Club drug use disorder	10.87 (3.56)	0 (0)
Inhalant use disorder	7.68 (4.63)	0 (0)
Hallucinogens use disorder	8.12 (3.18)	0 (0)
Other drug use disorder	1.33 (1.04)	1.55 (1.54)

OUD + 2: Two or more substance use disorder in addition to opioid use disorder.
OUD + 1: One substance use disorder in addition to opioid use disorder.

Table 4
Prevalence of each type of childhood maltreatment in both groups. No significant difference between any of the groups.

Childhood maltreatment	OUD only	OUD + 1	OUD + 2
	Prevalence (SE)		
Emotional abuse	24.65 (3.56)	31.51 (5.22)	30.26 (6.11)
Physical abuse	33.09 (4.63)	41.69 (5.56)	44.05 (6.31)
Sexual abuse	24.98 (4.28)	27.56 (4.27)	29.98 (6.16)
Physical neglect	53.45 (5.29)	46.02 (5.73)	59.46 (5.54)
Emotional neglect	13.56 (3.26)	19.88 (4.40)	21.78 (6.58)

disorders, and past-year PTSD with OUD + 2 or OUD + 1. Only past-year PTSD was associated with OUD + 2, after controlling for demographics and other clinical confounders, including childhood maltreatment. This final adjusted model was able to correctly classify 81.7% of the individuals with polydrug use disorders (sensitivity), and 56.4% of those without polydrug use disorders (specificity). Past-year PTSD showed a trend toward significance with OUD + 2, after excluding the OUD + 1 group and controlling for the same variables (OR: 3.58; 95% CI: 0.9–14.25; p = 0.07). No clinical disorder was associated with OUD + 1. Childhood maltreatment was associated with OUD + 1 after controlling for demographics and clinical variables (OR: 1.04; 95% CI: 1.00–1.07; p = 0.04).

Past-year PTSD and childhood maltreatment were not associated with past-year diagnoses of alcohol use disorder (p = 0.36 and p = 0.65, respectively), stimulant use disorder (p = 0.87, p = 0.88), cocaine use disorder (p = 0.61, p = 0.53) and cannabis use disorder (p = 0.21, p = 0.33). However, we found a significant association between past-year PTSD and past-year sedative use disorder (OR: 3.02; 95% CI: 1.40–6.51; p = 0.01). There was no association between childhood maltreatment and past-year sedative use disorder (p = 0.16).

4. Conclusion

Research on polydrug use disorders is scarce, and more is needed for future prevention and treatment (Connor et al., 2014). Over 90% of the individuals with OUD were using more than two additional substances within the same year. Also, in our sample, over a quarter had at least three classes of substance use disorders, including OUD, within the same period. Substance use disorders were ranked by prevalence in the same order as substance use. There is a need to provide psychoeducation to patients with OUD about the risks of using substances, even in moderate amounts, which could lead to problematic use.

The individuals in the OUD + 2 group were younger and more often single, male, and affected by psychiatric comorbidities (mood disorders, PTSD, and personality disorders) than the OUD only or OUD + 1 groups. They were also characterized by a younger age of onset of opioid use. This could indicate the need to use multiple substances to relieve the psychiatric symptoms, as reported in other studies (Blanco et al., 2013). The more severe the childhood maltreatment the more likely individuals would have OUD in the past year. However, there were no statistically significant differences in the childhood maltreatment scores or each type of maltreatment between the OUD + 2 or OUD + 1 group and the OUD only group. There was an association between PTSD and OUD + 2, also when controlling for demographics, familial history, age of onset of opioid use, axis I disorders, and childhood maltreatment.

Contrary to other studies on polydrug use disorders with multiple primary substances (Alvarez-Alonso et al., 2016; Evans et al., 2017), our results showed no difference in childhood maltreatment severity or prevalence between the two groups of individuals with OUD. The association between type of childhood maltreatment and polydrug use was inconsistent across previous studies; this could be due to the different populations studied, such as adolescent cohorts, differences in focus (disorder vs. use) and, more importantly, to the different primary substances studied. The range of prevalence of childhood maltreatment in our polydrug group was 21.8–59.5%, comparable to the reported range in the polydrug group in the Alvarez-Alonso et al. study (26.7–63%) (Alvarez-Alonso et al., 2016). However, the range of prevalence in our control group was much higher (Table 3). In addition, based on our results, childhood maltreatment severity is much higher in individuals with past year OUD than individuals without this disorder. This could indicate an overall strong relationship between childhood maltreatment and OUD, with or without other drug disorders, and the personal preference for opioids in the victims of childhood maltreatment.

Regardless of childhood maltreatment, PTSD was associated with polydrug use disorders. Our results showed that the OUD + 1 group was not significantly different from the OUD only group. The only differences concerned some demographic and social factors, such as the patients in the OUD + 1 group being younger and more often single. However, the OUD + 2 group had distinct characteristics, specifically regarding psychiatric comorbidities, and in particular the association with PTSD. Therefore, childhood maltreatment is a precursor of many types of substance use and mental health disorders (Afifi et al., 2012b; Scott et al., 2012). However, the presence of multiple (more than two) substance use disorders is more strongly associated to active PTSD symptoms, which could or could not be associated with childhood maltreatment.

Table 5
Childhood maltreatment and clinical disorders predicting polydrug use among patients with opioid use disorder.

	OUD + 1 (95% confidence interval)	OUD +2 (95% confidence interval)
Past-year PTSD	OR: 1.24 (0.57–2.70) (p = 0.59)	**OR: 2.41 (1.20–4.84) (p = 0.01)**
Adjusted for: demographics	OR: 1.00 (0.38–2.65) (p-0.99)	**OR: 3.02 (1.26–7.25) (p = 0.01)**
Adjusted for: demographics, other clinical and childhood maltreatment	OR: 0.72 (0.16–3.32) (p = 0.68)	**OR: 4.15 (1.27-13.54) (p = 0.02)**
Childhood maltreatment	OR: 1.01 (0.99–1.02) (p = 0.49)	OR: 1.01 (0.99–1.03) (p = 0.35)
Adjusted for: demographics	OR: 1.01 (0.99–1.03) (p = 0.47)	OR: 1.02 (1.0–1.05) (p = 0.05)
Adjusted for: demographics and other clinical diagnosis.	**OR: 1.04 (1.00-1.07) (p = 0.04)**	OR: 1.02 (0.99–1.05) (p = 0.21)
Past-year Mood disorders	OR: 1.64 (0.89–3.03) (p = 0.11)	**OR: 2.21 (1.18-4.13) (p = 0.01)**
Adjusted for: demographics	OR: 1.50 (0.80–2.83) (p = 0.21)	OR: 2.04 (1.02–4.10) (p = 0.05)
Adjusted for: demographics, other clinical diagnoses and childhood maltreatment	OR: 1.83 (0.41–8.27) (p = 0.43)	OR: 1.23 (0.49–3.08) (p = 0.69)
Past-year Anxiety disorders	OR: 0.85 (0.49–1.46) (p = 0.55)	OR: 1.19 (0.59–2.40) (p = 0.62)
Adjusted for: demographics	OR: 0.79 (0.43–1.42) (p = 0.40)	OR: 1.29 (0.59–2.84) (p = 0.53)
Adjusted for: demographics, other clinical diagnoses and childhood maltreatment	OR: 0.56 (0.13–2.35) (p- = 0.42)	OR: 0.50 (0.17–1.53) (p = 0.2)
Personality disorders	OR: 1.73 (0.96–3.13) (p = 0.07)	OR: 1.80 (1.00–3.22) (p = 0.05)
Adjusted for: demographics	OR: 1.53 (0.83–2.82) (p = 0.17)	OR: 1.80 (0.94–3.45) (p = 0.07)
Adjusted for: demographics, other clinical diagnoses and childhood maltreatment	OR: 0.49 (0.15–1.59) (p = 0.23)	OR: 1.35 (0.39–4.65) (p = 0.65)

OUD + 2: Two or more substance use disorder in addition to opioid use disorder.
OUD + 1: One substance use disorder in addition to opioid use disorder.
Bold: statistically significant.

Sedative use disorder was the only substance use disorder significantly associated with past-year PTSD diagnosis, and the third most common substance disorder, a worrying fact given that most overdose deaths are the result of combining opioids with benzodiazepines (Zoorob, 2018). This is consistent with other studies reporting that patients with severe PTSD symptoms are characterized by high use of opioids and sedatives (Peck et al., 2018). According to the self-medication hypothesis, it seems that many individuals use multiple substances to overcome a highly distressful disorder such as PTSD characterized by multiple, different, negative effects (i.e., trauma re-experience, anger, sleep difficulties, and negative cognitions). Patients with PTSD have difficulty regulating their emotions, and their use of multiple substances could be a coping mechanism to avoid negative emotions (Mirhashem et al., 2017). However, the use of multiple substances at the same time enhances certain effects (e.g. sedation), increasing the individual's chances of being exposed to traumatic events/victimization, and subsequently increases the risk of developing PTSD symptoms (high-risk model) (Kaysen et al., 2011). Another explanation for the comorbidity between polydrug use disorders and PTSD is that the effects of multiple substances and their withdrawal on the endogenous stress response system, the hypothalamic-pituitary-adrenal (HPA) axis, and the activation of stress hormones such as corticotropin-releasing factor (CRF), predispose the individuals to develop PTSD after exposure to trauma (susceptibility model) (Becker, 2012). The pattern of the drugs most commonly used in our sample indicates that many individuals might be using substances with similar actions (alcohol and opioids, sedatives and opioids) to enhance their effect on the central nervous system (e.g., reducing hypervigilant symptoms) (Connor et al., 2014). Cannabis can act as an analgesic in patients with pain disorders. It was recently found that even a small amount of smoked cannabis, if combined with opioids, can enhance the pain-suppression effect as well as increase the positive subjective feeling related to opioids, thus increasing the potential for abuse (Cooper et al., 2018). This may explain the high prevalence of cannabis use disorders in our sample. To a lesser degree, some individuals preferred combining opioids with stimulants, also known as speedball, a combination known to have a powerful synergistic effect on behavior (Trujillo et al., 2011). The most common secondary substance used in our sample was alcohol, which is legal, suggesting that availability could have contributed to its frequent use (Connor et al., 2014). Consistently with our results, several other trials, focused on separate substances, reported high use of a variety of substance classes, including alcohol, methamphetamine, benzodiazepine and cannabis, among individuals with OUDs (Anderson et al., 2018; Chen et al., 2011; Frost et al., 2018; Pikovsky et al., 2018; Schuman-Olivier et al., 2013).

The clinical presentation of patients with OUD and PTSD is complex. Individuals with comorbid PTSD and OUD have poor quality of life, poor functioning, and severe symptoms of OUD, a comorbidity that requires further evaluation to improve both screening and treatment (Hassan et al., 2017a; Ouimette et al., 2006; Schnurr et al., 2000). We strongly encourage clinicians facing challenging cases of OUD with polydrug use disorders to screen for active PTSD symptoms. More important, a key to the targeting of polydrug use disorders could be treating the active PTSD symptoms. Concurrent treatment of PTSD, using pharmacotherapy and psychotherapy, is highly recommended (Flanagan et al., 2016). Trauma-focused therapies such as prolonged exposure had promising effects in reducing PTSD symptomatology and craving for alcohol in an inpatient sample (Peck et al., 2018). The use of non-exposure therapy (i.e. cognitive behavioral therapy) was shown to be effective in reducing substance use among patients with OUD on opioid agonist therapy (OAT), but not effective in reducing PTSD symptoms compared to patients on OAT receiving standard care (Saunders et al., 2015). This is consistent with results showing that OAT by itself can be helpful for patients with OUD and PTSD, because of its efficacy in reducing psychiatric symptoms (Danovitch, 2016; Hassan et al., 2017b).

The main limitation of this study is that its methodology does not allow causal inferences; it is possible that polydrug use and diagnoses increase the risk of trauma exposure and susceptibility to stress. In addition, this is a retrospective study, thus subject to the risk of recall and information bias. Additionally, the relatively small sample size could have affected the results, in particular regarding the association with childhood maltreatment. Excluding the OUD + 1 group could have affected the power, resulting in smaller statistical significance.

In summary, there is a high prevalence of polydrug use disorders among OUD patients. More than a third of the individuals with polydrug use disorders exhibit active PTSD symptoms. Childhood maltreatment rates were high in both the polydrug and the control groups, but not statistically different between the two groups. PTSD was associated with polydrug use disorders, also when controlling for childhood maltreatment. Therefore, screening for PTSD symptoms in OUD patients with polydrug use disorders is critical. Future research should evaluate whether focused PTSD treatment in this population can reverse polydrug use disorders.

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Contributors

Dr. Hassan designed the study, analyzed the data, interpreted the results and wrote the manuscript. Dr. Le Foll contributed in study design, quality control and edited the manuscript. All authors approved final manuscript for submission.

Conflict of interest

No conflict declared.

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