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Multiple drug use disorder diagnoses among drug-involved hospitalizations in the United States: Results from the 2016 National Inpatient Sample

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ABSTRACT

Background: Having more than one drug use disorders (DUDs) is an increasing public health concern, but it has been understudied. The goal of this study is to investigate the prevalence and patterns of coexisting DUD diagnoses among inpatient hospitalizations due to DUD in the United States.

Methods: Data were from the 2016 National Inpatient Sample and included hospitalizations with a principal DUD diagnosis for patients aged ≥18 years (i.e., drug-involved hospitalizations, unweighted n = 31,707). The DUD diagnosis profile was categorized into three groups: single, two, and three or more DUD diagnoses. Generalized ordered logit models were used to examine correlates of DUD diagnosis groups.

Results: Among drug-involved hospitalizations, approximately 50.1 % had multiple coexisting DUD diagnoses (2 DUD diagnoses, 32.1 %; ≥3 DUD diagnoses, 18.0 %). Particularly, opioid use disorder accounted for 58.6 % of drug-involved hospitalizations. Among specific opioid-involved hospitalizations, about 51.2 % had multiple DUD diagnoses. The most common secondary DUD diagnoses among opioid-involved hospitalizations included cocaine (21.7 %), cannabis (18.5 %), and sedatives (18.1 %). Adjusted analyses showed that being aged 18−25 years (vs. ≥ 26), living in areas with the lowest quartile of household income (vs. highest), and having a secondary diagnosis of mental disorders or tobacco/alcohol use disorder were associated with increased odds of having multiple DUD diagnoses in the total sample and in the opioid subsample.

Conclusions: Findings suggest that healthcare providers should increase the awareness of multiple DUDs while treating patients with DUD, especially those with opioid use disorder. More research is needed to better characterize treatment needs for patients with multiple DUDs.

1. Introduction

Multiple drug use disorders are defined as having more than one drug use disorder (DUD) simultaneously or sequentially during a defined period, which it is an emerging public health concern (National Institute on Drug Abuse [NIDA], 2018). According to the 2012–2013 National Epidemiologic Survey on Alcohol and Related Conditions, 7.8 % and 2.3 % of U.S. adults had multiple DSM-5 substance use disorders (SUDs: DUD and alcohol use disorder [AUD]) in the lifetime and in the past year, respectively (McCabe et al., 2017). In the United States, national data indicate that as many as 77 % of persons aged 18–64 years with OUD have been found to have a co-occurring SUD (tobacco use disorder [TUD], AUD, and DUDs) in the past year (Jones and McCance-Katz, 2019). Compared to a single DUD, having multiple DUDs has been associated with poorer health and healthcare outcomes, and the resources needed to prevent and treat multiple DUDs are substantial and complex, yet they are understudied (Connor et al., 2014; Ives and Ghelani, 2006; Substance Abuse and Mental Health Services Administration [SAMHSA], 2014). Therefore, it is imperative to extend empirical research on patients diagnosed with multiple DUDs to inform

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early identification and integrated treatment in order to improve treatment for persons with severe drug use problems.

The terminology of DUDs used in this study was considered as DUDs for illicit drugs and prescription drugs. Most existing studies have examined multiple SUDs, which often include DUDs, AUD, or/and TUD, and limited information is available specifically for multiple DUDs. For example, one study reported that 73 %, 24 %, and 3% of veterans with any SUD (SUD: DUD and AUD) had 1, 2–3, and ≥4 SUDs in 2012, respectively (Bhalla et al., 2017). However, pooling drug, alcohol, or/and tobacco data may obscure the difference in the prevalence, pattern, and treatment needs among persons with DUD&AUD/TUD versus those with multiple-DUDs. A national study found that the prevalence of SUD (AUD and DUD) among specific DUD ranged from 57 % for prescription OUD to 98 % for inhalant use disorder, while the prevalence of SUD among AUD was only 15 % (McCabe et al., 2017). Thus, it is important to distinguish between those with multiple DUDs and those multiple SUDs in order to understand prevalently coexisting DUDs among drug users, which has implications for identifying strategies to increase the risk assessment and optimize the treatment planning and healthcare services.

Most previous studies have used the survey data to detect multiple DUDs, and there is a lack of clinical information on multiple DUDs to delineate the severity of DUD patterns and potential treatment needs (Connor et al., 2014; Hernández-Serrano et al., 2016; McCabe et al., 2017). By using the survey data of U.S. adults in 2001–2002, a latent class analysis identified five classes: no DUD (92.5 %), DUD for cannabis only (5.8 %), DUD for stimulants and hallucinogens (0.6 %), DUD for prescription drugs (0.6 %), and multiple DUDs (0.5 %) (Agrawal et al., 2007). Persons admitted to inpatient care due to a DUD usually have severe medical conditions (e.g., severe withdrawal symptoms), and multiple DUDs have been associated with a greater number of healthcare utilization, such as psychiatric hospitalizations and residential treatment (Bhalla, et al., 2017). The exploration of DUDs using a large inpatient sample could provide more empirical information to increase physicians' awareness of patients with multiple DUDs (Bhalla et al., 2017). Diagnosis of DUD in general hospitals is based on the International Classification of Diseases (ICD). The recent implementation of the ICD, Tenth Revision, Clinical Modification (ICD-10-CM) may provide the opportunity to improve DUD identification and classification. Unlike the ICD-9-CM, the ICD-10-CM splits the diagnosis codes for drug withdrawal into specific drug diagnosis groups, including a specific drug diagnosis for inhalants, and introducing a new category of "unspecific use" (Centers for Medicare and Medicaid Services [CMS], 2018; Heslin et al., 2017). In ICD-10-CM, DUDs include drug use related diagnoses for opioids, cannabis, sedatives, cocaine, stimulants, hallucinogens, inhalants, and other drugs. More information is provided in the Methods section. Therefore, this study used national inpatient data to identify treatment-based multiple DUDs to better inform essential clinical information.

Prior studies have suggested that several factors were associated with multiple SUDs; however, the majority of these studies have focused on specific populations, such as small clinical samples and persons with a DUD associated with a specific drug. In a primary care sample, adults who were younger, white, unemployed, less educated, or disabled were more likely to have multiple SUDs (TUD, AUD, and DUD) (John et al., 2018). An analysis of National Veterans Health Administration data showed that being black and being homeless were positively associated with having a higher number of multiple SUDs (AUD and DUD) (Bhalla et al., 2017). Among adults with OUD, having post-traumatic stress disorder was associated with increased odds of OUD with two or more other SUDs (AUD and DUD) (Hassan and Le Foll, 2019). Of admissions to publicly funded treatment programs in Tennessee, about 49 % reported multiple substance (alcohol or drug) abuse, odds of polysubstance abuse were higher for African Americans, those aged 18–44 years, or those admitted in an urban setting (Kedia et al., 2007). Hence, there is a need to better understand demographic and clinical factors associated with having multiple DUDs in a large representative sample, including treatment-seeking individuals, in order to better identify vulnerable drug users for facilitating the linkage to effective treatment.

Taken together, the present study uses a large national inpatient sample with the ICD-10-CM diagnosis codes to (1) examine the distribution of multiple coexisting DUD diagnoses, (2) determine the correlates of the DUD diagnosis profile, and (3) identify the potential pattern of multiple DUD diagnoses.

2. Methods

2.1. Data source

Data were from the National Inpatient Sample (NIS), part of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality (HCUP, 2018). The NIS is sampled from the State Inpatient Datasets (SID), which include inpatient data of U.S. community hospitals (excluding rehabilitation and long-term acute care hospitals) derived from billing data submitted by hospitals to statewide data organizations. The NIS data include the clinical and other information typically recorded in the discharge abstract for all-payer patients (HCUP, 2018). We used one-year (2016) data because the 2016 NIS was the first annual data using the ICD-10-CM coding system. The NIS datasets are anonymized that are publicly available for research. We aggregated the de-identified data at national level for the analysis. The use of NIS datasets for research was determined to be exempt from review by the Duke University Health System Institutional Review Board.

2.2. Study sample

In this study, the observation unit is the hospitalization encounter. We focused on a subsample of the NIS data: hospitalizations for adult patients aged ≥ 18 years with a principal DUD diagnosis (i.e., drug-involved hospitalizations). DUD diagnoses were identified by ICD-10-CM codes: opioid use disorder (F11.xx excluding F11.11, F11.21), cannabis use disorder (F12.xx excluding F12.11, F12.21), sedative/hypnotic/anxiolytic use disorder (F13.xx excluding F13.11, F13.21), cocaine use disorder (F14.xx excluding F14.11, F14.21), stimulant use disorder (F15.xx excluding F15.11, F15.21), hallucinogen use disorder (F16.xx excluding F16.11, F16.21), inhalant use disorder (F18.xx excluding F18.11, F18.21), and other psychoactive substance related disorders (F19.xx excluding F19.11, F19.21) (CMS, 2018). The excluded codes were the remission codes indicating that the patients did not currently met the full criteria for DUD (Fleury et al., 2016). The unweighted sample size is 31,707 (weighted N = 158,535). The study sample represented a national sample of hospitalizations of adult patients admitted to community hospitals for treatment due to DUD.

2.3. Study variables

2.3.1. DUD diagnoses

According to ICD-10-CM codes above, DUD diagnoses included DUD diagnoses for opioids, cannabis, sedatives, cocaine, stimulants, hallucinogens, inhalants and other drugs.

2.3.2. Principal and secondary DUD diagnosis

The principal diagnosis was defined as the condition chiefly responsible for a hospital admission (HCUP, 2018). Each hospitalization has only one principal diagnosis, and the principal DUD diagnoses were mutually exclusive based on the data source. The secondary diagnosis was defined as the preexisting condition at admission or newly developed condition during hospitalization, and each hospitalization could have 0–29 secondary diagnosis codes (HCUP, 2018).

2.3.3. Single and multiple DUD diagnoses

In order to analyze the pattern of DUD diagnoses, we further identified the DUD diagnosis profile (i.e., single and multiple DUD diagnosis groups) by the status of the principal and/or secondary DUD diagnosis: (1) single DUD diagnosis refers to hospitalization with 1 principal DUD diagnosis; (2) multiple-2 DUD diagnoses refer to hospitalization with 1 principal and 1 secondary DUD diagnosis; (3) multiple-≥3 DUD diagnoses refer to hospitalization with 1 principal and ≥2 secondary DUD diagnoses.

2.3.4. Other psychiatric disorder diagnoses

We also included TUD (ICD-10-CM codes: F17.xx [nicotine dependence] excluding F17.201, F17.211, F17.221, F17.291), AUD (ICD-10-CM codes: F10.xx excluding F10.11, F10.21), and mental disorders other than DUDs as clinical covariates that have been found to be associated with multiple DUDs (Bhalla et al., 2017; John et al., 2018). Definition of mental disorders was consistent with those described in the HCUP report, which included anxiety, bipolar, depressive, disruptive/impulse-control/conduct, eating, personality, schizophrenia, somatic symptom, and trauma/stress-related disorders (Owens et al., 2019).

2.3.5. Sociodemographics

For descriptive purposes and as covariates for the association analyses, we examined patient age group at admission (18 − 25, 26 − 34, 35 − 49, 50 − 64, ≥65), sex (male, female), race/ethnicity (non-Hispanic white, non-Hispanic African American, Hispanic, Asian/Pacific Islander, others), urban-rural location (large metropolitan, median/small metropolitan, rural), median household income quartiles based on ZIP code (lowest, 2nd, 3rd, and highest quartile), primary expected payer (Medicare, Medicaid, private, uninsured, other payers), and admitting hospital's region (Northeast, Midwest, South, West). Age group was categorized consistent with the groups from the National Survey on Drug Use and Health to increase the comparability, and the categories of other sociodemographics were directly used HCUP-defined groups. The selection of these possibly correlated variables was based on previous studies (Bhalla et al., 2017; Ding et al., 2011; Owens et al., 2019).

2.4. Statistical analysis

Descriptive analysis was first conducted, to examine the characteristics of the study sample. *Then*, we calculated the prevalence of single and multiple DUD diagnoses by the sociodemographic and clinical characteristics in the total sample and in the subsample with principal OUD diagnosis, respectively. *Furthermore*, we determined the correlates of DUD diagnosis groups in the total sample and in the opioid subsample (i.e., opioid-related hospitalizations). As the outcome was ordinal (single, 2 DUD, and ≥3 DUD diagnoses), the ordered logit regression was primarily considered; however, the parallel lines/proportional odds assumption for the ordered logit regression was tested and found to be violated, which indicated coefficient estimates were not the same for each of the ordered dichotomizations of the outcome variable (Williams, 2016). For example, being aged 35 − 49 (vs. 18 − 25) had different odds ratios (AOR 0.44, 95 %CI 0.39 − 0.49 for having 2 or ≥3 DUDs compared to 1 DUD and AOR 0.33, 95 %CI 0.29 − 0.39 for having ≥3 DUDs compared to 1 or 2 DUDs) (Table 2), and the estimates will fail to reflect the nature of correlations if the ordered logit regression was used and reported only one odds ratio in this case. Therefore, we switched to the generalized ordered logit regression (significance level, $p < 0.05$), which is a superior alternative because it relaxes the restrict assumption of the ordered logistic model and can be more parsimonious than multinomial logistic regression (Long and Freese, 2014; Williams, 2006, 2016). Specifically, the generalized ordered logit model reported the same coefficient for the variables where the proportional odds assumption is met and different coefficients for other variables where the assumption is violated in a series of panel contrasts in one model (Williams, 2006, 2016). *Finally*, the proportions of each secondary DUD diagnosis among each principal DUD diagnosis were estimated to further identify the common combinations of multiple DUDs.

The data were weighted properly in all statistical analyses to account for the NIS's complex designs excepted for the sample size in Stata 15.1 (StataCorp, 2017).

Table 1
Demographic and clinical characteristics of the study sample: The 2016 National Inpatient Sample.

Variables	Unweighted N	Weighted column % (95 % CI)
Overall	31,707	100
Principal drug use disorder diagnosis[a]		
Opioid	18,596	58.6 (55.3 − 62.0)
Stimulant	3521	11.1 (9.8 − 12.5)
Sedative	2383	7.5 (6.8 − 8.3)
Cocaine	2109	6.7 (5.9 − 7.4)
Cannabis	1077	3.4 (3.0 − 3.8)
Hallucinogen	250	0.8 (0.7 − 1.0)
Inhalant	24	0.1 (0.05 − 0.12)
Other drug[b]	3747	11.8 (10.2 − 13.6)
Age group, years		
18 − 25	5585	17.6 (16.5 − 18.8)
26 − 34	9285	29.3 (28.0 − 30.6)
35 − 49	9443	29.8 (28.8 − 30.8)
50 − 64	6097	19.2 (17.8 − 20.7)
≥65	1297	4.1 (3.8 − 4.5)
Sex		
Male	19,790	62.4 (61.1 − 63.7)
Female	11,911	37.6 (36.3 − 38.9)
Race/ethnicity		
White, non-Hispanic	20,368	64.2 (60.7 − 67.6)
African American, non-Hispanic	5641	17.8 (15.4 − 20.5)
Hispanic	2712	8.6 (7.1 − 10.2)
Asian/Pacific Islander	281	0.9 (0.6 − 1.3)
Other race/ethnicity[b]	1239	3.9 (3.2 − 4.8)
Primary expected payer		
Medicare	4646	14.7 (13.7 − 15.6)
Medicaid	14,545	45.9 (42.8 − 48.9)
Private	7466	23.5 (20.9 − 26.4)
Uninsured	3713	11.7 (10.0 − 13.7)
Other payer[b]	1275	4.0 (3.2 − 5.0)
Patient's residence location		
Large metropolitan	18,377	58.0 (53.7 − 62.1)
Median/small metropolitan	8481	26.7 (23.5 − 30.2)
Rural	4295	13.5 (11.5 − 15.8)
Median household income for patient's ZIP code		
Lowest quartile	11,693	36.9 (34.2 − 39.6)
2nd quartile	7261	22.9 (21.4 − 24.5)
3rd quartile	6242	19.7 (18.6 − 20.8)
Highest quartile	5539	17.5 (15.3 − 19.9)
Hospital region		
Northeast	9731	30.7 (25.5 − 36.4)
Midwest	8179	25.8 (21.3 − 30.8)
South	10,036	31.7 (27.7 − 35.9)
West	3761	11.9 (9.7 − 14.4)
Secondary tobacco use disorder diagnosis[c]		
No	13,999	44.2 (41.3 − 47.0)
Yes	17,708	55.8 (53.0 − 58.7)
Secondary alcohol use disorder diagnosis[c]		
No	25,525	80.5 (78.5 − 82.3)
Yes	6182	19.5 (17.7 − 21.5)
Secondary mental disorder diagnosis[c]		
No	13,632	43.0 (40.8 − 45.2)
Yes	18,075	57.0 (54.8 − 59.2)
Discharge status		
Routine	24,616	77.6 (75.7 − 79.4)

(*continued on next page*)

Table 1 (*continued*)

Variables	Unweighted N	Weighted column % (95 % CI)
Transfer/homecare	3236	10.2 (9.1 – 11.5)
Against medical advice	3791	12.0 (10.5 – 13.5)
Other discharge[b]	64	0.2 (0.1 – 0.5)

CI: confidence interval; DUD: drug use disorder.

[a] Each hospitalization included only one principal diagnosis, and the principal drug use disorder diagnoses were mutually exclusive in the study sample.

[b] Other drug was defined by the ICD-10-CM diagnosis group of other psychoactive substance related disorders; other race/ethnicity included Native American and other unspecified races/ethnicities; other payer included Worker's compensation, CHAMPUS, CHAMPVA, Title V, and other government programs; other discharge status included died in hospital, discharged alive but unknown destination, or unknown status. Missing values for sex (non-female/non-male), race/ethnicity (not reported), residence (not reported), household income (not reported), and payer (not reported) were counted as a valid group but not reported in the table.

[c] Each hospitalization could have 0–29 secondary diagnoses, and mental disorders included anxiety, bipolar, depressive, disruptive/impulse-control/conduct, eating, personality, schizophrenia, somatic symptom, and trauma/stress-related disorders.

3. Results

3.1. Characteristics of the study sample (Table 1)

In 2016, it was estimated that there were 158,535 drug-involved hospitalizations. Of this sample, 58.6 % had a principal diagnosis of OUD, and 41.4 % had a principal diagnosis of non-opioid DUD (stimulants, 11.1 %; sedatives, 7.5 %; cocaine, 6.7 %; cannabis, 3.4 %; hallucinogens, 0.8 %; inhalants, 0.1 %; other drugs, 11.8 %). Additionally, 57.0 %, 55.8 %, and 19.5 % had any secondary mental disorders other than DUDs, TUD, and AUD, respectively.

The majority of drug-involved hospitalizations involved patients who were aged 18–34 years (46.9 %), male (62.4 %), or non-Hispanic white (64.2 %); had Medicaid as primary payer (45.9 %); lived in a large metropolitan area (58.0 %); had family income in the lowest quartile (36.9 %); had been admitted to a hospital in the Northeast region (30.7 %); and who had been discharged routinely (77.6 %).

3.2. Multiple DUD diagnoses among drug-involved hospitalizations (Table 2)

Among all drug-involved hospitalizations, 50.1 % had multiple DUD diagnoses (2 DUD diagnoses, 32.1 %; ≥3 DUD diagnoses, 18.0 %). The prevalence of multiple DUD diagnoses varied by age group, sex, race/ethnicity, payer, residence location, and hospital region. For example, 34.4 % and 23.9 % of drug-involved hospitalizations of patients aged 18 – 25 years had 2 and ≥3 DUD diagnoses, respectively, and the prevalence of multiple DUD diagnoses decreased with increasing age. Also, whites had a higher prevalence of hospitalization with ≥3 DUD diagnoses than did African Americans (19.3 % vs. 13.1 %), whereas the other racial/ethnic group had a higher prevalence of 2 DUD diagnoses than did whites (36.3 % vs. 32.0 %).

Results from the generalized ordered logit regression showed that, in the total sample, being aged 18 – 25 years (vs. ≥ 26); male (vs. female); white (vs. Asian/Pacific Islander); in the lowest quartile of household income (vs. highest); admitted to a hospital in the Northeast (vs. Midwest); and having a secondary diagnosis of TUD, AUD, and mental disorders other than DUDs were associated with increased odds of having more DUD diagnoses. In the model, being aged 50 – 64 and ≥65 years, African American, and other races/ethnicities did not meet the proportional odds assumption, respectively, and had different odds ratios in two ordinal comparisons: 2, ≥3 vs. 1 DUD diagnosis and ≥3 vs. 1, 2 DUD diagnoses.

3.3. Multiple DUD diagnoses among opioid-involved hospitalizations (Table 3)

Among the subsample of opioid-involved hospitalizations, 51.2 % had multiple DUD diagnoses (2 DUD diagnoses, 33.2 %; ≥3 DUD diagnoses, 18.1 %). Across demographic groups, the prevalence of multiple DUD diagnoses was 61.6 % for young adults aged 18 – 25 years, 57.0 % for adults aged 26 – 34 years, 52.0 % for males, 49.9 % for females, 52.8 % for whites, 42.1 % for African Americans, and 55.2 % for Hispanics.

Adjusted analysis showed that, in the opioid subsample, being aged 18 – 25 years (vs. ≥ 26); being in the lowest and 2nd quartiles of household family income (vs. highest); being admitted to a hospital in the Northeast (vs. Midwest, South); and having a secondary diagnosis of TUD/AUD/mental disorders other than DUDs were associated with increased odds of having more DUD diagnoses. In this model, being aged 35 – 49, 50 – 64, and ≥65 years did not meet the proportional odds assumption and had different odds ratios in two ordinal comparisons: 2, ≥3 vs. 1 DUD diagnosis and ≥3 vs. 1, 2 DUD diagnoses. In contrast to the overall sample model, being female (vs. male) and white (vs. Asian/Pacific Islander) were not significant, but being in the 2nd quartile of household income (vs. highest) and admitted to a hospital in the South (vs. Northeast) became significant.

3.4. Principal DUD diagnosis and coexisting secondary DUD diagnosis (Table 4)

Of hospitalizations for each principal DUD diagnosis, 56.4 % of hallucinogens, 56.1 % of sedatives, 52.8 % of cocaine, 51.2 % of opioids, 50.3 % of stimulants, 44.0 % of other drugs, and 30.6 % of cannabis use disorder diagnoses had at least one secondary DUD diagnosis. Among opioid-involved hospitalizations, cocaine (21.7 %), cannabis (18.5 %), and sedatives (18.1 %) were the most common secondary DUD diagnoses. Over 40 % of sedative-involved hospitalizations had a secondary OUD diagnosis. Secondary cannabis use disorder diagnosis was the most prevalent secondary DUD among drug-involved hospitalizations for hallucinogens (44.8 %), cocaine (32.1 %), stimulants (30.1 %), and other drugs (22.8 %), respectively.

In addition, 35.4 % of cocaine-involved hospitalizations had a secondary AUD diagnosis, compared to around 20 % for other principal drug hospitalizations. About 61.8 % of opioid-involved hospitalizations had a secondary diagnosis of TUD, compared to a relatively lower prevalence for other principal drugs (e.g., cocaine, 53.9 %; stimulants, 48.5 %; cannabis, 42.9 %).

4. Discussion

To our knowledge, this study is the first to comprehensively examine the prevalence and pattern of multiple DUD diagnoses nationwide after the ICD-10-CM implementation. Despite the important clinical implications for treating patients with the most severe drug use problems, multiple DUDs are underrecognized and undertreated (Connor et al., 2014; National Institute on Drug Abuse (NIDA, 2018). Persons admitted to inpatient units due to a DUD usually indicate the need for urgent/intensive care, and this analysis of inpatient data provides important clinical information about the distribution and patterns of multiple DUDs. *First*, we found that about 1 in 2 drug-involved hospitalizations had multiple coexisting DUD diagnoses. *Second*, of the sample, OUD was the leading DUD (58.6 %). Multiple DUD diagnoses were also highly prevalent, specifically among opioid-involved hospitalizations (51.2 %), and commonly coexisting DUD diagnoses included sedative, cocaine, and cannabis use disorder. *Finally*, multiple DUD diagnoses in the total sample and in the opioid subsample differed by age groups, household income, and a secondary diagnosis of other

Table 2
Prevalence and adjusted odds ratios of multiple DUD diagnoses among drug-involved hospitalizations: The 2016 National Inpatient Sample.

	Prevalence (n = 31,707)			Generalized ordered logit regression (n = 29,274)[a]	
Number of DUD diagnoses Weighted %	1 DUD Row % (95 % CI)	2 DUDs Row % (95 % CI)	≥3 DUDs Row % (95 % CI)	2, ≥3 vs. 1 DUD(s) AOR (95 % CI)	≥3 vs. 1, 2 DUD(s) AOR (95 % CI)
Overall (DUD)	49.9 (47.4 – 52.5)	32.1 (30.8 – 33.4)	18.0 (16.2 – 19.8)	———	———
Age group, years					
18 – 25	41.7 (39.3 – 44.1)	34.4 (32.9 – 35.9)	23.9 (21.8 – 26.2)	1.00	1.00
26 – 34	44.0 (41.4 – 46.6)	33.8 (32.2 – 35.3)	22.3 (20.3 – 24.3)	**0.88 (0.81 – 0.95)**	**0.88 (0.81 – 0.95)**[b]
35 – 49	49.5 (46.1 – 52.9)	32.6 (30.9 – 34.4)	17.8 (15.5 – 20.4)	**0.69 (0.62 – 0.77)**	**0.69 (0.62 – 0.77)**[b]
50 – 64	61.3 (57.7 – 64.8)	29.2 (27.2 – 31.4)	9.4 (7.7 – 11.5)	**0.44 (0.39 – 0.49)**	**0.33 (0.29 – 0.39)**
≥65	77.4 (74.6 – 80.0)	19.9 (17.6 – 22.4)	2.7 (1.8 – 4.0)	**0.26 (0.22 – 0.31)**	**0.12 (0.08 – 0.18)**
Sex					
Male	48.7 (45.9 – 51.5)	32.9 (31.5 – 34.4)	18.4 (16.5 – 20.4)	1.00	1.00
Female	52.0 (49.5 – 54.4)	30.7 (29.3 – 32.2)	17.3 (15.6 – 19.1)	**0.90 (0.86 – 0.96)**	**0.90 (0.86 – 0.96)**[b]
Race/ethnicity					
White, non-Hispanic	48.7 (46.4 – 51.1)	32.0 (30.7 – 33.3)	19.3 (17.6 – 21.1)	1.00	1.00
African American, non-Hispanic	55.7 (50.8 – 60.6)	31.2 (28.3 – 34.2)	13.1 (10.7 – 15.9)	0.88 (0.77 – 1.01)	**0.78 (0.67 – 0.89)**
Hispanic	48.5 (42.3 – 54.8)	32.9 (30.2 – 35.8)	18.5 (14.0 – 24.1)	0.91 (0.77 – 1.07)	0.91 (0.77 – 1.07)[b]
Asian/Pacific Islander	63.7 (55.1 – 71.5)	26.0 (20.7 – 32.1)	10.3 (6.4 – 16.2)	**0.55 (0.41 – 0.75)**	**0.55 (0.41 – 0.75)**[b]
Other race/ethnicity[c]	44.9 (40.4 – 49.4)	36.3 (33.6 – 39.1)	18.8 (15.3 – 22.9)	1.08 (0.93 – 1.27)	0.88 (0.75 – 1.04)
Primary expected payer					
Medicare	60.7 (58.2 – 63.2)	27.7 (26.1 – 29.4)	11.6 (10.2 – 13.2)	0.98 (0.84 – 1.15)	0.98 (0.84 – 1.15)[b]
Medicaid	46.9 (43.7 – 50.1)	33.9 (32.2 – 35.7)	19.2 (17.1 – 21.4)	1.07 (0.89 – 1.29)	1.07 (0.89 – 1.29)[b]
Private	49.6 (44.7 – 54.4)	31.2 (29.1 – 33.5)	19.2 (15.9 – 23.0)	1.00	1.00
Uninsured	49.4 (46.5 – 52.3)	31.8 (29.9 – 33.7)	18.8 (16.3 – 21.6)	1.02 (0.84 – 1.24)	1.02 (0.84 – 1.24)[b]
Other payer[c]	49.1 (44.9 – 53.3)	33.7 (30.8 – 36.8)	17.2 (14.1 – 20.8)	1.11 (0.90 – 1.38)	1.11 (0.90 – 1.38)[b]
Patient's residence location					
Large metropolitan	50.2 (46.4 – 54.0)	32.2 (30.3 – 34.1)	17.6 (15.1 – 20.4)	1.00	1.00
Median/small metropolitan	50.0 (47.6 – 52.4)	31.4 (29.9 – 32.8)	18.7 (17.1 – 20.3)	0.95 (0.83 – 1.09)	0.95 (0.83 – 1.09)[b]
Rural	49.4 (45.5 – 53.4)	32.6 (30.6 – 34.7)	18.0 (15.2 – 21.1)	0.95 (0.79 – 1.15)	0.95 (0.79 – 1.15)[b]
Median household income for patient's ZIP code					
Lowest quartile	50.7 (47.1 – 54.3)	31.7 (29.9 – 33.5)	17.7 (15.4 – 20.2)	**1.17 (1.01 – 1.34)**	**1.17 (1.01 – 1.34)**[b]
2nd quartile	50.3 (47.9 – 52.8)	31.7 (30.3 – 33.2)	17.9 (16.2 – 19.8)	1.04 (0.92 – 1.18)	1.04 (0.92 – 1.18)[b]
3rd quartile	50.8 (48.2 – 53.3)	31.5 (30.0 – 33.0)	17.8 (16.1 – 19.6)	0.98 (0.89 – 1.08)	0.98 (0.89 – 1.08)[b]
Highest quartile	47.7 (44.0 – 51.4)	33.6 (31.0 – 36.3)	18.7 (16.3 – 21.4)	1.00	1.00
Hospital region					
Northeast	43.4 (38.4 – 48.4)	36.0 (33.8 – 38.3)	20.6 (16.8 – 25.1)	1.00	1.00
Midwest	56.7 (50.9 – 62.3)	28.7 (25.8 – 31.8)	14.6 (11.5 – 18.4)	**0.65 (0.48 – 0.88)**	**0.65 (0.48 – 0.88)**[b]
South	50.9 (48.2 – 53.7)	31.0 (29.3 – 32.7)	18.1 (16.3 – 19.9)	0.84 (0.67 – 1.04)	0.84 (0.67 – 1.04)[b]
West	49.5 (45.1 – 53.9)	32.4 (30.4 – 34.4)	18.1 (14.9 – 21.9)	0.94 (0.72 – 1.22)	0.94 (0.72 – 1.22)[b]
Secondary tobacco use disorder diagnosis[d]					
No	57.7 (55.3 – 60.1)	29.2 (27.7 – 30.8)	13.1 (11.8 – 14.4)	1.00	1.00
Yes	43.8 (40.6 – 47.0)	34.4 (32.8 – 36.0)	21.8 (19.5 – 24.3)	**1.62 (1.44 – 1.83)**	**1.62 (1.44 – 1.83)**[b]
Secondary alcohol use disorder diagnosis[d]					
No	52.7 (50.1 – 55.2)	31.1 (29.8 – 32.5)	16.2 (14.7 – 17.8)	1.00	1.00
Yes	38.6 (35.4 – 41.9)	36.1 (34.5 – 37.7)	25.3 (22.3 – 28.6)	**1.69 (1.53 – 1.87)**	**1.69 (1.53 – 1.87)**[b]
Secondary mental disorder diagnosis[d]					
No	54.3 (51.1 – 57.6)	30.5 (28.8 – 32.3)	15.1 (13.2 – 17.3)	**1.38 (1.27 – 1.51)**	**1.38 (1.27 – 1.51)**[b]
Yes	46.6 (44.2 – 49.1)	33.3 (32.0 – 34.6)	20.1 (18.4 – 22.0)	1.00	1.00

CI: confidence interval; DUD: drug use disorder. Bold face: $p < 0.05$.
[a] The outcome of the generalized ordered logit regression was an ordinal dependent variable of the number of DUD diagnoses (1, 2, ≥3). Missing values for sex, race/ethnicity, residence, household income, and payer were counted as a valid group but not reported in the table, and 2433 out of 31,707 hospitalizations were excluded due to missing values in these independent variables.
[b] The generalized ordered logit regression model produced identical AORs, with AORs of 2, ≥3 vs. 1 because the parallel lines assumption was met.
[c] Other race/ethnicity included Native American and other unspecified races/ethnicities; other payer included Worker's compensation, CHAMPUS, CHAMPVA, Title V, and other government programs.
[d] Each hospitalization could have 0–29 secondary diagnoses, and mental disorders included anxiety, bipolar, depressive, disruptive/impulse-control/conduct, eating, personality, schizophrenia, somatic symptom, and trauma/stress-related disorders.

psychiatric disorders. These results have important implications for research and clinical practices.

Consistent with estimates from the clinical trial and treatment data, our findings raise concerns regarding the high prevalence of multiple coexisting DUD diagnoses among hospitalized DUD patients (John et al., 2018; Kedia et al., 2007). Commonly identified reasons for using multiple drugs include: to enhance drug effects, to mitigate drug craving or withdrawal, and drug accessibility; consequently, multiple drug users may have perceived positive drug outcome expectancies or have expected reinforcing effects that may drive continued drug use (Connor et al., 2014; Kenna et al., 2007; Liu et al., 2018). Despite a lack of information on DUD treatment use among persons with multiple DUDs, the national estimates indicated a low treatment utilization rate for individual DUD, such as 8% for adults with past-year cannabis use disorder (Wu et al., 2017) and 13 % for adults with a past-year DUD (Grant et al., 2016). Both our results and prior studies demonstrate a strong need to address treatment needs and improve treatment co-ordination and management for people with multiple DUDs (Connor et al., 2014; Ives and Ghelani, 2006). Compared to single DUD, treatment targeting multiple DUDs is associated with substantial obstacles due to the number of different drugs that can be combined in a diagnosis of multiple DUDs as well as variations in addiction severity across drugs (Ives and Ghelani, 2006; Kenna et al., 2007). Clinicians may provide psychosocial intervention and/or pharmacotherapy treatment

Table 3
Prevalence and adjusted odds ratios of multiple DUD diagnoses among opioid-involved hospitalizations: The 2016 National Inpatient Sample.

	Prevalence (n = 18,596)			Generalized ordered logit regression (n = 17,358)[a]	
Number of DUD diagnoses	1 DUD	2 DUDs	≥3 DUDs	2, ≥3 vs. 1 DUD(s)	≥3 vs. 1, 2 DUD(s)
Weighted %	Row % (95 % CI)	Row % (95 % CI)	Row % (95 % CI)	AOR (95 % CI)	AOR (95 % CI)
Overall (OUD)	48.8 (45.0 – 52.5)	33.2 (31.3 – 35.0)	18.1 (15.6 – 20.8)	———	———
Age group, years					
18 – 25	38.4 (35.0 – 41.9)	34.8 (32.8 – 36.9)	26.8 (23.7 – 30.2)	1.00	1.00
26 – 34	43.0 (39.5 – 46.7)	34.8 (32.7 – 36.9)	22.2 (19.5 – 25.1)	**0.81 (0.74 – 0.89)**	**0.81 (0.74 – 0.89)**[b]
35 – 49	47.9 (43.1 – 52.8)	34.6 (32.1 – 37.1)	17.5 (14.3 – 21.3)	**0.67 (0.59 – 0.77)**	**0.58 (0.49 – 0.68)**
50 – 64	62.2 (57.2 – 66.8)	29.6 (26.6 – 32.8)	8.2 (6.2 – 11.0)	**0.39 (0.34 – 0.45)**	**0.25 (0.21 – 0.31)**
≥65	77.4 (73.6 – 80.8)	20.2 (17.1 – 23.7)	2.4 (1.3 – 4.3)	**0.26 (0.20 – 0.33)**	**0.10 (0.05 – 0.17)**
Sex					
Male	48.0 (43.9 – 52.1)	33.8 (31.8 – 35.9)	18.2 (15.6 – 21.2)	1.00	1.00
Female	50.1 (46.6 – 53.6)	32.1 (30.1 – 34.1)	17.9 (15.5 – 20.5)	0.95 (0.88 – 1.02)	0.95 (0.88 – 1.02)[b]
Race/ethnicity					
White, non-Hispanic	47.2 (43.8 – 50.6)	33.2 (31.4 – 35.0)	19.6 (17.3 – 22.2)	1.00	1.00
African American, non-Hispanic	57.9 (50.0 – 65.3)	30.5 (25.9 – 35.6)	11.6 (8.2 – 16.2)	0.88 (0.71 – 1.09)	0.88 (0.71 – 1.09)[b]
Hispanic	44.8 (36.9 – 52.9)	35.5 (31.8 – 39.4)	19.7 (13.4 – 27.9)	0.95 (0.77 – 1.17)	0.95 (0.77 – 1.17)[b]
Asian/Pacific Islander	60.5 (41.3 – 77.0)	28.9 (18.1 – 42.9)	10.5 (4.6 – 22.4)	0.65 (0.41 – 1.02)	0.65 (0.41 – 1.02)[b]
Other race/ethnicity[c]	43.1 (37.5 – 48.8)	37.3 (33.7 – 41.1)	19.6 (15.3 – 24.8)	1.01 (0.85 – 1.21)	1.01 (0.85 – 1.21)[b]
Primary expected payer					
Medicare	62.1 (58.8 – 65.3)	26.9 (24.8 – 29.2)	11.0 (9.1 – 13.1)	0.86 (0.72 – 1.04)	1.01 (0.82 – 1.24)[b]
Medicaid	46.4 (41.9 – 50.9)	34.6 (32.3 – 37.1)	19.0 (16.1 – 22.2)	1.03 (0.83 – 1.27)	1.03 (0.83 – 1.27)[b]
Private	47.6 (41.3 – 53.9)	32.7 (29.9 – 35.7)	19.7 (15.6 – 24.7)	1.00	1.00
Uninsured	46.4 (40.7 – 52.3)	34.6 (31.9 – 37.5)	18.9 (13.7 – 25.5)	1.10 (0.83 – 1.46)	1.10 (0.83 – 1.46)[b]
Other payer[c]	46.0 (40.1 – 52.0)	35.6 (31.3 – 40.0)	18.4 (14.4 – 23.3)	1.26 (0.98 – 1.63)	1.26 (0.98 – 1.63)[b]
Patient's residence location					
Large metropolitan	49.0 (43.9 – 54.1)	33.2 (30.6 – 35.9)	17.8 (14.6 – 21.6)	0.89 (0.73 – 1.08)	0.89 (0.73 – 1.08)[b]
Median/small metropolitan	49.5 (46.2 – 52.7)	32.1 (30.2 – 34.0)	18.5 (16.3 – 20.9)	0.94 (0.71 – 1.23)	0.94 (0.71 – 1.23)[b]
Rural	48.0 (41.4 – 54.6)	33.8 (30.6 – 37.2)	18.3 (13.9 – 23.6)	1.00	1.00
Median household income for patient's ZIP code					
Lowest quartile	50.0 (44.7 – 55.4)	32.7 (30.1 – 35.4)	17.3 (13.9 – 21.2)	**1.37 (1.17 – 1.59)**	**1.37 (1.17 – 1.59)**[b]
2nd quartile	48.2 (44.7 – 51.8)	32.5 (30.5 – 34.6)	19.3 (16.7 – 22.1)	**1.23 (1.05 – 1.44)**	**1.23 (1.05 – 1.44)**[b]
3rd quartile	50.8 (47.0 – 54.5)	31.9 (29.8 – 34.1)	17.4 (15.1 – 19.9)	1.00 (0.88 – 1.13)	1.00 (0.88 – 1.13)[b]
Highest quartile	46.0 (41.1 – 51.0)	35.4 (31.8 – 39.1)	18.6 (15.6 – 22.1)	1.00	1.00
Hospital region					
Northeast	40.4 (35.2 – 45.8)	37.8 (35.2 – 40.4)	21.8 (17.4 – 27.0)	1.00	1.00
Midwest	58.7 (50.4 – 66.6)	27.8 (23.7 – 32.2)	13.5 (9.3 – 19.1)	**0.56 (0.38 – 0.83)**	**0.56 (0.38 – 0.83)**[b]
South	51.2 (47.1 – 55.4)	31.9 (29.5 – 34.5)	16.8 (14.0 – 20.0)	**0.70 (0.53 – 0.93)**	**0.70 (0.53 – 0.93)**[b]
West	42.7 (36.5 – 49.1)	35.7 (32.7 – 38.7)	21.6 (16.5 – 27.9)	1.12 (0.80 – 1.57)	1.12 (0.8 – 01.57)[b]
Secondary tobacco use disorder diagnosis[d]					
No	57.1 (53.6 – 60.6)	30.4 (28.2 – 32.7)	12.5 (10.7 – 14.5)	1.00	1.00
Yes	43.6 (39.1 – 48.2)	34.8 (32.6 – 37.1)	21.6 (18.4 – 25.0)	**1.55 (1.32 – 1.81)**	**1.55 (1.32 – 1.81)**[b]
Secondary alcohol use disorder diagnosis[d]					
No	51.7 (48.0 – 55.4)	32.2 (30.2 – 34.2)	16.1 (14.0 – 18.5)	1.00	1.00
Yes	34.7 (30.7 – 39.0)	37.8 (35.4 – 40.2)	27.5 (23.2 – 32.3)	**1.84 (1.61 – 2.10)**	**1.84 (1.61 – 2.10)**[b]
Secondary mental health disorder diagnosis[d]					
No	53.4 (49.0 – 57.8)	31.5 (29.2 – 33.9)	15.1 (12.5 – 18.1)	1.00	1.00
Yes	44.6 (40.9 – 48.4)	34.6 (32.6 – 36.7)	20.8 (18.2 – 23.6)	**1.41 (1.26 – 1.59)**	**1.41 (1.26 – 1.59)**[b]

CI: confidence interval; DUD: drug use disorder. Bold face: $p < 0.05$.

[a] The outcome of the generalized ordered logit regression was an ordinal dependent variable of the number of DUD diagnoses (1, 2, ≥3). Missing values for sex, race/ethnicity, residence, household income, and payer were counted as a valid group but not reported in the table, and 1238 out of 18,596 hospitalizations were excluded due to missing values in these independent variables.

[b] The generalized ordered logit regression model produced identical AORs, with AORs of 2, ≥3 vs. 1 because the parallel lines assumption was met.

[c] Other race/ethnicity included Native American and other unspecified races/ethnicities; other payer included Worker's compensation, CHAMPUS, CHAMPVA, Title V, and other government programs.

[d] Each hospitalization could have 0–29 secondary diagnoses, and mental disorders included anxiety, bipolar, depressive, disruptive/impulse-control/conduct, eating, personality, schizophrenia, somatic symptom, and trauma/stress-related disorders.

for multiple DUDs based on single DUD treatment strategies or their own experience, but limited evidence is available on service models from clinical trials or single DUD treatment efficacy for multiple DUD treatment (Connor et al., 2014; Kenna et al., 2007). Future research is needed to improve the accurate identification of multiple DUDs and provide linkages to follow-up specialty services in order to customize treatment strategies and maximize treatment effects (Jones et al., 2012; Kenna et al., 2007).

Our findings on multiple DUDs reinforce concerns on the burden of the U.S. opioid epidemic on healthcare. We found that nationally, OUD accounted for about 59 % of overall drug-involved hospitalizations, and among them, 51 % had a secondary DUD diagnosis (most prevalent DUDs: cocaine, 22 %; cannabis, 19 %; sedatives, 18 %). It was estimated that the national rate of opioid-related ED visits and inpatient stays has increased by 99 % and 64 % between 2005 and 2014, respectively (Weiss et al., 2017). A new study has also shown that a high prevalence of co-occurring multiple DUDs among adults aged 18–64 years with OUD in a national survey sample: 16 % for sedatives, 16 % for cannabis, and 13 % for cocaine (Jones and McCance-Katz, 2019). Studies have hypothesized co-use of opioids and other drugs, for example, cocaine use was thought to lessen the severity of opioid withdrawal symptoms (Leri et al., 2003), cannabis use might be a substitute for prescription opioids to treat pain (Corroon et al., 2017), and benzodiazepine use appeared to enhance the effects of opioids (Jones et al., 2012). However, only 26 % of persons with OUD aged ≥ 12 years have received any alcohol or drug use-related treatment in the past year (Wu et al., 2016),

Table 4
Coexisting secondary drug use disorder diagnoses among the principal-specific drug use disorder diagnosis: The 2016 National Inpatient Sample.

	Principal drug use disorder (DUD) diagnosis[a]						
	Opioid[1st] (n = 18,596)	Stimulant[1st] (n = 3521)	Sedative[1st] (n = 2383)	Cocaine[1st] (n = 2109)	Cannabis[1st] (n = 1077)	Hallucinogen[1st] (n = 250)	Other drugs[1st] (n = 3747)
Weighted %	Column % (95 % CI)	Column % (95 % CI)	Column % (95 % CI)	Column % (95 % CI)	Column % (95 % CI)	Column % (95 % CI)	Column % (95 % CI)
Any DUD[2nd] diagnosis[b], yes	51.2 (47.5 – 55.0)	50.3 (47.9 – 52.6)	56.1 (52.2 – 59.9)	52.8 (50.3 – 55.4)	30.6 (27.7 – 33.8)	56.4 (48.8 – 63.7)	44.0 (39.6 – 48.5)
Opioid[2nd], yes	————	16.2 (14.6 – 17.9)	40.1 (36.0 – 44.3)	17.4 (15.7 – 19.4)	8.1 (6.5 – 10.1)	9.6 (6.4 – 14.2)	18.6 (16.7 – 20.7)
Stimulant[2nd], yes	8.1 (6.7 – 9.6)	————	7.6 (6.2 – 9.2)	8.3 (6.8 – 10.0)	9.4 (7.7 – 11.4)	6.4 (3.9 – 10.4)	12.5 (10.5 – 14.7)
Sedative[2nd], yes	18.1 (15.6 – 20.9)	6.5 (5.5 – 7.6)	————	5.8 (4.7 – 7.1)	4.4 (3.2 – 5.9)	5.6 (3.2 – 9.5)	6.1 (5.1 – 7.4)
Cocaine[2nd], yes	21.7 (19.0 – 24.6)	9.1 (8.0 – 10.2)	9.8 (7.5 – 12.8)	————	10.2 (8.3 – 12.4)	7.6 (4.8 – 11.8)	13.7 (11.6 – 16.1)
Cannabis[2nd], yes	18.5 (16.5 – 20.7)	30.1 (28.2 – 32.1)	17.7 (16.0 – 19.6)	32.1 (29.5 – 34.8)	————	44.8 (37.8 – 52.0)	22.8 (19.7 – 26.2)
Hallucinogen[2nd], yes	0.6 (0.4 – 0.8)	0.9 (0.6 – 1.2)	0.8 (0.5 – 1.3)	2.1 (1.5 – 2.9)	3.5 (2.6 – 4.7)	————	1.4 (0.9 – 2.2)
Other drugs[2nd], yes	7.5 (5.3 – 10.5)	7.7 (6.7 – 8.8)	7.0 (4.8 – 10.0)	7.5 (6.3 – 9.0)	4.9 (3.6 – 6.6)	5.2 (2.7 – 9.7)	————
Alcohol use disorder[2nd], yes	17.3 (14.8 – 20.2)	17.2 (15.8 – 18.6)	20.9 (18.0 – 24.1)	35.4 (32.4 – 38.5)	15.8 (13.1 – 18.9)	24.0 (18.8 – 30.1)	23.1 (20.3 – 26.2)
Tobacco use disorder[2nd], yes	61.8 (58.0 – 65.5)	48.5 (45.3 – 51.6)	47.6 (44.0 – 51.3)	53.9 (50.5 – 57.1)	42.9 (39.0 – 46.9)	42.8 (35.2 – 50.8)	44.0 (38.6 – 49.6)

DUDs included opioid, cannabis, sedatives, cocaine, stimulants, hallucinogens, inhalants, and other drug use disorder, but inhalant use disorder was not reported due to small cell size following the NIS privacy protection rule.
CI: confidence interval; DUD: drug use disorder.
[a] Principal diagnosis (1 st) was defined as the condition chiefly responsible for the hospitalization. Each hospitalization case only included one principal diagnosis, and the principal drug use disorder diagnoses were mutually exclusive in the study sample.
[b] Secondary diagnosis (2nd) was defined as pre-existing condition at admission or newly developed condition during hospitalization. Each secondary drug use disorder diagnosis is a binary variable, and we reported the percentage of having a secondary drug use disorder diagnosis among principal-specific drug use disorder diagnosis hospitalizations.

and persons with DUD or AUD were likely to have a greater risk of OUD and overdose (Dowell et al., 2016; Jones et al., 2012). Therefore, it is important to assess drug-using patients for multiple drug use problems and treat multiple DUDs to improve outcomes. Medication treatment for OUD has been promoted to expand OUD treatment (Jones and McCance-Katz, 2019). Additionally, medication treatment for OUD may potentially support treatment for multiple OUD-DUDs, and one register-based study suggested that, among patients receiving opioid maintenance treatment, those with adequate doses of methadone/sublingual buprenorphine/naloxone were significantly less abuse of benzodiazepines and amphetamines than those with inadequate medicine doses (Heikman et al., 2017). More efforts are needed to improve treatment for DUDs and to develop effective service models for those with multiple DUDs.

Our findings also concerned the subgroups that were at elevated risk for multiple DUDs, and we found that young adults aged 18 – 25 years (vs. ≥ 26), males (vs. females), whites (vs. Asians/Pacific Islanders), residents in the area with the lowest quartile of household income (vs. highest), and patients with mental disorders/TUD/AUD were associated with elevated odds of having multiple DUDs. These results are in line with factors related to multiple drug use and DUDs in previous studies (Bhalla et al., 2017; John et al., 2018; McCabe et al., 2017). The emerging drug use trend (e.g., synthetic cannabinoids [spice]), and/or misusing prescription drugs may contribute to multiple DUDs among young, low-income, or minority groups (Connor et al., 2014; McCabe et al., 2008; Ramo et al., 2010; Stogner and Miller, 2014). Comprehensive assessment and intervention are needed for accurate detection and early treatment among these subgroups. It has been suggested that ED-based screening, psychosocial/pharmacologic intervention, and a SUD treatment linkage service provide opportunities to improve care for SUD patients (Hawk and D'Onofrio, 2018), and treatment at hospital discharge that facilitates linkage to follow-up addiction treatment could increase completion of DUD treatment (Liebschutz et al., 2014; Saitz, 2019). Future studies should also address subgroup-specific treatment barriers to improve treatment outcomes.

The findings should be interpreted with caution. *First*, all analyses were based on encounter-level data rather than patient-level data, and some patients may have had readmissions during the study period (HCUP, 2018). However, the one-year data is a relatively short-term period. *Second*, these results may be considered as conservative estimates, as the NIS sampling excluded rehabilitation facilities. *Finally*, the diagnosis data are based on clinical care as part of treatment encounters, which could be biased by various sources, such as billing issues (e.g., reimbursement), under-reporting by patients, coding mistakes, and other sources of errors (e.g., a lack of validation by objective measures to confirm a diagnosis) (Wu et al., 2013). In order to reduce the potential impact from underreporting of DUDs, we limited our study sample to those with hospitalizations with DUD as a primarily responsible variable for inpatient admission rather than any diagnosis. Another potential coding bias might be due to the transition of ICD coding systems. For instance, inhalant-related diagnoses in the ICD-9-CM were included in the other specified/unspecified drug abuse/dependence category (i.e., no inhalant-specific codes), but there are inhalant-specific diagnosis codes in the ICD-10-CM (CMS, 2018). Therefore, inhalant use disorder diagnoses may be underrecognized or not given an isolated diagnosis. HCUP has implemented the quality control procedures on the data with ICD-10-CM coding to minimize the impact of coding bias or errors.

5. Conclusions

Multiple DUD diagnoses are highly prevalent among patients admitted to inpatient treatment for DUD in the United States. Findings suggest that healthcare providers should increase their assessments and identification for multiple DUDs to improve treatment planning and management while treating drug-using patients, which is particularly relevant for patients with opioid use disorder. Further research on delineating different combinations of co-occurring DUDs is needed to better evaluate patients' treatment needs for improving treatment outcomes.

Contributors

H Zhu contributed to study designs, conducted literature searches and data analyses, and drafted the manuscripts. LT Wu contributed to study designs and analyses, drafted the manuscripts, and supervised the work. All authors approved the final draft of the manuscript.

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Declaration of Competing Interest

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