

Geographical and Socioeconomic Disparities in Substance and Opioid Use Disorders Among Inflammatory Bowel Disease Hospitalizations in the United States From the National Inpatient Sample

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Abstract

Objective: We compared substance use disorder (SUD) prevalence among adult inflammatory bowel disease (IBD) hospitalizations with non-IBD controls from the 2016–2018 National Inpatient Sample, assessing correlations with demographics, socioeconomic status, geographic regions, depression, and anxiety.

Methods: The primary aim focused on SUD, defined as substance abuse or dependence (*International Statistical Classification of Diseases, Tenth Revision [ICD-10]: F10–F19*) excluding unspecified use or remission, among hospitalizations documenting IBD (Crohn's disease or ulcerative colitis; *ICD-10: K50–51*) as one admitting diagnosis (IBD-D). The prevalence of

SUD among hospitalizations with and without IBD was compared. The secondary aim further characterized factors influencing SUD among hospitalizations with IBD as the primary diagnosis (IBD-PD). Multivariable logistic regression was performed to estimate the adjusted odds ratios (ORs) for SUD including associated covariates.

Results: SUD prevalence was 20.9% for IBD-D and 20.8% for non-IBD controls ($P = .38$). After adjustments, there was less SUD (OR 0.92, 95% CI, 0.90–0.93) but more opioid use disorder (OUD) (OR 1.20, 95% CI, 1.15–1.24) among IBD-D; other substances were less likely among IBD-D. Among IBD-PD hospitalizations, SUD significantly associated with Crohn's disease (75.1% vs 58.8%, $P < .001$), Medicaid (30.4% vs 15.8%, $P < .001$), lowest-income quartile (32.8% vs 23.8%,

$P < .001$), depression (19.1% vs. 12.5%), and anxiety (24.7% vs. 14.9%). These factors were also associated with OUD. Notably, certain geographic regions and urbanization levels correlated with both elevated SUD and OUD among IBD-PD hospitalizations.

Conclusions: We comprehensively characterized SUD prevalence among adult IBD hospitalizations, identifying demographic, socioeconomic, geographic, and mental health risk factors for SUD and OUD in IBD. These findings inform efforts to decrease SUD among IBD patients by improving health care delivery through reducing health care disparities and improving psychiatric care.

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Inflammatory bowel disease (IBD), consisting of Crohn's disease (CD) and ulcerative colitis (UC), is a relapsing and remitting disease characterized by gastrointestinal and systemic inflammation. Given its chronicity and debilitating symptoms, comorbidity with psychiatric disorders is substantial.^{1–3} Specifically, depression and anxiety are associated with IBD and are linked to increased risk of IBD flare, worse clinical outcomes, and higher health care costs.^{4–8} Substance use

can exacerbate anxiety and depression, while anxiety and depression can reciprocally increase the likelihood of engaging in substance use.⁹

While substance use disorder (SUD) among IBD patients has been postulated, the epidemiology has not been thoroughly investigated. One prospective Canadian study reported 1 in 6 patients with IBD developed SUD.¹⁰ Another retrospective study from one tertiary center in the US found 21% prevalence of

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Clinical Points

- Association between substance use disorder (SUD) and hospitalizations among adult inflammatory bowel disease (IBD) patients has not been examined.
- Higher prevalence of SUD and opioid use disorder (OUD) is found among IBD hospitalizations and is associated with distinct demographic, socioeconomic, geographic, and psychiatric contributors.
- Initiatives targeting these risk factors may decrease SUD and OUD among IBD patients, potentially decreasing hospitalizations.

polysubstance use among IBD patients, with higher odds of SUD among those with anxiety, use of antidepressants, higher perceived pain, smoking status, and male sex.¹¹ There has not been a study examining the distribution of SUD among US hospitalizations for IBD. The use of several substances directly affects IBD clinical outcomes. For example, smoking increases the risk for CD and worsens disease course but may be protective against UC.¹² Opioid use among IBD patients is associated with higher health care costs, infections, and mortality,^{13–15} possibly by obfuscating earlier signs of disease flare which may be managed promptly in outpatient setting to prevent complications and hospitalization. Chronic opioid abuse has been linked to increased disease activity, surgeries, escalation of therapy, and noncompliance.^{13,16,17} Following increasing legal tolerance of cannabinoids resulting in a lower barrier to access and increased use among the general adult population, the use of marijuana for self-medication has garnered interest among IBD patients as alternative therapy for alleviating pain, diarrhea, and poor appetite although clinical utility and side effects continue to be under investigation.^{17–19}

Despite growing evidence of substance use among IBD patients, few studies have comprehensively investigated SUD in IBD. The prevalence of SUD in IBD in comparison to the general population is unclear. Furthermore, studies have not adequately assessed the impact of demographics and socioeconomic status in SUD among IBD, factors which heavily influence the prevalence and outcome of both illnesses individually.^{20–22} Finally, the distribution of SUD among national IBD hospitalization is not well-defined.^{16–18} To address these questions, our focus was to characterize SUD among IBD hospitalizations using a well-established US national database. We hypothesized that SUD, especially cannabinoids and opioids, is correlated with hospitalizations among IBD patients. To study this, our primary aim compared the prevalence of SUD among hospitalizations with and without IBD. Our

secondary aim further characterized factors influencing SUD among hospitalizations primarily for IBD.

METHODS

Data Source

We performed a cross-sectional study of inpatient hospitalizations utilizing the 2016–2018 US National Inpatient Sample (NIS) database. NIS is a stratified sample of all-payer hospital discharges from Healthcare Cost and Utilization Project (HCUP) participating hospitals, designed to reflect national estimates of hospital stays. In 2018, the sample captured data from 47 states and the District of Columbia, covering 97% of the US population.²³ Long-term acute care hospitals are excluded from the NIS. Given that this is a publicly available database in HCUP that contains only de-identified data, the study was exempt from the Institutional Review Board of the University of Southern California. All study materials are available via the 2016–2018 NIS database, which is publicly available in HCUP.

Study Population

The study population for the primary aim included inpatient hospitalizations of adults (age ≥18) from 2016–2018 in the US NIS database with and without IBD. We defined hospitalizations with IBD (IBD-D) utilizing the *International Classification of Diseases, 10th revision (ICD-10)*, as a diagnosis of Crohn's disease (K50.x) or ulcerative colitis (K51.x, refer to Supplemental Materials* for a detailed list of *ICD-10* codes). We utilized IBD-D to evaluate hospitalization of all IBD patients, including hospitalizations that may not be for the management of IBD-related symptoms. The study population for the secondary aim encompassed the subgroup of inpatient stays with a primary reason for hospitalization of IBD (IBD-PD), based on the first *ICD-10* code. IBD-PD was utilized to perform a more focused evaluation of SUD in those primarily hospitalized for IBD.

Outcomes

The primary outcome was SUD, defined as active substance use or dependence based on *ICD-10* codes. SUD included alcohol (F10.x), opioids (F11.x), cannabinoids (F12.x), sedatives or hypnotics (F13.x), cocaine or stimulants (F14.x and F15.x), nicotine (F17.x), and hallucinogens, inhalants, or other psychoactive substances (F16.x, F18.x, and F19.x, shown in Supplemental Materials*). Unspecified use of substances or remission did not qualify as SUD. Secondary outcomes included substance-specific use disorders.

Table 1.

Demographics for Adult Hospital Admissions With and Without IBD in the NIS Database, 2016–2018 (Total Weighted N 90,847,141)

	Non-IBD-D	IBD-D	P value
Age, mean (SE)	58 (0.06)	54 (0.09)	<.001
Female	51.8%	56.3%	<.001
Race			<.001
White	67.2%	78.7%	
Black	15.2%	11.2%	
Hispanic	11.2%	6.2%	
Asian	2.8%	1.2%	
Native American	0.6%	0.4%	
Other	3.0%	2.3%	
Insurance			<.001
Medicare	47.6%	42.2%	
Medicaid	18.5%	14.9%	
Private	26.8%	36.4%	
Self-pay	4.0%	3.5%	
No charge	0.4%	0.4%	
Other	2.8%	2.6%	
Hospital division			<.001
New England	4.7%	6.5%	
Middle Atlantic	14.0%	15.1%	
East North Central	15.4%	17.5%	
West North Central	6.9%	7.3%	
South Atlantic	20.9%	21.0%	
East South Central	7.0%	6.5%	
West South Central	11.6%	9.0%	
Mountain	6.1%	5.8%	
Pacific	13.3%	11.4%	
ZIP code income quartile			<.001
Q1: <\$46,000	30.4%	24.4%	
Q2: \$46,000 to \$58,999	26.4%	25.6%	
Q3: \$59,000 to \$78,999	23.6%	26.0%	
Q4: \$79,000+	19.5%	23.9%	
Major depressive disorder	12.8%	16.9%	<.001
Anxiety disorders	13.5%	19.3%	<.001
Urban/rural			<.001
Large central metro	29.5%	27.1%	
Large fringe metro	24.0%	27.6%	
Small/medium metro	30.0%	30.4%	
Rural (micropolitan and non-core)	16.4%	14.9%	

Abbreviations: IBD-D = hospitalizations documenting inflammatory bowel disease, NIS = National Inpatient Sample.

Variables

Demographic characteristics included sex, race/ethnicity, health insurance type, zip code income quartile, hospital division based on regional classifications by HCUP, and urban/rural designation. ZIP code income quartiles were based on NIS, corresponding to the following categories in 2018: (1) \$1–\$45,999; (2) \$46,000–\$58,999; (3) \$59,000–\$78,999; and (4) \$79,000 or more. Urban-rural designation was categorized as large central metro, large fringe metro, small and medium metro, and rural (micropolitan and noncore) based on National Center for Health Statistics urban-rural definitions. The regional classifications for hospital division and each of its compromising states can be found in Supplemental Materials*. Comorbidities of

anxiety (F41.x) and major depressive disorders (F32.x and F33.x) were also abstracted. Anxiety disorders included panic disorder and generalized or mixed anxiety disorders. Major depressive disorders included both single episode and recurrent (Supplemental Materials*).

Statistical Methods

All statistical analyses utilized survey procedures incorporating the NIS discharge weights, hospital clusters, and stratum to account for the complex survey design. The discharge weights were designed to reflect national estimates of discharges. Taylor-series linearization was used to estimate variance and produce unbiased SEs and CIs. Weighted percentages and means with standard errors were reported for categorical and continuous variables, respectively, and compared using Rao-Scott χ^2 and *t* tests.

For the primary aim, we estimated the prevalence of SUD among inpatient hospitalizations as a weighted percentage separately for hospitalizations with and without a diagnosis of IBD (the latter serving as non-IBD controls). To analyze the association between SUD and IBD, we used multivariable logistic regression to estimate the adjusted odds ratios (ORs) for SUD including the a priori selected covariates of age, sex, health insurance, zip code income quartile, hospital division, depression, and anxiety. In sensitivity analysis, we further adjusted for urban/rural classification and race. Distributions for SUD and opioid use disorder (OUD) by IBD hospitalizations are presented by regions defined in Supplemental Materials*. Our secondary aim focused on SUD among IBD-PD. Adjusted ORs for SUD among these hospitalizations were estimated via multivariable logistic regression as described above while additionally adjusting for urban/rural classification and race.

Statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, North Carolina). Regional maps of SUD among IBD hospitalizations were created utilizing STATA Version 17.0 (StataCorp, College Station, Texas).

RESULTS

Primary Aim

A weighted total of 90,869,381 adult hospitalizations were identified, of which 1.1% were identified with a diagnosis of IBD. IBD-D were 56.3% female and 78.7% White and had a mean age of 54 years (± 0.1) (Table 1). Compared to non IBD-D hospitalizations, IBD-D was more likely to have private insurance (36.4% vs 26.8%, $P < .001$) and be in the highest income quartile (23.9% vs 19.5%, $P < .001$). IBD-D also had higher rates of major depressive (16.9% vs 12.8%, $P < .001$) and anxiety (19.3% vs 13.5%, $P < .001$) disorders.

Table 2.

Weighted Prevalence and Odds Ratios of SUD for IBD-D vs. Non-IBD-D Hospitalizations in the NIS Database, 2016–2018, Multivariable Analysis Adjusted for Age, Sex, Health Insurance, ZIP Code Income Quartile, Depression, Anxiety, and Hospital Division (Total Weighted N 90,869,381 for Univariate Analysis and 89,106,978 for Multivariable Analysis)

Active substance use disorder	IBD-D weighted %	Non-IBD-D weighted %	Univariate			Multivariable		
			OR (IBD-D vs non-IBD-D)	95% CI	P value	OR (IBD-D vs non-IBD-D)	95% CI	P value
All substances (SUD)	20.9%	20.8%	1.01	0.99–1.02	.38	0.92	0.90–0.93	<.001
Alcohol	3.0%	5.3%	0.55	0.53–0.57	<.001	0.47	0.45–0.48	<.001
Opioids	3.0%	2.2%	1.39	1.35–1.44	<.001	1.20	1.15–1.24	<.001
Cannabinoids	1.1%	1.4%	0.79	0.76–0.83	<.001	0.62	0.59–0.65	<.001
Sedatives or hypnotics	0.3%	0.4%	0.89	0.82–0.97	.01	0.66	0.60–0.71	<.001
Cocaine or stimulants	0.9%	1.8%	0.50	0.48–0.53	<.001	0.45	0.43–0.48	<.001
Nicotine	16.8%	16.1%	1.05	1.04–1.07	<.001	0.99	0.97–1.00	.05
Inhalants, hallucinogens, and other psychoactive substances	0.5%	0.7%	0.68	0.63–0.72	<.001	0.57	0.53–0.61	<.001

Abbreviations: IBD-D = hospitalizations documenting inflammatory bowel disease, NIS = National Inpatient Sample, SUD = substance use disorder.

Overall prevalence of SUD was 20.9% for IBD-D and 20.8% for non IBD-D hospitalizations ($P = .38$). Upon multivariable analysis adjusting for demographic characteristics and hospital division, IBD-D was less likely to have SUD (OR 0.92, 95% CI, 0.90–0.93), but more likely to have OUD (OR 1.20, 95% CI, 1.15–1.24). Other substances were less likely among IBD-D including disorders of alcohol, cannabinoids, cocaine or stimulants, sedatives or hypnotics, and inhalants, hallucinogens, or other psychoactive substances (Table 2, all $P < .001$). We did not detect a significant difference in nicotine dependence by IBD, and overall prevalence of cannabis use disorder was low (1.1% in IBD-D and 1.4% in non IBD-D hospitalizations). These results remained statistically significant when multivariable models were further adjusted for race and urban/rural locations (see Supplemental Materials Table 5*).

Secondary Aim

Among IBD-PD hospitalizations, the diagnosis of SUD occurred more often with CD (75.1% vs 58.8%, $P < .001$) than UC, Medicaid insurance (30.4% vs 15.8%, $P < .001$), and in the lowest income quartile (32.8% vs 23.8%, $P < .001$) (see Supplemental Materials Table 6*). IBD-PD with SUD versus without also exhibited higher presence of major depressive disorder (19.1% vs 12.5%, $P < .001$) and anxiety disorders (24.7% vs 14.9%, $P < .001$). Moreover, rural counties and hospital divisions in East South Central, East North Central, and Mountain regions account for a higher proportion of IBD-PD with SUD than without ($P < .001$).

Substance Use Disorder. Compared to Whites, multivariable adjusted ORs for SUD were highest for Native Americans (OR 1.38, 95% CI, 1.00–1.92) and lowest for Asian or Pacific Islander (OR 0.41, 95% CI, 0.31–0.53) (Table 3). Odds of SUD were higher for

hospitalizations with CD compared to UC (OR 1.97, 95% CI, 1.88–2.07) and male sex (OR 1.34, 95% CI, 1.28–1.41). When compared to private insurance, all other types of insurance had higher ORs of hospitalizations with SUD. Compared to the fourth (highest) income quartile, hospitalizations with lower income quartiles had an incrementally higher ORs of SUD (Supplemental Materials Figure 1*). Finally, odds of SUD were higher among hospitalizations with major depressive disorder (OR 1.32, 95% CI, 1.24–1.41) and anxiety disorders (OR 1.69, 95% CI, 1.60–1.80).

The weighted percentages of hospitalizations with SUD among IBD-PD by hospital division are characterized via maps (Figure 1A). When compared to the West South Central, the East and West North Central, Mountain, and East South Central hospital divisions had higher adjusted ORs for SUD. However, only the Mountain hospital division had statistically significant higher odds of SUD (OR 1.18, 95% CI, 1.03–1.35). Urban/rural regions were also compared. Utilizing large central as the reference, small and medium metropolitan areas had higher likelihood of SUD (OR 1.11, 95% CI, 1.04–1.08).

Opioid Use Disorder. The identification of higher OUD among IBD-D hospitalizations encouraged further analyses of demographic, socioeconomic, and mental health factors correlating with OUD among IBD-PD hospitalizations. Odds of OUD among IBD-PD were lower for all races compared to Whites except Native American (OR 1.42, 95% CI, 0.64–3.13) (Table 3). Furthermore, the likelihood of OUD was increased for hospitalizations with CD (OR 1.76, 95% CI, 1.53–2.02), male sex (OR 1.27, 95% CI, 1.11–1.44), and decreased with increasing age (OR 0.98, 95% CI, 0.97–0.98). When compared to private insurance, Medicare, Medicaid, and self-pay had higher ORs of OUD. In reference to the 4th income quartile, lower quartiles had higher likelihood of

Table 3.

Odds Ratios of SUD and OUD vs Without Among IBD-PD in the NIS Database, 2016–2018, Upon Multivariable Analyses (Total Weighted N 265,585)

Variable ^a	SUD			OUD		
	OR	95% CI	P value	OR	95% CI	P value
Crohn disease (vs ulcerative colitis)	1.97	1.88–2.07	<.001	1.76	1.53–2.02	<.001
Age	0.99	0.99–1.00	<.001	0.98	0.97–0.98	<.001
Male (vs female)	1.34	1.28–1.41	<.001	1.27	1.11–1.44	<.001
Race^b						
<i>White</i>	—	—	—	—	—	—
Black	0.84	0.78–0.90	<.001	0.64	0.52–0.78	<.001
Hispanic	0.59	0.54–0.65	<.001	0.51	0.39–0.67	<.001
Asian or Pacific Islander	0.41	0.31–0.53	<.001	0.41	0.19–0.87	.02
Native American	1.38	1.00–1.92	.05	1.42	0.64–3.13	.39
Other	0.76	0.65–0.89	<.001	0.54	0.35–0.85	.01
Insurance						
<i>Private including HMO</i>	—	—	—	—	—	—
Medicare	1.54	1.43–1.65	<.001	3.59	2.94–4.38	<.001
Medicaid	2.79	2.63–2.97	<.001	3.13	2.65–3.70	<.001
Self-pay	3.39	3.09–3.70	<.001	1.92	1.46–2.53	<.001
No charge	3.13	2.41–4.07	<.001	1.90	0.93–3.91	.08
Other	1.59	1.39–1.82	<.001	1.16	0.74–1.80	.52
ZIP code income quartile (2018 values)						
Q1: <\$46,000	1.73	1.60–1.87	<.001	1.35	1.09–1.68	.01
Q2: \$46,000 to \$58,999	1.48	1.37–1.59	<.001	1.20	0.99–1.46	.06
Q3: \$59,000 to \$78,999	1.30	1.21–1.41	<.001	1.37	1.14–1.65	.001
Q4: \$79,000+	—	—	—	—	—	—
Major depressive disorder	1.32	1.24–1.41	<.001	1.50	1.28–1.75	<.001
Anxiety disorders	1.69	1.60–1.80	<.001	2.43	2.10–2.81	<.001
Hospital division						
New England	0.96	0.85–1.09	.55	1.24	0.84–1.82	.27
Middle Atlantic	0.94	0.85–1.05	.28	1.21	0.87–1.68	.26
East North Central	1.08	0.98–1.20	.14	0.79	0.56–1.09	.15
West North Central	1.09	0.95–1.24	.21	0.98	0.64–1.51	.94
South Atlantic	0.99	0.90–1.10	.91	1.63	1.19–2.24	.003
East south central	1.04	0.92–1.17	.56	1.12	0.76–1.66	.58
<i>West south central</i>	—	—	—	—	—	—
Mountain	1.18	1.03–1.35	.02	1.85	1.23–2.68	.001
Pacific	1.02	0.91–1.14	.78	1.93	1.39–2.68	<.001
Urban/rural						
<i>Large central metro</i>	—	—	—	—	—	—
Large fringe metro	1.06	1.00–1.14	.07	0.84	0.70–1.01	.06
Small/medium metro	1.11	1.04–1.18	.002	0.78	0.66–0.92	.004
Rural (micropolitan and noncore)	1.07	0.99–1.16	.10	0.58	0.46–0.74	<.001

^aItalics denote the comparator group within each category.

^bRace category includes analysis of Hispanics (ethnicity).

Abbreviations: HMO = health maintenance organization, IBD-PD = hospitalizations with inflammatory bowel disease as the primary diagnosis, NIS = National Inpatient Sample, OUD = opioid use disorder, SUD = substance use disorder.

OUD (Supplemental Materials Figure 2*). Again, odds of OUD were higher in hospitalizations with major depressive disorder (OR 1.50, 95% CI, 1.28–1.75) and anxiety disorders (OR 2.43, 95% CI, 2.10–2.81).

The weighted percentages of OUD among hospitalizations for IBD-PD are shown by region in the map (Figure 1B). Compared to the West South Central as the reference hospital division, the South Atlantic, Mountain, and Pacific hospital divisions had higher ORs for OUD. In comparison to large central areas, small and medium

metropolitan areas and rural areas were less likely to have hospitalizations with OUD. Urban large fringe had no statistically significant difference from large central areas.

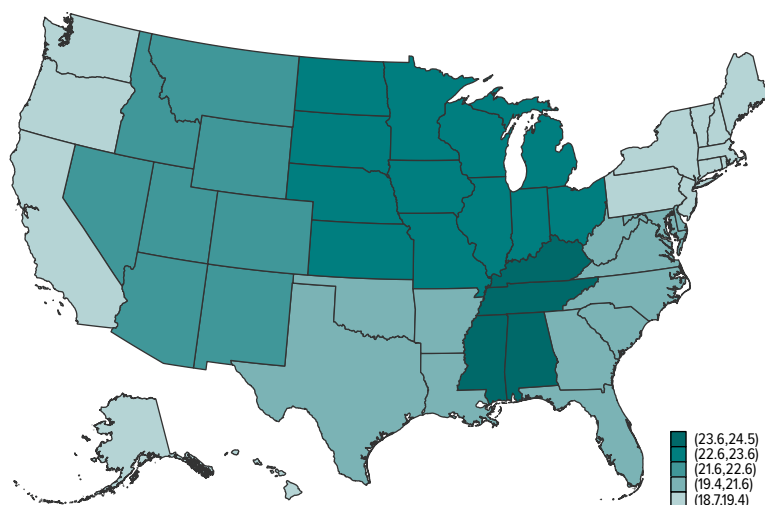
DISCUSSION

This study identified several national, regional, demographic, and disease-related characteristics of SUD among hospitalizations of patients with IBD and

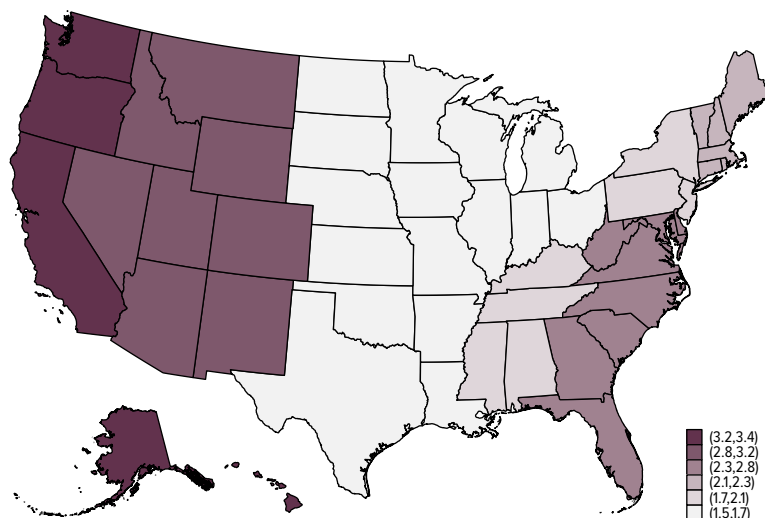
Figure 1.

Weighted Percent of (A) SUD^a and (B) OUD^b in Hospitalizations with IBD as Primary Diagnosis (IBD-PD), Mapped by Hospital Division

A. SUD in IBD Hospitalizations



B. OUD in IBD Hospitalizations



^aWeighted percent of SUD among IBD-PD mapped by hospital division. East South Central had the highest percent, but only the Mountain hospital division had statistically significant higher odds of SUD when compared to the West South Central. States of each hospital division listed in Supplemental Materials (available from the corresponding authors on request).

^bWeighted percent of OUD among IBD-PD mapped by hospital division. Pacific had the highest percent, and the South Atlantic, Mountain, and Pacific hospital divisions had higher odds ratio for OUD when compared to the West South Central. States of each hospital division listed in Supplemental Materials (available from the corresponding authors on request).

Abbreviations: IBD-PD = hospitalizations with inflammatory bowel disease as the primary diagnosis, OUD = opioid use disorder, SUD = substance use disorder.

hospitalizations with IBD as the primary admitting diagnosis. Among IBD-D hospitalizations, patients were more likely to be female, be White, have private insurance, and be in the highest income quartile, consistent with the demographics and socioeconomic

status of IBD patients previously reported.^{24–26} For IBD-PD, patients with SUD were younger, likely male, held nonprivate insurance, and in the lowest income quartile, consistent with published studies on SUD in the general US population.^{37,38} Patients with CD and comorbid

major depressive disorder or anxiety disorders were more likely to have SUD. Taken together, these patterns identified several characteristics of IBD patients associated with SUD. Targeting modifiable factors to reduce SUD may mitigate hospitalizations and reduce health care utilization among IBD patients.

Surprisingly, the prevalence of SUD among IBD-D was less than for non IBD-D hospitalizations after adjustments. Among the comprehensive list of substances we investigated, only OUD was higher among IBD patients. Tobacco continues to be one of the most abused substances in the US; however, there was no detectable difference between IBD-D and non IBD-D hospitalization cohorts. It is well-known that tobacco is an environmental risk factor for developing CD and worsens its course but may be protective against UC.^{27,28} Nevertheless, smoking is discouraged for its detrimental effects to overall health. While cannabinoid use among IBD has garnered interest as a form of self-medication, also likely reflecting its increasing legalizations, we found its use lower among IBD-D patients.^{29,30} Given other survey data have shown higher rates of cannabinoids use among IBD patients,^{31,32} we surmise this may reflect alternative forms of cannabinoid used including edibles, oils, and topicals, which may not be adequately captured during history taking of hospital admission. Most importantly, we found higher OUD among IBD-D. It has been reported that IBD is an independent risk factor for heavy opioid use, which is in turn associated with worse IBD outcomes.³³ Along with literature reporting high opioid use in both the outpatient and inpatient settings,¹³ our findings reinforce the need for ongoing effort to discourage opioid use among IBD patients through improving disease control, disseminating the detriments of opioid use on IBD outcomes, and establishing multidisciplinary efforts to limit opioid prescriptions. Our findings highlight potential racial and ethnic inequalities in the prescription of opioids in IBD-D, with Hispanic and non-White patients experiencing lower rates of opioid treatment for pain management.^{34–36}

Among IBD-PD, patients with CD, comorbid major depressive disorder or anxiety disorders, Medicaid insurance, lowest income quarter, and hospitalizations in rural counties and geographically located in East South Central, East North Central, and Mountain regions were more likely to have SUD. These findings suggest several contributors to increased IBD hospitalizations in SUD including underlying health care inequality in outpatient IBD management resulting in higher hospitalization rates, differences in symptom severity between CD and UC, and burden of mental disorders which are known to associate with poor disease control and outcomes.^{1,20,21}

Regional variations in SUD and OUD among hospitalizations for IBD-PD across the US were examined. Hospital admissions representing the Mountain region had higher odds of SUD, while those from the South Atlantic,

Mountain, and Pacific regions recorded higher OUD. Discrepancies in SUD and OUD were also found within hospital regions; SUD trended towards higher odds outside large central areas representing higher urbanization, whereas odds of OUD decreased in a stepwise fashion as areas became more rural. These findings likely reflect differences in the prevalence of SUD and OUD across geographic regions, access to adequate health care and specialists across different strata of urbanization, and variations in prescribers' practices reflecting their geography and urbanization levels. Specifically, obtaining opioids requires contact with the health care system in the forms of a prescriber and a pharmacy, and medical infrastructures are more geographically concentrated in urbanized versus rural areas. Finally, our findings offer novel insight of opioid use patterns among IBD patients, providing additional information to the FDA's initiative to combat the opioid crisis.

Several limitations merit consideration. First, the NIS database records individual hospitalizations and not individual patients. Therefore, it is possible that a small percentage of patients with frequent hospitalizations may skew the findings. However, this is the most comprehensive government-sponsored inpatient database. Second, our analyses found a surprisingly low prevalence of cannabis use disorder (1.1% in IBD hospitalizations and 1.4% in non-IBD hospitalizations); these rates were consistent with other publications utilizing the same database and likely underestimate cannabis use as aforementioned due to incomplete documentation of several forms of the substance.³⁹ Third, the NIS does not contain any information on disease-related factors including burden of symptoms, severity of disease, surgical history, age of onset, and other variables which may influence OUD and SUD among IBD patients. Finally, current findings are derived from the 2016–2018 NIS database and may not adequately capture transformative trends in response to the COVID-19 epidemic. Future studies utilizing updates to the NIS will elucidate the impact of COVID-19.

In conclusion, we comprehensively characterized the prevalence of SUD among hospitalizations for IBD. We also identified differences in SUD and OUD based on IBD type, demographic background and socioeconomic status, the presence of concomitant depression and anxiety, and variations reflecting geographic regions and urbanization levels. These findings may serve to guide efforts to reduce SUD, and especially OUD, through reducing health care inequalities and promoting the mental health of IBD patients.

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