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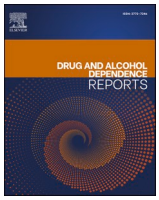

Characteristics and co-morbidities associated with hospital discharges for opioid and methamphetamine co-use, United States 2016–2019

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HIGHLIGHTS

- Hospitalizations for opioid and methamphetamine co-use increased between 2016 and 2019.
- A high proportion of co-use stays had co-morbid psychiatric and infectious diseases.
- Co-use was associated with a higher proportion of patient directed discharge.
- Co-use presents unique challenges for delivering hospital-based addiction services.

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ABSTRACT

Introduction: The US overdose crisis is increasingly characterized by opioid and methamphetamine co-use. Hospitalization is an important opportunity to engage patients in substance use treatment. Understanding characteristics of co-use-related hospital stays can inform the development of services to better support this growing patient population.

Methods: We used 2016–2019 National Inpatient Sample data to conduct a cross sectional analysis of hospitalizations involving use of opioids, methamphetamine, or both. We used bivariate analysis to compare patient demographics. We then used multinomial logistic regressions to compare the proportion of hospital stays which indicated co-morbid diagnosis. To account for correlated data, we used generalized linear models to compare outcomes in hospital mortality, patient-directed discharge, and length of stay.

Results: Co-use-related stays had a higher proportion of co-morbid mental health (60.7%; 95% CI: 59.9–61.4%) and infectious diseases (41.5%; 95% CI: 40.8–42.2%), than opioid- or methamphetamine-related stays. Co-use-related stays increased between 2016 and 2019 and were associated with a higher proportion of patient directed discharge (10.7%; 95% CI: 10.4–11.0%) and longer length of stay (6.3 days; 95% CI: 6.2–6.4 days) compared to opioid (8.1%; 95% CI: 7.9–8.3% and 5.8 days; 95% CI: 5.8–5.9 days) and methamphetamine-related stays (6.5%; 95% CI: 6.3–6.6% and 5.5 days; 95% CI: 5.4–5.5 days).

Conclusion: Patients discharged with co-use differ from patients with opioid or methamphetamine use alone, representing a range of challenges and opportunities. In addition to offering treatment for both substance use disorders, hospital-based services that address co-occurring conditions may better support patients with co-use through targeted and tailored approaches.

1. Introduction

The overdose crisis in the United States (US) is increasingly driven by both opioids and methamphetamine (Fischer et al., 2021). Between 2011 and 2021 overdose deaths involving both psychostimulants (predominantly methamphetamine) and opioids increased 21-fold, and in

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2021 opioids were present in 66% of all psychostimulant overdose deaths (Spencer et al., 2023). Increases in opioid and methamphetamine co-use have been identified in admissions to specialty substance use treatment facilities (Jones et al., 2020b), Veterans Health Administration hospitals (Warfield et al., 2022), and community hospitals (Fingar and Owens, 2021).

Hospital admissions offer a key opportunity to connect individuals with substance use treatment. Over 20% of individuals with opioid and/or methamphetamine use disorders were hospitalized at least once in the previous year (Gryczynski et al., 2016). A variety of hospital-based addiction medicine models have been developed (Englander et al., 2022), however most were designed specifically for patients with opioid use disorder (OUD) and focus on continuing or initiating treatment with medications for opioid use disorder (MOUD) (Weimer et al., 2019). These services may not support patients with multiple substance use disorders as effectively compared to patients with OUD alone (Englander et al., 2020; Nordeck et al., 2018; Tsui et al., n.d.). As the overdose crisis is increasingly characterized by opioid and methamphetamine co-use, it is important to better understand these patients' needs so that hospitals can develop and implement interventions to better serve this population.

Past research has identified high rates of mood disorders, psychotic disorders, and septicemia in methamphetamine-related (Winkelman et al., 2018) as well as opioid-related (Alemu et al., 2021) hospital stays. These studies also found hospitalized patients with opioid or methamphetamine use were more likely to be younger and White compared to other patients. However, the demographic characteristics and other medical needs of hospitalized patients with both opioid and methamphetamine co-use remain unknown. Findings from community surveys suggest hospital care for patients with co-use may be complicated by higher rates of chronic conditions, severe mental illness, infectious, and cardiovascular diseases (Shearer et al., 2020). One study has described the prevalence of hospital admissions indicating both opioid and stimulant use and compared demographic characteristics across substance use group (Fingar and Owens, 2021). Notably, this study included both methamphetamine and cocaine in a single aggregate stimulant use category despite differences in sociodemographic and health characteristics associated with methamphetamine and cocaine use (Booth et al., 2006; Jones et al., 2020a; Mustaquim et al., 2021). As hospitals respond to the shifting nature of the substance use epidemic, it is important to better understand the characteristics of hospitals where patients are admitted, patient demographic, and co-occurring medical needs associated with opioid and methamphetamine co-use specifically.

In this study we use four years of nationally representative data to describe hospital admissions indicating methamphetamine, opioid, and co-use. We estimate the 2016–2019 trends in hospitalizations for each substance use group. We compare the patient demographics, comorbidities, admitting hospital characteristics, and hospitalization outcomes between substance use groups.

2. Material and methods

2.1. Study sample and data source

We used data from the National Inpatient Sample (NIS) for hospital discharges between 2016 and 2019. The NIS is a nationally-representative all payer database and includes patient demographic, hospital characteristic, diagnosis, and stay outcome information for 20% of all inpatient discharges to acute care hospitals, representative of 97% of hospitalizations nationwide (Agency for Healthcare Research and Quality, 2020). For this cross-sectional analysis we used all admissions for adults aged 18 and older where opioid and/or methamphetamine use was indicated.

2.2. Methamphetamine and opioid use

We identified opioid and/or methamphetamine use with primary and secondary ICD-10-CM diagnosis codes (NIS data includes up to 40 diagnoses per record). Opioid use was identified with diagnosis codes for opioid abuse, dependence, or poisoning. Although there are not specific ICD-10-CM codes for methamphetamine abuse, dependence, or poisoning, we used codes for other stimulant related disorders and psychostimulant poisoning to identify methamphetamine use (Appendix A). Previous work has shown that these codes have a high predictive probability for methamphetamine-use (Shearer et al., 2021). After identifying all admissions with opioid and/or methamphetamine use, we categorized them into three mutually exclusive groups: opioid use without methamphetamine use, methamphetamine use without opioid use, and opioid and methamphetamine co-use.

2.3. Patient demographic characteristics

We include categorical variables for patient race and ethnicity (non-Hispanic Black, non-Hispanic White, and non-Hispanic Other [Asian/Pacific Islander, Native American, & other], and Hispanic), age (18–24, 25–34, 35–44, 45–54, 55+), and insurance coverage (Medicare, Medicaid, and other [includes Private, self-pay, no charge]) as well as a binary indicator for gender.

2.4. Patient co-morbidities

Based on a review of the literature and discussion with addiction medicine experts we identified disease which may be associated with opioid and/or methamphetamine use (Alemu et al., 2021; Curran et al., 2022; D'Amico et al., 2019; Dickson et al., 2021; Han et al., 2021b; Ronan and Herzig, 2016; Wen et al., 2020). We used groups of ICD-10-CM codes from the Clinical Classification Software Refined for ICD-10-CM diagnosis codes to define most disease categories (Appendix A). We then grouped diseases to identify medical services which may be involved in substance-related stays: mental health, infectious disease, cardiovascular, pulmonary, additional substance use, and injury. A single hospitalization may include diagnosis for multiple specific diseases but would only be counted in the overall category once. We tabulated the proportion of diseases and injuries by group. We also used Stata's *Elixhauser* module to calculate the Elixhauser Comorbidity Index for each hospital stay. We considered primary and secondary diagnosis codes when identifying co-morbid conditions.

2.5. Hospital characteristics

We included categorical variables for hospital region (Northeast, Midwest, South, West), size (small, medium, large), and ownership (public, non-profit, for-profit) and a combined rural/urban location/teaching status variable (rural, urban non-teaching, urban teaching). We classified hospital size using NIS definitions, which vary based on a hospital's region, location and teaching status (Agency for Healthcare Research and Quality, 2020).

2.6. Hospital outcomes

Based on the discharge disposition, we created binary indicators for whether the patient died while hospitalized or had a patient directed discharge (identified as "against medical advice" in the NIS). We calculated length of stay as a count variable by subtracting the admission date from the discharge date (2.2% of discharges had a stay length of zero days).

2.7. Statistical analysis

First, we estimated the weighted prevalence of opioid,

methamphetamine, and co-use-related hospitalizations from 2016 to 2019. We conducted separate bivariate analysis with chi-square and Wald-T tests to determine whether differences in frequency of demographic characteristics between co-use and opioid or methamphetamine use alone were statistically significant. We estimated the age- and sex-adjusted proportion of substance use involved admissions which also indicated each comorbidity using logistic regressions and Stata's postestimation margin command.

Next, we compared hospital characteristics across the three substance use groups. We used multinomial logistic regressions, controlling for demographic characteristics and overall health with an Elixhauser Comorbidity Index score, to estimate the proportion of admissions that were to each hospital type and whether this differed across groups.

Finally, we compared hospital stay outcomes across the three groups. Controlling for demographic characteristics, Elixhauser Comorbidity Index, and hospital characteristics we used generalized linear models with a binomial distribution and logit link to estimate the weighted proportion of hospital deaths and patient-directed discharges. We used a generalized linear model with a Poisson distribution and log link to compare the mean length of stay between the three substance use groups. To account for potential correlation at the hospital level, regression analyses of hospital characteristics and stay outcomes were estimated with standard errors calculated to account for hospital-year clusters. Observations with missing sociodemographic characteristics (0.02%, 0.2%, and 3.2%, missing gender, insurance, and race/ethnicity information, respectively) were excluded using case wise deletion. An additional 0.1% of observations were missing hospital outcome information and were excluded from that analysis. Appropriate strata and weight variables were used to account for the NIS's complex survey design in all analyses. Stata 18.0 was used for all analyses. This project was determined to not be human subjects research by the University of Minnesota's Institutional Review Board.

3. Results

3.1. Trends in opioid, methamphetamine, and co-use hospitalizations

Between 2016 and 2019, we identified over a million annual opioid and/or methamphetamine-related hospital stays using nationally representative discharge data (Appendix B). The weighted number of opioid-related stays decreased from 899,000 (95% CI: 852,000–946,000) in 2016 to 818,000 (95% CI: 775,000–861,000) in 2019, while methamphetamine-related stays increased from 229,000 (95% CI: 211,000–247,000) to 357,000 (95% CI: 331,000–382,000) and co-use-related stays increased from 67,000 (95% CI: 62,000–72,000) to 97,000 (95% CI: 90,000–105,000).

3.2. Patient demographic characteristics

A larger proportion of co-use-related stays were for younger patients aged 18–24 (10.8%; 95% CI: 10.5–11.1%) and 25–34 (38.5%; 95% CI: 38.0–39.0%), while a larger proportion of opioid-related stays were for older patients aged 55–64 (21.0%; 95% CI: 20.9–21.1%) and 65+ (23.6%; 95% CI: 23.3–24.0%) (Table 1). A majority of methamphetamine-related (62.7%; 95% CI: 62.4–63.0%) and co-use-related stays (57.1%; 95% CI: 56.5–57.6%) were for male patients, but only 48.1% (95% CI: 47.8–48.4%) of opioid-related stays were for males. Compared to other substance use groups, opioid-related stays were more common for non-Hispanic Black patients (14.9%; 95% CI: 14.4–15.4%) and methamphetamine-related stays were more common for Hispanic patients (15.0%; 95% CI: 14.3–15.7%). Both methamphetamine- and co-use-related stays were more common for patients enrolled in Medicaid (53.3%; 95% CI: 52.5–54.2% and 55.8%; 95% CI: 54.8–56.8%, respectively) than opioid-related stays (35.0%; 95% CI: 34.4–35.5%).

3.3. Comorbidities

We observed high proportion of comorbidities across each substance use-related stay group. Mental health diagnoses were the most common co-morbid disease identified. Co-use-related stays had the highest proportion of most co-morbid mental health disorders (60.7%; 95% CI: 59.9–61.4%) (Table 2). However, schizophrenia and related psychosis disorders were more common among methamphetamine-related stays (20.8%; 95% CI: 20.1–21.6%). The proportion of diagnosis for suicide ideation or attempt was also high among methamphetamine-related (16.0%; 95% CI: 15.4–16.6%) and co-use-related stays (15.3%; 95% CI: 14.7–15.8%).

Co-use-related stays had substantially higher proportions of co-morbid infectious diseases (41.5%; 95% CI: 40.8–42.2%), than opioid (30.1%; 95% CI: 29.8–30.4%) or methamphetamine-related stays (25.2%; 95% CI: 24.8–25.6%) (Table 2). Viral hepatitis, skin infections, and septicemia were the most common infectious diagnoses across all groups. Among opioid- and co-use-related stays, we also observed relatively high proportions of severe infections including endocarditis and osteomyelitis. Methamphetamine-related stays highest proportion of human immunodeficiency virus (HIV) diagnosis (2.7%; 95% CI: 2.6–2.8%). The proportion of stays indicating other sexually transmitted

Table 1
Demographic characteristics of opioid-, methamphetamine-, and co-use related hospital stays—United States, 2016–2019.

	Proportion% (95% CI) Opioid alone $n = 695{,}504$	Methamphetamine Alone $n = 234{,}252$	Co-use $n = 66{,}684$	Opioid alone vs. Co-use	Methamphetamine alone vs. Co-use
Race					
White	72.6 (71.9–73.2)	66.3 (65.4–67.2)	79.3 (78.5–80.0)	$P<0.001$	$P<0.001$
Black	14.9 (14.4–15.4)	11.6 (11.2–12.0)	5.9 (5.6–6.2)		
Hispanic	8.4 (8.1–8.8)	15.0 (14.3–15.7)	9.7 (9.1–10.3)		
Other	4.1 (3.9–4.3)	7.1 (6.7–7.6)	5.1 (4.7–5.5)		
Age					
18–24	4.9 (4.8–5.0)	9.5 (9.3–9.6)	10.8 (10.5–11.1)	$P<0.001$	$P<0.001$
25–34	17.5 (17.2–17.7)	26.1 (25.8–26.4)	38.5 (38.0–39.0)		
35–44	15.3 (15.1–15.4)	24.5 (24.3–24.7)	25.1 (24.7–25.5)		
45–54	17.7 (17.5–17.9)	21.8 (21.6–22.0)	14.6 (14.3–14.9)		
55–64	21.0 (20.9–21.2)	14.7 (14.4–15.0)	9.0 (8.7–9.3)		
65+	23.6 (23.3–24.0)	3.4 (3.3–3.5)	2.1 (1.9–2.2)		
Sex					
Female	51.9 (51.6–52.2)	37.3 (37.0–37.6)	42.9 (42.4–43.5)	$P<0.001$	$P<0.001$
Male	48.1 (47.8–48.4)	62.7 (62.4–63.0)	57.1 (56.5–57.6)		
Insurance					
Medicare	38.3 (37.8–38.7)	15.6 (15.3–15.8)	12.4 (12.1–12.8)	$P<0.001$	$P<0.001$
Medicaid	35.0 (34.4–35.5)	53.3 (52.5–54.2)	55.8 (54.8–56.8)		
Other	26.8 (26.4–27.2)	31.1 (30.3–31.9)	31.8 (30.8–32.8)		

Table 2
Proportion of opioid-, methamphetamine-, and co-use related hospital stays indicating each co-morbidity—United States, 2016–2019.

	Proportion% (95% CI)				
	Opioid alone	Methamphetamine Alone	Co-use	Opioid alone vs. Co-use	Methamphetamine alone vs. Co-use
Mental Health	52.3 (51.9–52.6)	58.1 (57.3–58.9)	60.7 (59.9–61.4)	$P<0.001$	$P<0.001$
Schizophrenia and psychosis disorders	4.5 (4.4–4.6)	20.8 (20.1–21.6)	11.9 (11.6–12.3)	$P<0.001$	$P<0.001$
Depression	26.8 (26.5–27.1)	21.7 (21.3–22.1)	28.1 (27.5–28.7)	$P<0.001$	$P<0.001$
Bipolar	11.1 (10.9–11.3)	14.7 (14.4–15.0)	15.5 (15.1–15.9)	$P<0.001$	$P<0.001$
Anxiety	28.9 (28.6–29.2)	21.8 (21.4–22.3)	29.2 (28.6–29.9)	$P = 0.279$	$P<0.001$
PTSD	7.0 (6.9–7.2)	7.9 (7.7–8.1)	9.7 (9.4–10.1)	$P<0.001$	$P<0.001$
Suicide	8.7 (8.5–8.9)	16.0 (15.4–16.6)	15.3 (14.7–15.8)	$P<0.001$	$P = 0.015$
Infectious Disease	30.1 (29.8–30.4)	25.2 (24.8–25.6)	41.5 (40.8–42.2)	$P<0.001$	$P<0.001$
Endocarditis	1.5 (1.5–1.6)	0.5 (0.5–0.6)	2.5 (2.3–2.6)	$P<0.001$	$P<0.001$
Osteomyelitis	2.5 (2.4–2.5)	1.5 (1.4–1.5)	2.6 (2.4–2.8)	$P = 0.059$	$P<0.001$
Infective Arthritis	0.4 (0.4–0.4)	0.2 (0.2–0.3)	0.6 (0.5–0.6)	$P<0.001$	$P<0.001$
Skin Infection	9.6 (9.5–9.8)	8.8 (8.6–9.0)	14.8 (14.4–15.2)	$P<0.001$	$P<0.001$
Septicemia	10.0 (9.8–10.2)	9.2 (8.9–9.4)	14.1 (13.7–14.6)	$P<0.001$	$P<0.001$
HIV	2.0 (1.8–2.1)	2.3 (2.2–2.5)	1.5 (1.4–1.6)	$P<0.001$	$P<0.001$
Hepatitis	14.4 (14.1–14.7)	9.6 (9.4–9.8)	23.1 (22.6–23.7)	$P<0.001$	$P<0.001$
STI	0.6 (0.6–0.6)	1.1 (1.0–1.1)	0.9 (0.8–1.0)	$P<0.001$	$P<0.001$
Cardiovascular	15.5 (15.3–15.7)	21.6 (21.2–22.1)	15.1 (14.6–15.5)	$P = 0.056$	$P<0.001$
Thrombophlebitis	2.8 (2.7–2.8)	1.4 (1.3–1.4)	2.4 (2.3–2.5)	$P<0.001$	$P<0.001$
Pulmonary Heart Disease	2.6 (2.5–2.7)	3.5 (3.3–3.6)	2.0 (1.9–2.2)	$P<0.001$	$P<0.001$
Myocardial Infarction	2.0 (1.9–2.0)	3.2 (3.1–3.4)	2.3 (2.1–2.4)	$P<0.001$	$P<0.001$
Heart Failure	10.4 (10.2–10.6)	18.2 (17.8–18.6)	10.3 (9.9–10.7)	$P = 0.552$	$P<0.001$
Ischemic Stroke	0.9 (0.8–0.9)	2.0 (1.9–2.0)	1.1 (1.0–1.2)	$P<0.001$	$P<0.001$
Pulmonary Disease	33.1 (32.8–33.4)	28.7 (28.3–29.0)	31.0 (30.5–31.5)	$P<0.001$	$P<0.001$
COPD	17.1 (16.9–17.3)	16.4 (16.0–16.7)	16.2 (15.7–16.6)	$P<0.001$	$P = 0.352$
Asthma	10.4 (10.2–10.5)	7.7 (7.5–7.9)	8.1 (7.9–8.3)	$P<0.001$	$P = 0.002$
Respiratory Arrest	15.0 (14.7–15.2)	11.8 (11.5–12.1)	15.1 (14.7–15.6)	$P = 0.526$	$P<0.001$
Chronic Pain	27.4 (27.0–27.9)	8.8 (8.6–9.0)	18.1 (17.6–18.5)	$P<0.001$	$P<0.001$
Additional Substance Use	36.3 (35.7–36.8)	44.5 (44.1–44.9)	51.6 (50.9–52.2)	$P<0.001$	$P<0.001$
Cocaine	12.8 (12.4–13.2)	8.2 (8.0–8.5)	14.3 (13.9–14.7)	$P<0.001$	$P<0.001$
Benzodiazepine	8.8 (8.5–9.1)	3.3 (3.2–3.4)	12.6 (12.1–13.0)	$P<0.001$	$P<0.001$
Cannabis	10.2 (10.0–10.5)	23.2 (22.8–23.5)	22.4 (22.0–22.8)	$P<0.001$	$P<0.001$
Alcohol	14.9 (14.5–15.2)	18.2 (18.0–18.5)	17.6 (17.2–18.0)	$P<0.001$	$P = 0.001$
Other	5.5 (5.2–5.7)	6.4 (6.2–6.6)	8.9 (8.6–9.2)	$P<0.001$	$P<0.001$
Injury	17.3 (17.1–17.6)	16.6 (16.3–17.0)	22.0 (21.5–22.6)	$P<0.001$	$P<0.001$
Poisoning by Drug	11.2 (11.1–11.4)	8.2 (8.0–8.4)	14.3 (13.9–14.7)	$P<0.001$	$P<0.001$
Other	6.8 (6.6–6.9)	9.2 (8.9–9.5)	8.8 (8.4–9.1)	$P<0.001$	$P = 0.010$

Proportion adjusted for age and sex.

infection diagnoses was much lower than HIV and hepatitis among all groups.

Co-morbid cardiovascular diagnoses were much more common among methamphetamine-related stays (21.6%; 95% CI: 21.2–22.1%) than opioid (15.5%; 95% CI: 15.3–15.7) or co-use-related stays (15.7%; 95% CI: 14.6–15.5%) (Table 2). Heart failure was the most common cardiovascular condition and diagnosed in 18.2% (95% CI: 17.8–15.6%) methamphetamine-related stays.

Over half of co-use-related stays indicated the use of at least one additional substance (51.5%; 95% CI: 50.9–52.2%) (Table 2). Among co-use related stays, cocaine, benzodiazepine, and other substance use was indicated in 14.3% (95% CI: 13.9–14.7%), 12.5% (95% CI: 21.1–13.0%), and 8.9% (95% CI: 8.6–9.2%) of stays, respectively. Furthermore, poisoning by drugs (14.3%; 95% CI: 13.9–14.7) was most

Table 3
Hospital characteristics of opioid-, methamphetamine-, and co-use-related stays—United States 2016–2019.

	Adjusted Proportion% (95% CI)				
	Opioid alone	Methamphetamine Alone	Co-use	Opioid alone vs. Co-use	Methamphetamine alone vs. Co-use
Region					
Northeast	26.1 (25.3–27.0)	3.4 (3.2–3.6)	6.8 (6.2–7.4)	$P<0.001$	$P<0.001$
Midwest	21.2 (20.5–22.0)	17.3 (16.3–18.3)	16.8 (15.8–17.8)	$P<0.001$	$P = 0.316$
South	34.1 (33.2–34.9)	28.7 (27.6–29.8)	31.9 (30.5–33.3)	$P = 0.001$	$P<0.001$
West	18.5 (17.9–19.1)	50.6 (49.3–51.9)	44.4 (43.0–45.9)	$P<0.001$	$P<0.001$
Location/Teaching					
Rural	7.1 (6.7–7.4)	10.2 (9.6–10.8)	9.4 (8.6–10.1)	$P<0.001$	$P = 0.019$
Urban-non Teaching	21.2 (20.6–21.9)	25.0 (23.8–26.2)	23.4 (22.2–24.5)	$P<0.001$	$P = 0.005$
Urban-Teaching	71.7 (71.0–72.5)	64.8 (63.5–66.0)	67.2 (65.9–68.6)	$P<0.001$	$P<0.001$
Bed Size					
Small	21.4 (20.6–22.2)	17.9 (17.0–18.9)	20.0 (18.7–21.3)	$P = 0.031$	$P<0.001$
Medium	29.0 (28.2–29.7)	25.5 (24.3–26.6)	24.5 (23.3–25.7)	$P<0.001$	$P = 0.069$
Large	49.6 (48.7–50.6)	56.6 (55.2–58.0)	55.5 (54.0–57.0)	$P<0.001$	$P = 0.108$
Ownership					
Public	12.5 (11.9–13.2)	16.7 (15.7–17.8)	16.4 (15.2–17.6)	$P<0.001$	$P = 0.571$
Non-Profit	75.2 (74.5–76.0)	64.7 (63.3–66.0)	68.3 (66.9–69.7)	$P<0.001$	$P<0.001$
For-Profit	12.2 (11.8–12.7)	18.6 (17.5–19.7)	15.3 (14.3–16.2)	$P<0.001$	$P<0.001$

Adjusts for patient race, age, sex, insurance, and Elixhauser comorbidity index.

common among co-use related stays. Other injuries were similarly common among methamphetamine-related (9.2%; 95% CI: 8.9–9.5%) and co-use related stays (8.8%; 95% CI: 8.4–9.1%).

3.4. Hospital characteristics

Methamphetamine- and co-use-related stays were more common in the West and less common in the Northeast than stays indicating opioid use alone. Methamphetamine (64.8%; 95% CI: 63.5–66.0%) and co-use-related stays (67.2%; 95% CI: 65.9–68.6%) were less commonly in urban teaching hospitals than opioid-related stays (71.7%; 95% CI: 71.0–72.5%) (Table 3). Additionally, a higher proportion of methamphetamine-related stays were at for-profit hospitals (18.6%; 95% CI: 17.5–19.7%) than opioid (12.2%; 95% CI: 11.8–12.7%) or co-use-related stays (15.3%; 95% CI: 14.3–16.2%).

3.5. Hospital outcomes

The proportion of stays ending with patient directed discharge were high among all groups (Co-use: 10.7%; 95% CI: 10.4–11.0%, opioid use: 8.1%; 95% CI: 7.9–8.3%, and methamphetamine use: 6.5%; 95% CI: 6.3–6.6%) (Table 4). Co-use related stays lasted longer (6.3 days; 95% CI: 6.2–6.4 days) than opioid (5.8 days; 95% CI: 5.8–5.9 days) or methamphetamine-related stays (5.5 days; 95% CI: 5.4–5.5 days).

4. Discussion

Between 2016 and 2019 we identified large increases in methamphetamine- and co-use-related US hospital stays. We found a high proportion of co-use related stays also had complex medical co-morbidities, patient directed discharge, and increased length of stay. The differences in demographic characteristics and medical needs across substance use groups can be leveraged to target and tailor interventional approaches to better support hospitalized patients with co-use.

A variety of hospital-based addiction care models have been developed to support hospitalized patients with substance use disorders (Englander et al., 2022). In many cases these services were developed to treat OUD and focus on initiating treatment with MOUD (Liebschutz et al., 2014; Weimer et al., 2019). However, these existing services may not effectively support patients with co-use. Previous research found methamphetamine co-use is associated with lower rates of MOUD initiation (Englander et al., 2020) and linkage to continuing outpatient treatment (Tsui et al., n.d.), than OUD alone. Our study highlights the unique needs of hospitalized patients with co-use, such as high proportions of certain mental health and infectious co-morbidities, that can inform a tailored and targeted approach. Hospitals may need to provide additional supports the address the comorbidities and referral process to outpatient treatment to improve patient outcomes for this unique population. For example, one safety-net hospital implemented an early identification, medication, and behavioral management protocol for methamphetamine use which was associated with increased outpatient addiction treatment attendance (Simpson et al., 2023). Additionally, the high proportion of methamphetamine- and co-use-involved stays which were paid for by Medicaid highlights the importance of Substance Use and Mental Health Block Grants and 1115 Waivers for developing and testing treatment approaches. Given the increasing prevalence of stimulant use we observe, it is important that these programs not be restricted to opioids alone.

Mental health conditions were the most common co-morbidity, suggesting that mental health professionals should play an important role supporting hospitalized patients with substance use. Hospitalizations indicating methamphetamine or co-use had a high proportion of schizophrenia and psychosis. It is important that care teams are able to differentiate between, and appropriately treat, methamphetamine-induced psychosis and other psychiatric conditions (Priest et al., 2023; Simpson et al., 2023). Additionally, we found a high proportion of methamphetamine- and co-use related stays also indicated PTSD or. Given the continued increase in methamphetamine-related stays, healthcare systems can adopt a trauma informed approach to better treat patients with substance use disorders and a history of trauma (Substance Abuse and Mental Health Services Administration, 2014). The associations between opioid, methamphetamine, and polysubstance use with suicide in outpatient treatment and community populations is well documented (Han et al., 2021a; Wilcox et al., 2004; Yuodelis-Flores and Ries, 2015). In this paper we found that this association extends to hospitalized stays indicating opioid and methamphetamine co-use which had the highest proportion of suicide-related diagnosis. Unfortunately, there are limited effective interventions to prevent suicide among people with opioid and/or methamphetamine use disorders highlighting a need for continued research and development of suicide prevention interventions for people with SUD (Padmanathan et al., 2020). In the meantime, recent interventions developed for outpatient SUD treatment facilities could be adapted for administration during hospital admissions (Ries et al., 2022).

All substance use groups had a high proportion of co-morbid infectious diseases, emphasizing the importance of multidisciplinary care teams and hospital-based interventions to identify and treat infection. Harm reduction education and resources, such as sterile injection equipment, should be provide as part of hospital-based care of patients with opioid and/or methamphetamine use who are at high risk (Chan et al., 2022; Priest et al., 2023). These resources may be particularly important and reduce the incidence of infectious disease, such as hepatitis, among hospitalized patients with co-use. Adopting hospital-based multidisciplinary care teams may also benefit patients with co-use who have higher rates endocarditis, osteomyelitis, and septicemia than patients with opioid or methamphetamine use alone (O'Donnell et al., 2022; Weimer et al., 2022). The proportion of admissions indicating a STI diagnosis was much lower than self-reported rates of STI among individuals with opioid and/or methamphetamine use (Shearer et al., 2020). This finding may suggest there is an opportunity to increase testing, diagnosis, and treatment of STIs during hospital admissions.

We found that co-use-related stays were on average longer than hospital stays involving only opioids or methamphetamine. Multidisciplinary teams may reduce the length of stays while addressing patients' other medical needs. Both a multidisciplinary psychiatric consult service (Sledge et al., 2015) and a substance use intervention team (Thompson et al., 2020) reduced the average length of stay. The association between substance use and increased risk for patient directed discharge is well documented in the literature (Ti and Ti, 2015). In this paper we build on previous findings by showing that this risk is substantially higher for co-use-related stays compared to stays involving only opioid or methamphetamine use. In addition to interrupting treatment, patient

Table 4
Outcomes associated with opioid-, methamphetamine-, and co-use-related stays—United States, 2016–2019.

	Adjusted proportion (95% CI)				
	Opioid alone	Methamphetamine Alone	Co-use	Opioid alone vs. Co-Use	Methamphetamine alone vs. Co-use
Died while hospitalized	1.6 (1.6–1.7)	1.3 (1.2–1.3)	1.6 (1.5–1.8)	$P = 0.987$	$P<0.001$
Patient directed discharge	8.1 (7.9–8.3)	6.5 (6.3–6.6)	10.7 (10.4–11.0)	$P<0.001$	$P<0.001$
Length of Stay (Days)	5.8 (5.8–5.9)	5.5 (5.4–5.5)	6.3 (6.2–6.4)	$P<0.001$	$P<0.001$

Adjusts for patient race, age, sex, insurance, Elixhauser comorbidity index, hospital region, location/teaching, size, and control.

directed discharges are associated with higher readmission and mortality rates (Alagappan et al., 2023; Tan et al., 2020). Although findings are mixed, both the initiation of MOUD during a hospital stay (Kays et al., 2022) and an addiction medicine consultation services (Marks et al., 2019) have reduced rates of patient directed discharge in some hospitals. These interventions may support patients hospitalized with co-use.

Identifying hospital characteristics associated with SUD-admissions may help inform a targeted approach to expanding SUD treatment services. A study of OUD-related emergency department visits found that stratifying hospitals by OUD visit rate categorized more rural hospitals in the top quartile of OUD related use, than stratifying hospitals by OUD visit volume (Khatri et al., 2022). We expand on this finding by showing that an even higher percentage of methamphetamine and co-use involved admissions were to rural hospitals while a lower percent were to urban teaching hospitals, compared to opioid use alone. While hospital-based addiction medicine services may be developed and tested in large academic medical centers it will be important that they are designed to be adopted in rural and non-academic settings to support patients affected by next waves of the overdose crisis.

There are limitations which may affect the interpretation of findings from this study. The NIS does not include admissions to substance use treatment facilities, psychiatric, short-term rehabilitation, and long-term acute care hospitals and so our results may not be reflective of all individuals who seek substance use treatment. However, the NIS is representative of 97% of stays in community hospitals nationwide so is an ideal source for characterizing patients admitted to hospitals who may benefit from substance use treatment in addition to other medical care (Gacutan, 2019). The identification of substance use group and medical co-morbidities was determined using ICD-10-CM diagnosis codes for each admission. The specificity and sensitivity of these codes likely varies across conditions and previous research has shown diagnosis codes may misclassify some substance-involved stays (Howell et al., 2021; Lagisetty et al., 2021). For example, some admissions involving opioid use maybe for patients taking prescribed chronic opioid analgesics especially among patients 55 and older (Howell et al., 2021). Furthermore, the ICD-10-CM diagnosis codes are not specific to methamphetamine use and so this group could include admissions for other substances such as amphetamines. However, an analysis from one health system found a high positive predictive value for using these ICD-10-CM diagnosis codes to identify methamphetamine use specifically (Shearer et al., 2021).

5. Conclusions

Using a nationally representative sample, we describe the similarities and differences of acute care hospital stays involving opioid, methamphetamine, or co-use. Between 2016 and 2019, co-use-related stays steadily increased and were associated with a higher proportion of patient directed discharge. Co-use was also associated with high proportions of both psychiatric and infectious comorbidities compared to opioid or methamphetamine use alone, highlighting the importance of multidisciplinary care teams and widespread knowledge of appropriate addiction treatment. As hospitals continue to develop services in response to the overdose crisis it is important that they consider the unique needs of people who use both opioids and methamphetamine to better support this growing patient population.

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CRediT authorship contribution statement

Riley D. Shearer: Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Writing – original draft. **Nathan D. Shippee:** Conceptualization, Funding acquisition, Methodology, Supervision, Writing – review & editing. **Beth A. Virnig:** Conceptualization, Writing – review & editing. **Timothy J. Beebe:** Conceptualization, Writing – review & editing. **Tyler N.A. Winkelman:** Conceptualization, Funding acquisition, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

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References

Agency for Healthcare Research and Quality, H.C. adn U.P., 2020. Introduction to the HCUP National Inpatient Sample (NIS), p. 2018.

Alagappan, A., Chambers, T.J.G., Brown, E., Grecian, S.M., Lockman, K.A., 2023. How does discharge against medical advice affect risk of mortality and unplanned readmission? A retrospective cohort study set in a large UK medical admissions unit. BMJ Open. 13, e068801 https://doi.org/10.1136/bmjopen-2022-068801.

Alemu, B.T., Olayinka, O., Martin, B.C., 2021. Characteristics of hospitalized adults with opioid use disorder in the United States: nationwide inpatient sample. Pain. Physi. 24, 327–334.

Booth, B.M., Leukefeld, C., Falck, R., Wang, J., Carlson, R., 2006. Correlates of rural methamphetamine and cocaine users: results from a multistate community study. J. Stud. Alcohol 67, 493–501. https://doi.org/10.15288/jsa.2006.67.493.

Chan, C.A., Canver, B., McNeil, R., Sue, K.L., 2022. Harm reduction in health care settings. Med. Clin. 106, 201–217. https://doi.org/10.1016/j.mcna.2021.09.002.

Curran, L., Nah, G., Marcus, G.M., Tseng, Z., Crawford, M.H., Parikh, N.I., 2022. Clinical correlates and outcomes of methamphetamine-associated cardiovascular diseases in hospitalized patients in California. J. Am. Heart. Assoc. 11, e023663 https://doi.org/10.1161/JAHA.121.023663.

D'Amico, M.J., Walley, A.Y., Cheng, D.M., Forman, L.S., Regan, D., Yurkovic, A., Samet, J.H., Weinstein, Z.M., 2019. Which patients receive an addiction consult? A preliminary analysis of the INREACH (INpatient REadmission post-Addiction Consult Help) study. J. Subst. Abuse Treat. 106, 35–42. https://doi.org/10.1016/j.jsat.2019.08.013.

Dickson, S.D., Thomas, I.C., Bhatia, H.S., Nishimura, M., Mahmud, E., Tu, X.M., Lin, T., Adler, E., Greenberg, B., Alshawabkeh, L., 2021. Methamphetamine-associated heart failure hospitalizations across the United States: geographic and social disparities. JAHA 10. https://doi.org/10.1161/JAHA.120.018370.

Englander, H., Jones, A., Krawczyk, N., Patten, A., Roberts, T., Korthuis, P.T., McNeely, J., 2022. A taxonomy of hospital-based addiction care models: a scoping review and key informant interviews. J. Gen. Intern. Med. 37, 2821–2833. https://doi.org/10.1007/s11606-022-07618-x.

Englander, H., King, C., Nicolaidis, C., Collins, D., Patten, A., Gregg, J., Korthuis, P.T., 2020. Predictors of opioid and alcohol pharmacotherapy initiation at hospital discharge among patients seen by an inpatient addiction consult service. J. Addict. Med. 14, 415–422. https://doi.org/10.1097/ADM.0000000000000611.

Fingar, K.R., Owens, P.L., 2021. Opioid-related and stimulant-related adult inpatient stays, 2012–2018: statistical Brief #271. Healthcare Cost and Utilization Project (HCUP) Statistical Briefs. Agency for Healthcare Research and Quality (US), RockvilleMD.

(Min-H. Fischer, B., O'Keefe-Markman, C., Lee, A., Daldegan-Bueno, D., 2021. 'Resurgent', 'twin' or 'silent' epidemic? A select data overview and observations on increasing psycho-stimulant use and harms in North America Subst. Abuse Treat. Prev. Policy. 16, 17. https://doi.org/10.1186/s13011-021-00350-5.

Gacutan, K., 2019. Healthcare Cost and Utilization Project — HCUP 53.

Gryczynski, J., Schwartz, R.P., O'Grady, K.E., Restivo, L., Mitchell, S.G., Jaffe, J.H., 2016. Understanding patterns of high-cost health care use across different substance user groups. Health Aff. (Millwood) 35, 12–19. https://doi.org/10.1377/hlthaff.2015.0618.

Han, B., Compton, W.M., Jones, C.M., Einstein, E.B., Volkow, N.D., 2021a. Methamphetamine use, methamphetamine use disorder, and associated overdose deaths among US adults. JAMA Psychiatry. https://doi.org/10.1001/jamapsychiatry.2021.2588.

Han, B., Cotto, J., Etz, K., Einstein, E.B., Compton, W.M., Volkow, N.D., 2021b. Methamphetamine overdose deaths in the US by sex and race and ethnicity. JAMA Psychiatry. https://doi.org/10.1001/jamapsychiatry.2020.4321.

Howell, B.A., Abel, E.A., Park, D., Edmond, S.N., Leisch, L.J., Becker, W.C., 2021. Validity of incident opioid use disorder (OUD) diagnoses in administrative data: a chart verification study. J. Gen. Intern. Med. 36, 1264–1270. https://doi.org/10.1007/s11606-020-06339-3.

Jones, C.M., Compton, W.M., Mustaquim, D., 2020a. Patterns and characteristics of methamphetamine use among adults — United States, 2015–2018. MMWR. Morb. Mortal. Wkly. Rep. 69, 317–323. https://doi.org/10.15585/mmwr.mm6912a1.

Jones, C.M., Underwood, N., Compton, W.M., 2020b. Increases in methamphetamine use among heroin treatment admissions in the United States, 2008–17. Addiction 115, 347–353. https://doi.org/10.1111/add.14812.

Kays, L.B., Steltenpohl, E.D., McPheeters, C.M., Frederick, E.K., Bishop, L.B., 2022. Initiation of buprenorphine/naloxone on rates of discharge against medical advice. Hosp. Pharm. 57, 88–92. https://doi.org/10.1177/0018578720985439.

Khatri, U.G., Samuels, E.A., Xiong, R., Marshall, B.D.L., Perrone, J., Delgado, M.K., 2022. Variation in emergency department visit rates for opioid use disorder: implications for quality improvement initiatives. Am. J. Emerg. Med. 51, 331–337. https://doi.org/10.1016/j.ajem.2021.10.047.

Lagisetty, P., Garpestad, C., Larkin, A., Macleod, C., Antoku, D., Slat, S., Thomas, J., Powell, V., Bohnert, A.S.B., Lin, L.A., 2021. Identifying individuals with opioid use disorder: validity of International Classification of Diseases diagnostic codes for opioid use, dependence and abuse. Drug Alcohol Depend. 221, 108583 https://doi.org/10.1016/j.drugalcdep.2021.108583.

Liebschutz, J.M., Crooks, D., Herman, D., Anderson, B., Tsui, J., Meshesha, L.Z., Dossabhoy, S., Stein, M., 2014. Buprenorphine treatment for hospitalized, opioid-dependent patients: a randomized clinical trial. JAMA Intern. Med. 174, 1369–1376. https://doi.org/10.1001/jamainternmed.2014.2556.

Marks, L.R., Munigala, S., Warren, D.K., Liang, S.Y., Schwarz, E.S., Durkin, M.J., 2019. Addiction medicine consultations reduce readmission rates for patients with serious infections from opioid use disorder. Clin. Infect. Dis. 68, 1935–1937. https://doi.org/10.1093/cid/ciy924.

Mustaquim, D., Jones, C.M., Compton, W.M., 2021. Trends and correlates of cocaine use among adults in the United States, 2006–2019. Addict. Behav. 120, 106950 https://doi.org/10.1016/j.addbeh.2021.106950.

Nordeck, C.D., Welsh, C., Schwartz, R.P., Mitchell, S.G., Cohen, A., O'Grady, K.E., Gryczynski, J., 2018. Rehospitalization and substance use disorder (SUD) treatment entry among patients seen by a hospital SUD consultation-liaison service. Drug Alcohol Depend. 186, 23–28. https://doi.org/10.1016/j.drugalcdep.2017.12.043.

O'Donnell, M., Englander, H., Strnad, L., Bhamidipati, C.M., Shalen, E., Riquelme, P.A., 2022. Expanding the team: optimizing the multidisciplinary management of drug use-associated infective endocarditis. J. Gen. Intern. Med. 37, 935–939. https://doi.org/10.1007/s11606-021-07313-3.

Padmanathan, P., Hall, K., Moran, P., Jones, H.E., Gunnell, D., Carlisle, V., Lingford-Hughes, A., Hickman, M., 2020. Prevention of suicide and reduction of self-harm among people with substance use disorder: a systematic review and meta-analysis of randomised controlled trials. Compr. Psychiatry 96, 152135. https://doi.org/10.1016/j.comppsych.2019.152135.

Priest, K.C., Balasanova, A.A., Levander, X.A., Chan, B., Blazes, C.K., Mahan, J., Brown, J., Mahoney, Stacey, Peng, L., Mahoney, Sean, Lundy, T., Englander, H., 2023. Caring for hospitalized adults with methamphetamine use disorder: a proposed clinical roadmap. Am. J. Med. 136, 507–509. https://doi.org/10.1016/j.amjmed.2023.01.012.

Ries, R.K., Livengood, A.L., Huh, D., Kerbrat, A.H., Fruhbauerova, M., Turner, B., Comtois, K.A., 2022. Effectiveness of a suicide prevention module for adults in substance use disorder treatment. JAMA Netw. Open. 5, e222945 https://doi.org/10.1001/jamanetworkopen.2022.2945.

Ronan, M.V., Herzig, S.J., 2016. Hospitalizations related to opioid abuse/dependence and associated serious infections increased sharply, 2002–12. Health Aff. 35, 832–837. https://doi.org/10.1377/hlthaff.2015.1424.

Shearer, R.D., Howell, B.A., Bart, G., Winkelman, T.N.A., 2020. Substance use patterns and health profiles among US adults who use opioids, methamphetamine, or both, 2015-2018. Drug Alcohol Depend. 214, 108162 https://doi.org/10.1016/j.drugalcdep.2020.108162.

Shearer, R.D., Shippee, N.D., Winkelman, T.N.A., 2021. Characterizing trends in methamphetamine-related health care use when there is no ICD code for "methamphetamine use disorder. J. Subst. Abuse Treat. 127, 108369 https://doi.org/10.1016/j.jsat.2021.108369.

Simpson, S.A., Wolf, C., Loh, R.M., Camfield, K., Rylander, M., 2023. Evaluation of the BEAT meth intervention for emergency department patients with methamphetamine psychosis. J. Addict. Med. 17, 67–73. https://doi.org/10.1097/ADM.0000000000001037.

Sledge, W.H., Gueorguieva, R., Desan, P., Bozzo, J.E., Dorset, J., Lee, H.B., 2015. Multidisciplinary proactive psychiatric consultation service: impact on length of stay for medical inpatients. PsychOther. Psychosom. 84, 208–216. https://doi.org/10.1159/000379757.

Spencer, M.R., Miniño, A.M., Garnett, M.G, 2023. Co-involvement of opioids in drug overdose deaths involving cocaine and psychostimulants, 2011–202. NCHS. Data Brief.

Substance Abuse and Mental Health Services Administration, 2014. SAMHSA's Concept of Trauma and Guidance for a Trauma-Informed Approach. Substance Abuse and Mental Health Services Administration, Rockville, MD.

Tan, S.Y., Feng, J.Y., Joyce, C., Fisher, J., Mostaghimi, A., 2020. Association of hospital discharge against medical advice with readmission and in-hospital mortality. JAMA Netw. Open. 3, e206009 https://doi.org/10.1001/jamanetworkopen.2020.6009.

Thompson, H.M., Faig, W., VanKim, N.A., Sharma, B., Afshar, M., Karnik, N.S., 2020. Differences in length of stay and discharge destination among patients with substance use disorders: the effect of Substance Use Intervention Team (SUIT) consultation service. PLoS. One 15, e0239761. https://doi.org/10.1371/journal.pone.0239761.

Ti, L., Ti, L., 2015. Leaving the hospital against medical advice among people who use illicit drugs: a systematic review. Am. J. Public Health 105, e53–e59. https://doi.org/10.2105/AJPH.2015.302885.

Tsui, J.I., Stephens, D., Collins, B., Denisiuk, E., Hallgren, K.A., Blalock, K.L., Klein, J.W., Jack, H.E., Merrill, J.O., n.d. Co-use of methamphetamine is associated with lower rates of linkage to outpatient treatment for hospitalized patients who initiate buprenorphine. J. Addict. Med. 10.1097/ADM.0000000000001129. https://doi.org/10.1097/ADM.0000000000001129.

Warfield, S.C., Bharat, C., Bossarte, R.M., DePhilippis, D., Farrell, M., Hoover, M., Larney, S., Marshalek, P., McKetin, R., Degenhardt, L., 2022. Trends in comorbid opioid and stimulant use disorders among Veterans receiving care from the Veterans Health Administration, 2005–2019. Drug Alcohol Depend. 232, 109310 https://doi.org/10.1016/j.drugalcdep.2022.109310.

Weimer, M., Morford, K., Donroe, J., 2019. Treatment of opioid use disorder in the acute hospital setting: a critical review of the literature (2014–2019). Curr. Addict. Rep. 6, 339–354. https://doi.org/10.1007/s40429-019-00267-x.

Weimer, M.B., Falker, C.G., Seval, N., Golden, M., Hull, S.C., Geirsson, A., Vallabhajosyula, P., 2022. The need for multidisciplinary hospital teams for injection drug use-related infective endocarditis. J. Addict. Med. 16, 375. https://doi.org/10.1097/ADM.0000000000000916.

Wen, H., Barnett, M.L., Saloner, B., 2020. Clinical risk factors for COVID-19 among people with substance use disorders. Psychiatric Serv. appi.ps., 2020002 https://doi.org/10.1176/appi.ps.202000215.

Wilcox, H.C., Conner, K.R., Caine, E.D., 2004. Association of alcohol and drug use disorders and completed suicide: an empirical review of cohort studies. Drug and Alcohol Dependence. Drug Abuse Suici. Behav. 76, S11–S19. https://doi.org/10.1016/j.drugalcdep.2004.08.003.

Winkelman, T.N.A., Admon, L.K., Jennings, L., Shippee, N.D., Richardson, C.R., Bart, G., 2018. Evaluation of amphetamine-related hospitalizations and associated clinical outcomes and costs in the United States. JAMA Netw. Open. 1, e183758 https://doi.org/10.1001/jamanetworkopen.2018.3758.

Yuodelis-Flores, C., Ries, R.K., 2015. Addiction and suicide: a review. Am. J. Addict. 24, 98–104. https://doi.org/10.1111/ajad.12185.