

# Substance abuse and inpatient outcomes in inflammatory bowel disease hospitalizations in the United States: a propensity matched analysis

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## Abstract

**Background** Inflammatory bowel disease (IBD) is a chronic intestinal inflammation resulting in a genetically susceptible population. The present study aimed to look at the effect of substance abuse on IBD hospitalizations in the United States.

**Methods** We identified primary IBD hospitalizations with substance abuse using the National Inpatient Sample database (2016-2019). A matched comparison cohort of IBD hospitalizations without substance abuse was identified by 1:N propensity score matching using the nearest-neighbor method, based on demographics, hospital-level factors, and comorbidities.

**Results** We matched 4437 IBD hospitalizations with a diagnosis of substance abuse to 4528 hospitalizations without abuse. The median age was higher in the substance abuse group than no abuse (44 vs. 38 years,  $P<0.001$ ). There was a higher prevalence of discharge to care facilities (2.9% vs. 2.2%) and against medical advice (4.9% vs. 1.8%) in the substance abuse group compared to the no abuse ( $P<0.001$ ). The median length of hospital stays (LOS) ( $P=0.74$ ) and hospitalization charge did not differ significantly ( $P=0.57$ ). There was no significant difference in 30-day inpatient mortality among cohorts (adjusted hazard ratio 0.74, 95% confidence interval 0.32-1.81;  $P=0.54$ ). There was a higher prevalence of psychoses (2.5% vs. 1.3%) and depression (18.8% vs. 15.7%) in IBD hospitalizations with substance abuse compared to those without abuse ( $P<0.001$ ).

**Conclusions** This study reports no difference in median LOS, hospitalization charge, or mortality risk in IBD hospitalizations based on substance abuse. There is a higher prevalence of psychoses and depression in IBD patients, requiring screening for substance abuse to improve overall outcomes.

**Keywords** Inflammatory bowel disease, alcoholism, length of stay, substance-related disorders, National Inpatient Sample database

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## Introduction

Inflammatory bowel disease (IBD) includes Crohn's disease (CD) and ulcerative colitis (UC), and is characterized by chronic relapsing intestinal inflammation. Several risk factors have been associated with the rising prevalence of this debilitating disease, including genetic, environmental and psychological factors [1,2]. Although not definitive, IBD is thought to be secondary to a dysregulated host-microbe interaction or abnormal immune response in genetically susceptible individuals [3]. Substance abuse, including alcohol, has pro-inflammatory and direct cytotoxic effects, which can damage the physical and immunological barrier of the intestinal epithelium and lymphoid tissue, possibly contributing to worsening IBD [4].

There is a reported higher prevalence of psychological disorders in IBD patients, concurrently associated with greater consumption

of substances such as cocaine, cannabis, and opioids [5,6]. Consumption of these substances and alcohol can complicate the management of IBD. Substance abuse has been associated with IBD relapse, especially in the adult population [7-9]. There is a higher rate of IBD-related hospitalizations associated with substance abuse, and it is also considered a barrier to treatment adherence, remission and self-care [10]. Substance abuse in IBD patients can result in unwanted flares and inadvertently increase healthcare charges and poor patient outcomes [9]. The present study aimed to look at the effect of substance abuse on inpatient outcomes of IBD hospitalizations in the United States (US).

## Materials and methods

### Data source

The National Inpatient Sample (NIS) database was developed as a stratified probability sample to represent all non-federal hospitals in the US. It is the US's largest publicly available all-payer inpatient database [11]. In the present study, the NIS was analyzed to extract data from January 1<sup>st</sup>, 2016, to December 31<sup>st</sup>, 2019. In the NIS, all hospital discharges are weighted to ensure adequate national representation. Details on the design and sampling methods of the NIS are available at <https://www.hcup-us.ahrq.gov>.

### Sample population

The International Classification of Diseases, 10<sup>th</sup> revision, Clinical Modification (ICD-10-CM) was used to identify adult patients ( $\geq 18$  years of age) with a primary diagnosis of IBD. Additionally, data were extracted to indicate those patients with substance abuse (defined by dependence on alcohol, opioids, cocaine, or cannabis). The ICD-10 diagnosis codes are given in Supplementary Table 1. Patients were split into 2 cohorts based on the presence or absence of substance abuse. Exclusion criteria included ages  $< 21$  years, incomplete data, and patient transfers. These were considered high-risk conditions that could influence the outcomes.

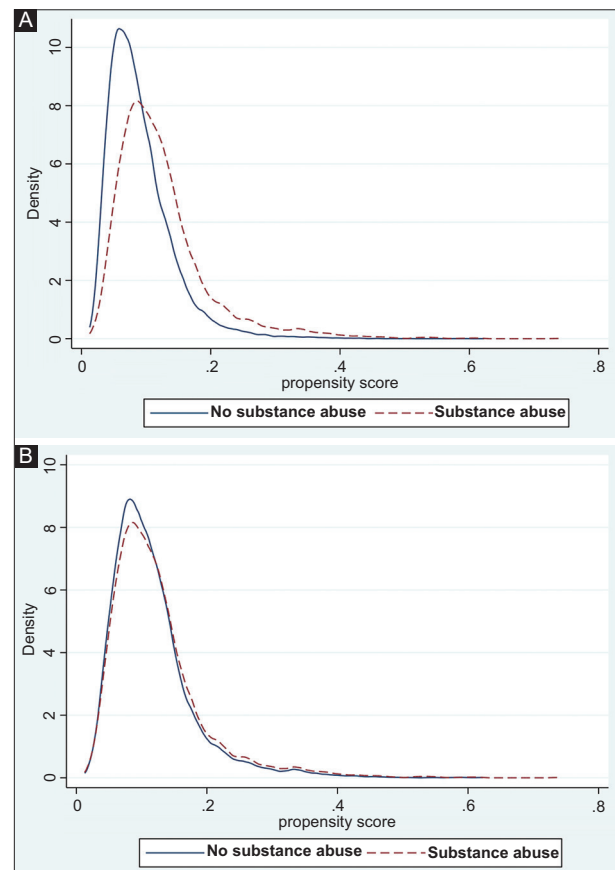
### Outcome measures

The primary outcomes were comparing the length of stay (LOS), hospitalization charge, and mortality between the 2 groups. Secondary outcomes included prevalence of depression and psychoses. Additional covariates included a demographic comparison between both groups.

### Statistical analysis

The present study developed matched cohorts using propensity score matching to minimize the effect of imbalances

between demographic, hospital level and comorbidity data. A propensity score was assigned to each hospitalization using a multivariate logistic regression model that included race, sex, age, and hospital-level factors, and the comorbidities shown in Tables 1 and 2. Propensity scores between the 2 cohorts were matched using a nearest-neighbor method within 0.01 standard deviations of the calculated score, based on demographics, hospital factors and comorbidities as matching variables and inpatient mortality as the outcome [12]. A standardized difference with an absolute value greater than 0.10 determined the covariate balance, which was then visualized using a 2-way plot as shown in Fig. 1A (before match) and 1B (after match). We used the chi-square test for categorical variables and the Wilcoxon rank-sum (Mann-Whitney) test for continuous variables, as NIS is a nonparametric database. Categorical variables were presented as frequency (N) and percentage (%), and continuous variables were reported as medians with interquartile range (IQR) as appropriate. The threshold for statistical significance was kept at 0.05, with all P-values being 2-sided. For primary outcomes such as median length of stay (LOS) and median inpatient charges, we utilized weighted hierarchical linear regression models and adjusted for confounding variables, as previously reported [5]. We used hierarchical Cox regression models for inpatient mortality and adjusted for patient and hospital-level confounders, including discharge disposition, where indicated. Inpatient mortality risk



**Figure 1** Covariate balance before propensity score matching in the present study

**Table 1** Comparative analysis of characteristics for IBD hospitalizations with substance abuse compared to no abuse before and after propensity matching

Variables	Substance abuse	No Substance abuse (Unmatched)	P-value	No Substance abuse (Matched)	P-value
	4437	42872		4528	
Median age, years (IQR)	44 (IQR 32-59)	41 (IQR 31-53)	<0.001	38 (IQR 29-52)	<0.001
Age group (years)			<0.001		<0.001
21-34	1514 (34.1%)	13400 (31.3%)		1823 (40.3%)	
35-49	1489 (33.6%)	12115 (28.3%)		1365 (30.1%)	
50-64	1116 (25.2%)	10265 (23.9%)		887 (19.6%)	
65-79	318 (7.2%)	7092 (16.5%)		453 (10.0%)	
Sex					
Male	2705 (61.0%)	20205 (47.1%)	<0.001	2820 (62.3%)	0.20
Female	1732 (39.0%)	22667 (52.9%)		1708 (37.7%)	
Race			<0.001		<0.001
White	3071 (69.2%)	31811 (74.2%)		3374 (74.5%)	
Black	818 (18.4%)	5540 (12.9%)		574 (12.7%)	
Hispanic	369 (8.3%)	3460 (8.1%)		381 (8.4%)	
Asian	35 (0.8%)	710 (1.7%)		66 (1.5%)	
Native American	30 (0.7%)	163 (0.4%)		17 (0.4%)	
Other	114 (2.6%)	1188 (2.8%)		116 (2.6%)	
Elixhauser Comorbidity Index Score			<0.001		<0.001
0	421 (9.5%)	9345 (21.8%)		1288 (28.4%)	
1	866 (19.5%)	11297 (26.4%)		1081 (23.9%)	
2	1009 (22.7%)	9191 (21.4%)		882 (19.5%)	
≥ 3	2141 (48.3%)	13039 (30.4%)		1277 (28.2%)	
Hospital region			<0.001		0.002
Northeast	876 (19.7%)	9373 (21.9%)		832 (18.4%)	
Midwest	961 (21.7%)	10396 (24.2%)		1061 (23.4%)	
South	1710 (38.5%)	16075 (37.5%)		1836 (40.5%)	
West	890 (20.1%)	7028 (16.4%)		799 (17.6%)	
Hospital location and teaching status			0.005		<0.001
Rural	295 (6.6%)	2591 (6.0%)		302 (6.7%)	
Urban nonteaching	902 (20.3%)	8015 (18.7%)		782 (17.3%)	
Urban teaching	3240 (73.0%)	32266 (75.3%)		3444 (76.1%)	
Expected primary payer			<0.001		<0.001
Medicare	881 (20.9%)	10148 (24.5%)		812 (18.7%)	
Medicaid	1391 (32.9%)	7080 (17.1%)		832 (19.2%)	
Private	1494 (35.4%)	21903 (53.0%)		2397 (55.2%)	
Other	458 (10.8%)	2217 (5.4%)		301 (6.9%)	
Median household income (quartile)			<0.001		0.037
1 <sup>st</sup> (0-25 <sup>th</sup> )	1447 (32.6%)	10452 (24.4%)		1369 (30.2%)	
2 <sup>nd</sup> (26 <sup>th</sup> -50 <sup>th</sup> )	1160 (26.1%)	10752 (25.1%)		1183 (26.1%)	
3 <sup>rd</sup> (51 <sup>st</sup> -75 <sup>th</sup> )	1043 (23.5%)	11185 (26.1%)		1088 (24.0%)	
4 <sup>th</sup> (76 <sup>th</sup> -100 <sup>th</sup> )	787 (17.7%)	10483 (24.5%)		888 (19.6%)	
Disposition of patient			<0.001		<0.001
Discharged to home or self-care (routine discharge)	3651 (82.3%)	35276 (82.3%)		3807 (84.1%)	
Transfer to short-term hospital	79 (1.8%)	679 (1.6%)		67 (1.5%)	
Transfer other: includes skilled nursing facility, intermediate care facility, another type of facility	129 (2.9%)	1311 (3.1%)		101 (2.2%)	
Home health care	351 (7.9%)	4814 (11.2%)		460 (10.2%)	
Against medical advice	218 (4.9%)	673 (1.6%)		81 (1.8%)	
Died	12 (0.3%)	119 (0.3%)		9 (0.2%)	
Admission day			0.027		<0.001
Weekday admissions	3489 (78.6%)	34312 (80.0%)		3705 (81.8%)	
Weekend admissions	948 (21.4%)	8560 (20.0%)		823 (18.2%)	
Opioid, cocaine, and cannabis abuse	3664 (82.6%)	0 (0.0%)		0 (0.0%)	

(Contd...)

**Table 1** (Continued)

Variables	Substance abuse	No Substance abuse (Unmatched)	P-value	No Substance abuse (Matched)	P-value
Alcohol abuse	1013 (22.8%)	0 (0.0%)		0 (0.0%)	
Median hospitalization charge, US\$ (IQR)	31513 (IQR 18671-56428)	32007 (IQR 18270-58383)	0.45	31537 (IQR 18114-56181)	0.57
Median LOS, days (IQR)	4 (IQR 2-6)	4 (IQR 2-6)	0.74	4 (IQR 2-6)	0.74

IBD, inflammatory bowel disease; IQR, interquartile range; LOS, length of hospital stay

**Table 2** Elixhauser comorbidities for IBD hospitalizations with substance abuse vs. no abuse before and after propensity matching

Variables	Substance abuse	No Substance abuse (Unmatched)	P-value	No Substance abuse (Matched)	P-value
	4437	42872		4528	
Congestive heart failure	125 (2.8%)	1314 (3.1%)	0.36	121 (2.7%)	0.67
Cardiac arrhythmias	376 (8.5%)	4265 (9.9%)	0.002	337 (7.4%)	0.071
Valvular disease	54 (1.2%)	598 (1.4%)	0.33	54 (1.2%)	0.92
Pulmonary circulation disorders	30 (0.7%)	444 (1.0%)	0.022	24 (0.5%)	0.37
Peripheral vascular disease	119 (2.7%)	1101 (2.6%)	0.65	113 (2.5%)	0.58
Uncomplicated hypertension	1009 (22.7%)	9965 (23.2%)	0.45	884 (19.5%)	<0.001
Paralysis	8 (0.2%)	115 (0.3%)	0.27	10 (0.2%)	0.67
Other neurological disorders	210 (4.7%)	1328 (3.1%)	<0.001	173 (3.8%)	0.033
Chronic pulmonary diseases	723 (16.3%)	5190 (12.1%)	<0.001	607 (13.4%)	<0.001
Uncomplicated diabetes	184 (4.1%)	2402 (5.6%)	<0.001	180 (4.0%)	0.68
Complicated diabetes	139 (3.1%)	1939 (4.5%)	<0.001	137 (3.0%)	0.77
Hypothyroidism	190 (4.3%)	2983 (7.0%)	<0.001	179 (4.0%)	0.43
Renal failure	145 (3.3%)	1936 (4.5%)	<0.001	134 (3.0%)	0.40
Liver disease	447 (10.1%)	1781 (4.2%)	<0.001	372 (8.2%)	0.002
Peptic ulcer disease excluding bleeding	64 (1.4%)	510 (1.2%)	0.14	63 (1.4%)	0.84
AIDS/HIV	18 (0.4%)	83 (0.2%)	0.004	15 (0.3%)	0.56
Lymphoma	3 (0.1%)	136 (0.3%)	0.003	2 (<1%)	0.64
Metastatic cancer	18 (0.4%)	315 (0.7%)	0.013	13 (0.3%)	0.34
Solid tumor without metastasis	55 (1.2%)	658 (1.5%)	0.12	50 (1.1%)	0.55
Rheumatoid arthritis/collagen vascular disorder	145 (3.3%)	1568 (3.7%)	0.19	133 (2.9%)	0.37
Coagulopathy	197 (4.4%)	1441 (3.4%)	<0.001	158 (3.5%)	0.021
Obesity	329 (7.4%)	4155 (9.7%)	<0.001	306 (6.8%)	0.23
Protein calorie malnutrition	845 (19.0%)	7168 (16.7%)	<0.001	742 (16.4%)	<0.001
Fluid and electrolyte disorder	1803 (40.6%)	15432 (36.0%)	<0.001	1623 (35.8%)	<0.001
Blood loss anemia	215 (4.8%)	2131 (5.0%)	0.72	182 (4.0%)	0.057
Iron deficiency anemia	443 (10.0%)	4410 (10.3%)	0.53	373 (8.2%)	0.004
Psychoses	111 (2.5%)	321 (0.7%)	<0.001	60 (1.3%)	<0.001
Depression	833 (18.8%)	5996 (14.0%)	<0.001	712 (15.7%)	<0.001
Complicated hypertension	177 (4.0%)	1999 (4.7%)	0.041	172 (3.8%)	0.64

IBD, inflammatory bowel disease

was then reported as adjusted hazard ratios (aHR) with 95% confidence intervals (CI) and P-value. Analyses were performed using Statistical software for data science (STATA) version 16.0 software (StataCorp LLC, Station, TX, USA).

### Ethical consideration

NIS contains de-identified patient data. Therefore, it was deemed exempt from the institutional review board as in prior

studies using NIS [13]. In view of the public availability of this database, patient consent was also waived.

## Results

In the present study, before matching, there were 47,309 primary IBD hospitalizations (9.37% with abuse, 90.63% without abuse) that fulfilled the selection criteria. Using nearest-neighbor matching, we matched 4437 IBD hospitalizations with a secondary diagnosis of substance abuse (cases) to 4528 IBD hospitalizations without a secondary diagnosis of substance abuse (controls). After matching, the median age was higher in hospitalizations with abuse than those without abuse (44 vs. 38 years,  $P<0.001$ ). The median age was higher in the substance abuse group (44 years [IQR 32-59]) than no abuse (38 years [IQR 29-52]) ( $P<0.001$ ). The matched cohorts showed no statistical difference in relation to sex. There was a higher prevalence of the Black race in IBD hospitalizations with substance abuse than those without abuse. Hospitalizations with substance abuse had a higher prevalence of Elixhauser Comorbidity Index Score  $\geq 3$  (48.3% vs. 28.2%) compared to those without abuse ( $P<0.001$ ). Private insurance, followed by Medicaid and Medicare, was the primary payer for both cohorts (Table 1). Most hospitalizations with substance abuse belonged to the lowest median household income group. There was a higher prevalence of patients discharged to care facilities (2.9% vs. 2.2%) and against medical advice (4.9% vs. 1.8%) in the substance abuse group compared to the no abuse group ( $P<0.001$ ). There was a higher number of weekend admissions in IBD hospitalizations with substance abuse.

The median LOS did not show any significant difference between the cohorts (4 days each) ( $P=0.74$ ). Similarly, the median hospitalization charge did not reveal any significant difference between cohorts after matching, as shown in Table 1. Inpatient mortality was slightly higher in hospitalizations with substance abuse than in those without (0.3% vs. 0.2%,  $P<0.001$ ). After matching, there was no significant difference between cohorts in major comorbidities (Table 2). There was a higher prevalence of uncomplicated hypertension (22.7% vs. 19.5%,  $P<0.001$ ), neurological disorders (4.7% vs. 3.8%,  $P=0.033$ ), liver disease (10.1% vs. 8.2%,  $P=0.002$ ), coagulopathies (4.4% vs. 3.5%,  $P=0.021$ ), protein-calorie malnutrition (19% vs. 16.4%,  $P<0.001$ ), fluid and electrolyte disorders (40.6% vs. 35.8%,  $P<0.001$ ), iron deficiency anemia (10% vs. 8.2%,  $P=0.004$ ), psychoses (2.5% vs. 1.3%,  $P<0.001$ ), and depression (18.8% vs. 15.7%,  $P<0.001$ ) in IBD hospitalizations with substance abuse compared to those without abuse ( $P<0.05$ ) (Table 2). In the matched cohorts, there was no significant difference in all-cause 30-day inpatient mortality (aHR 0.74, 95%CI 0.32-1.81;  $P=0.54$ ).

## Discussion

We performed a retrospective study of IBD hospitalizations in the US over 4 years (2016-2019) to better understand the

relationship between substance abuse and IBD. We determined that median LOS and hospitalization charges did not differ for primary IBD hospitalizations based on substance abuse history. Males, and patients in age groups 35-49 years and 50-64 years, had a higher prevalence of substance abuse. There was no sex-based disparity in matched cohorts. There was a higher prevalence of the Black race in IBD hospitalizations with substance abuse than among those without abuse. Most hospitalizations with substance abuse belonged to the lowest median household income group. There was a higher prevalence of psychoses (2.5% vs. 1.3%) and depression (18.8% vs. 15.7%) in IBD hospitalizations with substance abuse compared to those without abuse ( $P<0.001$ ). Inpatient mortality was slightly higher in hospitalizations with abuse than without abuse (0.3% vs. 0.2%,  $P<0.001$ ); however, there was no significant difference in all-cause 30-day inpatient mortality ( $P=0.54$ ).

Substance use complicates the management of IBD, as comorbid substance use has been associated with higher hospitalization rates than chronic conditions alone [10]. When we examined patient characteristics, a higher prevalence of substance abuse was observed in males compared to females in the present study (61% vs. 39%). Men have more impulsivity and risk-taking behavior, which may explain their greater use of alcohol and drugs [10]. Patients with IBD are more likely to seek coping mechanisms like alcohol and other substances to respond to the disease burden and its effects on quality of life. No prior literature reveals disparity among races for IBD and substance abuse. We report a higher prevalence of the Black race with substance abuse for IBD hospitalizations. This could be secondary to differences in addiction treatment completion for Blacks, explained by differences in socioeconomic status and housing instability [14].

Prior studies report that substance use, particularly alcohol, can cause inflammation within the gastrointestinal tract, contributing to exacerbation of IBD. In the gastrointestinal tract, alcohol disrupts bacterial balance and homeostasis, resulting in bacterial overgrowth [15]. Bacterial overgrowth leads to an increase in endotoxin production, which compounds inflammation. Additionally, alcohol increases the effect of Kupffer cells in the liver, increasing the production of inflammatory markers such as interleukin-1, interleukin-6, and tumor necrosis factor- $\alpha$  [16]. Substance abuse also alters the permeability of the gut membrane, permitting the systemic spread of inflammation and thus promoting multiple organ involvement. These factors may increase IBD flare-ups and admissions and can explain the greater number of weekend admissions in our study, as more drinks are consumed on the weekends [17].

In the present matched analysis, there was no difference in LOS and hospitalization charge in IBD hospitalizations based on substance abuse. Studies have shown that IBD patients often self-medicate with substances for symptom management [10,18]. The slightly greater mortality could be secondary to the use of substances; however, further prospective data regarding the cause of death will be needed before any definitive conclusion can be drawn.

Substance abuse is a well-established factor that affects nutritional status, leading to deficiencies and malnutrition [19].

This is consistent with the present study, which reports a significantly higher prevalence of protein-calorie malnutrition, fluid and electrolyte disorders and iron deficiency anemia in IBD hospitalizations with substance abuse compared to those without abuse. These deficiencies can additionally be exacerbated as IBD is linked to poor appetite, resorption and chronic blood loss [20].

Our study reveals a greater prevalence of psychoses and depression in IBD hospitalizations with substance abuse, consistent with prior reports [21,22]. Patients who suffer from anxiety and depression often use alcohol and other drugs as a form of self-medication to alleviate their symptoms. The rate of depression in those with IBD is approximately 27% [23]. The complex relationship between the central nervous and enteric nervous systems, known as the brain-gut-microbiome signaling pathway, may explain the higher prevalence of depression and psychiatric conditions in IBD [24,25]. Literature has shown that inflammatory pathways triggered in IBD reduce the production of serotonin, resulting in higher rates of depression [24]. Management of IBD with comorbid psychiatric conditions is complex. Studies have noted increased disability, medication noncompliance and IBD disease activity in this population [26].

There are a few limitations to this study. As it was a database study, the data are limited to the variables available through the database. This limits the ability to evaluate other objective variables affecting inpatient mortality and length of stay. Given the use of ICD codes, confounding factors and misclassifications may arise that are not coded by ICD-10 and may not be added as comorbidities. Additionally, there is a potential for missing data in the NIS database. There is a lack of information regarding the cause of inpatient mortality. However, despite these limitations, the selection of data over a 4-year period resulted in a large number of admissions being included in the analysis. Additionally, this is one of the largest inpatient databases available in the US and can approximate up to 95% of the US population, allowing for generalizable results. In addition, various propensity matching, regression models and adjustments allowed a more accurate and detailed analysis.

In conclusion, the present study using matched cohorts revealed no difference in LOS and hospitalization charge between IBD hospitalizations with or without substance abuse. Per our analysis, despite the higher prevalence of inpatient mortality, there is no increased risk based on substance use. However, given the lack of information regarding the cause of death, further prospective data will be required before any definitive conclusion can be drawn. There was a high rate of weekend admissions in the substance abuse cohort, probably linked to weekend binge drinking and alteration of gut microbiota. There was also a greater prevalence of psychoses and depression in IBD hospitalizations with substance abuse. As comorbid psychiatric and substance abuse disorders complicate the management of IBD, clinicians should screen for these conditions. Based on the findings of this study, patients with IBD, especially men of the Black race, and those with depression or psychosis, should be screened for substance abuse to improve overall outcomes.

## Summary Box

### What is already known:

- Inflammatory bowel disease (IBD) is a chronic relapsing intestinal inflammation
- Substance abuse has proinflammatory and direct cytotoxic effects, which can damage the intestinal epithelium's physical and immunological barrier, contributing to IBD flares
- Substance abuse in IBD patients is considered a barrier to treatment adherence, remission, and self-care

### What the new findings are:

- There was no difference in the median length of stay, hospitalization charge, or mortality risk in IBD hospitalizations based on substance abuse
- There was a higher prevalence of males and the Black race in IBD hospitalizations with substance abuse than those without abuse
- There was a higher prevalence of hypertension, neurological disorders, protein-calorie malnutrition, electrolyte disorders, iron deficiency anemia, psychoses, and depression in IBD hospitalizations with substance abuse than in those without abuse

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## Supplementary material

**Supplementary Table 1** List of ICD-10 codes utilized in the present study

Irritable bowel disease	K5100, K51011, K51012, K51013, K51014, K51015, K51016, K51017, K51018, K51019, K5120, K51211, K51212, K51213, K51214, K51218, K51219, K5130, K51311, K51312, K51313, K51314, K51318, K51319, K5140, K51411, K51412, K51512, K51513, K51514, K51518, K51519, K5180, K51811, K51812, K51813, K51814, K51818, K51819, K5190, K51911, K51912, K51913, K51914, K51918, K51919, K50011, K50012, K50013, K50014, K50018, K50019, k5010, K50111, K50112, K50113, K50114, K50118, K50119, k5080, K50811, K50812, K50813, K50814, K50818, K50819, k5090, K50911, K50912, K50913, K50914, K50918, K50919, k5000
Substance abuse	F19939, F19950, F19951, F15920, F19921, F1997, F1996, F1994, F11182, F11282, F11982, F13182, F13282, F13982, F14182, F14282, F14982, F15182, F15282, F15982, F19182, F19282, F19982, F11159, F11181, F11188, F11222, F11259, F11281, F11288, F11922, F11959, F11981, F11988, F12122, F12159, F12180, F12188, F12222, F12259, F12280, F12288, F12922, F12959, F12980, F12988, F13159, F13180, F13181, F13188, F13259, F13280, F13281, F13288, F13959, F13980, F13981, F13988, F14122, F14159, F14180, F14181, F14188, F14222, F14259, F14280, F14281, F14288, F14922, F14959, F14980, F14981, F14988, F15122, F15159, F15180, F15181, F15188, F15222, F15259, F15280, F15288, F15922, F15959, F15980, F15981, F15988, F16122, F16159, F16180, F16183, F16188, F16259, F16280, F16283, F16288, F16959, F16980, F16983, F16988, F17208, F17218, F17228, F17298, F18159, F18180, F18188, F18259, F18280, F18288, F18959, F18988, F19122, F19159, F19180, F19181, F19188, F19222, F19259, F19280, F19281, F19288, F19922, F19959, F19980, F19981, F19988, F1120, F1121, F1320, F1321, F1420, F1421, F1220, F1221, F1520, F1521, F1620, F1620, F1620, F1621, F1920, F1921, F1210, F1290, F1211, F1211, F1610, F1611, F1310, F1311, F1110, F1111, F1410, F1411, F1510, F1511, F1910, F1911, F1810, F1811, F1911, F17200, Z720, Z715
Alcohol abuse	E52, F10, G62.1, I42.6, K29.2, K70.0, K70.3, K70.9, T51, Z50.2, Z71.4, Z72.1
Congestive heart failure	I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5–I42.9, I43, I50, P29.0
Cardiac arrhythmia	I44.1–I44.3, I45.6, I45.9, I47–I49, R00.0, R00.1, R00.8, T82.1, Z45.0, Z95.0
Valvular disease	A52.0, I05–I08, I09.1, I09.8, I34–I39, Q23.0–Q23.3, Z95.2–Z95.4
Pulmonary circulation disorders	I26, I27, I28.0, I28.8, I28.9
Peripheral vascular disorders	I70, I71, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9
Hypertension without complications	I10
Diabetes without complications	E10.0, E10.1, E10.9, E11.0, E11.1, E11.9, E12.0, E12.1, E12.9, E13.0, E13.1, E13.9, E14.0, E14.1, E14.9
Diabetes with complications	E10.2–E10.8, E11.2–E11.8, E12.2–E12.8, E13.2–E13.8, E14.2–E14.8
Hypothyroidism	E00–E03, E89.0
Liver disease	B18, I85, I86.4, I98.2, K70, K71.1, K71.3–K71.5, K71.7, K72–K74, K76.0, K76.2–K76.9, Z94.4
Peptic ulcer disease excluding bleeding	K25.7, K25.9, K26.7, K26.9, K27.7, K27.9, K28.7, K28.9
Metastatic cancer	C77–C80
Solid tumor without metastasis	C00–C26, C30–C34, C37–C41, C43, C45–C58, C60–C76, C97
Coagulopathy	D65–D68, D69.1, D69.3–D69.6
Obesity	E66
Protein calorie malnutrition	E40–E46, R63.4, R64
Fluid and electrolyte disorders	E22.2, E86, E87
Psychoses	F20, F22–F25, F28, F29, F30.2, F31.2, F31.5
Depression	F20.4, F31.3–F31.5, F32, F33, F34.1, F41.2, F43.2