

High Burden of Obesity and Low Rates of Weight Loss Pharmacotherapy in Inflammatory Bowel Disease: 10-Year Trend

Abbinaya Elangovan, MD,^{*,§, ID} Raj Shah, MD,^{†, §} Sajjadh M.J. Ali, MD,[‡] Jeffry Katz, MD,[†] and Gregory S. Cooper, MD^{†, ID}

^{*}Department of Internal Medicine-Pediatrics, Case Western Reserve University/MetroHealth Medical Center, Cleveland, Ohio, USA

[†]Division of Gastroenterology and Hepatology, Case Western Reserve University/University Hospitals Cleveland Medical Center, Cleveland, Ohio, USA

[‡]Department of Internal Medicine, Saint Vincent Hospital, Worcester, Massachusetts, USA

[§]Co-first authors.

Address correspondence to: Gregory S. Cooper, MD, Division of Gastroenterology and Hepatology, Case Western Reserve University/University Hospitals Cleveland Medical Center, 11100 Euclid Avenue, Wearn 244, Cleveland, OH 44106-5066, USA (gregory.cooper@uhhospitals.org).

Background: The prevalence of obesity and inflammatory bowel disease (IBD) has increased in the last decade. There is a paucity of data on the recent trend of obesity and the utilization of anti-obesity pharmacotherapy in IBD. We aimed to use a population-level database to analyze their trends.

Methods: A retrospective analysis of population-level data from 2010 to 2019 was performed among individuals ≥ 18 years of age using a commercial database, IBM Explorys. The prevalence and trends of obesity, diabetes mellitus type 2 (DM2), essential hypertension, dyslipidemia and/or hyperlipidemia, sleep apnea, and anti-obesity pharmacotherapy were studied. Univariate analysis using chi-square test and trend analysis using the Cochran Armitage test were performed.

Results: Among 39 717 520 adults, 37.3% of IBD patients have a diagnosis of obesity (Crohn's disease 36.9% vs ulcerative colitis 38.5%, $P < .0001$). The proportion of IBD adults with obesity and metabolic comorbidities increased from 2010 to 2019: obesity (19.7%–30.1%), DM2 (8.3%–12.5%), hypertension (25.1%–33.9%), hyperlipidemia (22.1%–32.2%), and sleep apnea (4.1%–10.8%). All comparisons were statistically significant ($P < .0001$). Only 2.8% of eligible adults with obesity were prescribed anti-obesity pharmacotherapy in the last 10 years, with trends increasing from 1.4% to 3.6%, 2010–2019.

Conclusions: With obesity being a harbinger for metabolic syndrome, the increase in obesity in IBD patients was accompanied by a concomitant increase in the diseases associated with obesity in the past decade. However, this alarming rise in obesity was accompanied by a disproportionately small increase in anti-obesity pharmacotherapy similar to general population.

Lay Summary

With the prevalence of obesity, metabolic comorbidities, and inflammatory bowel disease (IBD) in the last decade, this study utilized a dataset to analyze trends. While 1 in 3 adults with IBD were obese, only 3.6 per 100 eligible adults were prescribed anti-obesity pharmacotherapy.

Key Words: inflammatory bowel disease, obesity, metabolic syndrome, epidemiology

Introduction

Inflammatory bowel disease (IBD) affects 1.3% of the US population.¹ Between 15% and 40% of adults with IBD also live with obesity.² IBD and obesity result in derangements in adipokine secretion.³ An increase in the release of resistin, adiponectin, TNF- α , and IL-1 β was observed in both Crohn's disease (CD) and ulcerative colitis (UC), and an increase in the release of IL-8 and leptin was observed in CD and UC, respectively.³ The relationship between IBD and obesity is further demonstrated in epidemiological studies. For every 1 unit rise in body mass index (BMI) z-score between 7 and 13 years of age, the risk of CD is increased 1.2 times.⁴ Obese BMI at 18 years of age increases the risk of CD 2.3-fold in women compared with those with normal BMI.⁵ In contrast

to obesity and CD, evidence on the causal relationship between UC and obesity is limited.

Obesity could be a cause, a consequence, and/or a coexistence in IBD but the impacts of obesity in IBD need careful consideration. For every 1 kg m⁻² increase in BMI, there is a 4% increase in the risk of treatment failure with biologics and an 8% increase in the risk of surgery/hospitalization among individuals with UC.⁶ Patients with obesity have a higher number of hospitalizations due to preventable causes and cardiopulmonary complications, have a longer length of stay annually and higher hospitalization-related costs compared with patients without obesity.^{7,8} Intraoperative time, blood loss, and conversion rates to open surgery are higher in those with IBD and obesity compared with nonobese.⁹

Received for publication: August 1, 2022. Editorial Decision: January 24, 2023

© The Author(s) 2023. Published by Oxford University Press on behalf of Crohn's & Colitis Foundation.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

As the prevalence of obesity has exponentially increased in the past decade among US adults, the trends of obesity among IBD may have also increased during this time, however the exact trend of obesity and pharmacological management of obesity in IBD is not well established. In addition to the ill effects of obesity in IBD, the metabolic comorbidities add to the burden of the disease and their trends need careful exploration. We aimed to analyze the trends of obesity among individuals with IBD over a 10-year period.

Methods

Database

We performed a retrospective trend analysis of individuals ≥ 18 years old from 2010 to 2019, using a commercial database (Explorys, IBM Watson Health). Explorys is a deidentified cloud-based platform which gathers clinical information from inpatient and outpatient encounters of 64 million unique patients across 26 leading healthcare networks.¹⁰ Various types of clinical data including demographics, history, symptoms, diagnoses, procedures, and medications are extracted from each participating institution's electronic health record. The data then enter Explorys data grid where they are standardized and normalized. The database uses Systematized Nomenclature of Medicine—Clinical Terms (SNOMED CT) to list International Classification of Diseases (ICD-9 and ICD-10) diagnoses retrieved from the institutions.^{11,12} Explorys is a Health Insurance Portability and Accountability Act (HIPAA) compliant platform, and hence approval from institutional review board is not required.

Study Population

The study population included individuals, ≥ 18 years of age, who were active in the Explorys database in the last 10 years (2010–2019). This information was obtained by identifying individuals who had at least 1 hospital encounter (inpatient, outpatient, surgery, procedure, emergency, or urgent care visit) during the study period. “Crohn's disease” (CD), “ulcerative colitis” (UC), “diabetes mellitus type 2” (DM2), “essential hypertension”, “dyslipidemia and/or hyperlipidemia”, and “sleep apnea” were defined using SNOMED CT diagnosis codes as outlined in [Supplementary Table S1](#). Individuals were considered to have obesity if they had at least 1 BMI in the obese category ($\text{BMI} \geq 30 \text{ kg m}^{-2}$) in the corresponding period (eg, an individual is considered to have obesity in 2019 if he or she had at least 1 BMI in the obese category in 2019).

For the analysis of anti-obesity pharmacotherapy among IBD individuals with obesity, we determined individuals eligible for the treatment. We defined eligibility as individuals with IBD who also have obesity and do not have contraindications to anti-obesity pharmacotherapy^{10,13} listed in [Supplementary Table S2](#). Among the eligible adults, we studied the proportion of adults with obesity who were prescribed anti-obesity pharmacotherapy at least 30 days after the diagnosis of CD and UC. Among the individuals with IBD and obesity who were prescribed obesity pharmacotherapy, we also assessed the use of biologics (prescription of any one of the following: infliximab, adalimumab, certolizumab, vedolizumab, ustekinumab, and tofacitinib) in the year 2019. The anti-obesity medications studied include drugs approved for short-term use (< 12 weeks)—phentermine, phendimetrazine, benzphetamine, and diethylpropion,

and those approved for long-term use (≥ 12 weeks)—orlistat, liraglutide, phentermine/topiramate, lorcaserin, and naltrexone/bupropion ([Supplementary Table S3](#)).^{10,13} Lorcaserin was withdrawn by FDA in February 2020 due to potential risk of cancer.¹⁴ However as our prespecified time period was inclusive of the period when lorcaserin was used clinically, this medication was still used in our analysis.

Statistical Analysis

The primary aim of the study is to analyze the yearly trends of obesity and metabolic comorbidities in the last 10 years. The secondary aim is to study the yearly trends of anti-obesity pharmacotherapy in the last 10 years. Categorical data were analyzed using the chi-square test. Period prevalence of IBD per 100 000 population was calculated by dividing the number of individuals with IBD who had at least 1 hospital encounter in a given year by the total number of patients who had at least one of the encounters in that specific period. The demographic variables of IBD patients with obesity were compared with those without obesity using univariate chi-square test to obtain unadjusted odds ratio. Age was categorized into < 50 and ≥ 50 years as IBD exhibits a bimodal age distribution with peak incidence at 25–34 and 55–64 years.¹⁵ Similar univariate comparisons were performed for those with metabolic comorbidities—DM2, hypertension, hyperlipidemia, and sleep apnea individually. Further, the demographic variables of IBD patients with obesity who were prescribed anti-obesity medications were compared with those who were not prescribed anti-obesity medications. The trends of metabolic comorbidities and anti-obesity pharmacotherapy among IBD patients were performed using the Cochrane Armitage test for the study period of 2010–2019 and mean annual percentage change (APC) was calculated. $P < .05$ was considered statistically significant. Microsoft Excel 2016 and Addinsoft XLSTAT 2019.1 were used for statistical analysis.

Results

Among 39 717 520 adults active in the database in the last 10 years, the prevalence of CD and UC over a 10-year period was 443 and 361 per 100 000 population, respectively. 176 110 (0.44%) CD and 143 460 (0.36%) UC patients had at least 1 hospital encounter in the last 10 years. The prevalence of obesity in IBD was 37 300 per 100 000 population, $\text{UC} > \text{CD}$ (CD 36.9% vs UC 38.5%, $P < .0001$). The demographic characteristics of IBD individuals with and without obesity are presented in [Table 1](#). There was a higher proportion of adults ≥ 50 years of age (42%), women (62%), Non-Hispanics (85%), Caucasians (85%), and public insurance payors (42%) in the IBD population with obesity compared with those without obesity ([Table 1](#)). Among adults with IBD, obesity was more likely in adults ≥ 50 years, women, African Americans, and Medicaid payors ([Table 2](#)); DM2 and hypertension were more likely in those who were ≥ 50 years of age, men and African Americans; hyperlipidemia and sleep apnea were more common in adults ≥ 50 years, men and Caucasians ([Table 3](#)).

Percentage of Metabolic Comorbidities in Adults With IBD

The percentage of DM2, hypertension, hyperlipidemia, and sleep apnea among IBD patients was 14.3%, 37.2%,

Table 1. Demographic comparison of IBD population with and without obesity.

Variables		Adults with IBD (N = 286 760)	Adults with IBD and obesity (N = 107 070, 37%)	Adults with IBD without obesity (N = 179 690)	OR (CI)
Age	<50 years	121 770	41 740 (34%)	87 190 (49%)	0.68 (0.67–0.68)
	≥50 years	164 990	65 330 (61%)	92 500 (52%)	1
Gender	Male	118 660	40 310 (38%)	79 610 (45%)	1
	Female	168 100	66 760 (62%)	100 100 (57%)	1.32 (1.30–1.34)
Ethnicity	Non-Hispanic	225 130	90 760 (85%)	132 580 (75%)	1
	Hispanic	16 600	7950 (7%)	8640 (5%)	1.34 (1.30–1.39)
Race	Caucasian	229 800	90 520 (85%)	137 520 (78%)	1
	African American	23 360	10 500 (10%)	12 860 (7%)	1.24 (1.21–1.27)
Insurance	Medicare	69 430	29 560 (28%)	35 930 (20%)	1
	Medicaid	33 260	14 820 (14%)	16 980 (10%)	1.06 (1.03–1.09)
	Commercial	155 160	56 090 (52%)	107 380 (61%)	0.63 (0.62–0.65)
	Self-pay	28 910	6600 (6%)	10 600 (6%)	0.76 (0.73–0.78)

Abbreviations: IBD, inflammatory bowel disease; OR, odds ratio.
P < .001 in all comparisons.

34.2%, and 11.8%, respectively. All metabolic comorbidities analyzed in the study were higher in UC compared with CD—DM2: CD 13.3% vs UC 14.8%; hypertension: CD 35.0% vs UC 37.5%; hyperlipidemia: CD 31.1% vs UC 36.7%; sleep apnea: CD 12.1% vs UC 11.2% (*P* < .0001 for all comparisons).

Utilization of Anti-obesity Pharmacotherapy in IBD

Among 107 070 adults with IBD and obesity included in the study, 78 200 were eligible for anti-obesity pharmacotherapy. Among the eligible adults, 2170 (2.8%) adults with obesity were prescribed weight loss pharmacotherapy in the last 10 years. 76.5% were prescribed drugs approved for short-term use and 35.5% were prescribed drugs approved for long-term use. Phentermine was the most prescribed medication (74.2% of total, 97% of short-term drugs) followed by naltrexone-bupropion (15.2%), phentermine-topiramate (11.1%), lorcaserin (10.6%), liraglutide (3.2%), diethyl propion (2.8%), orlistat (1.8%), phendimetrazine (1.4%), and benzphetamine (0.5%). Adults <50 years, women, African Americans, those with Medicaid, commercial insurance and self-pay were more likely to be prescribed anti-obesity pharmacotherapy (Table 3). In the year 2019, 26% of CD patients and 17% of UC patients were prescribed obesity pharmacotherapy as well as one of the biologics.

Trend Analysis

The rates of obesity among IBD patients increased from 19.7% in 2010 to 30.1% in 2019, (CD: 18.4%–29.7%; UC: 19.8%–30.9%, *P* < .0001) (Figure 1). The mean APC of obesity among individuals with IBD was +5.7%. A significant increase in metabolic comorbidities was seen in IBD patients from 2010 to 2019, DM2 (8.3%–12.5%, *P* < .0001, mean APC +4.8%), hypertension (25.1%–33.9%, *P* < .0001, mean APC +3.4%), hyperlipidemia (22.1%–32.2%, *P* < .0001, mean APC +4.3%), and sleep apnea (4.1%–10.8%, *P* < .0001, mean APC +11.7%). All comparisons were statistically significant. (*P* < .0001).

The trend of anti-obesity pharmacotherapy decreased between 2010 and 2012 by 24%. But overall, the rates

increased from 1.4% in 2010 to 3.6% in 2019 (Figure 2). Among short-term drugs, the trend analysis was limited to phentermine, as it constituted 97% of the prescription for short-term drugs. Phentermine rates increased from 1.0% to 2.5%, 2012–2019 with a mean APC of +15%. The trend of long-term medications increased from 0.2% in 2013 to 1.5% in 2019 with a 4 times higher mean APC of +60%.

Discussion

In a large population-level database, this study showed that obesity and metabolic comorbidities have increased at an alarming rate among the IBD population in the past decade. Consistent with many other studies, our study continues to affirm that obesity and metabolic comorbidities are higher in UC compared with CD.^{16–18} Our study also reports an extremely low rate of anti-obesity pharmacotherapy in this population.

Obesity

The prevalence of obesity in IBD has been described in US-based as well as international studies. The rate of obesity in our study (30.1%) in 2019 is slightly lower than earlier single center studies 2000–2012 (31.5%–32.7%)^{16,17} probably related to the more recent timeline and a study population inclusive of inpatients as well as outpatients, unlike Sztembis et al¹⁸ which exclusively analyzed hospitalized IBD adults. Most importantly, the overall prevalence of obesity in the general population has also increased in this time period from 33.7% in 2007–2008 to 39.6% in 2015–2016.¹⁹ Even though central obesity is reported to occur in both CD and UC,²⁰ obesity rates are higher in UC than CD (36.9% vs 38.5% *P* < .0001) consistent with published studies (CD 27–30.3 % vs UC 32–35.2%).^{16,17} This is likely due to multiple factors such as fat malabsorption, decreased calorie intake and higher lipid oxidation rate leading to an overall lower fat mass in Crohn's patients. The effect was accentuated in CD with ileal involvement.²¹

The demographic differences between IBD adults with obesity and those without obesity are useful in the identification

Table 2. Demographic comparison of IBD population with and without metabolic comorbidities.

Variables	Adults with IBD and DM2 (N = 40 570)			Adults with IBD and HTN (N = 106 660)			Adults with IBD and HLD (N = 179 690)			Adults with IBD and sleep apnea (N = 33 760)		
	N (%)	OR (CI)		N (%)	OR (CI)		N (%)	OR (CI)		N (%)	OR (CI)	
Age												
<50 years	5080 (13%)	0.16 (0.15–0.16)		14 950 (14%)	0.11 (0.11–0.11)		13 170 (13%)	0.11 (0.11–0.12)		6920 (7%)	0.31 (0.30–0.32)	
≥50 years	35 490 (87%)	1		91 710 (86%)	1		84 920 (87%)	1		26 840 (27%)	1	
Gender												
Male	17 490 (33%)	1		45 240 (42%)	1		41 620 (42%)	1		16 080 (16%)	1	
Female	23 080 (57%)	0.92 (0.90–0.94)		61 420 (58%)	0.93 (0.92–0.95)		56 470 (58%)	0.94 (0.92–0.95)		17 680 (18%)	0.75 (0.73–0.77)	
Ethnicity												
Non-Hispanic	33 230 (82%)	1		89 410 (84%)	1		82 660 (84%)	1		28 460 (19%)	1	
Hispanic	2720 (7%)	1.13 (1.08–1.18)		4700 (4%)	0.60 (0.58–0.62)		5550 (6%)	0.87 (0.84–0.90)		2570 (3%)	1.27 (1.21–1.32)	
Race												
Caucasian	32 860 (14%)	1		88 710 (83%)	1		83 650 (85%)	1		28 540 (29%)	1	
African American	4700 (20%)	1.50 (1.46–1.56)		10 760 (10%)	1.36 (1.32–1.40)		7360 (8%)	0.80 (0.78–0.83)		2780 (3%)	0.96 (0.92–0.99)*	
Insurance												
Medicare	19 460 (48%)	1		46 840 (44%)	1		42 850 (44%)	1		13 370 (14%)	1	
Medicaid	5100 (13%)	0.47 (0.45–0.48)		11 050 (10%)	0.24 (0.23–0.25)		9620 (10%)	0.25 (0.25–0.26)		4520 (5%)	0.66 (0.54–0.68)	
Commercial	11 860 (29%)	0.21 (0.21–0.22)		38 330 (36%)	0.16 (0.15–0.16)		36 160 (37%)	0.19 (0.18–0.19)		12 080 (12%)	0.35 (0.34–0.36)	
Self-pay	4150 (10%)	0.43 (0.41–0.45)		10 440 (10%)	0.27 (0.26–0.28)		9460 (10%)	0.30 (0.29–0.31)		3790 (4%)	0.63 (0.61–0.66)	

Abbreviations: DM2, diabetes mellitus type 2; HLD, hyperlipidemia; HTN, hypertension; IBD, inflammatory bowel disease; OR, odds ratio.
 $P < .001$ except * where $P = .03$.

of high-risk cohorts. Among adults with IBD, women were more likely to have obesity compared with men correlating with the literature.¹⁷ Hispanics and African Americans were more likely to have obesity than Caucasians similar to the racial/ethnic disparities in the general population.²² Public insurance payors were more likely to live with obesity than commercial insurance payors in concordance to previous reports among the general population.²³ Identifying these high-risk groups will help us target anti-obesity interventions and help prevent adverse outcomes related to obesity among IBD patients.

Metabolic Comorbidities

There are considerable metabolic derangements reported in IBD. Although obesity rates are typically higher in UC than CD,^{16,17} metabolic abnormalities have not always followed a similar pattern.^{20,24,25} In a prospective study based on an IBD registry, DM2 rates were higher in the CD population (44% UC vs 56% CD, $P = .0059$) and the inflammatory markers were higher in IBD patients with DM compared with those without DM2.²⁴ In another retrospective nationwide cohort study, CD but not UC had elevated risk of DM compared with the non-IBD population after adjusting for steroid use and serum glucose levels.²⁵ In contrast to the literature, DM2 rates were higher in UC than CD in our study even among patients with obesity probably due to the relatively higher number of older adults in UC. Similarly, UC patients in our study had higher rates of hyperlipidemia in contrast to the literature.²⁰ But it is important to note that those studies also varied in obesity status and disease activity among IBD patients. While there is limited literature exclusively studying the relationship between obesity and hypertension, the duration of IBD inversely correlates with arterial elasticity.²⁶ Stiffness of arteries leads to essential hypertension with time.²⁷ Our study found a high percentage of hypertension (37%) among IBD patients with higher rates in UC than CD. In contrast to the above metabolic diseases, sleep apnea was slightly more commonly reported in CD in this study. Here, the rate of sleep apnea in IBD (11.4%) is similar to prior studies.²⁸

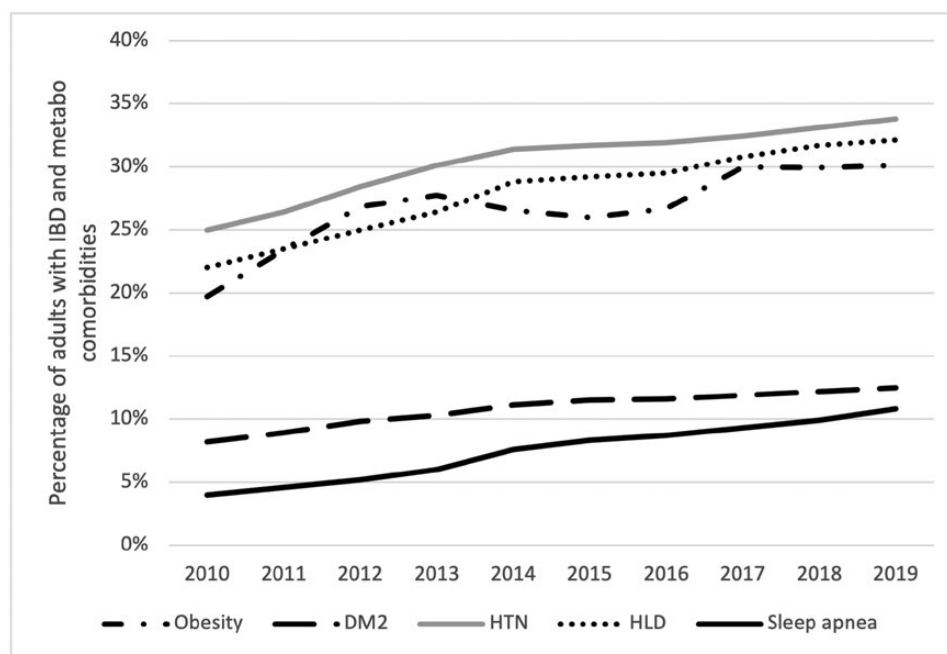
Obesity Pharmacotherapy in IBD

The management of obesity may require interventions at multiple levels including behavioral, lifestyle changes, pharmacotherapy, and bariatric surgeries. In this study, we quantified the proportion of IBD adults with obesity who were prescribed weight loss medications. Recent guidelines from American Gastroenterological Association recommend adding pharmacological agents to lifestyle interventions in adults with BMI ≥ 30 kg m⁻², and those with BMI ≥ 27 kg m⁻² with weight-related comorbidities, who have had an inadequate response to lifestyle interventions.²⁹ We found a small percentage (2.5%) of IBD adults who were prescribed anti-obesity pharmacotherapy similar to the general US population reported in recent studies.^{30,31} These low rates are in part due to lack of insurance coverage. Data from Centers for Medicare & Medicaid Services, the STOP Obesity Alliance, and the US Census Bureau's American Community Survey showed that <20 Medicaid programs had coverage for these drugs.²⁸ Medicare does not cover anti-obesity medications or subsidize them.^{32,33} Even among

Table 3. Demographics of adults with IBD and obesity who were prescribed anti-obesity pharmacotherapy.

Variables		IBD adults with obese BMI (N = 78 200)	Adults with obese BMI and anti-obesity drugs (N = 2170)		OR (CI)
Age	<50	30 590	1090	50.2%	1.59 (1.46–1.73)
	≥50	47 610	1080	49.8%	1
Gender	Male	30 730	340	15.7%	1
	Female	47 470	1830	84.3%	3.65 (3.25–4.10)
Ethnicity	Non-Hispanic	67 190	1850	85.3%	1
	Hispanic	3390	90	4.1%	0.96 (0.78–1.19)*
Race	Caucasian	66 210	1790	82.5%	1
	African American	7740	300	13.8%	1.45 (1.28–1.64)
Insurance	Medicare	19 040	300	13.8%	1
	Medicaid	8640	220	10.1%	1.63 (1.37–1.95)
	Commercial	43 200	1450	66.8%	2.17 (1.91–2.46)
	Self-pay	7320	200	9.2%	1.75 (1.46–2.10)

Abbreviations: BMI, body mass index; IBD, inflammatory bowel disease; OR, odds ratio.
P < .001 except * where *P* = .732.

**Figure 1.** Trends of obesity and comorbidities in inflammatory bowel disease 2010–2019.

marketplace health insurance plans, there are state-to-state disparities.³² Fewer state employee health plans covered obesity pharmacotherapy in 2021 (16 states) compared with 2017 (23 states).³⁴ Furthermore, beneficiaries are limited by factors such as prior authorization, determination of medical necessity by failing behavioral therapy and achieving effective weight loss within timeframe to be eligible for drug reapproval.³³ Legislative bills such as “Treat and Reduce Obesity Act (TROA)” can help obtain coverage for FDA-approved anti-obesity medications under Medicare Part D.³³

It is possible that the barriers for the prescription of weight loss medications in the general population such as lack of

insurance, difference in provider training and limited experience in prescribing those medications exist for the IBD population as well.^{35–37} But it is uncertain whether the providers are more hesitant to prescribe weight loss medications such as sympathomimetics in IBD patients especially due to the lack of high-quality data on obesity pharmacotherapy in IBD patients. The European Society for Clinical Nutrition and Metabolism (ESPEN) and United European Gastroenterology (UEG) recommends patients to focus on weight loss during their remission and prior to elective surgeries to improve therapeutic response and surgical outcomes. A stepwise approach is advised starting from dietary modifications, anti-obesity therapy followed by bariatric surgery as indicated. The use

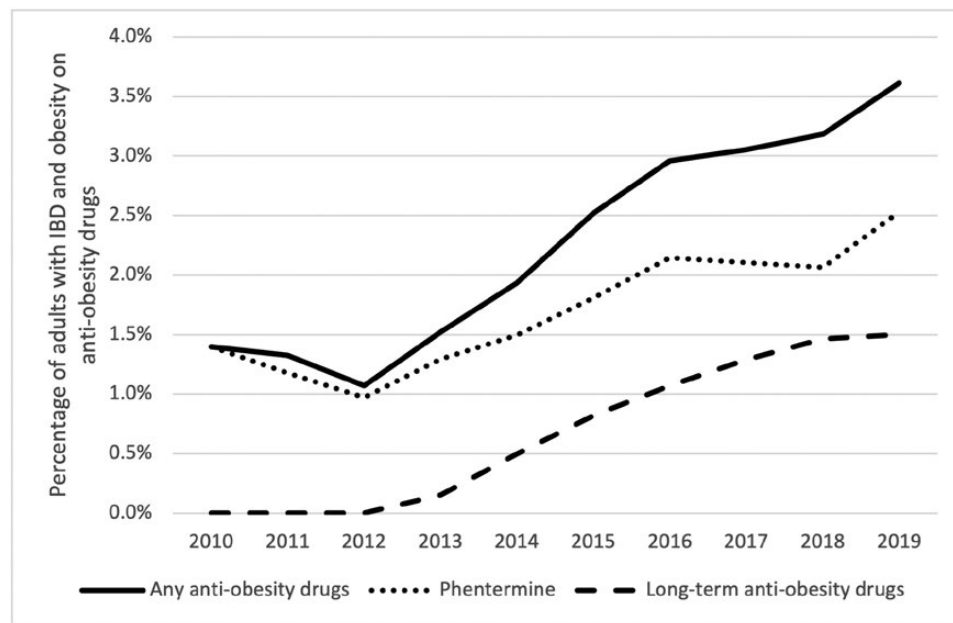


Figure 2. Trends of anti-obesity pharmacotherapy in inflammatory bowel disease 2010–2019.

of orlistat in IBD individuals is discouraged as it is a lipase inhibitor which can increase malabsorption.³⁸

Worrisome Trends

A time-trend analysis of 40 RCTs on CD patients from 1991 to 2008 showed a significant increase in weight ($r = 0.36$; 95% CI: 0.46–0.88) and BMI ($r = 0.14$; 95% CI: 0.03–0.23).³⁹ It is difficult to pinpoint to 1 etiology for the increasing trend but multifarious reasons such as lifestyle changes, increased smoking, dietary habits, steroid use could be responsible,²⁴ but analyzing them is beyond the scope of this study. In contrast to the steep increase in the prevalence of obesity and diseases of metabolic syndrome in the IBD population, there was a decrease in the rate of anti-obesity pharmacotherapy between 2010 and 2012 by 24%. This decline was most noticeable for phentermine (33%). One potential reason could be the withdrawal of a similar sympathomimetic, sibutramine in 2010 due to cardiovascular adverse effects.⁴⁰ This decline was followed by an increase in the overall prescription rates from 2012 to 2019, the rise being most prominent for drugs approved for long-term use. Efforts to understand and address the barriers to therapeutic management of obesity might help us mitigate the cardiovascular risks that are well established in metabolic syndrome.^{41–45}

Limitations

The study reports the prevalence of obesity and the disproportionately small percentage anti-obesity medication use in a big sample of individuals across multiple healthcare systems inclusive of inpatients and outpatients. The deidentified nature of our dataset limits our ability to validate SNOMED CT codes making it entirely dependent on the provider entered ICD. But SNOMED CT is superior to many other terminologies and it designed to include more concepts per clinical document than ICD-9.⁴⁶ The database is deidentified and we do not have access to any patient-level data that would require manual chart review. This registry depends

on individuals who had at least 1 medical visit within the Explorys integrated healthcare networks. Since IBD patients tend to be more connected with medical care, it is possible that screening and treatment for metabolic derangements are more frequent in IBD due to the higher rates of healthcare visits⁴⁷ as opposed to non-IBD patients. However, this should not affect the trends analysis which is the main focus of the paper. It has been reported that there was an increase in the documentation of procedure-related medications in Explorys in the last 2 decades.⁴⁸ We acknowledge this as a possibility in the documentation of diseases and medication prescriptions. In the analysis of anti-obesity pharmacotherapy, our study could not exclude conditions that were temporary such as pregnancy, lactation, uncontrolled hypertension or conditions that do not have specific ICD-10 code such as family history of medullary thyroid carcinoma. The database provides information on the drug brand name, dosage and method of administration. However, details of the duration of medication prescription and compliance are beyond the scope of the database. Our study was also unable to account for potential drug interactions which could be contraindication for prescribing weight loss medications such as concurrent use of monoamine oxidase inhibitors. Since the prescription rate of anti-obesity medications was extremely small, we do not think the above contraindications would affect our results markedly. NAFLD was not included in the analysis as the reported prevalence of NAFLD in Explorys was negligible (4720 cases identified) and did not match the US prevalence of 10%–20%.⁴⁰ To create a comprehensive study sample, we included IBD patients who visited outpatient, emergency, and inpatient settings. Still, we acknowledge the potential ascertainment bias from event driven visitation. Further, we acknowledge limitations of large database such as lack of longitudinal data.

Despite the limitations, the large size and the mixed demographic profile of our subjects from community and tertiary care hospital systems inclusive of inpatients and outpatients allow our study to be applicable to the vast majority of the

US population. Knowledge of increasing obesity trend and the seemingly low rate of anti-obesity pharmacotherapy is a call for action as obesity can affect the course and treatment outcomes of IBD patients adversely.

Conclusions

Obesity is emerging as one of the biggest threats to health-care costs and utilization. This large population-level study shows that IBD is characterized by obesity and metabolic derangements at rates that have consistently increased in the last decade. In a disease population with a complicated disease course, the growing trend of obesity can complicate the existing profile and lead to unprecedented consequences in IBD patients. This study also brings to light the low rates of pharmacological management of obesity in the IBD population. This can be addressed through robust interventions to optimize preventative care and aggressive treatment of obesity and metabolic comorbidities among adults with IBD.

Supplementary Data

Supplementary data is available at *Crohn's and Colitis* 360 online.

Funding

None declared.

Conflicts of Interest

None declared.

Data Availability

Data not publicly available.

References

- Loftus EV, Jr. Update on the incidence and prevalence of inflammatory bowel disease in the United States. *Gastroenterol Hepatol (N Y)*. 2016;12(11):704–707.
- Singh S, Dulai PS, Zarrinpar A, Ramamoorthy S, Sandborn WJ. Obesity in IBD: epidemiology, pathogenesis, disease course and treatment outcomes. *Nat Rev Gastroenterol Hepatol*. 2017;14(2):110–121.
- Sideri A, Stavrakis D, Bowe C, et al. Effects of obesity on severity of colitis and cytokine expression in mouse mesenteric fat. Potential role of adiponectin receptor 1. *Am J Physiol Gastrointest Liver Physiol*. 2015;308(7):G591–G604.
- Jensen CB, Angquist LH, Mendall MA, Sorensen TIA, Baker JL, Jess T. Childhood body mass index and risk of inflammatory bowel disease in adulthood: a population-based cohort study. *Am J Gastroenterol*. 2018;113(5):694–701.
- Khalili H, Ananthakrishnan AN, Konijeti GG, et al. Measures of obesity and risk of Crohn's disease and ulcerative colitis. *Inflamm Bowel Dis*. 2015;21(2):361–368.
- Kurnool S, Nguyen NH, Proudfoot J, et al. High body mass index is associated with increased risk of treatment failure and surgery in biologic-treated patients with ulcerative colitis. *Aliment Pharmacol Ther*. 2018;47(11):1472–1479.
- Nguyen NH, Ohno-Machado L, Sandborn WJ, Singh S. Obesity is independently associated with higher annual burden and costs of hospitalization in patients with inflammatory bowel diseases. *Clin Gastroenterol Hepatol*. 2019;17(4):709–718.e7.
- Pavelock N, Masood U, Minchenberg S, Heisig D. Effects of obesity on the course of inflammatory bowel disease. *Proc (Bayl Univ Med Cent)*. 2019;32(1):14–17.
- Krane MK, Allaix ME, Zoccali M, et al. Does morbid obesity change outcomes after laparoscopic surgery for inflammatory bowel disease? Review of 626 consecutive cases. *J Am Coll Surg*. 2013;216(5):986–996.
- Keith JN. Pharmacotherapy in treatment of obesity. *Gastroenterol Clin North Am*. 2016;45(4):663–672.
- IBM Watson Health. The IBM Explorys Platform 2016. 2016. Accessed March 3, 2023. <https://www.ibm.com/watson-health/about/explorys>
- Medicine NLo. Unified Medical Language System (UMLS). 2018. Accessed March 3, 2023. https://www.nlm.nih.gov/research/umls/mapping_projects/snomedct_to_icd10cm.html
- Pilitsi E, Farr OM, Polyzos SA, et al. Pharmacotherapy of obesity: available medications and drugs under investigation. *Metabolism*. 2019;92(Epub):170–192.
- Administration UFaD. FDA requests the withdrawal of the weight-loss drug Belviq, Belviq XR (lorcaserin) from the market 2020. 2020. Accessed March 3, 2023. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-requests-withdrawal-weight-loss-drug-belviq-belviq-xr-lorcaserin-market>
- Hou JK, Kramer JR, Richardson P, Mei M, El-Serag HB. The incidence and prevalence of inflammatory bowel disease among U.S. veterans: a national cohort study. *Inflamm Bowel Dis*. 2013;19(5):1059–1064.
- Flores A, Burstein E, Cipher DJ, Feagins LA. Obesity in inflammatory bowel disease: a marker of less severe disease. *Dig Dis Sci*. 2015;60(8):2436–2445.
- Seminario JL, Koutroubakis IE, Ramos-Rivers C, et al. Impact of obesity on the management and clinical course of patients with inflammatory bowel disease. *Inflamm Bowel Dis*. 2015;21(12):2857–2863.
- Sztembis J, Filip R, Pekala A, et al. P834 Metabolic syndrome occurrence in patients with inflammatory bowel disease in Poland—preliminary results from the POLIBD study. *J Crohns Colitis*. 2018;12(suppl 1):S538.
- Hales CM, Fryar CD, Carroll MD, Freedman DS, Ogden CL. Trends in obesity and severe obesity prevalence in US youth and adults by sex and age, 2007–2008 to 2015–2016. *JAMA*. 2018;319(16):1723–1725.
- Dragasevic S, Stankovic B, Kotur N, et al. Metabolic syndrome in inflammatory bowel disease: association with genetic markers of obesity and inflammation. *Metab Syndr Relat Disord*. 2020;18(1):31–38.
- Capristo E, Addolorato G, Mingrone G, Greco AV, Gasbarrini G. Effect of disease localization on the anthropometric and metabolic features of Crohn's disease. *Am J Gastroenterol*. 1998;93(12):2411–2419.
- Petersen R, Pan L, Blanck HM. Racial and ethnic disparities in adult obesity in the United States: CDC's tracking to inform state and local action. *Prev Chronic Dis*. 2019;16:E46. doi:10.5888/pcd16.180579.
- Mylona EK, Benitez G, Shehadeh F, et al. The association of obesity with health insurance coverage and demographic characteristics: a statewide cross-sectional study. *Medicine (Baltimore)*. 2020;99(27):e21016.
- Din H, Anderson AJ, Ramos Rivers C, et al. Disease characteristics and severity in patients with inflammatory bowel disease with co-existent diabetes mellitus. *Inflamm Bowel Dis*. 2020;26(9):1436–1442.
- Kang EA, Han K, Chun J, et al. Increased risk of diabetes in inflammatory bowel disease patients: a nationwide population-based study in Korea. *J Clin Med*. 2019;8(3):343–343.
- Zanoli L, Cannavò M, Rastelli S, et al. Arterial stiffness is increased in patients with inflammatory bowel disease. *J Hypertens*. 2012;30(9):1775–1781.
- Prijic R, Premuzic V, Brinar M, Krznarić Ž, Jelaković B, Čuković-Čavka S. Increased arterial stiffness—similar findings in patients

- with inflammatory bowel disease without prior hypertension or diabetes and in patients with well-controlled hypertension. *Blood Press*. 2018;27(4):240–246.
28. Stephenson J. Report finds large variation in states' coverage for obesity treatments. *JAMA Health Forum*. 2022;3:e220608.
 29. Grunvald E, Shah R, Hernaez R et al. AGA clinical practice guideline on pharmacological interventions for management of obesity. *Gastroenterology*. 2022;163(5):1198–1225.
 30. Saxon DR, Iwamoto SJ, Mettenbrink CJ, et al. Antiobesity medication use in 2.2 million adults across eight large health care organizations: 2009–2015. *Obesity (Silver Spring)*. 2019;27(12):1975–1981.
 31. Elangovan A, Shah R, Smith ZL. Pharmacotherapy for obesity—trends using a population level national database. *Obes Surg*. 2020;31(3):1105–1112.
 32. Gomez G, Stanford FC. US health policy and prescription drug coverage of FDA-approved medications for the treatment of obesity. *Int J Obes (Lond)*. 2018;42(3):495–500.
 33. United States Government Accountability Office Report to Congressional Committees. *GAO-19-577 Obesity Drugs: Few Adults Used Prescription Drugs for Weight Loss and Insurance Coverage Varied*. 2019. Accessed March 3, 2023. <https://www.gao.gov/products/gao-19-577>.
 34. Hughes S, Dietz WH, Gallagher C. Coverage for obesity prevention and treatment: analysis of state employee health plans and use of benefits. *Obesity (Silver Spring)*. 2022;30(8):1573–1578.
 35. Simon R, Lahiri SW. Provider practice habits and barriers to care in obesity management in a large multicenter health system. *Endocr Pract*. 2018;24(4):321–328.
 36. Petrin C, Kahan S, Turner M, Gallagher C, Dietz WH. Current practices of obesity pharmacotherapy, bariatric surgery referral and coding for counselling by healthcare professionals. *Obes Sci Pract*. 2016;2(3):266–271.
 37. Bessesen DH, Van Gaal LF. Progress and challenges in anti-obesity pharmacotherapy. *Lancet Diabetes Endocrinol*. 2018;6(3):237–248.
 38. Bischoff SC, Barazzoni R, Busetto L, et al. European guideline on obesity care in patients with gastrointestinal and liver diseases—Joint ESPEN/UEG guideline. *Clin Nutr*. 2022;41(10):2364–2405.
 39. Moran GW, Dubeau M-F, Kaplan GG, Panaccione R, Ghosh S. The increasing weight of Crohn's disease subjects in clinical trials: a hypothesis-generating time-trend analysis. *Inflamm Bowel Dis*. 2013;19(13):2949–2956.
 40. US Food and Drug Administration. FDA Drug Safety Communication: FDA Recommends Against the Continued Use of Meridia (Sibutramine) 2010. 2018. Accessed March 3, 2023. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-recommends-against-continued-use-meridia-sibutramine>
 41. Singh S, Singh H, Loftus EV, Jr., Pardi DS. Risk of cerebrovascular accidents and ischemic heart disease in patients with inflammatory bowel disease: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. 2014;12(3):382–393.e1: quiz e22.
 42. Feng W, Chen G, Cai D, Zhao S, Cheng J, Shen H. Inflammatory bowel disease and risk of ischemic heart disease: an updated meta-analysis of cohort studies. *J Am Heart Assoc*. 2017;6(8):e005892.
 43. Panhwar MS, Mansoor E, Al-Kindi SG, et al. Risk of myocardial infarction in inflammatory bowel disease: a population-based national study. *Inflamm Bowel Dis*. 2019;25(6):1080–1087.
 44. Rungoe C, Basit S, Ranthe MF, Wohlfahrt J, Langholz E, Jess T. Risk of ischaemic heart disease in patients with inflammatory bowel disease: a nationwide Danish cohort study. *Gut*. 2013;62(5):689–694.
 45. Yarur AJ, Deshpande AR, Pechman DM, Tamariz L, Abreu MT, Sussman DA. Inflammatory bowel disease is associated with an increased incidence of cardiovascular events. *Am J Gastroenterol*. 2011;106(4):741–747.
 46. Nadkarni PM, Darer JA. Migrating existing clinical content from ICD-9 to SNOMED. *J Am Med Inform Assoc*. 2010;17(5):602–607.
 47. Park KT, Ehrlich OG, Allen JI, et al. The cost of inflammatory bowel disease: an Initiative from the Crohn's & Colitis Foundation. *Inflamm Bowel Dis*. 2020;26(1):1–10.
 48. Smith ZL, Elmunzer BJ, Cooper GS, Chak A. Real-world practice patterns in the era of rectal indomethacin for prophylaxis against post-ERCP pancreatitis in a high-risk cohort. *Am J Gastroenterol*. 2020;115(6):934–940.