

Sex Differences in Cannabis Use Disorder Diagnosis Involved Hospitalizations in the United States

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Objectives: The study examined sex differences in trend and clinical characteristics of cannabis use disorder (CUD) diagnosis involved hospitalizations among adult patients.

Methods: We analyzed hospitalization data from the 2007–2011 Nationwide Inpatient Samples for patients aged 18–64 years (N = 15,114,930). Descriptive statistics were used to characterize demographic variables and to compare the proportions of CUD diagnosis and comorbid patterns between male and female hospitalizations. Logistic regressions were performed to examine the association of sex and other demographic variables with CUD diagnosis.

Results: During the study period, 3.3% of male and 1.5% of female hospitalizations had any-listed CUD diagnoses, and both sexes presented an upward trend in the number, rate, and proportion of CUD diagnosis. Among hospitalizations for patients aged 18–25 years, about 1 in 10 males and 1 in 20 females included a CUD diagnosis, and this proportion decreased with age strata. Mental

disorders accounted for the highest proportion of CUD involved inpatient hospitalizations, and female CUD involved hospitalizations included a higher proportion of mental disorders that required hospitalized care compared with male hospitalizations (41% vs 36%). In each sex group, younger age, black race, lower household income, large metropolitan residence, non-private insurance, substance use diagnosis, and mental disorders were associated with elevated odds of having CUD diagnosis.

Conclusion: The large sample of clinical hospitalization data suggest an increased trend in CUD diagnosis and sex differences in several comorbidities with CUD-involved hospital admissions. Prevention and treatment for CUD should consider sex differences in clinical comorbidities.

Key Words: cannabis use disorder, hospitalization, mental disorder, sex

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Cannabis use disorders (CUDs) are among the most prevalent illicit/nonmedical drug use disorders globally and in the United States (Center for Behavioral Health Statistics and Quality [CBHSQ], 2016; Hall et al., 2016). It was estimated that 1.4% to 2.9% of U.S. adults aged ≥ 18 years met criteria for CUD in the past year (Hasin et al., 2015; CBHSQ, 2016; Wu et al., 2016). CUD is potentially associated with various health risks, such as psychiatric disorders, motor vehicle injuries, respiratory and cardiovascular diseases (Volkow et al., 2014; Hall et al., 2016). For example, a recent review suggested that the use of cannabis-based products was associated with an increased likelihood of a variety of cardiovascular diseases, particularly ischemic strokes (Jouanjus et al., 2017). The ongoing shifts in recreational and medical cannabis laws, decreased perceived risk of cannabis use (CU), as well as an increase in the prevalence of CUD could have a potential impact on health (Cerdá et al., 2012; Volkow et al., 2014; Okaneku et al., 2015). CUDs have been found to be associated with an increase in healthcare utilization and costs (Gubatan et al., 2016; Gryczynski et al., 2016; Kim et al., 2016). The CUD-related hospital costs were estimated to be approximate \$4.5 billion annually (Gryczynski et al., 2016). However, most previous studies used self-reported healthcare utilization data, and there is a need to investigate CUD and related comorbidities in large clinical samples (Lynskey and Hall, 2016). Meanwhile, studies of the community samples in general have suggested that men and women manifest differently in the prevalence of CUD, drug tolerance, health

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consequences, and treatment-seeking behaviors (Cotto et al., 2010; Fattore and Fratta, 2010; Craft et al., 2013; Khan et al., 2013; Ketcherside et al., 2016). However, little is known about sex differences in CUDs in a large clinical sample, which can provide useful information to guide intervention and treatment for both sexes. Thus, this study is designed to explore recent trends and clinical characteristics of CUD in a national inpatient dataset in order to better inform intervention efforts.

Prior studies reported that males had a higher CUD prevalence than females in the general population, which suggest sex differences in the demand and utilization of healthcare. Wu et al. (2014) estimated that approximately 2.3% of males aged ≥ 12 years met criteria for past-year CUD compared with 1.1% of females between 2005 and 2011. Hasin et al. (2016) estimated that 1.6% and 1.9% of males aged ≥ 18 years had moderate/severe and mild CUDs in the past year, respectively, compared with 0.7% and 0.9% of females between 2012 and 2013. The potential reason for higher CUD prevalence among males was that males were more likely than females to use cannabis for both medical and recreational purposes, and an estimated 16.5% of males aged ≥ 12 years used cannabis compared with 10.2% of females in the past year (CBHSQ, 2016). Fairman (2016) found that two-thirds of registered medical cannabis participants were male in 13 states and District of Columbia, and Lin et al. (2016) estimated that 62% of recreational cannabis users aged ≥ 18 years in a national sample of adults were male. Men usually initiated cannabis at a younger age than women, and have more opportunities than women in access to drugs (Wagner and Anthony, 2002; CBHSQ, 2016). In addition, males appeared to have a greater likelihood of problem CU than females (Wu et al., 2014; Cuttler et al., 2016).

Prior studies also suggest sex differences in psychiatric comorbidities in the population-based surveys or small clinical samples; however, there is limited information about CUD and its comorbidities among hospitalized patients (Greenfield et al., 2007; Goldstein et al., 2012; National Institute on Drug Abuse [NIDA], 2016). Because CUD and comorbidities are generally more severe at inpatient settings that could place a high burden on the healthcare resource utilization, it is critical to examining sex differences in CUD and other comorbidities among inpatients (Moore et al., 2007; Wittchen et al., 2007; Volkow et al., 2014; Hunt et al., 2016). Khan et al. (2013) found that, among adults with a lifetime CUD, over 94% of men and women had a psychiatric comorbidity in 2001/2002, and that men with lifetime CUD were more likely to have any psychiatric disorder, any substance use disorder (SUD; other than CUD) and antisocial personality disorder, whereas women with CUD were more likely to have mood and anxiety disorders. Foster et al. (2016) found that women aged between 18 and 22 years with CUD had a higher likelihood of anxiety and suicide than the same age-group men with CUD in a clinical trial sample ($n = 600$). These 2 studies indicate sex differences in psychiatric disorders among adults with CUD. This sex difference in psychiatric disorders may be attributed to the observed differences in the interaction of cannabis and hormones, cannabis effects on brain structure, and function between males and females in the clinical and laboratory studies

(Fattore and Fratta, 2010; Craft et al., 2013; Ketcherside et al., 2016).

This study aims to analyze a national hospitalization database and examine sex differences in (1) recent trends in CUD diagnosis among hospitalizations, (2) proportion of CUD diagnosis among hospitalizations across demographic groups, (3) comorbid patterns of CUD diagnosis, and (4) association of demographic variables and comorbidities with CUD diagnosis.

METHODS

Data Source

We analyzed the hospitalization data from the 2007–2011 Nationwide Inpatient Sample (NIS) of the Healthcare Cost and Utilization Project (HCUP) sponsored by Agency for Healthcare Research and Quality (HCUP, 2013). The NIS is the largest publicly available all-payer hospitalization database in the United States, which was constructed by a 20% stratified sample of non-federal community hospitals (excluding short-term rehabilitation, long-term non-acute care hospitals, psychiatric hospitals, and alcoholism/chemical dependency treatment facilities) in the participating states (HCUP, 2013). The NIS database included 40 to 46 states/year between 2007 and 2011, and detailed information about NIS states can be found at the HCUP website (<https://www.hcup-us.ahrq.gov/>). The NIS dataset annually included about 8 million inpatient discharges from over 1000 hospitals, and it has been widely used to produce national inpatient treatment estimates for various conditions. We used the NIS data from 2011 and before because the NIS has made substantial changes in designs since 2012. For example, the old NIS data from 2011 and before included a sample of hospitals, whereas the subsequent NIS data from 2012 and after included a sample of hospital discharges.

In this study, the unit of observation is a hospitalization encounter rather than an individual patient. We focused on non-maternal/non-neonatal hospitalizations for patients aged between 18 and 64 years between 2007 and 2011 ($n = 15,114,930$; male = 7,393,657, female = 7,721,273). Hospitalizations for patients aged ≤ 17 years and ≥ 65 years were excluded because of state variation in children's healthcare benefit and high hospital readmission rate, respectively (Schildhaus et al., 2013; Barrett et al., 2015). The use of NIS data was determined to be exempt from review by the institutional review board of Duke University Health System.

Study Variables

Demographic variables included patients' age in years at admission, sex, race/ethnicity (non-Hispanic white, non-Hispanic black, Asian/Pacific-Islander/Native-American, Hispanic and other/unknown), residential location (large, small, and micropolitan/non-metropolitan area), and primary expected payer (Medicaid/Medicare, private, self-pay, and other), as well as median household income based on zip code (1st [lowest], 2nd, 3rd, and 4th [highest] quartiles) and census region of the hospital (Northeast, Midwest, South, and West).

Diagnosis variables were based on the *International Classification of Diseases, 9th Revision, Clinical Modification*

(ICD-9-CM) and the HCUP Clinical Classifications Software (CCS) for ICD-9-CM (Centers for Medicare & Medicaid Services, 2014; Elixhauser et al., 2015). There were 15 to 25 original ICD-9-CM and reclassified CCS diagnosis codes for each hospitalization, and the first-listed diagnosis code was the primary diagnosis (Heslin et al., 2015). Our analysis was based on diagnosis codes and definitions from the NIS data. We used ICD-9-CM codes to identify a specific condition (eg, CUD, tobacco use disorder, etc), and used CCS codes to describe a small number of clinically meaningful diagnosis categories by collapsing related ICD-9-CM codes. CUD was defined by ICD-9-CM codes 304.3 (cannabis dependence) and 305.2 (non-dependent cannabis abuse). The diagnosis of any SUD other than CUD was defined by ICD-9-CM codes: alcohol (291, 303, 305.0, 357.5, 425.5, 535.3, 571.0–571.3), tobacco (305.1), cocaine (304.2 and 305.6), opioid (304.0, 304.7, 305.5), and other drugs (292, 304.1, 304.4–304.6, 304.8, 304.9, 305.3, 305.4, 305.7–305.9). Any drug use disorder other than CUD did not include tobacco and alcohol diagnoses. Because mental disorders (non-SUD diagnoses) were common among drug users (Heslin et al., 2015), we examined mental disorders among CUD-involved hospitalizations by using CCS codes (Appendix Table S1, <http://links.lww.com/JAM/A57>): adjustment disorders (650), anxiety disorders (651), attention-deficit, conduct, and disruptive behavior disorders (652), impulse control disorders, not elsewhere classified (NEC) (656), mood disorders (657), personality disorders (658), and schizophrenia and other psychotic disorders (659).

In addition to CUD, any other SUDs, and mental disorders, we also used a multilevel CCS scheme to define 6 other medical diagnosis categories: (1) diseases of the nervous system and sense organs (76–95); (2) diseases of the circulatory system (96–121); (3) diseases of the respiratory system (122–134); (4) diseases of the digestive system (135–155); (5) diseases of the genitourinary system (156–175); and (6) diagnosis of injury and poisoning (225–244); Appendix Table S1, <http://links.lww.com/JAM/A57>; Elixhauser et al., 2015).

Data Analyses

Descriptive statistics were used to characterize demographic variables of the study sample (hospitalization data among adults aged 18–64 years) and to compute the frequency, rate (per 100,000 population) and proportions of CUD diagnoses over time, stratified by sex. We calculated and compared the proportion of CUD diagnosis in each demographic group between male and female hospitalizations. We examined the distributions of primary and any-listed comorbidities among hospitalizations involving CUD diagnosis, and we computed specific categories for mental disorders and other SUDs separately for each sex. Chi-square and *t* tests were used to examine the significance for discrete and continuous variables, respectively. Finally, logistic regressions were performed to examine the association of sex and other demographic variables with CUD diagnosis by controlling for the discharge year. We reported the significance level $P < 0.0001$ in tables due to a large sample size. All results were weighted estimates except for the sample size by considering NIS complex designs and using Stata 13.0 (Stata-Corp, 2013).

RESULTS

Characteristics of the Study Sample

Among non-maternal/non-neonatal hospitalizations for adults aged 18 to 64 years (unweighted $N = 15,114,930$), 49% were male, 82% were aged 35 to 64 years, 54% were non-Hispanic whites, 30% resided in areas with the lowest median household income, and 10% were self-payers for healthcare. Male and female hospitalizations showed similar distributions across demographic groups. Compared with male hospitalizations, female hospitalizations had slightly higher proportions of middle-age (26–49 years) and private insurance (Table 1).

Trends in CUD Diagnosis by Sex

Overall, 3.3% of male and 1.5% of female hospitalizations had any CUD diagnosis. Between 2007 and 2011, males and females presented a similar upward trend in the number, rate, and proportion of hospitalizations involving any CUD diagnosis. Males accounted for 68% of all CUD diagnoses (weighted $N = 1,713,469$), and had a higher rate of hospitalizations per 100,000 population than females. In 2011, the estimated rate of hospitalizations was 285 CUD diagnoses per 100,000 males aged 18 to 64 years (which increased by 38% from 206 in 2007), and 135 CUD diagnoses per 100,000 females aged 18 to 64 years (which increased by 39% from 97 in 2007) (Table 2).

Males had a double proportion of CUD compared with females across each demographic group. Notably, among hospitalizations for patients aged 18 to 25 years, about 1 in 10 males and 1 in 20 females included a CUD diagnosis, and this proportion decreased with age strata for both sexes. Also, non-Hispanic blacks had a higher proportion of CUD than other race/ethnic groups (5.6% male; 2.3% female).

Comorbid Pattern of CUD by Sex

Among CUD-involved hospitalizations, 99% were listed as secondary diagnosis. SUDs (other than CUD) and mental disorders (other than SUD) were the most common primary/any-listed diagnosis for both sexes. For example, 36% and 41% were primary mental disorders and 14% and 11% were primary other SUDs for males and females, respectively. Compared with hospitalizations without CUD diagnosis, both male and female hospitalizations with CUD diagnosis had significantly higher rates of other SUD and any mental disorder diagnoses ($P < 0.0001$) for both primary and any-listed diagnosis (Tables 3 and 4, Appendix Table S2 and S3, <http://links.lww.com/JAM/A57>).

Females with CUD were more likely than males with CUD to have any-listed diagnosis of any mental disorder (71% vs 57%, $P < 0.0001$), mood disorders (57% vs 38%, $P < 0.0001$), anxiety disorders (20% vs 11%, $P < 0.0001$), and personality disorders (13% vs 8%, $P < 0.0001$). Compared with males with CUD, females with CUD had fewer alcohol-related disorder diagnoses (32% vs 42%, $P < 0.0001$). In addition to this, mental and other SUD diagnoses, common comorbidities (any-listed) among hospitalizations with CUD included diseases of the circulatory system (38% male; 36% female), diseases of the digestive system (26% male; 29%

TABLE 1. Characteristics of Hospitalizations for Adults Aged 18–64 Years by Sex: 2007–2011 Nationwide Inpatient Sample

Sex	Overall		Male		Female		<i>P</i>
	Sample Size, Unweighted N (%)	15,114,930 (100%)	7,393,657 (48.97%)		7,721,273 (51.03%)		
Weighted Column, %	%	95% CI	%	95% CI	%	95% CI	
Mean of age, y	47.10	47.02–47.17	47.31	47.21–47.40	46.90	46.84–46.96	<0.0001
Age group, y							<0.0001
18–25	7.27	7.16–7.38	7.53	7.40–7.66	7.02	6.92–7.11	
26–34	10.91	10.78–11.03	10.62	10.46–10.78	11.19	11.08–11.29	
35–49	31.91	31.78–32.05	30.43	30.24–30.61	33.34	33.22–33.47	
50–64	49.91	49.65–50.17	51.43	51.09–51.76	48.45	48.24–48.67	
Race/ethnicity*							<0.0001
White, non-Hispanic	53.95	52.59–55.31	54.10	52.68–55.51	53.81	52.47–55.14	
Black, non-Hispanic	15.52	14.77–16.31	15.09	14.33–15.88	15.94	15.18–16.74	
Hispanic	9.05	8.39–9.75	9.30	8.60–10.05	8.80	8.18–9.48	
Asian/Pacific-Islander/Native-American	2.24	2.07–2.42	2.22	2.05–2.42	2.25	2.08–2.43	
Other/unknown [†]	15.93	14.54–17.42	15.94	14.53–17.46	15.91	14.53–17.40	
Household income*							<0.0001
Lowest quartile	30.08	29.15–31.04	30.18	29.21–31.16	29.99	29.07–30.93	
2nd quartile	25.05	24.42–25.68	24.75	24.12–25.39	25.33	24.70–25.97	
3rd quartile	22.53	21.96–23.11	22.29	21.72–22.88	22.76	22.19–23.34	
Highest quartile	19.09	18.17–20.04	19.00	18.08–19.97	19.17	18.25–20.12	
Residential location*							<0.0001
Large metropolitan	53.67	51.70–55.62	54.03	52.04–56.01	53.32	51.37–55.26	
Small metropolitan	25.68	24.15–27.28	25.32	23.79–26.92	26.03	24.50–27.63	
Micropolitan/non-metropolitan	17.39	16.72–18.07	17.07	16.38–17.79	17.69	17.04–18.35	
Hospital region							<0.0001
Northeast	20.27	19.42–21.14	21.14	20.20–22.10	19.43	18.62–20.27	
Midwest	22.79	21.96–23.64	22.56	21.68–23.46	23.01	22.20–23.84	
South	38.71	37.62–39.82	37.92	36.76–39.10	39.47	38.41–40.54	
West	18.23	17.54–18.95	18.39	17.62–19.17	18.08	17.42–18.77	
Primary expected payer*							<0.0001
Private	45.62	44.80–46.44	43.25	42.37–44.14	47.89	47.13–48.66	
Medicaid/Medicare	36.87	36.28–37.47	35.74	35.12–36.38	37.96	37.38–38.54	
Self-pay	10.32	9.92–10.73	12.35	11.88–12.84	8.37	8.03–8.72	
Other [‡]	6.87	6.50–7.26	8.31	7.85–8.79	5.49	5.18–5.81	
CUD diagnosis*							<0.0001
Any-listed CUD diagnosis	2.39	2.31–2.48	3.31	3.19–3.43	1.51	1.46–1.57	
Non-CUD diagnosis	97.58	97.49–97.66	96.66	96.54–96.78	98.45	98.40–98.51	
Diagnosis array among CUD [§]							0.0008
Primary CUD diagnosis	0.52	0.44–0.63	0.56	0.46–0.68	0.46	0.37–0.56	
Secondary CUD diagnosis	99.48	99.37–99.56	99.44	99.32–99.54	99.54	99.44–99.63	

*Missing values were not reported.

†Some states in certain years did not provide race/ethnicity information, and these hospitalizations were coded into other/unknown races/ethnicities.

‡Other primary expected payer included no charge, Worker's Compensation, CHAMPUS, CHAMPVA, Title V, and other government programs.

§The distribution of primary and secondary diagnosis was calculated among hospitalizations involving any-listed CUD diagnosis instead of among all hospitalizations in the sample.

||We reduced the significance level to $P < 0.0001$ due to a large sample size. CI, confidence interval; CUD, cannabis use disorder.

female), and diseases of the respiratory system (23% male; 29% female).

Adjusted Analysis of CUD Diagnosis Among Hospitalizations

In the overall sample, female hospitalizations were less likely to have a CUD diagnosis than male hospitalizations (adjusted odds ratio: 0.54, 95% confidence interval [CI] 0.53–0.55) after controlling age, race/ethnicity, household income, residential location, hospital region, primary payer, mental and other SUDs, and discharge year. In each sex group, younger age, non-Hispanic blacks, lower household income, large metropolitan, non-private insurance, SUD (tobacco, alcohol and drugs other than cannabis), and mental disorders were associated with elevated odds of CUD diagnosis (Table 5).

DISCUSSION

This analysis of a large national sample of adult hospitalizations extends research on CUD and comorbidities in community surveys to inpatient settings. To our knowledge, this study is the first to provide a comprehensive clinical view of CUD and comorbidities among hospitalized patients. First, our findings suggest that both sexes showed an upward trend in the number and proportion of hospitalizations involving CUD diagnosis from 2007 to 2011, and hospitalizations by patients aged 18 to 25 years had the highest proportion of CUD diagnosis. Second, among adult hospitalizations, non-private insurance, lower household income, diagnoses of other SUDs, and mental disorders were associated with elevated odds of CUD diagnosis. Both male and female hospitalizations with CUD were disproportionately affected by these sociodemographic factors. Third, compared with male

TABLE 2. Hospitalizations Involving Any-listed Cannabis Use Disorder Diagnosis for Adults Aged 18–64 Years by Sex: 2007–2011 Nationwide Inpatient Sample

Sex	Overall with CUD				Male with CUD				Female with CUD						
	Unweighted N	Weighted N	Rate* %†	95% CI	Unweighted N	Weighted N	Rate* %†	95% CI	Unweighted N	Weighted N	Rate* %†	95% CI			
Total/mean‡	359,675	1,713,469	177	2.39	2.31–2.48	243,503	1,161,100	242	3.31	3.19–3.43	116,172	552,369	114	1.51	1.46–1.57
Year															
2007	59,683	286,190	151	2.04	1.87–2.22	40,421	194,059	206	2.83	2.61–3.08	19,262	92,131	97	1.28	1.18–1.40
2008	62,741	294,595	154	2.06	1.89–2.24	42,284	198,409	209	2.85	2.63–3.09	20,457	96,186	100	1.31	1.20–1.43
2009	70,166	340,892	177	2.37	2.18–2.57	47,424	230,737	241	3.27	3.01–3.55	22,742	110,155	113	1.50	1.37–1.63
2010	78,521	380,349	195	2.61	2.42–2.82	53,664	260,166	269	3.61	3.33–3.91	24,857	120,182	123	1.63	1.52–1.75
2011	88,564	411,445	210	2.88	2.67–3.10	59,710	277,729	285	3.96	3.68–4.26	28,854	133,715	135	1.84	1.70–1.98
% change 2011 vs 2007	48.39	43.77	39.07	41.18	NA	47.72	43.12	38.35	39.93	NA	49.80	45.14	39.18	43.75	NA
Age group															
18–25	86,172	410,839	237	7.89	7.61–8.17	58,952	281,288	317	10.65	10.28–11.02	27,220	129,551	153	5.05	4.86–5.25
26–34	90,758	432,532	237	5.54	5.34–5.74	61,170	291,743	319	7.83	7.56–8.12	29,588	140,789	155	3.44	3.31–3.58
35–49	117,254	559,129	174	2.45	2.35–2.54	77,425	369,526	232	3.46	3.33–3.60	39,829	189,604	117	1.56	1.49–1.62
50–64	65,491	310,969	108	0.87	0.83–0.91	45,956	218,543	157	1.21	1.16–1.26	19,535	92,426	63	0.52	0.50–0.54
Race/Ethnicity§															
White, non-Hispanic	165,370	784,737	80	2.03	1.95–2.11	109,773	521,483	108	2.75	2.64–2.86	55,597	263,254	53	1.34	1.28–1.39
Black, non-Hispanic	90,209	430,347	231	3.87	3.67–4.08	62,052	296,406	331	5.60	5.32–5.90	28,157	133,941	138	2.30	2.18–2.42
Hispanic	26,186	125,582	148	1.94	1.81–2.08	19,855	95,168	232	2.92	2.73–3.12	6,331	30,414	69	0.94	0.87–1.02
Asian/Pacific-Islander/ Native-American	5,615	27,228	11	1.70	1.42–2.03	3,822	18,514	15	2.37	2.02–2.79	1,793	8,714	7	1.06	0.84–1.33
Other/unknown	61,083	292,578	NA	2.56	2.35–2.79	40,511	194,106	NA	3.47	3.19–3.77	20,572	98,472	NA	1.69	1.54–1.85

*Rate was defined as CUD involved hospitalizations per 100,000 persons/males/females aged 18–64 years.

†The weighted percentage of hospitalizations involving any-listed cannabis use disorder diagnosis among all hospitalizations for adults aged 18–64 years.

‡Total unweighted and weighted numbers and mean of rate and proportions between 2007 and 2011.

§We used the population of 1 race/non-Hispanic white, 1 race/non-Hispanic black, 1 race/non-Hispanic Asian, American Indians and Alaska Natives, Native Hawaiian& Pacific Islander, Hispanic, respectively, as the denominators to calculate rates of CUD across racial/ethnic groups.

||Logistic regression estimated the rate differed from the estimate in 2007 (P<0.0001). Bold: the estimates were different between male and female hospitalizations (P<0.0001). CI, confidence interval; CUD, cannabis use disorder; NA, not available.

TABLE 3. Primary Diagnosis Pattern of Substance Use Disorders, Mental Disorders and Other Medical Diseases Among Hospitalizations for Adults Aged 18–64 Years by Cannabis Use Disorder and Sex: 2007–2011 Nationwide Inpatient Sample

Sex	Overall						Male			Female				
	Cannabis Use Disorder (CUD) Diagnosis		Non-CUD		CUD		CUD		Non-CUD		CUD		Non-CUD	
	Sample Size, Unweighted N	%	95% CI	%	95% CI	243,503	%	95% CI	7,148,030	%	95% CI	116,172	%	95% CI
Primary Diagnosis														
Substance use disorders (SUD other than CUD)														
Any SUD (other than CUD) [*]	12.63	11.73–13.59	3.00	2.82–3.20	13.63	12.66–14.66	4.28 [§]	4.00–4.57	10.54	9.72–11.42	1.80 [§]	1.69–1.91		
Alcohol-related disorders	6.11	5.68–6.57	1.99	1.9–2.09	7.04	6.53–7.58	3.00 [§]	2.86–3.15	4.16	3.85–4.50	1.05 [§]	1.00–1.10		
Any drug use disorder (other than CUD) [†]	6.52	5.96–7.13	1.01	0.89–1.13	6.59	6.02–7.20	1.28 [§]	1.12–1.46	6.38	5.78–7.02	0.75 [§]	0.67–0.83		
Cocaine use disorders	0.83	0.67–1.02	0.07	0.05–0.09	0.83	0.67–1.03	0.09 [§]	0.07–0.13	0.83	0.66–1.04	0.04 [§]	0.03–0.05		
Opioid use disorders	1.73	1.46–2.06	0.26	0.22–0.31	1.79	1.51–2.14	0.35 [§]	0.28–0.44	1.61	1.35–1.92	0.18 [§]	0.15–0.20		
Other drug use disorders [‡]	3.95	3.59–4.35	2.88	2.81–2.96	3.96	3.61–4.35	0.83 [§]	0.72–0.97	3.94	3.53–4.39	0.53 [§]	0.47–0.60		
Mental disorders (other than SUD)														
Any mental disorder	37.52	36.10–38.96	6.54	6.22–6.88	35.79	34.36–37.26	6.46 [§]	6.12–6.81	41.15	39.67–42.64	6.62 [§]	6.31–6.95		
Mood disorders	23.60	22.61–24.63	4.05	3.85–4.25	20.21	19.30–21.14	3.59 [§]	3.41–3.79	30.74	29.53–31.98	4.47 [§]	4.25–4.70		
Schizophrenic, psychotic, delusional disorders	11.52	10.88–12.19	2.04	1.90–2.19	13.32	12.57–14.10	2.42 [§]	2.24–2.61	7.75	7.29–8.22	1.69 [§]	1.58–1.80		
Adjustment disorders	1.32	1.18–1.47	0.20	0.18–0.21	1.33	1.17–1.50	0.21 [§]	0.19–0.23	1.31	1.17–1.47	0.18 [§]	0.17–0.20		
Anxiety disorders	0.65	0.59–0.71	0.18	0.18–0.19	0.50	0.45–0.54	0.15 [§]	0.14–0.16	0.97	0.87–1.07	0.22 [§]	0.21–0.23		
Impulse control disorders, NEC	0.20	0.18–0.22	0.04	0.03–0.044	0.25	0.22–0.28	0.05 [§]	0.048–0.06	0.09	0.07–0.11	0.023 [§]	0.02–0.03		
Personality disorders	0.17	0.14–0.20	0.024	0.02–0.03	0.13	0.11–0.16	0.02 [§]	0.016–0.022	0.24	0.20–0.30	0.03 [§]	0.025–0.04		
Attention-deficit, conduct, disruptive behavior disorders	0.06	0.05–0.07	0.008	0.007–0.009	0.07	0.05–0.08	0.01 [§]	0.009–0.012	0.04	0.03–0.06	0.006 [§]	0.005–0.007		
Selected other medical diseases														
Injury and poisoning	10.65	10.19–11.13	10.62	10.41–10.83	11.31	10.77–11.88	12.18	11.89–12.48	9.26	8.91–9.62	9.15	9.01–9.29		
Diseases of the circulatory system	8.89	8.57–9.22	17.10	16.87–17.33	9.72	9.37–10.09	20.55 [§]	20.24–20.85	7.13	6.83–7.45	13.85 [§]	13.66–14.04		
Diseases of the digestive system	6.80	6.57–7.04	13.54	13.4–13.68	6.74	6.50–6.99	12.87 [§]	12.73–13.02	6.93	6.65–7.21	14.17 [§]	14.03–14.31		
Diseases of the respiratory system	4.34	4.18–4.50	8.31	8.21–8.42	4.17	4.01–4.33	7.67 [§]	7.57–7.76	4.69	4.48–4.91	8.92 [§]	8.80–9.04		
Diseases of the nervous system and sense organs	3.14	3.02–3.27	3.39	3.33–3.44	3.04	2.92–3.17	2.95	2.90–3.00	3.36	3.20–3.52	3.80 [§]	3.73–3.87		
Diseases of the genitourinary system	1.92	1.84–2.01	6.17	6.09–6.26	1.46	1.39–1.53	3.59 [§]	3.54–3.64	2.90	2.75–3.06	8.61 [§]	8.49–8.73		

*Any SUD include tobacco, alcohol and drug other than cannabis use disorder, and tobacco was not reported due to small sample size (N < 10).

†Any other drug use disorder includes drugs other than cannabis.

‡Other drug use disorders include amphetamine, hallucinogen, sedatives, hypnotics, anxiolytics, tranquilizers, barbiturates, and other not specified drugs based on ICD-9-CM codes.

§Chi square tests reported estimates in males/females with CUD differed with estimates in males/females without CUD (P < 0.0001). Bold: the estimates were different between male and female hospitalizations with CUD (P < 0.0001). CI, confidence interval; CUD, cannabis use disorder; NEC, not elsewhere classified; SUD, substance use disorder.

TABLE 4. Any-listed Diagnosis Pattern of Substance Use Disorders, Mental Disorders and Other Medical Diseases Among Hospitalizations for Adults Aged 18–64 Years by Cannabis Use Disorder and Sex: 2007–2011 Nationwide Inpatient Sample

Cannabis Use Disorder (CUD) Diagnosis	Overall						Male			Female		
	CUD		Non-CUD		Non-CUD		CUD		Non-CUD		CUD	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Sample Size, Unweighted N	359,675		14,750,325		7,148,030		243,503		7,602,295		116,172	
Any-listed Diagnosis												
Substance use disorders (SUD other than CUD)												
Any SUD (other than CUD)*	81.74	81.31–82.15	29.29	28.88–29.70	82.10	81.66–82.53	34.77 [§]	34.30–35.25	80.97	80.50–81.44	24.12 [§]	23.76–24.99
Alcohol-related disorders	38.64	37.97–39.31	9.12	8.92–9.32	41.86	41.17–42.56	13.55 [§]	13.25–13.85	31.87	31.17–32.58	4.95 [§]	4.83–5.06
Tobacco use disorder	51.29	50.35–52.23	21.19	20.82–21.55	50.89	49.90–51.87	23.80 [§]	23.39–24.21	52.15	51.20–53.09	18.73 [§]	18.39–19.06
Any drug use disorder (other than CUD)†	44.37	43.64–45.09	6.61	6.38–6.85	43.78	43.04–44.53	8.00 [§]	7.69–8.33	45.59	44.80–46.37	5.30 [§]	5.14–5.47
Cocaine use disorders	26.60	25.85–27.36	2.11	2.00–2.22	26.55	25.76–27.35	2.79 [§]	2.64–2.95	26.70	25.94–27.48	1.46 [§]	1.39–1.53
Opioid use disorders	13.66	13.09–14.25	2.55	2.40–2.71	13.22	12.66–13.81	3.03 [§]	2.83–3.25	14.58	13.93–15.26	2.10 [§]	1.99–2.21
Other drug use disorders‡	20.19	19.52–20.87	3.56	3.43–3.69	19.54	18.88–20.21	4.16 [§]	4.00–4.33	21.55	20.80–22.31	3.00 [§]	2.90–3.10
Mental disorders (other than SUD)												
Any mental disorder	61.78	60.66–62.88	27.28	26.90–27.66	57.40	56.20–58.58	22.88 [§]	22.49–23.26	70.98	69.96–71.99	31.43 [§]	31.02–31.84
Mood disorders	44.26	43.26–45.25	19.49	19.18–19.80	38.07	37.11–39.04	15.18 [§]	14.91–15.46	57.25	56.21–58.29	23.55 [§]	23.20–23.90
Schizophrenic, psychotic, delusional disorders	15.58	14.90–16.28	3.94	3.76–4.12	17.62	16.84–18.43	4.58 [§]	4.36–4.80	11.29	10.79–11.80	3.33 [§]	3.20–3.47
Adjustment disorders	2.52	2.33–2.72	0.64	0.61–0.67	2.43	2.23–2.64	0.62 [§]	0.58–0.65	2.72	2.50–2.95	0.65 [§]	0.62–0.69
Anxiety disorders	13.45	12.94–13.97	7.47	7.34–7.61	10.50	10.07–10.94	5.71 [§]	5.60–5.82	19.65	18.97–20.35	9.14 [§]	8.98–9.30
Impulse control disorders, NEC	0.95	0.87–1.03	0.16	0.14–0.17	1.10	1.01–1.20	0.21 [§]	0.19–0.22	0.63	0.56–0.70	0.11 [§]	0.10–0.12
Personality disorders	9.29	8.72–9.88	1.41	1.33–1.48	7.63	7.13–8.17	1.14 [§]	1.07–1.21	12.77	12.05–13.52	1.66 [§]	1.57–1.75
Attention-deficit, conduct, disruptive behavior disorders	3.02	2.83–3.22	0.63	0.61–0.65	3.20	3.01–3.41	0.68 [§]	0.65–0.70	2.64	2.43–2.86	0.58 [§]	0.56–0.60
Selected other medical diseases												
Diseases of the circulatory system	37.54	36.84–38.24	59.01	58.71–59.32	38.43	37.71–39.16	62.41 [§]	62.03–62.79	35.66	34.89–36.44	55.81 [§]	55.52–56.11
Diseases of the digestive system	26.76	26.19–27.33	40.32	40.02–40.62	25.67	25.09–26.26	38.15 [§]	37.83–38.48	29.04	28.43–29.66	42.36 [§]	42.07–42.66
Diseases of the respiratory system	25.32	24.87–25.77	30.74	30.50–30.97	23.35	22.90–23.81	29.26 [§]	29.03–29.49	29.45	28.90–30.00	32.13 [§]	31.88–32.38
Diseases of the nervous system and sense organs	24.01	23.52–24.50	25.81	25.55–26.07	22.63	22.13–23.14	24.60 [§]	24.35–24.85	26.90	26.36–27.44	26.95	26.68–27.22
Injury and poisoning	20.57	20.00–21.16	21.05	20.77–21.34	21.41	20.74–22.10	23.34 [§]	22.98–23.70	18.81	18.32–19.31	18.90	18.68–19.13
Diseases of the genitourinary system	16.17	15.75–16.60	28.63	28.40–28.86	13.70	13.27–14.15	25.26 [§]	25.01–25.52	21.35	20.87–21.85	31.80 [§]	31.57–32.02

*Any SUD include tobacco, alcohol and drug other than cannabis use disorder.

†Any other drug use disorder includes drugs other than cannabis.

‡Other drug use disorders include amphetamine, hallucinogen, sedatives, hypnotics, anxiolytics, tranquilizers, barbiturates, and other not specified drugs based on ICD-9-CM codes.

§Chi square tests reported estimates in males/females with CUD differed with estimates in males/females without CUD ($P < 0.0001$). Bold: the estimates were different between male and female hospitalizations with CUD ($P < 0.0001$). CI: confidence interval. CUD, cannabis use disorder; NEC, not elsewhere classified; SUD, substance use disorder.

TABLE 5. Adjusted Odds Ratios of Hospitalizations With Cannabis Use Disorder Diagnosis Versus Non-CUD Diagnosis: 2007–2011 Nationwide Inpatient Sample

Sex	Overall*			Male*			Female*			
	Adjusted Odds Ratio (AOR)	AOR	95% CI	P	AOR	95% CI	P	AOR	95% CI	P
Sex (vs male)										
Female	0.54	0.53–0.55	<0.0001							
Age in years (vs 18–25)										
26–34	0.55	0.53–0.56	<0.0001	0.55	0.54–0.57	<0.0001	0.55	0.53–0.56	<0.0001	
35–49	0.24	0.23–0.24	<0.0001	0.23	0.22–0.23	<0.0001	0.25	0.25–0.26	<0.0001	
50–64	0.12	0.11–0.12	<0.0001	0.12	0.11–0.12	<0.0001	0.13	0.12–0.13	<0.0001	
Race/Ethnicity (vs white, non-Hispanic)										
Black, non-Hispanic	1.85	1.79–1.91	<0.0001	1.86	1.80–1.93	<0.0001	1.84	1.77–1.91	<0.0001	
Hispanic	0.92	0.88–0.97	0.001	0.95	0.90–0.99	0.031	0.88	0.83–0.93	<0.0001	
Asian/Pacific-Islander/Native-American	1.08	0.93–1.24	0.322	1.05	0.92–1.19	0.512	1.14	0.95–1.37	0.164	
Other/unknown†	1.18	1.11–1.26	<0.0001	1.17	1.10–1.25	<0.0001	1.20	1.12–1.28	<0.0001	
Household income (highest quartile)										
Lowest quartile	1.39	1.33–1.45	<0.0001	1.33	1.27–1.39	<0.0001	1.52	1.45–1.60	<0.0001	
2nd quartile	1.19	1.15–1.24	<0.0001	1.16	1.12–1.21	<0.0001	1.28	1.22–1.33	<0.0001	
3rd quartile	1.12	1.08–1.15	<0.0001	1.10	1.06–1.13	<0.0001	1.16	1.12–1.21	<0.0001	
Patient location (vs large metropolitan)										
Small metropolitan	1.00	0.95–1.05	0.924	1.00	0.95–1.06	0.921	0.98	0.93–1.04	0.574	
Micropolitan/non-metropolitan	0.86	0.81–0.92	<0.0001	0.86	0.81–0.92	<0.0001	0.86	0.80–0.91	<0.0001	
Hospital region (vs northeast)										
Midwest	1.11	1.03–1.21	0.010	1.11	1.02–1.20	0.013	1.11	1.02–1.21	0.017	
South	0.86	0.80–0.93	0.0001	0.86	0.79–0.93	0.0002	0.85	0.79–0.92	0.0001	
West	1.10	1.01–1.19	0.023	1.13	1.04–1.22	0.005	1.03	0.95–1.13	0.473	
Primary payer (vs private)										
Medicaid/Medicare	1.42	1.39–1.46	<0.0001	1.38	1.34–1.41	<0.0001	1.49	1.45–1.54	<0.0001	
Self-pay	1.69	1.63–1.75	<0.0001	1.61	1.55–1.67	<0.0001	1.84	1.77–1.92	<0.0001	
Other‡	1.52	1.44–1.60	<0.0001	1.45	1.37–1.53	<0.0001	1.63	1.54–1.73	<0.0001	
Tobacco use disorder§ (vs no diagnosis)										
All-listed diagnosis	2.38	2.32–2.43	<0.0001	2.23	2.18–2.29	<0.0001	2.62	2.54–2.70	<0.0001	
Alcohol-related disorder§ (vs no diagnosis)										
All-listed diagnosis	2.78	2.71–2.85	<0.0001	2.62	2.56–2.69	<0.0001	3.21	3.12–3.31	<0.0001	
Any drug use disorder other than CUD§ (vs no diagnosis)										
All-listed diagnosis	4.07	3.92–4.24	<0.0001	3.68	3.53–3.84	<0.0001	4.88	4.70–5.08	<0.0001	
Mental disorders other than SUD (vs no diagnosis)										
All-listed diagnosis	2.61	2.53–2.69	<0.0001	2.48	2.40–2.56	<0.0001	2.90	2.8–3.00	<0.0001	
Year (vs 2007)										
2008	1.03	0.95–1.12	0.523	1.03	0.95–1.12	0.473	1.02	0.93–1.11	0.663	
2009	1.11	1.02–1.20	0.019	1.11	1.02–1.21	0.014	1.09	1.00–1.19	0.048	
2010	1.15	1.06–1.25	0.001	1.16	1.07–1.26	0.001	1.12	1.03–1.22	0.006	
2011	1.26	1.16–1.37	<0.0001	1.27	1.17–1.39	<0.0001	1.23	1.13–1.35	<0.0001	

*Each adjusted logistic regression included all variables listed in the first column.

†Some states in certain years did not provide race/ethnicity information, and these hospitalizations were coded into other races/ethnicities.

‡Other primary expected payer included no charge, Worker's Compensation, CHAMPUS, CHAMPVA, Title V, and other government programs.

§Any-listed diagnosis and the definition can be found in Table S1, <http://links.lww.com/JAM/A57>. AOR, adjusted odds ratio; CI, confidence interval; CUD, cannabis use disorder. Boldfaced: $P < 0.0001$.

hospitalizations, female CUD-involved hospitalizations had higher proportions of mental disorders and genitourinary diseases and lower proportions of other SUDs, injuries, and circulatory diseases. These findings point toward the need to further study sex differences in mechanisms underlying CUD, comorbidities, and healthcare utilization pathways in order to inform prevention and treatment strategies.

An Increase in CUD-involved Hospitalizations Among Both Sexes

Importantly, our data showed that the number and proportion of CUD diagnoses were on the rise for both sexes in a large inpatient sample. This finding is consistent with the growing utilization in other healthcare settings. During the same time interval (2007–2011), the Treatment Episode Data

Set reported that the number of treatment facility admissions aged ≥ 12 years with cannabis as a primary substance increased by 11% (Substance Abuse and Mental Health Services Administration [SAMHSA], 2016), and the HCUP Nationwide Emergency Department Sample reported that the number of all-aged emergency department admissions with a primary CUD diagnosis increased by 66% (HCUPnet, 2016). Between 2007 and 2011, some of the NIS participating states have decriminalized CU or/and legalized medical CU (eg, Arizona, Connecticut, Michigan, and New Jersey), which may be associated with an increase in the number of CUD diagnoses among hospitalizations. Cerdá et al. (2012) found that residents in states with medical cannabis laws had higher odds of CUD than states without such laws. In addition, CUD appeared to be associated with other psychiatric and medical

health conditions that could contribute to inpatient utilization. In this study, most CUDs among hospitalizations were secondary diagnoses. Although NIS data do not allow us to examine causal associations between CUD and co-occurring diseases, comorbid patterns with CUD diagnoses were in line with findings from self-reported data (surveys or epidemiological studies) and laboratory-based studies (Volkow et al., 2014). For example, chronic or heavy CU has been found to be associated with increased odds of mental disorders (Moore et al., 2007; Goldstein et al., 2012; Hunt et al., 2016), injuries (Asbridge et al., 2012), cardiovascular diseases (Rumalla et al., 2016; Jouanjus et al., 2017), and respiratory diseases (Martinasek et al., 2016), which also were top primary diagnoses for both sexes in inpatient patients. Also, over 80% of hospitalizations with CUDs in this sample had at least 1 other SUD for both sexes, and combinations of CUD and other SUDs may have more harmful effects on health problems and healthcare utilization (SAMHSA, 2014; Zhu and Wu, 2016). Only a small proportion of CUD diagnoses was considered a primary diagnosis, but about 40% of CUD diagnoses was the secondary diagnosis following mental disorder diagnosis. Our data also indicated that mental disorders with comorbid CUD may increase the burden on inpatient care. More researches are needed to study whether early intervention of CUD could reduce the incidence of mental disorders.

Although young people are generally healthier in physical health and accounted for fewer hospitalizations than older people, we found that over 10% and 5% of male and female hospitalizations aged 18 to 25 years, respectively, had any-listed CUD diagnosis. Young adults also were more likely to meet criteria for CUD than older adults (Wu et al., 2016). Since the CUD prevalence in the community sample was 5.7% among young adults aged 18 to 25 years, this pattern suggested a high burden of healthcare use (Wu et al., 2014). Future research could clarify whether CUD among young adults may be associated with particularly severe illnesses requiring multiple treatment admissions. We also found a higher magnitude of association between non-private insurance and lower household income with CUD diagnosis, respectively, in both male and female hospitalizations, which suggest the need to further study the severity of CUD and related comorbidities as well as health-seeking patterns (eg, lacking access to timely ambulatory or SUD care) for lower-income individuals with CUD (Hasin et al., 2015; Wu et al., 2012, 2016). Having a better understanding of sex differences in CUD and clinical comorbidity may help improve early intervention for CUD and reduce health disparities.

High Proportions of Mental Disorders Among Female CUD Involved Hospitalizations

We compared comprehensive CUD comorbidity profiles between male and female hospitalizations with CUD diagnosis by using patients' medical records data. The critical findings were that mental disorders accounted for the highest proportion of CUD involved inpatient utilizations, especially among female hospitalizations with CUD. These findings imply that CUD involved mental disorders are a clinical burden on the healthcare system. Despite the limitation that

causality remained unclear, regular CU has been associated with psychiatric disorders (Volkow et al., 2014), which implies the challenge of treating patients with CUD and comorbidity and a need for research to identify effective treatment approaches. For example, Moore et al. (2007) estimated that regular cannabis users were twice more likely to have psychotic disorders than non-users by using meta-analysis. This study also adds clinical data for CUD-involved hospitalizations for women, as there is a limited number of studies on sex differences in psychiatric comorbidities among persons with CUD. We found that 41% of female CUD-related hospitalizations admitted to inpatient care were primarily related to mental disorders compared to 36% of male hospitalizations. Similarly, prior studies suggested that females with CUD were more likely to have a psychiatric disorder in a clinical sample (Chen et al., 2011), and to have anxiety and mood disorders in the general population (Goldstein et al., 2012; Khan et al., 2013). On the other hand, people with mental and physical problems may use cannabis to self-medicate their conditions. Lee et al. (2007) found that 5% of young adult cannabis users used cannabis to deal with stress and depression (coping motives) as a primary motive. Bonn-Miller et al. (2008) found a positive association of the level of anxiety vulnerability with the frequency of CU and/or coping motives among young cannabis users. Furthermore, compared with female CUD involved hospitalizations, we found that male CUD involved hospitalizations had slightly higher proportions of other SUDs, injury and poisoning, and circulatory diseases as primary admission reasons. However, sex-specific effects on these comorbidities remain limited in the literature and need further exploration. Rumalla et al. (2016) also used NIS data and found that CUD was more prevalent among male hospitalizations with a primary diagnosis of acute ischemic stroke (AIS) than among female hospitalizations with AIS.

Sex differences in comorbid patterns among hospitalized patients with CUD may be affected by biological factors and treatment-seeking behaviors. Biological differences between men and women may account for different pharmaceutical effects and active mechanisms of CU and CUD (Fattore and Fratta, 2010; Craft et al., 2013). For example, laboratory studies have observed that cannabis interacted with different hormones between 2 sexes (Brown and Dobs, 2002; Ketcherside et al., 2016). Also, female users were found to develop CUD and admit to treatment more quickly from first CU than male users (eg, telescoping effect; Hernandez-Avila et al., 2004; Khan et al., 2013), and to have a higher incidence and greater severity of cannabis withdrawal symptoms (Herrmann et al., 2015). Furthermore, there may be some sex differences in health-seeking and utilization of treatments. The Treatment Episode Data Set data showed that fewer female admissions aged 12 to 24 years were treated for primary CU than male admissions in the SUD related treatment facilities (SAMHSA, 2014). Compared with males, female users may be more likely to seek healthcare through general medical or mental health settings, and may not receive specialty addiction treatment (Greenfield et al., 2007, 2010). In fact, it was indicated that the majority of existing treatment programs for SUDs were designed primarily for men (Greenfield et al., 2007; NIDA, 2016). The hospitalization data tend to capture the subset of patients with the most

severe medical conditions. Therefore, sex differences CUD and its comorbidities may be influenced by severity and health-seeking patterns. Although more males had CUD, the sex gap in CUD prevalence has been decreasing with increasing cannabis availability (Johnson et al., 2015). There is a need to monitor sex differences in the CUD prevalence and related treatment admissions.

Limitations

Our results should be interpreted within the following limitations. First, NIS datasets represent encounter data, and an individual may have multiple admissions during the study period. We excluded old adults aged ≥ 65 years from the analysis to reduce potential bias associated with a high rate of readmission. Second, the NIS sample does not include substance use treatment facilities and psychiatric hospitals, where the prevalence of CUD is relatively high. It is also possible that there were low detection rates of SUDs in the sampling hospitals, which may underestimate the treatment use for CUD and other SUD diagnoses (Smothers et al., 2004). Third, the NIS data may have coding bias on diagnosis, which may affect our diagnosis estimates including CUD and other diseases (Yoshihara and Yoneoka, 2014). Nonetheless, HCUP has implemented the quality control procedures to improve the data quality. Fourth, the limitation of the broad definition for “other medical diseases” is that the analysis could not precisely identify a specific diagnosis subgroup. For example, the “disease of the circulatory system” included a number of cardiovascular diseases defined by CCS codes 96–121, such as heart valve disorders, pulmonary heart disease, and acute myocardial infarction. Finally, causal relations between CUD and comorbidities cannot be established due to a lack of data on the onset time of diseases.

CONCLUSIONS

This study provides a comprehensive analysis of CUD and comorbidities by using a large hospitalization dataset. We found an increased trend in CUD diagnosis among hospitalized patients for both sexes during the study period, and females with CUD diagnosis displayed disproportionately higher proportions of most comorbidities (eg, mental disorders) than males with CUD. Future research may be needed to develop effective sex-specific treatment models for individuals with CUD and comorbid mental disorders. There is a continuous need to monitor the CUD prevalence as well as CUD-related comorbidities, including how cannabis legalization differentially influences CUD and CUD-related problems across demographic groups and their treatment needs.

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