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Substance Use Among Patients With Incident Crohn's Disease in the United States, 2010 to 2019: A Medicaid Observational Study

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Abstract

BACKGROUND AND AIMS: Substance use among persons with Crohn's disease (CD) is associated with symptomatic exacerbation and poorer quality of life. However, data on the prevalence of substance use among individuals with CD are limited. Therefore, our study aimed to estimate the burden of alcohol and drug use among individuals with incident CD in the United

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States. We also assessed the associations between CD-related interventions and substance use after CD diagnosis.

METHODS: Our retrospective cohort study of the national Medicaid databases from 2010 to 2019 identified participants with newly diagnosed CD and defined substance use (ie, alcohol, opioids, cocaine, amphetamine, and cannabis) using diagnosis codes. Multivariable logistic regression models assessed the associations between CD-related interventions and substance use after CD diagnosis.

RESULTS: Overall, 16.3% of Medicaid enrollees with incident CD had substance ever-use, most commonly alcohol or opioids (each 8.0%). Any substance use saw an absolute decrease of 3.8% after CD diagnosis, but changes were less than 1% in either direction for each substance. CD-related hospitalization was associated with increased alcohol or opioid use post-CD diagnosis. Surgery was associated with lower use post-CD of opioids but not alcohol. CD medications (except steroids) were generally associated with decreased post-CD alcohol or opioid use.

CONCLUSION: Among Medicaid enrollees with incident CD, alcohol and opioid use were more frequent than previously published estimates for the general US population (6% and 4%, respectively, in 2019). Consequently, medical communities must be more aware of substance use by patients with CD to provide quality patient-centered care.

Introduction

Crohn's disease (CD) is a chronic inflammatory disorder of the gastrointestinal tract that afflicts more than 500,000 individuals in the United States.[1] Morbid complications of CD include intestinal obstruction, malnutrition, and chronic pain. Additionally, 25% of patients with CD manifest depressive symptoms, which have well-established connections with substance use disorders.[2,3] Preliminary data have linked alcohol or opioid use to worse CD outcomes. First, prior literature has speculated on the causative role of alcohol consumption in CD symptom exacerbation,[4,5] one possible mechanism being ethanol and adjuvants (eg, sulfites) in alcohol beverages disrupting the gut mucosal barrier and increasing intestinal infections.[6,7] Studies on chronic opioid use in CD have also described positive correlations with CD severity, endoscopies, and emergency room visits.[8] Finally, alcohol or opioid use by CD patients has been associated with comorbid mental health diagnoses and poorer quality of life.[9,10]

Unfortunately, data specific to the burden of substance use among individuals with CD are relatively scarce. In 2018, Mantzouranis et al. published a comprehensive literature review on alcohol and opioid use in inflammatory bowel disease. The authors identified only 4 studies presenting usage frequencies: one on alcohol and 3 on opioids.[9] Small sample sizes limited these early studies. All but one study involved less than 100 participants; the fourth study reported more than 300 enrollees with inflammatory bowel disease but did not specify CD.

Given the literature gap, the present study aimed to define the burden of alcohol and drug misuse among persons with incident CD in the United States. Additionally, we sought to assess the associations between CD-related interventions and substance use after CD diagnosis.

Methods

We adhered to the Strengthening the Reporting of Observational Studies in Epidemiology statement to report our retrospective cohort study.

Study population

Our retrospective cohort study used administrative claims data from the national Medicaid databases. Medicaid is a federal program administered by states and territories to provide health coverage primarily for individuals with low income. Other populations who may qualify for Medicaid include children, pregnant women, the elderly, and people with disabilities. Eligibility criteria, including exact income requirements and other covered cohorts, differ by state because each state administers its own Medicaid program.[11]

We used the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes and the corresponding Tenth Revision, Clinical Modification (ICD-10-CM) codes to identify our study population with CD and to capture substance misuse (ie, alcohol, tobacco, opioids, cocaine, amphetamine, and cannabis) (Tables A1 and A2, complete programming codes at https://github.com/susanmhutfless/playground).[12-21] Study inclusion required individuals to be Medicaid recipients with 2 CD encounters (ie, bearing diagnosis codes 555.* [ICD-9-CM] or K50.* [ICD-10-CM]). Individuals with diagnosis codes for ulcerative colitis (556.* [ICD-9-CM], K51.* [ICD-10-CM]) were excluded. All study participants had 1 year of Medicaid eligibility before the first CD diagnosis, which isolated the population to newly diagnosed (ie, incident) patients. Participants also were Medicaid-eligible for 1 year following diagnosis, ensuring sufficient follow-up time to observe substance use encounters. We defined Medicaid eligibility at the month level: each month with 15 days of eligibility counted as a Medicaid-eligible month. If an individual was not Medicaid-eligible for 3 consecutive months, their person-time contribution to our study stopped at the last eligible month. We excluded individuals whose records were missing birthdates or gender. We also excluded all encounters with a missing encounter date. Our study period spanned 10 years, from January 2010 through December 2019.

Substances

We analyzed alcohol, opioids, cocaine, amphetamine, and cannabis misuse in our study population. Associations with CD and tobacco-related disease exacerbation are well established.[22,23] Thus, we described tobacco use as a covariable but did not include it as an outcome of interest in our study. Finally, we defined prevalent substance use as a substance use diagnosis that coincided with or preceded the first CD diagnosis.

Data analysis

The primary outcome of our analysis was the use prevalence of the 5 substances among persons with incident CD. Additionally, we analyzed associations between CD-related interventions (ie, hospitalization, surgery, or medications) and alcohol or opioid misuse after CD diagnosis. Medications of interest included steroids, antitumor necrosis factor (TNF) agents, immunomodulators, and aminosalicylic acid compounds. To assess the associations, we created multivariable logistic regression models that adjusted for covariables comprising prevalent substance use (alcohol, opioids, and tobacco), gender, race/ethnicity, and age (in decades) at CD diagnosis. An exploratory analysis of our data demonstrated minimal missingness in key variables. For instance, our study inclusion criteria required a birthdate and gender to be available; these 2 variables individually had less than 1% missing data. Finally, we calculated null E-values to conduct a sensitivity analysis on the robustness of our statistical findings. The null E-value quantifies on the risk ratio scale the strength of potential unmeasured or uncontrolled confounding needed to explain away an observed association between an exposure (eg, hospitalization for CD) and an outcome (eg, alcohol misuse after CD diagnosis).[24]

All statistical analyses were performed using SAS Enterprise 8.3 (SAS Institute, Cary, North Carolina). *P* values less than .05 were considered statistically significant. We calculated E-values using the online calculator at https://www.evalue-calculator.com/. The Johns Hopkins Institutional Review Board reviewed and approved our study (IRB00206614).

Results

We identified 37,323 Medicaid recipients with incident CD from 2010 through 2019. Overall, 6091 (16.3%) patient records noted ever-use of alcohol, opioids, cocaine, amphetamine, or cannabis. Alcohol and opioids were the 2 most common ever-used substances, each separately involving 8.0% of individuals with incident CD. Cannabis (4.3%) was the next most common. By contrast, study subjects reported lower ever-use of cocaine (2.3%) and amphetamine (1.3%).

Of participants ever using alcohol, 54.1% were women and 64.3% identified as non-Hispanic White. The median age at CD diagnosis was 45 years (range 10–93 years). Fistulizing complications occurred in 5.0% of individuals, including 2.7% with perianal fistulae. Hospitalization and surgery for CD occurred in 44.5% and 15.4% of the patients with alcohol ever-use, respectively. CD treatments received were total parenteral nutrition (TPN) in 7.7% of patients, steroids in 60%, immunomodulators in 4.9%, anti-TNF in 7.1%, and antibiotics in 59.3% (Table 1). Demographics and clinical characteristics were not substantially different when examining those with alcohol use pre-CD or post-CD diagnosis. One minor deviation was a slightly lower proportion of anti-TNF treatments (5.8%) among individuals with pre-CD alcohol use (Tables A3 and A4).

Among patients with opioid ever-use, 67.7% were women and 73.1% were non-Hispanic White. The median CD diagnosis age was 41 years (range 11–89 years). Fistulizing complications occurred in 4.8% of individuals, including 2.9% with intestinal fistulae. CD-related hospitalization and surgery affected 48.4% and 14.0% of patients with opioid

ever-use, respectively. CD treatments received were TPN in 8.9% of patients, steroids in 62.8%, anti-TNF in 6.8%, and antibiotics in 62.6% (Table 1). Demographics and clinical characteristics were not substantially different when examining those with pre-CD or post-CD opioid use. Similar to alcohol, one slight difference was less common anti-TNF treatments (4.8%) among individuals with pre-CD opioid use (Tables A3 and A4).

The substance never-use cohort was 64.1% women and 59.6% non-Hispanic White. The median CD diagnosis age was 41 years (range 10–103). Fistulae complicated the disease in 5.8% of individuals; 3.3% had perianal fistulae. CD-related hospitalization occurred in 32.4% of patients with substance never-use and 14.1% underwent CD-related surgery. CD treatments received were TPN in 7.4% of patients, steroids in 55.5%, anti-TNF in 15.5%, and antibiotics in 49.6% (Table 1).

In our cohort, the prevalence of any substance use decreased from 12.7% before CD diagnosis to 8.9% after CD diagnosis (Figure). However, substance-specific consumption was largely stable. Opioids (+0.9%) and alcohol (−0.4%) saw the 2 biggest absolute changes in use after the CD diagnosis.

After adjustments, CD-related hospitalization, but not surgery, was associated with alcohol misuse after CD diagnosis (adjusted odds ratio [aOR] 1.70; 95% confidence interval [CI] 1.53, 1.89) (Table 2). Steroid use was also associated with increased odds of post-CD alcohol misuse (aOR 1.19; 95% CI 1.07, 1.33). All other CD medications had lower odds of post-CD alcohol misuse.

CD-related hospitalization had higher odds of opioid misuse after CD diagnosis (aOR 1.86; 95% CI 1.69, 2.06) (Table 3). However, CD-specific surgery was associated with lower odds of post-CD opioid misuse (aOR 0.83; 95% CI 0.72, 0.96). Among medications, steroid treatment was associated with increased odds of post-CD opioid misuse (aOR 1.29; 95% CI 1.16, 1.43), whereas all other CD medications saw lower odds.

In the sensitivity analysis, we noted null E-values ranging from 1.16 to 2.64 for point estimates (1.00–2.30 for confidence limits closest to the null) of alcohol use after CD diagnosis (Table 2). In comparison, null E-values ranged from 1.70 to 3.12 for point estimates (1.25–2.77 for confidence limits closest to the null) of opioid use after CD diagnosis (Table 3).

Discussion

We used Medicaid claims databases from 2010 to 2019 to estimate the burden of alcohol and drug use among persons newly diagnosed with CD in the United States. Overall, substance use was considerable in our study cohort: 16.3% reported ever using at least one substance (not including tobacco). Alcohol and opioids were the most commonly consumed substances, more so than cannabis; amphetamines were the least common. Tobacco use was predictably less prevalent among those who had never used other substances.

Our substance use estimates in persons with incident CD (Table 1, Figure) were generally higher than data for the general US population. Per the 2019 National Survey on Drug Use

and Health (NSDUH), 5.8% of persons aged 12 years reported heavy alcohol use—defined as 5 + drinks for men or 4 + drinks for women during the same session on at least 5 of the past 30 days.[25] Heavy alcohol use was particularly prevalent (8.4%) among persons aged 18–25 years. In comparison, 8.0% of Medicaid participants aged 10 years with incident CD ever noted alcohol misuse; the prevalence climbed to 15.1% for the 21–30 age subcohort. In addition, the 2019 NSDUH reported that 3.7% of the surveyed US population aged 12 years stated opioid misuse in the previous year. This was down from 4.4% in 2016, the year of the initial Surgeon General's report on the opioid epidemic in the United States.[26] In comparison, 8.0% of our study cohort ever had opioid misuse. However, the different data collection methods between NSDUH (ie, self-report surveys) and Medicaid data (ie, clinician-documented billing codes) may account for part of the findings.

In contrast to other substances, the estimated cannabis use in our Medicaid study cohort was notably less than described for the general US population. In the 2019 NSDUH, 17.5% of respondents aged 12 years reported cannabis use in the previous year. But among Medicaid enrollees with incident CD, the prevalence of cannabis ever-use was only 4.3%. As mentioned previously, methodological differences between NSDUH and Medicaid data may partly contribute to the divergent estimates. Another possible source of the discordance may be under-documentation by clinicians who have acknowledged cannabis use as acceptable behavior. The first state to decriminalize the possession of cannabis was Oregon in 1973, and California was the first to legalize medical cannabis in 1996.[27,28] Recreational cannabis legalization did not emerge at the state level until Colorado's constitutional amendment in 2012.[29] Moreover, clinicians have increasingly perceived cannabis as a possible, albeit still unproven, palliative treatment for CD.[30,31] The joint effect of cannabis legalization and clinician acceptance may have contributed to a lower estimate of cannabis use among Medicaid enrollees with incident CD compared to NSDUH's general US population.

Because low income is a predominant criterion for a person's Medicaid eligibility,[11] economic factors may have also impacted the substance use observations in our study cohort. However, persons who use drugs are not a monolithic group. Prior literature demonstrates complex associations between socioeconomic status (SES) and substance use that can vary depending on age, gender, the substance of choice, and other factors. For instance, higher SES appears to be associated with increased alcohol and cannabis use, particularly among young adults.[32] In contrast, lower SES has been associated with more opioid use and related adverse events (eg, fatal overdoses),[33,34] and women of low SES may have higher opioid utilization than men.[35]

Curiously, the absolute change in any substance use in our study cohort after the CD diagnosis was −3.8%, but changes were more limited (less than 1% in either direction) for individual substances (Figure). This phenomenon may suggest that less individuals engaged in any alcohol or drug use after the CD diagnosis but polysubstance use became more common. The subgroup of patients with polysubstance use may share certain features (eg, extra-intestinal CD)[36] but future patient-level analyses are needed to test this theory.

In our cohort, CD-related interventions had varying associations with post-CD alcohol and opioid use. For example, surgery for CD was not associated with alcohol use. But it was counterintuitively associated with lower odds of post-CD opioid misuse, presumably due to the surgical improvement—on average—of painful CD complications like intestinal structures.[37] In contrast, CD-related hospitalization was associated with increased alcohol or opioid consumption post-CD diagnosis. Chronic illnesses like CD are well described to cause anxiety and depression, with chronic pain being a frequent mediator.[2,38] Concomitantly, 5%–60% of hospitalized patients experience depressive symptoms.[39] Depression, in turn, often co-occurs with substance use as both cause and effect in a potentially unrelenting cycle.[3,40] Finally, except for steroids, medications treating CD were mostly associated with decreased post-CD alcohol or opioid misuse, possibly by reducing CD severity. In addition, alcohol use is contraindicated in the setting of certain CD medications (eg, methotrexate), which also may have contributed to our observations. Steroid treatment notably had opposite associations with post-CD alcohol or opioid misuse. While steroids may initially play a role in CD management, their chronic use is associated with many long-term morbid outcomes (eg, hip fracture) and reduced quality of life,[41,42] which may ultimately motivate substance use.

We acknowledge several limitations in our study. First, commonly applied case definitions for identifying CD have not yet been validated in Medicaid administrative claims data. In response, we chose a more complex case definition requiring 2 CD encounters to enhance positive predictive value and specificity.[43] Second, to ensure incident diagnoses of CD and adequate follow-up time, we mandated all study participants have 1 year of Medicaid enrollment before and after their first CD diagnosis. However, our study sample's representation of the larger US population may be compromised by the possibility that not every CD patient experiences continuous Medicaid coverage. Third, Medicaid claims data lack some granular covariables (eg, adverse childhood experiences, job loss) that may inform substance use studies.[44,45] Our sensitivity analysis noted null E-values that were larger than many, but not all, previously published associations between these unmeasured covariables and substance use.[44,46,47] Thus, while our study findings appeared fairly robust, unmeasured confounding was theoretically possible and—if sufficiently large —could account for the observed associations in our regression models. Finally, relative to self-reporting, administrative claims data may underestimate the prevalence of substance use or other chronic health conditions,[48,49] although conflicting literature exists.[50] Moreover, any discordance between administrative data and self-reporting may not be entirely random. Certain subcohorts (eg, older and more highly educated) have shown a lower likelihood of self-reporting mental health or substance use concerns.[51]

Conclusion

Among US Medicaid enrollees with newly diagnosed CD, substance use—headed by alcohol and opioids—was more frequent than published estimates for the general US population. Although hospitalization was associated with increases in post-CD substance use, medical therapies (excluding steroids) may limit substance use, presumably by controlling CD severity. Unfortunately, alcohol and opioid consumption among CD patients correlates with increased CD severity, comorbid mental health diagnoses, and poorer quality

of life.[9,10] Thus, to provide high-quality patient-centered care, medical and public health communities must heighten our shared awareness of substance use by patients with CD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments:

Abbreviations used in this paper:

aOR	adjusted odds ratio
CD	Crohn's disease
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
NSDUH	National Survey on Drug Use and Health
SES	socioeconomic status
TNF	tumor necrosis factor
TPN	total parenteral nutrition

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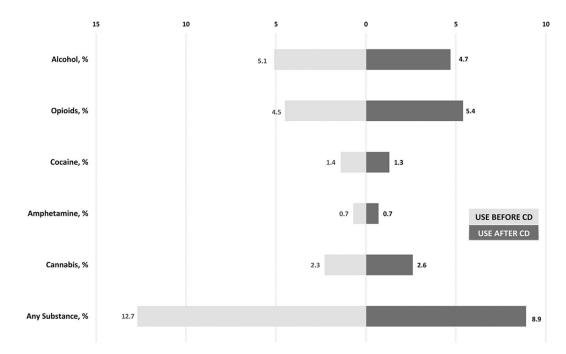
Figure.

Proportion of Medicaid participants with incident Crohn's disease (CD) who used substance before or after CD diagnosis, from 2010 through 2019 (N = 37,323).

Table 1.

Demographics and Clinical Characteristics of Medicaid Study Participants With Incident Crohn's Disease From 2010 Through 2019, Stratified by Substance Use Status (N = 37,323)

Characteristic	Substance never-use	Alcohol ever-use	Opioids ever-use	Cannabis ever-use	Cocaine ever-use	Amphetamine ever-use
	N = 31,232	N = 3001	N = 2979	N = 1607	N = 849	N = 473
Women, %	64.1	54.1	67.7	56.0	59.8	60.0
Race/Ethnicity, %						
White, non–Hispanic	59.6	64.3	73.1	61.9	54.3	75.3
Black, non–Hispanic	14.9	18.9	13.2	22.6	29.1	6.1
Other	25.6	16.8	13.7	15.5	16.6	18.6
Age at CD diagnosis, %						
10–20 y	17.5	4.2	3.4	12.0	2.1	4.0
21–30 y	14.3	15.1	18.3	28.5	16.8	19.9
31–40 y	16.7	20.9	26.4	27.1	23.2	32.8
41–50 y	16.3	25.6	25.0	18.1	29.6	23.9
51–60 y	16.8	24.7	20.2	12.6	24.4	15.4
61–70 y	10.3	7.8	5.4	1.6	3.7	3.8
71–105 y	8.0	1.8	1.3	< 1	< 2	< 3
Age at CD diagnosis, median (min, max), y	41 (10,103)	45 (10, 93)	41 (11, 89)	33 (11, 72)	43 (14, 76)	38 (14, 76)
First CD encounter, %						
Office	32.5	22.2	23.4	21.7	19.2	20.5
Inpatient hospital	22.8	35.2	33.5	32.3	40.2	37.2
Outpatient hospital	18.9	19.7	20.7	23.3	20.5	18.8
Emergency room	5.8	10.1	10.3	11.6	10.8	8.2
Unknown	20.0	12.9	12.1	11.2	9.3	15.2
Tobacco ever, %	19.4	64.0	66.6	72.2	78.9	70.2
Fistula, %						
Any	5.8	5.0	4.8	6.9	6.4	4.0
Intestinal	2.7	2.4	2.9	3.5	3.4	2.1
Perianal	3.3	2.7	2.1	3.8	3.1	2.7
Rectovaginal	0.6	0.6	0.6	0.8	0.7	0.4

Characteristic	Substance never-use	Alcohol ever-use	Opioids ever-use	Cannabis ever-use	Cocaine ever-use	Amphetamine ever-use
	N = 31,232	N = 3001	N = 2979	N = 1607	N = 849	N = 473
Hospitalization for CD, %	32.4	44.5	48.4	48.0	49.4	48.0
Surgery for CD, %	14.1	15.4	14.0	15.9	16.6	16.9
Total parenteral nutrition, %	7.4	7.7	8.9	6.7	8.5	8.9
Steroids, %	55.5	60.0	62.8	62.9	64.0	60.5
Anti-TNF, %	15.5	7.1	6.8	10.5	6.2	5.9
Immunomodulators, %						
Any	12.2	4.9	4.8	8.7	3.8	7.4
Methotrexate	4.2	1.4	1.6	2.2	0.7	2.7
Azathioprine	4.9	2.3	2.1	4.5	1.6	3.0
6-Mercaptopurine	4.2	1.4	1.4	2.6	1.4	2.3
Aminosalicylic acid, %	20.2	13.4	13.4	17.4	13.0	13.3
Antibiotics, %	49.6	59.3	62.6	65.1	67.4	65.5
Follow-up time before CD, median (min, max), y	2.2 (1.0, 9.0)	2.2 (1.0, 9.0)	2.2 (1.0, 8.9)	2.2 (1.0, 9.0)	2.3 (1.0, 9.0)	2.3 (1.0, 8.9)
Follow-up time after CD, median (min, max), y	2.7 (1.0, 9.0)	2.8 (1.0, 9.0)	3.0 (1.0, 9.0)	2.9 (1.0, 9.0)	2.9 (1.0, 9.0)	3.1 (1.0, 9.0)

CD, Crohn's disease; TNF, tumor necrosis factor.

Table 2.

Adjusted Odds Ratios (aOR) and 95% Confidence Intervals (CI) for Associations Between Crohn's Disease (CD)–Related Interventions and Alcohol Use After CD Diagnosis Among Medicaid Participants With Incident CD From 2010 Through 2019 (N = 37,323)

Characteristic	Alcohol use after CD		
	aOR[a]	95% CI	Null E-value for aOR (for CI)
Hospitalized for CD	1.63	1.47, 1.81	2.64 (2.30)
Surgery for CD	0.98	0.84, 1.13	1.16 (1.00)
Steroids	1.04	1.02, 1.28	1.24 (1.16)
Anti-TNF	0.64	0.52, 0.79	2.50 (1.85)
Immunomodulator	0.67	0.52, 0.85	2.35 (1.63)
Aminosalicylic acid	0.67	0.57, 0.78	2.35 (1.88)

CD, Crohn's disease; TNF, tumor necrosis factor.

[a]Multivariable logistic regression model adjusted for prevalent substance use (alcohol, opioids, and tobacco), gender, race/ethnicity, age at CD, diagnosis, CD-related hospitalization, surgery for CD, and CD medications.

Table 3.

Adjusted Odds Ratios (aOR) and 95% Confidence Intervals (CI) for Associations Between Crohn's Disease (CD)–Related Interventions and Opioid Use After Crohn's Disease (CD) Diagnosis Among Medicaid Participants With Incident CD From 2010 Through 2019 (N = 37,323)

| Characteristic | Opioid use after CD | | |
	aOR[a]	95% CI	Null E-value for aOR (for CI)
Hospitalized for CD	1.86	1.69, 2.06	3.12 (2.77)
Surgery for CD	0.83	0.72, 0.96	1.70 (1.25)
Steroids	1.29	1.16, 1.43	1.90 (1.59)
Anti-TNF	0.68	0.56, 0.82	2.30 (1.74)
Immunomodulator	0.65	0.52, 0.81	2.45 (1.77)
Aminosalicylic acid	0.79	0.68, 0.90	1.85 (1.46)

CD, Crohn's disease; TNF, tumor necrosis factor.

[a]Multivariable logistic regression model adjusted for prevalent substance use (alcohol, opioids, and tobacco), gender, race/ethnicity, age at CD, diagnosis, CD-related hospitalization, surgery for CD, and CD medications.