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Sex differences in the prevalence and correlates of emergency department utilization among adults with prescription opioid use disorder

William S. John^a and Li-Tzy Wu^{a,b,c,d}

^aDepartment of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, North Carolina, USA; ^bDepartment of Medicine, Division of General Internal Medicine, Duke University Medical Center, Durham, North Carolina, USA; ^cDuke Clinical Research Institute, Duke University Medical Center, Durham, North Carolina, USA; ^dCenter for Child and Family Policy, Sanford School of Public Policy, Duke University, Durham, North Carolina, USA

ABSTRACT

Background: The emergency department (ED) is well-suited as an opportunity to increase treatment access for prescription opioid use disorder (POUD). We examined sex differences in ED utilization among individuals with POUD to understand potential sex-specific treatment barriers and needs. **Methods:** Data from the 2005–2014 National Surveys on Drug use and Health were analyzed to examine the prevalence and correlates of past-year ED utilization among male and female adults aged 18 or older with POUD ($n = 4412$). **Results:** Overall, 58.2% of adults with POUD reported past-year ED utilization. Adjusted logistic regression revealed that females (vs. males) with POUD were more likely to report past-year ED utilization. Among females with POUD, older age, lower income, obtaining opioids from a physician, major depressive episode, and greater POUD severity were associated with increased odds of ED utilization. Among males with POUD, public insurance and obtaining opioids from a physician were associated with ED utilization. A larger proportion of males with POUD reporting ED use had multiple substance use disorders than those with no ED use. Treatment history (lifetime or past-year) for alcohol, drugs, or opioid use was associated with increased odds of ED use among males and females with POUD. **Conclusions/Importance:** Males and females with POUD presenting to the ED may have distinct predisposing, enabling, and need-related correlates. Sex-specific screening and intervention strategies may be useful to maximize the utility of the ED to address POUD.

KEYWORDS


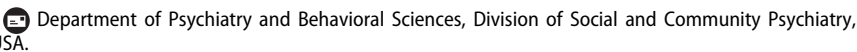
Opioid; opioid use disorder; emergency department; National Survey on Drug Use and Health


Background

The misuse of prescription opioids and related overdoses in the United States have emerged to epidemic proportions over the past two decades in terms of both morbidity and mortality (Cai, Crane, Poneleit, & Paulozzi, 2010; Coben et al., 2010; Guy, Pasalic, & Zhang, 2018; Rudd, Aleshire, Zibbell, & Gladden, 2016; Tedesco et al., 2017; Van Handel et al., 2016). Of the 42,249 U.S. opioid deaths in 2016, the most in any year on record, nearly half involved a prescription opioid (Department of Health and Human Services, 2018). According to the 2017 National Survey on Drug Use and Health (NSDUH), approximately 10.3 million adults aged 18 years or older misused prescription opioids in the past year and 1.6 million adults met criteria for past-year prescription opioid use disorder (POUD) (CBHSQ, 2018). Moreover, the number

of overdose deaths involving opioids has quadrupled since 1999 and continue to rise (Hedegaard, Warner, & Minino, 2017). An approach vital to reducing opioid-involved overdoses is expanding access to opioid agonist treatment (OAT), such as office-based buprenorphine treatment for POUD, and other addiction services (Volkow & Collins, 2017). However, less than one in five adults with POUD report receiving opioid-specific treatment in the past 12 months (Saha et al., 2016; Wu, Zhu, & Swartz, 2016). Thus, new strategies are needed to increase treatment access, such as collaborative care models to link patients to OAT and further or specialized care.

The emergency department (ED) is an important contact point with the healthcare system for many individuals with substance use problems that may be leveraged to identify patients with unmet treatment

CONTACT William S. John  william.john@duke.edu 

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need for POUD (Houry, Haegerich, & Vivolo-Kantor, 2018). That is, many individuals with POUD do not have access to healthcare elsewhere and therefore rely on the ED as their primary source of care for adverse effects from opioid use itself (e.g., overdose, injury) or other comorbid medical and psychiatric conditions, acute illnesses, or trauma (D'Onofrio et al., 2015). Indeed, prior research has indicated that individuals with frequent ED use have a higher prevalence of POUD than those who did not use the ED in the past year (Wu et al., 2012). Moreover, a national sample of U.S. hospitals indicated that ED discharge rates for opioid use disorders and poisonings significantly increased from 2006 to 2014 (Tedesco et al., 2017) while recent data estimated a 30% increase in the rate of opioid overdose ED visits in the U.S. from 2016 to 2017 (Vivolo-Kantor et al., 2018). The ED may also be leveraged to initiate interventions for OUD and to provide linkage to OAT and other addiction-related care. For instance, one study found that ED-initiated buprenorphine treatment for OUD, compared to a brief intervention and referral, significantly reduced opioid use and increased addiction treatment engagement (D'Onofrio et al., 2015).

To inform the most effective use of strategies for addressing POUD in the ED, it is crucial to understand the factors associated with ED utilization among individuals with POUD. In particular, previous research suggests that factors may differ between males and females with OUD thereby requiring targeted approaches and treatment planning in the ED to address sex-specific treatment needs and/or barriers to successful treatment linkage, engagement, and outcome. For example, clinical and national survey data indicate that females with POUD, compared to their male counterparts, have greater functional impairment, more co-occurring psychiatric problems (e.g., major depressive episode, post-traumatic stress disorder), and shorter time from initial use to regular use (Green, Grimes Serrano, Licari, Budman, & Butler, 2009; Kerridge et al., 2015; McHugh et al., 2013). Escalated opioid misuse among females has led to increased numbers of infants born dependent on opioids (i.e., neonatal abstinence syndrome) (Brown, Goodin, & Talbert, 2018). Moreover, the rate in opioid overdoses since 1999 has increased at a greater rate among females than males (Hedegaard et al., 2017). Few studies, however, have examined sex differences in ED utilization among those with POUD. A better understanding of the sex-specific factors associated with ED-utilization may have implications for

guiding efforts at optimizing ED-initiated screening and intervention for POUD.

Although useful, previous studies examining sex differences among ED patients with OUD are limited to ED encounter data (Choo, Douriez, & Green, 2014; Ryoo & Choo, 2016). The nature of this data source, however, does not allow for in-depth patient-level analysis regarding socioeconomic status, physical/mental health comorbidities, concurrent substance use, severity of OUD, or prior treatment utilization, all of which are factors that may affect treatment-seeking for POUD, engagement, and outcome (Dreifuss et al., 2013; Sharma et al., 2017; Wu et al., 2016). To this end, the objective of the present study was to utilize a nationally representative sample, the NSDUH, to examine sex differences in the extent to which predisposing, enabling, and need-related factors are associated with ED utilization among persons with POUD. Notably, ED utilization in the context of this study included self-reported visits to the ED for any reason (i.e., not only substance-related), which is useful for understanding the full extent of ED utilization among those with POUD. Such information may have implications for informing additional ED-based screening and intervention opportunities.

Methods

Data source

The annual NSDUH is a cross-sectional survey designed to provide ongoing estimates of substance use and mental health in the United States (CBHSQ, 2015). The survey used multistage area probability sampling methods to select a nationally representative sample of the civilian, noninstitutionalized population aged ≥ 12 years from all 50 states and the District of Columbia. Specifically, the sample was drawn from residents of households as well as residents of noninstitutional group quarters (e.g., college dormitories, group homes, civilians living on military bases), and individuals with no permanent residence (e.g., homeless people in shelters, hotel residents).

Data for this study were combined from the 2005 through 2014 NSDUH public-use data sets (CBHSQ, 2006; CBHSQ, 2015). This survey period included similar sampling methodology for our variables of interest, which allowed for analysis across years. Ranges of weighted response weights of household screening and interviewing for these years were 81.9–90.2% and 71.2–75.6%, respectively. Our sample for analysis was restricted to adult respondents aged 18 years or older. Among the total adult sample in the 2005–2014 NSDUH, 0.7% ($n = 4412$) met criteria for

past-year POUD, which formed the sample for analysis.

Study variables

Nonmedical prescription opioid use/use disorder

The NSDUH defined nonmedical prescription opioid use (NMPOU) as any self-reported use of prescription pain relievers that were not prescribed to the respondent or that the respondent took only for the experience or feeling they caused. Among respondents who responded affirmatively to any past-year NMPOU, additional questions were administered to determine whether criteria for prescription opioid abuse or dependence was met based on DSM-4 criteria (APA, 2000). Criteria for prescription opioid abuse included the presence of ≥ 1 prescription opioid-specific abuse symptoms and absence of dependence. Criteria for prescription opioid dependence included the presence of ≥ 3 prescription opioid-specific dependence symptoms, regardless of abuse status. Past-year POUD was operationalized as having met criteria for either abuse or dependence during the preceding 12 months of assessment. Severity of POUD was categorized by the overall number of symptoms to indicate mild (i.e., 1–3 symptoms), moderate (i.e., 4–5 symptoms), and severe (i.e., ≥ 6 symptoms) POUD. We also examined the frequency of past-year nonmedical use of prescription opioids (i.e., 1–29 days, 30–99 days, 100–199 days, and 200–365 days), number of prescription opioid abuse or dependence symptoms (i.e., 1–3, 4–5, 6–11), age at first NMPOU (i.e., < 18 , 18–25, and > 25), and number of different groups of prescription opioids ever used nonmedically among adults with POUD.

Past-year ED utilization

The primary dependent variable was past-year ED utilization (i.e., one or more admissions to the ED in the previous 12 months from when the survey was conducted). Past-year ED utilization was recoded as a binary variable (i.e., yes and no) from the following NSDUH question: “During the past 12 months ... how many different times have you been treated in an emergency room for any reason?”

Predisposing/demographic, enabling, and need-related variables

We examined the prevalence and correlates of ED utilization among adults with POUD across three domains found to influence treatment-seeking based on Anderson’s healthcare utilization model (Andersen, 1995; Wu et al., 2016): 1) predisposing/demographic

variables, 2) enabling variables, and 3) need-related factors.

Predisposing/demographic variables included self-reported sex, age, and race/ethnicity. We categorized race/ethnicity into four mutually exclusive groups including non-Hispanic White, non-Hispanic Black, Hispanic, and other (i.e., non-Hispanic Native American (American Indian/Alaska-native), non-Hispanic native Hawaiian/Pacific-Islander, non-Hispanic Asian-American, and mixed race (> 1 race)).

Enabling variables included self-reported education, household income, and population density of residence (large metropolitan (i.e., segment in a Core Based Statistical Area (CBSA) with 1 million or more persons), small metropolitan (segment in a CBSA with fewer than 1 million persons), and non-metropolitan (i.e., segment not in a CBSA) areas). We created a variable for respondents’ health insurance status, which was categorized as having public, private, or no health insurance. We also created a variable for respondents’ source of most recent (i.e., past 30 days) nonmedical use of prescription pain relievers, which was categorized as from one or more physicians, friends or family, or other sources (i.e., wrote fake prescription, stole, drug dealer, or unspecified).

Need-related factors included other past-year non-medical substance use, comorbid substance use disorders (SUDs), and mental health. As with POUD, other SUDs were defined as meeting substance-specific DSM-4 criteria for abuse or dependence. We included past-year use (illicit or nonmedical prescription drug use) and SUD for alcohol, cannabis, tranquilizers, cocaine, heroin, stimulants, sedatives, hallucinogens, and inhalants. We also included current (i.e., past month) nicotine dependence as assessed by the Nicotine Dependence Syndrome Scale and Fagerström Test of Nicotine Dependence (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991; Shiffman, Waters, & Hickcox, 2004). Binge alcohol use was assessed as well, which was defined as having 5 or more alcoholic beverages within a couple of hours of each other on at least one day in the past 30 days. Moreover, mental health characteristics included past-year major depressive episode (MDE) and serious psychological distress due to their association with opioid misuse (Frank, Binswanger, Calcaterra, Brenner, & Levy, 2015; Wu, Woody, Yang, & Blazer, 2010; Wu et al., 2016). Assessment for past-year MDE was based on DSM-4 criteria (Kessler et al., 2010; Kessler & Merikangas, 2004). Past-year serious psychological distress was defined as having a score of ≥ 13 on the K6 Psychological Distress Scale for the level of symptoms

during the worst month of the past year (Kessler et al., 2003).

Treatment history

Current and prior receipt of treatment for substance use problems was examined as a correlate of ED utilization due to the association of prior receipt of treatment and worse treatment outcome for POUD (Dreifuss et al., 2013). NSDUH respondents' were administered separate questions that asked about lifetime and past-year receipt of treatment for alcohol and/or drug use (e.g., "During the past 12 months, ... have you received treatment or counseling for your use of alcohol or any drug, not counting cigarettes?"). Respondents' were also asked about receiving their last or current treatment for specific substances. Last/current treatment for prescription opioids was assessed by the following questions, "The last time you entered treatment, did you receive treatment or counseling for your use of prescription pain relievers? Are you currently receiving treatment or counseling for your use of prescription pain relievers?"

Data analysis

We calculated descriptive statistics of adults with POUD by past-year ED utilization. The prevalence of past-year ED utilization was estimated among subgroups of adults with POUD. Logistic regression was used to examine factors associated with past-year ED utilization among adults with POUD, adjusting for predisposing variables (i.e., sex, age, and race/ethnicity), enabling variables (i.e., education, household income, population density of residence, insurance, and source of prescription opioids), and need variables (i.e., MDE, nicotine dependence, and other past-year SUDs). We also controlled for survey year, which was recoded as a categorical variable. Additionally, adjusted logistic regression was used to examine the association of lifetime treatment use for alcohol/drug use problems and past-year ED utilization among adults with POUD. To examine sex differences in ED utilization, all analyses were stratified by sex in addition to being performed among the total sample. Additionally, we explored interaction effects of sex in the fully adjusted logistic regression models to assess whether factors associated with ED utilization were different between males and females. All results were reported as weighted estimates whereas sample sizes were unweighted. Analyses were performed using survey procedures in SAS, version 9.4 (SAS Institute Inc., Cary, NC), which adjusted for the complex survey design of the NSUDH including weighting and clustering.

Results

Characteristics of adults with POUD by past-year ED utilization

Overall, the majority of adults with past-year POUD were male (58.8%), young adults aged 18–25 (35.0%), and white (74.0%) (Table 1). Over half of adults with POUD (58.2%) reported past-year ED utilization. Among those reporting ED utilization, 38.0% reported one ED encounter, 45.1% reported 2–4 encounters, and 11.2% reported 5 or more. Compared to adults with POUD who did not report past-year ED utilization, a greater proportion of those utilizing the ED were black, had high school education only, household income of <\$20,000, public insurance, reported a physician source of opioids used non-medically, and received treatment for opioid use disorder.

Prevalence of comorbid mental health problems and multiple SUDs

Overall, a greater proportion of adults with POUD who reported past-year ED use had past-year MDE, serious psychological distress, current nicotine dependence, past-year tranquilizer use disorder, and past-year sedative use disorder compared to ED non-users (Table 2). Among males with POUD, ED users compared to non-users had a greater proportion of serious psychological distress, any comorbid past-year SUD, and tranquilizer use disorder. Among females with POUD, a greater proportion of those who reported ED utilization had past-year MDE than those who did not report ED utilization. There were no significant differences in past-year use (illicit or non-medical) of other substances by ED utilization status and sex (supporting information Table S1).

The past-year frequency of NMPOU, age at first NMPOU, and the number of different groups of prescription opioids used nonmedically did not significantly differ by ED utilization status (supporting information Table S2). However, among the overall sample, a greater proportion of ED users met criteria for severe POUD (i.e., ≥ 6 symptoms) than ED non-users. Stratified by sex, the prevalence of severe POUD was only greater in ED users vs. non-users among females with POUD (supporting information Table S2).

Prevalence of past-year ED utilization among adults with POUD

Among the overall sample of adults with POUD, the prevalence of past-year ED utilization was higher

Table 1. Sample characteristics of adults aged 18 years or older with past-year prescription opioid use disorder with and without past-year emergency department (ED) utilization: 2005–2014 NSDUH ($n = 4412$).

	Total	ED utilization— past year	
		Yes	No
Sample size, unweighted	$n = 4412$	$n = 2506$	$n = 1906$
Weighted estimates	Column % (SE)	Column % (95% CI)	Column % (95% CI)
Overall	100 (0.0)	58.2 (56.2–60.2)	41.8 (39.8–43.8)
Sex			
Male	58.8 (1.3)	56.0 (52.1–59.9)	62.6 (58.7–66.4)
Female	41.2 (1.3)	44.0 (40.1–47.9)	37.4 (33.6–41.3)
Age in years			
18–25	35.0 (1.1)	33.6 (31.1–36.0)	37.1 (33.8–40.3)
26–34	27.7 (1.2)	27.3 (24.1–30.5)	28.2 (24.9–31.4)
35–49	23.3 (1.3)	21.5 (18.4–24.6)	25.8 (22.3–29.4)
50+	14.0 (1.5)	17.6 (13.7–21.5)	8.9 (6.2–11.6)
Race/ethnicity			
White, Non-Hispanic	74.0 (0.9)	71.2 (68.0–74.4)	77.9 (75.0–80.8)
Black, Non-Hispanic	8.9 (0.9)	11.1 (8.4–13.8)	5.9 (4.2–7.6)
Hispanic	12.0 (0.8)	12.8 (10.4–15.1)	11.1 (9.0–13.1)
Other	5.0 (0.5)	4.9 (3.6–6.3)	5.1 (3.6–6.7)
Education			
Less than high school	25.1 (1.1)	26.1 (23.4–28.9)	23.6 (20.7–26.5)
High school	35.3 (1.2)	38.3 (34.9–41.7)	31.1 (28.3–34.0)
Some college or more	39.6 (1.3)	35.6 (32.3–38.9)	45.2 (41.5–49.0)
Household income			
<\$20,000	30.1 (1.1)	34.4 (31.0–37.9)	24.0 (21.7–26.3)
\$20,000–\$49,999	37.5 (1.4)	37.3 (33.7–40.8)	37.8 (33.8–41.9)
\$50,000–\$74,999	14.0 (0.8)	13.4 (11.3–15.6)	14.8 (12.2–17.4)
≥\$75,000	18.4 (1.0)	14.9 (12.5–17.3)	23.4 (20.3–26.4)
County type			
Non-metro	6.1 (0.6)	6.4 (4.7–8.0)	5.8 (4.4–7.1)
Small metro	45.4 (1.1)	45.7 (42.4–48.9)	45.1 (41.8–48.4)
Large metro	48.5 (1.2)	48.0 (44.7–51.2)	49.2 (45.8–52.5)
Insurance			
None	31.3 (1.3)	30.1 (26.8–33.5)	33.0 (29.5–36.5)
Private	40.3 (1.2)	34.0 (30.7–37.4)	49.0 (45.7–52.3)
Public	28.4 (1.3)	35.8 (32.1–39.6)	18.0 (15.3–20.7)
Source of prescription opioids			
Family or friends	52.9 (1.2)	48.0 (44.2–51.7)	59.9 (56.7–63.0)
Physician	26.0 (1.0)	31.8 (28.6–34.9)	17.9 (15.2–20.6)
Other ^a	16.4 (1.0)	16.1 (13.3–18.8)	16.9 (14.6–19.2)
Unknown/invalid	4.7 (0.6)	4.2 (2.4–6.0)	5.3 (4.0–6.7)
Rx opioid use disorder treatment – last/current^b			
No	83.9 (1.0)	81.1 (78.1–84.1)	87.8 (85.6–89.9)
Yes	16.1 (1.0)	18.9 (15.9–21.9)	12.2 (10.1–14.4)

Boldface: estimate significantly differed from those reporting no past-year ED utilization.

^aOther source included theft, drug dealer, bought on internet, fake prescription, or other.

^bDefined as whether the last substance treatment or counseling received was for prescription opioids or whether treatment or counseling for prescription opioids was being received at the time of assessment.

among adults aged 50 or older compared to young adults aged 18–25; Blacks compared to Whites; those with less than high school education compared to some college or more; those with a household income of <\$20,000 compared to >\$20,000, those with public insurance compared to none; those obtaining opioids from a physician source compared to family or friends; adults with a past-year MDE than those without; those with current nicotine dependence than those without; and those greater severity of POUD (Table 3).

Among males, but not females, with POUD, the prevalence of ED use was higher among Blacks than Whites and among those with public insurance compared to no insurance. The prevalence of ED use among those with low education compared to having

some college or more and among those with a comorbid drug use disorder than those without was higher only among females with POUD.

Correlates of past-year ED utilization among persons with POUD

Among the overall sample of adults with POUD, adjusted logistic regression indicated that female sex, ages 50+ (vs. 18–28 years old), high school education (vs. less than high school), having public insurance (vs. none), physician source of opioids, past-year MDE, and greater number of POUD symptoms were associated with increased odds of ED utilization in the past year (Table 4). High income (vs. <\$20,000) and

Table 2. Prevalence of mental health problems and comorbid substance use disorders among adults aged 18 and older with past-year prescription opioid use disorder, stratified by past-year emergency department (ED) utilization status: 2005–2014 NSDUH ($n = 4412$).

Past-year ED utilization status	Overall $n = 4412$ Column % (SE)	ED utilization- past year					
		Total		Males		Females	
		Yes $n = 2506$ Column % (95% CI)	No $n = 1906$ Column % (95% CI)	Yes $n = 1234$ Column % (95% CI)	No $n = 1110$ Column % (95% CI)	Yes $n = 1272$ Column % (95% CI)	No $n = 796$ Column % (95% CI)
Sample size, unweighted	28.1 (1.2)	31.4 (28.0–34.9)	23.4 (20.2–26.6)	25.7 (21.1–30.3)	19.9 (15.7–24.1)	38.8 (33.5–44.0)	29.1 (24.8–33.4)
Weighted estimates	49.3 (1.3)	54.6 (51.2–58)	41.9 (38.2–45.6)	47.9 (43.3–52.5)	34.8 (30.4–39.3)	63.1 (57.7–68.5)	53.7 (48.2–59.3)
Mental health problems – past year							
Major depressive episode	19.9 (1.0)	17.8 (14.9–20.7)	22.8 (19.5–26.2)	14.3 (11.1–17.4)	22.3 (18.1–26.6)	22.3 (17.7–26.9)	23.7 (17.8–29.5)
Serious psychological distress ^a	80.1 (1.0)	82.2 (79.3–85.1)	77.2 (73.8–80.5)	85.7 (82.6–88.9)	77.7 (73.4–81.9)	77.7 (73.1–82.3)	76.3 (70.5–82.2)
Nicotine dependence – past month	53.5 (1.3)	56.8 (53.1–60.5)	49.0 (45.2–52.7)	58.4 (53.0–63.7)	51.0 (46.0–55.9)	54.7 (49.5–59.8)	45.6 (39.7–51.6)
Alcohol use disorder	40.3 (1.1)	40.6 (37.3–43.8)	40.0 (36.8–43.3)	43.9 (39.3–48.4)	41.2 (37.1–45.3)	36.4 (31.4–41.4)	38.0 (32.9–43.1)
Cannabis use disorder	20.1 (0.9)	19.8 (17.4–22.3)	20.4 (17.6–23.1)	22.9 (19.2–26.5)	22.8 (19.0–26.6)	16.0 (13.0–19.0)	16.3 (12.2–20.4)
Tranquilizer use disorder	14.6 (0.8)	17.3 (14.8–19.9)	10.7 (8.8–12.7)	16.8 (13.0–20.7)	9.7 (7.2–12.2)	18.0 (14.1–21.9)	12.4 (9.0–15.8)
Cocaine use disorder	12.9 (0.9)	14.8 (12.0–17.5)	10.2 (7.8–12.6)	17.1 (12.9–21.3)	10.0 (6.8–13.2)	11.8 (9.2–14.3)	10.6 (7.5–13.8)
Heroin use disorder	10.3 (0.7)	11.3 (9.0–13.7)	8.8 (6.7–10.9)	14.6 (11.1–18.1)	10.8 (7.8–13.8)	7.2 (5.2–9.2)	5.4 (2.8–8.0)
Stimulant use disorder	9.4 (0.9)	10.9 (8.3–13.5)	7.4 (5.3–9.4)	10.7 (7.6–13.8)	8.1 (5.2–10.9)	11.1 (6.7–15.5)	6.3 (4.2–8.3)
Sedative use disorder	3.7 (0.5)	5.0 (3.6–6.5)	1.7 (0.9–2.6)	4.0 (2.1–6.0)	1.2 (0.2–2.1)	6.3 (4.1–8.5)	2.6 (1.1–4.2)
Hallucinogen use disorder	3.9 (0.4)	4.6 (3.2–5.9)	3.1 (2.3–3.8)	5.7 (3.8–7.6)	2.9 (1.9–3.9)	3.1 (1.9–4.4)	3.4 (2.0–4.7)
Inhalant use disorder	1.2 (0.2)	1.0 (0.5–1.5)	1.4 (0.7–2.1)	1.4 (0.6–2.2)	1.6 (0.6–2.6)	0.6 (0.1–1.1)	1.0 (0.2–1.8)

Boldface: estimate significantly differed from those reporting no past-year ED utilization; Rx: prescription.

^aDefined as a K6 score of ≥ 13 on the K6 Psychological Distress Scale.

^bOther substance use disorder including nicotine dependence, alcohol use disorder, or any illicit drug use disorder.

Table 3. Prevalence of past-year emergency department (ED) utilization among adults aged 18 and older with past-year prescription opioid use disorder: 2005–2014 NSDUH ($n = 4412$).

	ED utilization – past year		
	Overall – yes $n = 4412$ Row % (95% CI)	Males – yes $n = 2344$ Row % (95% CI)	Females – yes $n = 2068$ Row % (95% CI)
Weighted estimates			
Sex			
Male†	55.5 (52.2–58.8)	–	–
Female	62.1 (58.3–66.0)	–	–
Age in years			
18–25†	55.8 (53.4–58.2)	52.0 (48.7–55.3)	60.6 (57.1–64.0)
26–34	57.5 (52.6–62.5)	54.6 (47.8–61.3)	62.5 (54.8–70.2)
35–49	53.7 (49.4–58.0)	51.9 (45.5–58.3)	55.9 (47.9–63.9)
50+	73.3 (67.1–79.6)	69.6 (59.9–79.3)	80.6 (69.7–91.5)
Race/ethnicity			
White, Non-Hispanic†	56.0 (53.5–58.6)	52.8 (49.4–56.2)	60.6 (56.0–65.1)
Black, Non-Hispanic	72.4 (64.9–80.0)	74.9 (63.8–86.0)	69.2 (56.3–82.1)
Hispanic	61.7 (54.7–68.6)	58.8 (49.6–68.1)	66.6 (56.2–76.9)
Other	57.3 (47.8–66.8)	53.4 (39.5–67.4)	62.7 (47.6–77.9)
Education			
Less than high school†	60.7 (56.8–64.6)	56.5 (50.8–62.3)	67.6 (62.3–72.9)
High school	63.2 (59.5–66.8)	60.3 (55.1–65.5)	68.1 (63.4–72.7)
Some college or more	52.3 (48.8–55.9)	49.7 (44.4–55.0)	55.2 (49.0–61.4)
Household income			
<\$20,000†	66.7 (63.3–70.1)	65.1 (59.6–70.6)	68.8 (63.2–74.4)
\$20,000–\$49,999	57.9 (53.8–61.9)	52.0 (46.4–57.6)	65.8 (59.5–72.1)
\$50,000–\$74,999	55.8 (49.7–62.0)	58.2 (50.6–65.9)	52.1 (41.7–62.5)
≥\$75,000	47.1 (41.4–52.7)	45.9 (39.0–52.9)	48.9 (39.3–58.6)
County type			
Non-metro†	60.7 (52.3–69.0)	60.6 (47.6–73.5)	60.8 (50.7–70.8)
Small metro	58.5 (55.5–61.6)	56.9 (52.1–61.7)	61.1 (56.2–66.0)
Large metro	57.7 (54.3–61.1)	53.6 (48.4–58.7)	63.2 (57.2–69.3)
Insurance status			
None†	56.0 (51.8–60.3)	52.4 (46.7–58.1)	62.2 (56.1–68.3)
Private	49.2 (45.9–52.6)	47.1 (42.2–52.0)	52.4 (46.4–58.4)
Public	73.5 (69.6–77.5)	73.8 (67.3–80.2)	73.3 (67.7–78.9)
Source of prescription opioids			
Family or friend†	52.8 (49.6–55.9)	48.9 (44.4–53.4)	57.6 (52.3–62.9)
Physician	71.2 (66.6–75.8)	70.6 (64.2–77.0)	72.0 (65.3–78.8)
Other ^a	57.1 (51.7–62.4)	55.4 (48.2–62.5)	61.0 (52.3–69.8)
Unknown/invalid	52.4 (40.4–64.5)	47.6 (30.7–64.5)	63.7 (50.5–77.0)
Major depressive episode – past year			
No†	55.5 (52.8–58.2)	53.7 (49.5–57.8)	58.6 (53.8–63.5)
Yes	65.2 (61.0–69.4)	61.7 (54.9–68.4)	68.6 (62.9–74.2)
Binge alcohol use			
No†	60.5 (57.4–63.7)	58.1 (52.6–63.7)	63.1 (57.4–68.7)
Yes	56.1 (53.0–59.2)	53.5 (49.6–57.4)	60.9 (55.5–66.2)
Other drug use^b			
No†	61.3 (56.0–66.6)	57.7 (49.9–65.5)	66.3 (58.4–74.1)
Yes	57.3 (54.8–59.8)	54.8 (51.2–58.5)	60.8 (56.8–64.9)
Nicotine dependence			
No†	54.2 (50.5–57.8)	51.4 (45.6–57.3)	57.8 (51.7–63.8)
Yes	61.8 (58.7–64.9)	58.8 (54.2–63.5)	66.3 (61.5–71.1)
Alcohol use disorder			
No†	58.0 (55.0–61.0)	54.4 (49.2–59.5)	62.7 (57.7–67.8)
Yes	58.6 (55.3–61.8)	57.1 (53.3–60.8)	61.1 (55.4–66.9)
Other drug use disorder^b			
No†	55.8 (52.7–58.9)	52.4 (47.6–57.2)	60.3 (54.9–65.8)
Yes	61.4 (57.9–65.0)	59.4 (54.3–64.4)	64.6 (59.3–70.0)
Rx OUD symptoms			
1–3†	53.1 (48.9–57.3)	51.1 (45.2–57.1)	55.7 (49.7–61.6)
4–5	58.7 (54.2–63.1)	57.2 (50.2–64.3)	60.7 (53.3–68.0)
6–11	63.7 (59.7–67.6)	58.7 (53.7–63.7)	71.3 (66.1–76.5)

Boldface: Estimate significantly differed from reference category (†) within each column ($p < 0.05$); Rx: prescription; OUD: opioid use disorder.

^aOther source included theft, drug dealer, bought on internet, fake prescription, other.

^bDrugs other than prescription opioids including marijuana, heroin, cocaine, hallucinogens, nonmedical Rx tranquilizers, nonmedical Rx sedatives, nonmedical Rx stimulants, or inhalants.

ages 35–49 were associated with decreased odds of past-year ED utilization. Among males with POUD, public insurance and obtaining opioids from one or

more physicians were associated with increased odds of ED utilization. Among females, physician source of opioids was also associated with increased odds of ED

Table 4. Adjusted odds ratios of past-year emergency department (ED) utilization among males and females with prescription opioid use disorder: 2005–2014 NSDUH ($n = 4412$).

	Overall ED utilization (yes vs. no)	Males ED utilization (yes vs. no)	Females ED utilization (yes vs. no)
Sample size, unweighted	$n = 4,412$	$n = 2,344$	$n = 2,068$
Adjusted odds ratio, AOR	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)
Sex			
Male	1.00	–	–
Female	1.33 (1.05–1.68)	–	–
Age in years			
18–25	1.00	1.00	1.00
26–34	0.98 (0.77–1.26)	0.99 (0.70–1.40)	0.98 (0.68–1.41)
35–49	0.79 (0.64–0.98)	0.81 (0.59–1.13)	0.81 (0.55–1.18)
50+	1.78 (1.19–2.66)	1.46 (0.85–2.51)	2.89 (1.40–5.97)
Race			
White, Non-Hispanic	1.00	1.00	1.00
Black, Non-Hispanic	1.49 (0.98–2.24)	1.53 (0.82–2.84)	1.42 (0.75–2.66)
Hispanic	1.18 (0.87–1.61)	1.15 (0.75–1.76)	1.25 (0.78–1.99)
Other	0.98 (0.63–1.53)	0.93 (0.50–1.73)	1.06 (0.60–1.87)
Education			
Less than high school	1.00	1.00	1.00
High school	1.28 (1.03–1.59)	1.30 (0.96–1.77)	1.25 (0.94–1.68)
Some college or more	0.92 (0.71–1.19)	0.98 (0.71–1.35)	0.83 (0.60–1.15)
Household income			
<\$20,000	1.00	1.00	1.00
\$20,000–\$49,999	0.82 (0.64–1.04)	0.73 (0.53–1.02)	0.93 (0.62–1.41)
\$50,000–\$74,999	0.96 (0.70–1.32)	1.24 (0.84–1.83)	0.67 (0.40–1.12)
≥\$75,000	0.68 (0.52–0.87)	0.74 (0.51–1.07)	0.58 (0.37–0.91)
County type			
Non-metro	1.00	1.00	1.00
Small metro	1.09 (0.78–1.53)	1.00 (0.60–1.66)	1.33 (0.81–2.19)
Large metro	1.13 (0.82–1.57)	0.94 (0.55–1.61)	1.55 (0.98–2.47)
Insurance			
None	1.00	1.00	1.00
Private	0.83 (0.64–1.06)	0.85 (0.61–1.19)	0.75 (0.53–1.06)
Public	1.74 (1.29–2.34)	2.09 (1.33–3.27)	1.33 (0.91–1.93)
Source of prescription opioids			
Family or friends	1.00	1.00	1.00
Physician	2.20 (1.65–2.93)	2.54 (1.82–3.56)	1.85 (1.27–2.69)
Other ^a	1.13 (0.86–1.49)	1.23 (0.86–1.77)	0.96 (0.63–1.46)
Unknown/invalid	0.92 (0.59–1.44)	0.90 (0.47–1.72)	1.12 (0.56–2.23)
Major depressive episode (yes vs. no)	1.36 (1.07–1.74)	1.28 (0.89–1.85)	1.45 (1.07–1.97)
Nicotine dependence (yes vs. no)	1.22 (0.98–1.52)	1.21 (0.90–1.62)	1.22 (0.88–1.70)
Alcohol use disorder (yes vs. no)	1.16 (0.94–1.43)	1.26 (0.97–1.64)	1.04 (0.78–1.40)
Other drug use disorder^b (yes vs. no)	1.19 (0.94–1.50)	1.30 (0.96–1.75)	1.05 (0.75–1.46)
Rx OUD symptoms			
1–3	1.00	1.00	1.00
4–5	1.18 (0.91–1.52)	1.09 (0.80–1.50)	1.34 (0.92–1.94)
6–11	1.44 (1.10–1.88)	1.17 (0.83–1.66)	1.96 (1.37–2.80)

Note: Each column represents a separate binary logistic regression model. All models also controlled for survey year; Rx: prescription; OUD: opioid use disorder.

Boldface: estimate significantly differed from reference group ($p < 0.05$).

^aOther source included theft, drug dealer, bought on internet, fake prescription, or other.

^bOther drugs included any drug other than prescription opioids used illicitly or for nonmedical purposes.

utilization, in addition to ages 50 years or older, low income, past-year MDE, and greater number of POUD symptoms. Survey year was not associated with ED utilization among males or females with POUD. There were no significant interaction effects between sex and other variables (i.e., age, race/ethnicity, other SUDs, MDE, or POUD severity, respectively).

Association between SUD treatment and past-year ED utilization among persons with POUD

Lifetime and past-year drug or alcohol use disorder treatment was associated with increased odds of past-year ED utilization among persons with POUD (Table

5). Past-year alcohol use disorder treatment, past-year drug use disorder treatment, and having received the last or current treatment specifically for opioid use were also associated with increased odds of past-year ED utilization. SUD treatment service use was associated with increased odds of ED utilization among both males and females with OUD. There were no significant interaction effects between sex and any of the substance use treatment variables.

Discussion

Drawing from a large, nationally representative sample, we found that the majority of adults with

Table 5. Prevalence and adjusted odds ratios of past-year emergency department (ED) utilization by substance use treatment service utilization among adults with past-year prescription opioid use disorder: 2005–2014 NSDUH ($n = 4412$).

Treatment service use	ED utilization – past year			ED utilization – past year		
	Total ED utilization – yes $n = 4412$	Males ED utilization – yes $n = 2344$	Females ED utilization – yes $n = 2068$	Total ED utilization (yes vs. no) $n = 4412$	Males ED utilization (yes vs. no) $n = 2344$	Females ED utilization (yes vs. no) $n = 2068$
Weighted estimates/AOR	Row% (95% CI)	Row% (95% CI)	Row% (95% CI)	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)
Drug or alcohol use disorder treatment-lifetime						
Not	54.7 (51.5–57.8)	52.3 (47.4–57.2)	57.9 (52.6–63.1)	1.00	1.00	1.00
Yes	63.5 (59.8–67.2)	60.0 (55.1–64.9)	69.0 (63.8–74.2)	1.53 (1.21–1.93)	1.44 (1.07–1.93)	1.71 (1.27–2.32)
Drug or alcohol use disorder treatment – past year						
Not	55.2 (52.6–57.7)	52.3 (48.2–56.3)	59.2 (54.5–63.9)	1.00	1.00	1.00
Yes	68.1 (63.3–72.9)	65.6 (59.2–72.0)	71.9 (65.9–78.0)	1.67 (1.28–2.19)	1.69 (1.19–2.39)	1.65 (1.17–2.32)
Alcohol use disorder treatment – past year						
Not	56.6 (54.4–58.8)	54.0 (50.5–57.5)	60.3 (56.0–64.6)	1.00	1.00	1.00
Yes	70.1 (63.9–76.3)	66.0 (57.9–74.2)	76.5 (68.0–85.0)	1.65 (1.2–2.28)	1.51 (1.05–2.18)	2.01 (1.21–3.35)
Drug use disorder treatment – past year						
Not	55.8 (53.4–58.2)	52.9 (48.8–56.9)	59.9 (55.4–64.4)	1.00	1.00	1.00
Yes	67.7 (62.4–72.9)	65.4 (58.5–72.3)	71.0 (64.4–77.6)	1.64 (1.23–2.18)	1.68 (1.15–2.46)	1.58 (1.1–2.26)
Opioid use disorder treatment – last/current						
Not	56.3 (53.9–58.7)	53.5 (49.6–57.4)	60.3 (56.1–64.6)	1.00	1.00	1.00
Yes	68.3 (62.8–73.9)	66.1 (58.5–73.7)	71.4 (64.2–78.7)	1.65 (1.23–2.21)	1.68 (1.11–2.53)	1.58 (1.09–2.29)

Note: A separate logistic regression model was conducted for each treatment service variable. Each separate logistic regression model controlled for sex, age, race/ethnicity, education, household income, county type, insurance status, source of prescription opioids, past-year major depressive episode, and survey year. AOR: adjusted odds ratio.

Boldface: estimate significantly differed from reference (†) group ($p < 0.05$).

past-year POUD reported ED utilization in the past year, many of whom had multiple encounters. These data serve to extend previous research highlighting the ED as a potentially salient opportunity to identify POUD, initiate treatment, and provide referral for continued care. This study also extended previous research by examining sex differences in ED utilization among adults with POUD. While a higher proportion of adults with POUD who used the ED were male, our study found that past-year ED utilization was more likely among females with POUD. These findings stand in contrast to a previous study, also analyzing data from the NSDUH, which found greater odds of past-year ED utilization among males who reported past-year non-medical opioid use (Frank et al., 2015). It is important to note, however, that the sample of Frank et al. (2015) included any past-year non-medical opioid users, while the present analysis focused on those meeting criteria for POUD. Therefore, these findings suggest that sex differences in ED utilization may differ as a function of problem severity of prescription opioid misuse and/or need for treatment.

One contributing factor to the increased odds of ED utilization among females with POUD may be associated with higher rates of comorbid conditions for which treatment in the ED is sought. To this end,

previous studies of national survey or treatment samples have shown greater psychiatric and medical problems in females than males with POUD (Cicero, Lynskey, Todorov, Inciardi, & Surratt, 2008; Katz, El-Gabalawy, Keyes, Martins, & Sareen, 2013; McHugh et al., 2013). We did not, however, find significant interactions of need-related covariates (i.e., MDE or other SUDs) or POUD severity (i.e., number of symptoms) with sex. These findings suggest that other factors, requiring further investigation, may be driving excess ED use among females compared to males. For instance, the difference may be due to biological factors in females that are associated with more vulnerability to adverse events from opioid misuse or lower thresholds of healthcare seeking among females than males with OUD.

Despite a lack of significant differences between females compared to males with POUD who used the ED, sex-specific factors associated with ED use were found. These findings have important clinical implications in that there may be distinct treatment needs and/or barriers among individuals with POUD who use the ED compared to those who do not use the ED, which may be further differentiated by sex. For instance, we found that past-year MDE was associated with increased odds of ED utilization only among females with POUD. These results may in part reflect

the association between depression and nonmedical benzodiazepine use among those with OUD, which is relatively more prevalent among females (Stein et al., 2017) and associated with increased risk of overdose and ED visits (Herbert, Gilbert, Cottrell, & Li, 2017; Jones & McAninch, 2015; Sun et al., 2017). While further research is needed to better understand the causal mechanisms between ED utilization and depression, these findings underscore major depression as an important treatment consideration among females with OUD who use the ED. Furthermore, these findings suggest that depression may be a useful indicator for identifying POUD in the ED.

We also extended prior work by examining the association of POUD severity (i.e., number of symptoms) and ED utilization. We found that greater severity of POUD was associated with increased odds of ED utilization among females but not males. These findings suggest that females may be relatively more vulnerable to adverse events requiring ED care as a function of POUD severity. Another possibility may be that females with high treatment need are more likely to seek treatment services from the ED compared to other locations or none at all. Hence, it will be important for EDs to establish a network of higher level treatment services (e.g., methadone treatment and/or residential treatment programs) and protocols for facilitating linkage to those services in order to prevent future adverse events and related ED visits among patients presenting with more severe POUD.

Other sex-specific factors of ED utilization were also found, which have implications for targeted screening and intervention strategies. For instance, older age was associated with greater odds of ED utilization only among females with POUD. Specifically, an overwhelming majority of over 80% of females with POUD who were aged 50 or older reported past-year ED use. Age-related physiological factors, higher rates of comorbid conditions, persistent pain, concomitant medications, or social factors (e.g., loss and loneliness) may make older female adults particularly susceptible to adverse events associated with opioid misuse leading to ED presentation. Another possible explanation for excess ED utilization among this subgroup may include the use of the ED as an attempt to obtain opioids for pain-related complaints. Indeed, previous work has found a positive relationship between age and rates of a physician source of opioids among females with opioid dependence (Cicero et al., 2008). While the causal relationships between older age, POUD, and ED utilization warrant further investigation, our study underscores the ED as a key

opportunity to identify and address POUD among older adults with POUD, particularly those who are female. Given the prominence of comorbid medical conditions and chronic pain among older adults with POUD, ED-based linkage to multidisciplinary settings may be useful.

Among males with POUD, a greater proportion of those who reported past-year ED use met criteria for comorbid past-year SUDs than those who did not (85.7% vs. 77.7%). There was no significant difference in the prevalence of comorbid past-year SUDs among females with POUD by ED use status. Prior research indicates that comorbid SUDs are associated with increased odds of overdose, suicide, sexual risk behaviors, infectious disease, and poorer treatment outcome (Connor, Gullo, White, & Kelly, 2014; Petry, 2001). Thus, screening for and addressing comorbid SUDs should be an important component of POUD treatment, especially among males with POUD who use the ED. Moreover, having public insurance was an enabling correlate of ED utilization only among males with POUD. While public insurance programs like Medicaid are important funders of treatment (Sharma et al., 2017), coverage varies widely from state to state (Burns et al., 2016). Thus, certain financial barriers to accessing opioid agonist treatment associated with some public insurance programs may be particularly relevant to the POUD population presenting to the ED.

Prior (lifetime or past-year) treatment for SUD was associated with increased odds of ED utilization among both males and females with POUD. Previous studies have shown that patients with a prior SUD treatment history are more likely to have greater substance use severity, more severe psychosocial functioning, medical problems, psychiatric problems, and worse treatment outcome compared to those with no treatment history (Cacciola, Dugosh, & Camilleri, 2009; Clark et al., 2015; Dennis, Scott, Funk, & Foss, 2005; Dreifuss et al., 2013; Simon et al., 2017). These findings lend further support to the notion that patients with POUD presenting to the ED may need an additional level of support to improve rates of engagement following ED-initiated treatment for POUD and referral for other SUD-related conditions (D'Onofrio et al., 2017).

Our findings should be considered in the context of some methodological limitations of NSDUH data. First, this was a cross-sectional study, which precluded causal interpretation of ED utilization among survey respondents with POUD. Additionally, the temporal pattern of events, such as whether POUD or other

factors occurred before, after, or simultaneously with ED utilization, could not be determined from the dataset, which should be considered when interpreting the findings. Our study was also limited to the extent that specific reasons for ED encounters were not captured. Nevertheless, our results provide important information on the subgroups most likely to seek care in the ED, which have implications for prevention, treatment engagement, and linkage efforts. Our results also suggest that these subgroups should be targeted to increase recruitment for randomized clinical trials for POUD conducted in the ED. Moreover, it was not possible from the dataset to determine the extent of other non-behavioral healthcare utilization (e.g., primary care visits) in which screening and intervention for POUD may have also occurred relative to the ED. Thus, it remains to be determined whether the ED represents a relatively more salient opportunity for treatment engagement among some individuals with POUD (e.g., high ED users with few to no primary care visits) more than others (e.g., infrequent ED users with many primary care visits). Furthermore, our findings are based on respondents' self-reported data, which may have been subject to recall or social desirability biases. However, the use of audio computer-assisted self-interviewing for the NSDUH serves to minimize these biases (Turner et al., 1998). Finally, individuals in institutional group quarters are excluded from the NSDUH such as those in hospitals, prisons, or residential treatment centers. It is possible that ED utilization in our study was underestimated given the exclusion of some high-risk subgroups of individuals. Notwithstanding these limitations, the NSDUH provides one of the largest nationally representative sample of adults with POUD available in the U.S. Thus, our results have increased generalizability compared to a sample recruited from a local area or a convenience sample.

Conclusions

In summary, our study suggests that males and females with POUD presenting to the ED may have distinct treatment needs and barriers to treatment access, many of which are associated with greater problem severity. These findings support the need for more intensive intervention protocols in the ED to increase treatment engagement and linkage to further care. One such strategy includes adding ED-initiated pharmacotherapy (e.g., buprenorphine) to the screening, brief intervention, and referral to treatment (SBIRT) model of care. While this approach has

shown efficacy compared to only brief-intervention and referral, longer term (i.e., 6-12 month) treatment retention rates following ED- or hospital-initiated buprenorphine treatment are only modest (Cushman, Liebschutz, Anderson, Moreau, & Stein, 2016; D'Onofrio et al., 2017). Addressing sex-specific treatment needs and barriers may be one useful strategy to promote sustained treatment beyond the initial linkage. Going forward, a concerted effort from providers, researchers, policymakers, and other stakeholders will be critical for reducing barriers to ED-initiated treatment and maximizing the utility of the ED to address POUD.

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