

Epidemiology of metabolic syndrome in patients with inflammatory bowel disease: a population-level cohort study from the United States

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Abstract

Background Epidemiological data on metabolic syndrome (MetS) in patients with inflammatory bowel disease (IBD) are limited.

Methods A retrospective cohort study was conducted using the United States (US) Collaborative Network (TriNetX) to obtain data for patients with IBD between 2010 and 2023. The primary aim of the study was to estimate the prevalence of MetS in ulcerative colitis (UC) and Crohn's disease (CD). Prevalence was further characterized by age, sex, race, disease location, IBD medications, history of surgery, and IBD phenotype.

Results Among 100,890 patients with IBD, metabolic syndrome (MetS) affected 34.4% overall (UC 32.4%, CD 34.3%). Prevalence rose sharply with age (12-14% at 18-39 to 47-50% at ≥65) and was higher in men than women. Rates were greatest among American Indian (CD 45.2%), Black (40%) and Hispanic (38-39%) populations, and lowest in Asian patients (26%). MetS clustered with more severe phenotypes (stricturing CD, prior CD surgery) and was not elevated among patients receiving advanced therapy. MetS was associated with greater systemic corticosteroid use and higher surgery/colectomy risk, while stricture and fistula risks in CD were similar; advanced therapy was not initiated more frequently in CD.

Conclusion Our study provides updated epidemiological estimates of MetS in patients with IBD in the US.

Keywords Inflammatory bowel disease, ulcerative colitis, Crohn's disease, metabolic syndrome, epidemiology

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Introduction

Inflammatory bowel disease (IBD), comprising ulcerative colitis (UC) and Crohn's disease (CD), is a chronic inflammatory condition of the gastrointestinal tract that poses a significant global health burden, affecting an increasing number of patients worldwide [1,2]. In a recent paper based on the Global Burden of Disease database, the United States (US) had the highest age-standardized prevalence rate globally, with nearly a quarter of the total global patients with IBD in 2017 [3]. Metabolic syndrome (MetS) is characterized by central obesity, insulin resistance, hypertension (HTN) and dyslipidemia, with visceral adiposity driving insulin resistance through proinflammatory cytokine production [4,5]. Among US adults aged 18 years or older, the prevalence of MetS in the general population rose by more than 35% from 1988-1994 to 2007-2012, increasing from 25.3% to 34.2% [6]. Emerging data suggest that the metabolic disturbances associated with

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MetS, including inflammation driven by visceral adiposity, may intersect with the pathophysiological mechanisms of IBD, potentially exacerbating disease progression and complicating management strategies [7,8]. However, despite this plausible biological interplay, the epidemiology of MetS in IBD remains incompletely understood and underreported in the US, during this ever-rising epidemic of obesity.

Earlier studies have reported widely varying prevalence estimates for MetS in IBD, typically ranging from 15-40%, depending on the population characteristics and diagnostic criteria used [9-12]. Indeed, both obesity and MetS are increasingly recognized in IBD, with the shifting demographics of IBD reflecting broader societal trends in obesity [2]. Moreover, there is evidence that obesity, through altered microbiota composition and chronic low-grade inflammation, may contribute to the pathogenesis of IBD [13]. However, most of the existing studies examining the co-occurrence of MetS and IBD predate the widespread use of biologic therapies, or are limited by modest sample sizes and geographically constrained cohorts. This lack of contemporary, large-scale data hampers our understanding of the epidemiology of MetS in patients with IBD and its impact on their disease course in the biologic era.

Given the rising prevalence of obesity and MetS globally, the role of visceral adiposity in driving insulin resistance, and the potential for these metabolic derangements to worsen IBD outcomes, updated epidemiological data are urgently needed [4,7]. Previous estimates may no longer reflect current trends, particularly with the rapidly evolving treatment landscape in which biologics and other advanced therapies are increasingly used. The primary aim of this study was to provide contemporary estimates of the prevalence of MetS in IBD, stratified by patient demographics and IBD characteristics.

Materials and methods

Database

A retrospective cohort study was conducted using the TriNetX database (Cambridge, MA, USA), a global federated research network that provides real-time access to de-identified electronic health records of more than 120 million patients within 69 healthcare organizations in the US. Most of these organizations are large academic medical institutions comprising both inpatient and outpatient facilities. Data in TriNetX represent the entire patient population of these institutions.

The de-identification process is performed at a network-level according to a formal determination by a qualified expert, as defined in the HIPAA Privacy Rule. TriNetX obfuscates

patient counts <10 to ensure anonymity. Clinical variables are derived directly from the electronic health records, and through a built-in natural language processing system that extracts variables from clinical documents. Robust quality assurance is conducted at the time of extraction, before inclusion in the database, incorporating data cleaning to reject patient records that do not meet TriNetX quality standards. The database does not include claims data or data collected from randomized clinical trials. It includes patient demographics, diagnoses, procedures, laboratory values and medication records. Only aggregate counts and statistical summaries are provided, ensuring that the data remain de-identified at all levels. Because the data are fully de-identified, Institutional Review Board approval was not required.

Study participants and cohorts

We performed a real-time search and analysis of the US Collaborative Network in the TriNetX platform. Patients aged ≥ 18 years old who were diagnosed with UC or CD were identified using at least 2 International Classification of Disease, Tenth Revision, Clinical Modification (ICD-10-CM) codes (K51.* for UC or K50.* for CD), plus a Rxnorm code for ≥ 1 IBD-related medication, between January 1, 2010, and December 31, 2023. Medications included mesalamine, balsalazide, olsalazine, sulfasalazine, azathioprine, mercaptopurine, methotrexate, infliximab, adalimumab, golimumab, certolizumab, vedolizumab, ustekinumab, tofacitinib, upadacitinib, ozanimod, etrasimod, and risankizumab. Complex case definitions requiring ≥ 1 ICD-10-CM code plus a relevant IBD-related prescription have demonstrated $\geq 80\%$ positive predictive value and $\geq 85\%$ specificity in prior administrative or claims-based studies [14]. The TriNetX database has been used in multiple previously published IBD studies [15-17]. All patients were required to have lab values for high-density lipoprotein (HDL) and triglycerides (TG). Individuals without available HDL or TG data were excluded. ICD-10, Rxnorm, CPT codes used for cohort design have been reported in Supplementary Tables 1 and 2.

Study aims and outcomes

The primary aim of the study was to determine the prevalence of MetS in patients with IBD. MetS was defined by any 3 or more of the following criteria: HTN, type 2 diabetes mellitus (T2DM), obesity, HDL <45 mg/dL, and TG ≥ 150 mg/dL. These criteria were largely based on the Adult Treatment Panel III (ATP III) and International Diabetes Federation guidelines, which can be applied to the US population [18,19]. We used ICD-10-CM codes for HTN and T2DM, instead of recorded blood pressure measurements or fasting glucose, to better reflect the chronic disease status, rather than a single elevated measurement. Similarly, we employed ICD-10-CM codes for obesity, rather than waist circumference, given the limited availability of anthropometric data, and because obesity diagnosis codes have been shown to

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have high specificity [20–22]. An HDL cutoff of <45 mg/dL was used uniformly for both men and women, because the database does not allow for gender-specific cutoffs. We believe these criteria are clinically practical and can be used for future MetS studies using administrative or claims-based databases.

MetS prevalence was reported by age group (18–39, 40–65, and >65 years), sex and race, for both UC and CD. Additionally, prevalence was stratified by disease location, IBD therapy, IBD-related surgery, and disease phenotype (for CD). We also analyzed the incidence proportion and prevalence of each MetS component from 2010–2023.

In exploratory analyses, we also evaluated 5-year IBD outcomes among adults with and without MetS in separate UC and CD propensity-matched cohorts (UC: 9850 MetS vs. 9850 controls; CD: 10,563 MetS vs. 10,563 controls). Outcomes included advanced therapy initiation (biologic/small-molecule agents), intravenous (IV) corticosteroid use, oral corticosteroid use, and surgery (colectomy for UC; any IBD-related surgery for CD). CD-specific endpoints also included stricture and fistula development.

Statistical analysis

All statistical analyses were conducted within the TriNetX browser-based real-time analytics platform. Baseline characteristics were summarized by means, standard deviations and proportions. We identified covariates based on demographics, comorbid diseases, laboratory parameters, and historical IBD medication use. Prevalence was expressed as proportions and percentages. Incidence and incidence rate (per 1000-person years) were calculated from 2010–2023 for obesity stratified by sex and race. Incidence and incidence rate were also reported for each component of MetS.

Results

Baseline characteristics

A total of 115,316 patients with IBD were identified: 60,691 (52.6%) with UC and 54,625 (47.4%) with CD (Table 1). In the UC cohort, the mean age was 58.1±17.8 years, 45% were male and 75% were White. Comorbidities included HTN in 51%, T2DM in 21% and obesity in 44.7%. Among those with available data on disease extent, 67.4% had pancolitis and 13.7% had proctitis. Approximately 36% were on advanced therapy, 44% had a history of acute severe ulcerative colitis (ASUC), and 1.38% had an ileal pouch-anal anastomosis (IPAA). In the CD cohort, the mean age was 55.3±18 years, 43% were male and 76% were White. Of those with documented disease location, 13.1% had small-bowel disease, and 61.3% had small and large bowel involvement. Regarding disease phenotype, 17.8% had stricturing disease and 18.2% had fistulizing disease. More than half of the patients (59%) were on advanced therapy. Nearly one third (31.6%) had a history of CD-related surgery.

Table 1 Baseline characteristics of the UC and CD cohort

Characteristics	UC cohort (n=60,691)	CD cohort (n=54,625)
Mean age (±SD)	58.1±17.8	55.3±18
Male sex	27,359 (45%)	23,493 (43%)
Race		
White	45,581 (75%)	41,509 (76%)
African American or Black	4,323 (7%)	4,604 (8%)
Hispanic or Latino	2,737 (5%)	1,824 (3%)
Asian	1,482 (2.4%)	872 (1.5%)
American Indian or Alaska Native	132 (0.2%)	146 (0.2%)
Native Hawaiian or Other Pacific Islander	75 (0.12%)	48 (0.08%)
Comorbid conditions		
Hypertension	30,828 (51%)	27,157 (50%)
Type 2 diabetes mellitus	12,863 (21%)	10,660 (20%)
Obesity	27,142 (44.7%)	24,890 (45.5%)
Mean HDL (mg/dL)	53.5±19.6	51.9±19
Mean triglycerides (mg/dL)	122±80.3	134±95.7
Nicotine dependence	7,932 (13%)	10,603 (19%)
Alcohol related disorders	3,145 (5%)	2,957 (5%)
Primary sclerosing cholangitis	2,186 (4%)	1,109 (2%)
Celiac disease	939 (1.5%)	1,018 (1.8%)
Rheumatoid arthritis	4,255 (7%)	4,886 (9%)
Psoriasis	3,545 (6%)	4,395 (8%)
Ankylosing spondylitis	997 (1.6%)	1,424 (2.6%)
Systemic lupus erythematosus	933 (1.5%)	1,149 (2.1%)
Mood disorders	20,445 (34%)	21,407 (39%)

UC, ulcerative colitis; CD, Crohn's disease; SD, standard deviation; HDL, high-density lipoprotein cholesterol

Prevalence of MetS in UC

Overall, 19,701 UC patients met the criteria for MetS, with a prevalence of 32.4%. After stratification by age, the prevalence was 11.7% in those aged 18–39, 30.8% in those aged 40–65, and 46.8% in those >65 years old. MetS prevalence was higher in males compared to females (39.4% vs. 30%). The prevalence based on race was 34.1% for White, 40.2% for Black, 38.1% for Hispanic or Latino, 25.7% for Asian, 37.3% for Native Hawaiian or Pacific Islander, and 35.6% for American Indian. The prevalence in patients with proctitis was 29.1%, whereas in those with pancolitis it was 33.8%. MetS was less common among patients on advanced therapy (31.9%) compared to those on 5-aminosalicylic acid ([5-ASA] 36.2%). Patients with a history of ASUC had a prevalence of 47.1%, and those with IPAA had 29.5% (Table 2). MetS was present in 5755 patients on tumor necrosis factor inhibitors ([TNFi] 33.3%), 2795 on vedolizumab (33.8%), 2068 on interleukin (IL)-23 inhibitors (32.3%) and 1193 on Janus kinase (JAK) inhibitors (24.3%).

Prevalence of MetS in CD

MetS was identified in 18,738 CD patients, with a prevalence of 34.3%. After stratification by age, the prevalence was 13.7% in those aged 18–39, 35.9% in those aged 40–65, and 50% in those

Table 2 Prevalence of metabolic syndrome among different subgroups in the UC cohort

Ulcerative colitis (UC)	
Subgroups	N (%)
Age (years)	
18-39	1262 (11.7%)
40-65	7898 (30.8%)
>65	10,541 (46.8%)
Sex	
Male	10,447 (39.4%)
Female	8922 (30.0%)
Race	
White	15,569 (34.1%)
African American or Black	1738 (40.2%)
Hispanic or Latino	1043 (38.1%)
Asian	381 (25.7%)
Native Hawaiian or Pacific Islander	28 (37.3%)
American Indian or Alaska Native	47 (35.6%)
Location	
Pancolitis	9230 (33.8%)
Proctosigmoiditis or left-sided colitis	2451 (32.1%)
Proctitis	1618 (29.1%)
Therapy	
5-ASA	11,774 (36.2%)
Advanced therapy	6987 (31.9%)
ASUC	12,590 (47.18%)
IPAA	248 (29.5%)
Crohn's disease (CD)	
Subgroups	N (%)
Age (years)	
18-39	1643 (13.7%)
40-65	8502 (35.9%)
>65	8593 (50.0%)
Sex	
Male	8911 (39.3%)
Female	9615 (32.9%)
Race	
White	14,958 (36.0%)
African American or Black	1848 (40.1%)
Hispanic or Latino	713 (39.0%)
Asian	223 (25.8%)
Native Hawaiian or Pacific Islander	19 (39.5%)
American Indian or Alaska Native	66 (45.2%)
Location	
Small bowel	1851 (35.2%)
Small and large bowel	8412 (34.2%)
Large bowel	4063 (39.7%)
Phenotype	
Stricturing	3786 (39.5%)
Fistulizing	3556 (36.4%)
Inflammatory	12,453 (36.4%)
Advanced therapy	10,709 (33.2%)
Surgery	7237 (41.9%)

5-ASA, 5-aminosalicylic acid; ASUC, acute severe ulcerative colitis; IPAA, ileal pouch anal anastomosis

>65 years old. MetS prevalence was higher in males compared to females (39.3% vs. 32.9%). The prevalence based on race was 36% for White, 40.1% for Black, 39% for Hispanic or Latino, 25.8% for Asian, 39.5% for Native Hawaiian or Pacific Islander, and 45.2% for American Indian. The prevalence was 39.7% for large bowel disease, 34.2% for small bowel disease and 35.2% for small-and-large-bowel disease. The prevalence was 39.5% for stricturing disease, 36.4% for fistulizing disease and 36.4% for inflammatory disease. MetS prevalence was 33.2% in those on advanced therapy and 41.9% in those with a history of CD-related surgery (Table 2). In CD, MetS prevalences were 9693 (34.4%) patients on TNFi, 3126 (39.3%) on vedolizumab, 4738 (34.6%) on IL-23 inhibitors and 736 (26.5%) on JAK inhibitors.

Incidence and prevalence of MetS components in IBD

The incidence of obesity in UC was 9.81%, with 58.4 cases per 1000 person-years in 2010-11, and remained stable in 2022-23 with an incidence of 8.45%, representing 51.1 cases per 1000 person-years (Table 3). The prevalence of obesity in UC rose from 18.25% in 2010-11 to 45.67% in 2022-23 (Fig. 1). Similarly, the incidence of obesity in CD was 10.07% in 2010-11, with 59.9 cases per 1000 person-years, and remained stable in 2022-23 with an incidence of 8.36%, representing 50.4 cases per 1000 person-years (Fig. 1). The prevalence of obesity in CD rose from 18.25% in 2010-11 to 45.67% in 2022-23 (Supplementary Figure 1 and Table 3).

The incidence of T2DM and HTN in UC was 2.86% (16.44 cases per 1000 person-years) and 8.09% (47.85 cases per 1000 person-years), respectively, in 2010-11, increasing to 3.66% (21.18 cases per 1000 person-years) and 10.58% (63.55 cases per 1000 person-years), respectively, in 2022-23. The prevalence was 19.73% for T2DM and 48.7% for HTN in 2022-23. Similarly, the incidence of T2DM and HTN in CD was 2.53% (14.24 cases per 1000 person-years) and 7.69% (45.29 cases per 1000 person-years), respectively, in 2010-11, increasing to 3.33% (18.99 cases per 1000 person-years) and 10.53% (62.82 cases per 1000 person-years), respectively, in 2022-23 (Table 3). The prevalence was 18.03% for T2DM and 47.8% for HTN in 2022-23. The incidence and prevalence of HDL <45 mg/dL and TG >150 mg/dL can be found in Table 3.

IBD outcomes in patients with MetS

In UC, advanced therapy use was reported in 2469 (25.06%) patients with MetS vs. 2334 (23.69%) controls (adjusted odds ratio [aOR] 1.07, 95% confidence interval [CI] 1.009-1.15; P=0.02); colectomy in 1502 (15.24%) vs. 1074 (10.90%) (aOR 1.47, 95%CI 1.35-1.59; P<0.001); IV steroid use in 2018 (20.48%) vs. 1196 (12.14%) (aOR 1.86, 95%CI 1.72-2.105; P<0.001); and oral steroid use in 4291 (43.56%) vs. 3220 (32.69%) (aOR 1.58, 95%CI 1.50-1.68; P<0.001). In CD, advanced therapy use was reported in 4501 (42.61%) patients with MetS vs. 4621 (43.74%) controls (aOR 0.95, 95%CI 0.90-

Table 3 Incidence proportion and prevalence of obesity, type 2 diabetes mellitus, hypertension, HDL < 45 mg/dL and TG > 150 in the UC and CD cohort from 2010-2023

Ulcerative colitis				Crohn's disease			
Obesity				Obesity			
Year	Incidence Proportion % (n)	Cases per 1000 person-years	Prevalence % (n)	Year	Incidence Proportion % (n)	Cases per 1000 person-years	Prevalence % (n)
2010-11	9.81% (3186)	58.44	18.25% (6537)	2010-11	10.07% (3025)	59.9	18.97% (6320)
2012-13	9.32% (3346)	54.06	23.17% (9817)	2012-13	9.40% (3097)	54.42	23.85% (9344)
2014-15	8.71% (3354)	50.4	26.95% (12961)	2014-15	8.67% (3025)	50.04	27.66% (12180)
2016-17	9.42% (3686)	60.63	31.52% (16301)	2016-17	9.87% (3488)	63.55	32.50% (15333)
2018-19	10.27% (3948)	57.71	36.85% (20135)	2018-19	10.51% (3580)	58.81	38.16% (18796)
2020-21	9.77% (3454)	54.79	41.53% (22656)	2020-21	9.76% (3024)	54.42	42.84% (20949)
2022-23	8.45% (2578)	51.13	45.67% (23477)	2022-23	8.36% (2223)	50.4	46.95% (21552)
T2DM				T2DM			
Year	Incidence Proportion % (n)	Cases per 1000 person-years	Prevalence % (n)	Year	Incidence Proportion % (n)	Cases per 1000 person-years	Prevalence % (n)
2010-11	2.86% (981)	16.44	7.16% (2564)	2010-11	2.53% (814)	14.24	6.19% (2064)
2012-13	3.16% (1263)	17.53	8.92% (3782)	2012-13	3.09% (1148)	17.17	8.08% (3167)
2014-15	3.74% (1664)	20.82	11.05% (5317)	2014-15	3.28% (1347)	18.26	10.05% (4425)
2016-17	3.26% (1520)	20.09	12.78% (6611)	2016-17	3.11% (1338)	18.99	11.78% (5561)
2018-19	3.95% (1905)	21.18	15.27% (8344)	2018-19	3.46% (1521)	18.63	14.04% (6920)
2020-21	3.69% (1729)	19.72	17.47% (9532)	2020-21	3.22% (1367)	17.17	15.97% (7814)
2022-23	3.66% (1570)	21.18	19.73% (10145)	2022-23	3.33% (1296)	18.99	18.03% (8276)
HTN				HTN			
Year	Incidence Proportion % (n)	Cases per 1000 person-years	Prevalence % (n)	Year	Incidence Proportion % (n)	Cases per 1000 person-years	Prevalence % (n)
2010-11	8.09% (2558)	47.85	18.86% (6755)	2010-11	7.69% (2292)	45.29	17.45% (5815)
2012-13	9.63% (3443)	55.88	23.80% (10086)	2012-13	9.26% (3102)	53.33	22.47% (8805)
2014-15	10.34% (3959)	59.9	28.60% (13754)	2014-15	9.56% (3392)	55.15	27.16% (11961)
2016-17	10.18% (3915)	65.75	33.26% (17201)	2016-17	10.19% (3638)	65.75	32.09% (15140)
2018-19	12.39% (4662)	70.49	39.70% (21689)	2018-19	11.61% (3983)	65.38	38.44% (18937)
2020-21	10.59% (3609)	59.17	44.17% (24094)	2020-21	10.14% (3148)	56.25	42.96% (21011)
2022-23	10.58% (3119)	63.55	48.73% (25050)	2022-23	10.53% (2817)	62.82	47.87% (21973)
HDL <45 mg/dL				HDL <45 mg/dL			
Year	Incidence Proportion % (n)	Cases per 1000 person-years	Prevalence % (n)	Year	Incidence Proportion % (n)	Cases per 1000 person-years	Prevalence % (n)
2010-11	7.40% (2357)	43.83	17.70% (6339)	2010-11	7.63% (2261)	44.93	17.90% (5966)
2012-13	6.53% (2364)	37.26	20.25% (8583)	2012-13	6.95% (2320)	39.45	20.79% (8147)
2014-15	7.33% (2917)	41.64	23.31% (11207)	2014-15	7.59% (2746)	43.1	24.11% (10619)

(Contd...)

Table 3 (Continued)

HDL <45 mg/dL				HDL <45 mg/dL			
Year	Incidence Proportion % (n)	Cases per 1000 person-years	Prevalence % (n)	Year	Incidence Proportion % (n)	Cases per 1000 person-years	Prevalence % (n)
2016-17	8.97% (3680)	57.34	27.86% (14409)	2016-17	9.81% (3633)	62.82	29.22% (13786)
2018-19	10.60% (4295)	59.17	33.73% (18430)	2018-19	11.56% (4137)	64.65	35.79% (17631)
2020-21	11.27% (4198)	63.19	39.44% (21513)	2020-21	11.93% (3867)	66.48	41.62% (20354)
2022-23	12.47% (3984)	75.24	45.63% (23456)	2022-23	13.39% (3692)	80.36	47.98% (22024)

TG ≥150 mg/dL				TG ≥150 mg/dL			
Year	Incidence Proportion % (n)	Cases per 1000 person-years	Prevalence % (n)	Year	Incidence Proportion % (n)	Cases per 1000 person-years	Prevalence % (n)
2010-11	6.03% (1959)	35.06	14.827% (5309)	2010-11	6.49% (1943)	37.99	16.06% (5352)
2012-13	5.56% (2065)	31.41	17.208% (7291)	2012-13	6.19% (2104)	35.06	18.71% (7332)
2014-15	6.35% (2607)	35.79	20.121% (9674)	2014-15	7.09% (2621)	40.18	22.05% (9710)
2016-17	7.31% (3105)	46.02	23.962% (12392)	2016-17	8.38% (3177)	53.33	26.43% (12470)
2018-19	9.04% (3829)	50.04	29.472% (16100)	2018-19	10.35% (3829)	57.71	32.69% (16105)
2020-21	9.68% (3814)	53.69	34.821% (18992)	2020-21	11.43% (3859)	63.92	38.90% (19023)
2022-23	11.07% (3770)	66.48	41.074% (21111)	2022-23	13.01% (3719)	78.53	45.83% (21035)

HDL, high-density lipoprotein cholesterol; TG, triglycerides; T2DM, type 2 diabetes mellitus; HTN, hypertension

1.008; $P=0.09$); surgery in 2698 (25.54%) vs. 2032 (19.23%) (aOR 1.44, 95%CI 1.34-1.53; $P<0.001$); IV steroid use in 2601 (24.62%) vs. 1556 (14.73%) (aOR 1.89, 95%CI 1.76-2.02; $P<0.001$); and oral steroid use in 5305 (50.22%) vs. 4020 (38.05%) (aOR 1.64, 95%CI 1.55-1.73; $P<0.001$). Stricture development was reported in 2134 (20.20%) vs. 2067 (19.56%) (aOR 1.04, 95%CI 0.97-1.11; $P=0.24$), and fistula development in 1578 (14.93%) vs. 1623 (15.36%) (aOR 0.96, 95%CI 0.89-1.04; $P=0.38$) (Table 4).

Discussion

Our study provides updated epidemiological estimates for MetS to characterize the prevalence, trends, and sociodemographic distribution of this condition among patients with IBD in the US, leveraging data from a large administrative database spanning over a decade. We observed that more than one-third of patients with UC and CD met the criteria for MetS, with the highest rates in elderly patients, males, and among the American Indian or Alaska native, Black and Hispanic populations. The increasing trend in the prevalence of MetS is explained by the increase in the prevalence of all individual components of MetS over a decade. The rapid increase in prevalence with age indicates that, given the demographic trend of an aging population, further increases in MetS are likely, accompanied by higher rates of associated chronic conditions. Disease phenotype also correlated with

MetS prevalence; more extensive UC involvement (pancolitis), a history of ASUC, stricturing CD and CD-related surgery were associated with higher prevalence of MetS. Interestingly, patients on advanced therapy had a lower MetS prevalence, though it is unclear if this was due to differences in disease behavior, less corticosteroid use or other confounding factors. Overall, our findings highlight a significant overlap between metabolic disturbances and IBD in a contemporary real-world setting.

Our results align with earlier reports documenting the rising burden of MetS in patients with IBD, although previous estimates have ranged from 15-40% [9,23-29]. Shen *et al* conducted a meta-analysis, revealing that MetS is a relatively common comorbidity in patients with IBD, with a pooled prevalence estimated at 19.4% (95%CI 15.1-23.8%) [11]. In another population-based study of 489 patients with IBD, 18% of patients were diagnosed with obesity (compared with 23% of the general population), and 38% of patients were overweight; this proportion was comparable between patients with CD (18% with obesity) or UC (17.5% with obesity) [10]. In a study by Flores *et al*, the authors reported that up to 25% of USA patients with IBD were diagnosed with obesity, which paralleled the obesity rate in the US back in 2015 [9]. Our data showed that the prevalence was approximately 45% for obesity and over 30% for MetS. European and Asian cohorts previously had generally lower MetS rates (10-30%), perhaps attributable to geographic variations in obesity prevalence, healthcare practices and the overall health of the population [30-36]. After stratification of IBD into UC and CD, our study reported

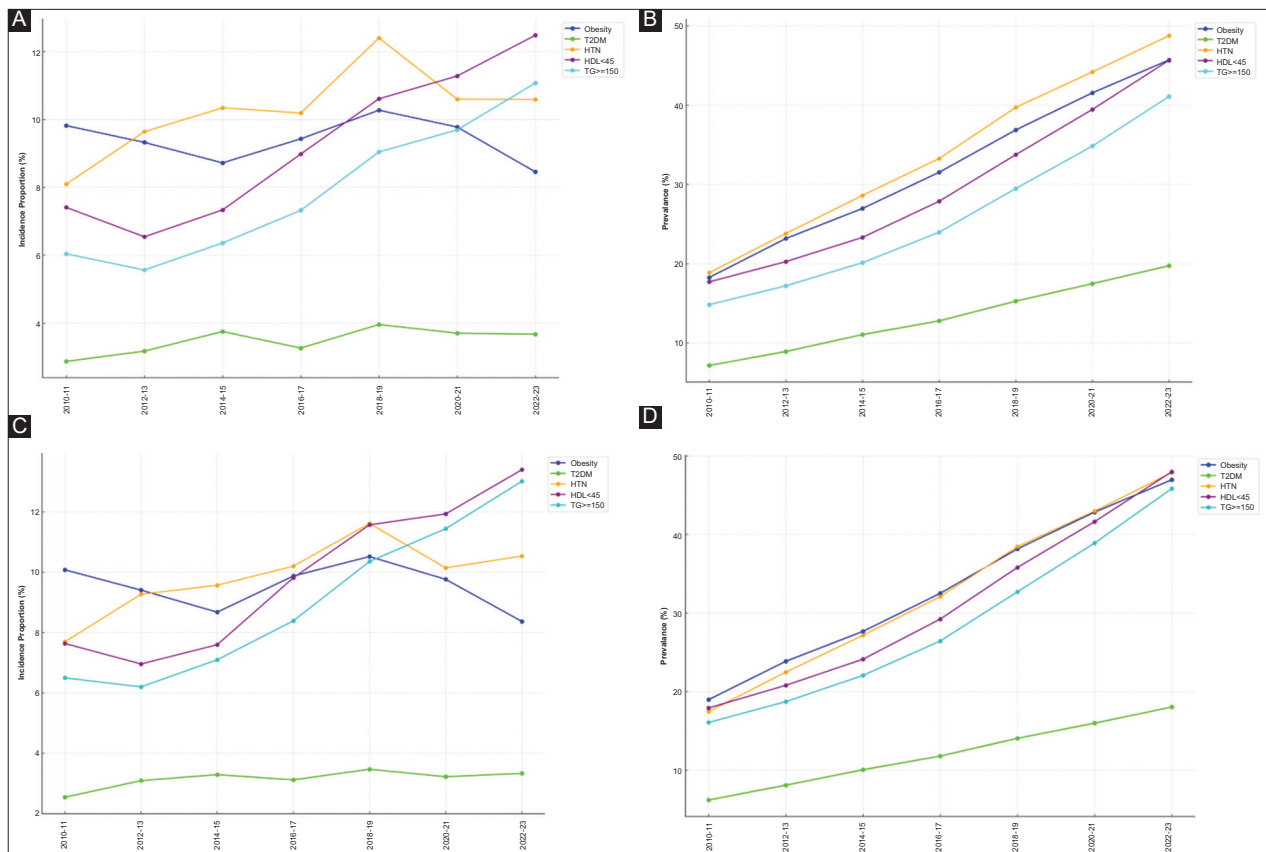


Figure 1 Incidence proportion (A1, A2) and prevalence (B1, B2) of each component of metabolic syndrome in patients with ulcerative colitis (1) and Crohn's disease (2) from 2010-2023

a MetS prevalence of 32.4% and 34.3% among these groups. Previously a meta-analysis reported that the prevalence of MetS is significantly higher in UC (38.2%, 95%CI 20.4-59.9%) compared to CD (13.6%, 95%CI 6.4-26.7%), with sensitivity analyses suggesting up to twice the risk in UC (OR 2.11, 95%CI 1.19-3.74) [11]. This was probably due to variations in study design, study setting and prevalence of MetS in IBD in the studies included.

In terms of risk factors, our study reported that MetS was much more prevalent in the older age group (>65 years) with 46.8% in UC and 50% in CD. Similarly, a study by Nagahori *et al* reported that patients with IBD and MetS were significantly older than those without at the time of evaluation (50.2 ± 15.0 vs. 38.0 ± 11.9 years, $P=0.013$), and at the time of diagnosis (41.6 ± 16.7 vs. 30.9 ± 11.5 years, $P=0.011$), with age identified as an independent predictor of MetS (OR 1.064, 95%CI 1.017-1.114) [30]. Similarly, Fitzmorris *et al* reported that patients with IBD and MetS were older as compared with those without MetS ($P<0.001$) [37]. Our study also reported that male patients were more likely to have MetS and IBD. Nagahori *et al* reported that the prevalence of MetS was higher in male patients with IBD (21.1%) than in females (12.9%), but the difference was not statistically significant ($P=0.414$) [30]. This difference was probably due to the small sample size in the comparison study. The racial and ethnic distribution of both IBD and

MetS in the US remains poorly understood, with a significant paucity of data. A recent study by Lewis *et al* reported that IBD prevalence is nearly twice as high among non-Hispanic White Americans, compared to Black, Hispanic and Asian Americans [38]. Similarly, national data reveal notable racial disparities in MetS prevalence, with non-Hispanic Black men showing lower rates, but non-Hispanic Black women exhibiting higher rates compared to their White counterparts [6]. However, our study is the first to highlight that MetS is more prevalent among the Black and Hispanic populations within the IBD cohort. On a similar note, a study by Zhang *et al* reported that patients from China have a lower prevalence of MetS compared to non-Hispanic Whites, non-Hispanic Blacks and Mexican Americans across all age groups [39]. This supports our finding that the Asian patients with IBD had a lower prevalence of MetS compared to other racial and ethnic groups. Future research exploring the underlying causes of MetS in patients with IBD is essential to understanding how risk factors contribute to racial and ethnic disparities in its prevalence, providing insights into the inequalities observed among diverse population groups over time.

Recent epidemiologic data indicate that the burden of MetS in the general US adult population now ranges from 34-36% [40,41]. For instance, a 2023 analysis of National Health and Nutrition Examination Survey data (2011-2018)

Table 4 Association of metabolic syndrome with 5-year clinical outcomes in ulcerative colitis and Crohn's disease: propensity-matched cohorts

Ulcerative colitis (UC)						
5-year Outcomes	Cohort (n=9,850)	N	%	aOR	95%CI	P-value
Advanced therapy use	UC MetS	2469	25.06%	1.07	1.009-1.15	0.02
	Control	2334	23.69%			
Colectomy	UC MetS	1502	15.24%	1.47	1.35-1.59	<0.001
	Control	1074	10.90%			
IV steroid use	UC MetS	2018	20.48%	1.86	1.72-2.105	<0.001
	Control	1196	12.14%			
Oral steroid use	UC MetS	4291	43.56%	1.58	1.50-1.68	<0.001
	Control	3220	32.69%			
Crohn's disease (CD)						
5-year outcomes	Cohort (n=10,563)	N	%	aOR	95%CI	P-value
Advanced therapy use	CD MetS	4501	42.61%	0.95	0.90-1.008	0.09
	Control	4621	43.74%			
Surgery	CD MetS	2698	25.54%	1.44	1.34-1.53	<0.001
	Control	2032	19.23%			
IV steroid use	CD MetS	2601	24.62%	1.89	1.76-2.02	<0.001
	Control	1556	14.73%			
Oral steroid use	CD MetS	5305	50.22%	1.64	1.55-1.73	<0.001
	Control	4020	38.05%			
Stricture development	CD MetS	2134	20.20%	1.04	0.97-1.11	0.24
	Control	2067	19.56%			
Fistula development	CD MetS	1578	14.93%	0.96	0.89-1.04	0.38
	Control	1623	15.36%			

aOR, adjusted odds ratio; CI, confidence interval; MetS, metabolic syndrome

reported MetS rates exceeding 35%, similar to earlier figures of roughly 34.7% from 2011-2016 [29,42]. Meanwhile, the latest national report notes that the prevalence of obesity among US adults, a major contributor to MetS, has surpassed 40% [29]. Compared to our findings of 32.4-34.3% in patients with IBD, it appears that MetS now affects individuals with IBD at rates mirroring those seen in the general population, underscoring a shift away from the traditional perception that IBD is primarily associated with malnutrition or low body weight. In our study, MetS prevalence correlated with potentially worse disease phenotypes, such as ASUC and stricturing phenotype in CD. This can probably be translated to outcomes in patients with obesity and UC, where in a study by Jain *et al* reported obesity was independently associated in a dose-dependent fashion with worsening disease activity [43]. On the other hand, systemic steroids remain a cornerstone of therapy for acute flares in both UC and CD; however, they are also well recognized to induce or exacerbate features of MetS—such as central obesity, hyperglycemia, and dyslipidemia—through complex effects on glucose metabolism, adipose tissue distribution and insulin sensitivity [44,45]. Prolonged

or repeated steroid use is frequently necessitated by more severe or refractory disease, and can drive weight gain and insulin resistance, heightening the risk for MetS in susceptible individuals. Several reports have documented an increased incidence of obesity and metabolic abnormalities in patients with IBD treated with chronic corticosteroids, underscoring the fact that disease severity, pharmacologic management and cardiometabolic outcomes are closely intertwined [46,47]. Consequently, patients with more aggressive or extensive disease, and those who receive higher cumulative doses of corticosteroid, may be at greater risk for MetS. Our matched analyses also showed higher systemic steroid exposure and greater colectomy/surgery among patients with IBD and MetS, consistent with evidence that obesity, a core MetS component, is linked to worse disease activity, poorer patient-reported outcomes and higher hospitalization risk in IBD [13,37,43]. Therapeutically, MetS may diminish biologic effectiveness and necessitate escalation, as a higher body mass index predicts earlier loss of response to infliximab and dose escalation with adalimumab [48,49]. These data support routine assessment and management of MetS to guide steroid-

sparing, treat-to-target decisions and biologic optimization, aiming to improve long-term outcomes while minimizing corticosteroid-related metabolic harm [13,44-47].

Our study also reports trends of each component of MetS from 2010-2023. The increasing prevalence of MetS in the IBD population parallels trends seen in the general population. MetS, characterized by visceral adiposity, insulin resistance and systemic inflammation, may exacerbate intestinal inflammation and complicate disease management in IBD patients [48,49]. Emerging evidence suggests that MetS components, such as dyslipidemia and HTN, may influence the disease course and therapeutic response, including altered pharmacokinetics of biologic agents. Despite these insights, data on the long-term impact of MetS on IBD progression, complications and comorbidities remain scarce. With MetS rates expected to rise further in this population, integrating targeted interventions, such as lifestyle modification and metabolic risk management into IBD care is crucial for improving outcomes.

The key strengths of our study include its large sample size and real-world nature, which encompasses diverse geographical regions within the US. Our use of clinically pragmatic MetS criteria allows reproducibility in other administrative and claims databases. This large-scale approach can capture trends that smaller or single-center studies might miss, shedding light on the intersection of MetS and IBD in the contemporary era of biologic and small-molecule therapies. Our study reports the prevalence of MetS across different demographic groups and is stratified by disease location, phenotype and medication use.

Our study also has several limitations that merit discussion. First, misclassification bias remains possible, given our reliance on ICD-10-CM and procedure codes. While the accuracy of identification of patients with IBD from an administrative database has been studied, identification of subgroups within patients with IBD, based on disease extent and phenotype, has not been validated. Given our large sample sizes, we utilized a combination of >1 ICD-10-CM codes and procedure codes commonly utilized in clinical practice, which our group felt would increase the accuracy of identifying different subgroups of UC and CD. The definitions of subgroups have been included in the Supplementary document, and can be used in future studies for consistency, as well as validation of diagnostic and procedure codes. Second, our MetS definition used a single HDL threshold for both men and women, and substituted ICD-10-CM codes for waist circumference and blood pressure; comparisons to strictly ATP III-defined cohorts should therefore be interpreted with caution. Third, socioeconomic factors, lifestyle behaviors and medication adherence, which are important in both IBD and MetS, were not fully captured. Fourth, owing to restrictions of the de-identified TriNetX platform, and the lack of patient-level data export and support for user-defined time-to-event endpoints, we could not construct a comprehensive multivariable “independent predictors” model or implement a Cox proportional hazards analysis for our composite IBD outcome; future studies with patient-level datasets

are needed to address these questions rigorously. Finally, as with all database studies, there is always concern over misdiagnosis, residual confounding and under-reporting of some variables.

In conclusion, our study highlights the epidemiology of MetS among patients with IBD in the US, with a prevalence of more than one-third of patients with UC and CD. This rising trend mirrors broader societal shifts in metabolic dysfunction, and underscores the association of MetS with severe IBD phenotypes. Future research should explore the mechanistic interplay between metabolic and inflammatory pathways to guide targeted interventions and to clarify whether metabolic interventions could favorably alter the disease course or improve treatment outcomes in IBD. These findings provide critical insights into the evolving epidemiology of IBD and offer a foundation for strategies to improve patient outcomes while addressing health disparities.

Summary Box

What is already known:

- Metabolic syndrome (MetS) affects about one-third of United States (US) adults and is rising with population aging and obesity
- Inflammatory bowel disease (IBD) and MetS share inflammatory and metabolic pathways, but contemporary large US data quantifying MetS in IBD have been limited and heterogeneous
- The clinical impact of MetS on IBD course (e.g., need for steroids or surgery) is incompletely defined

What the new findings are:

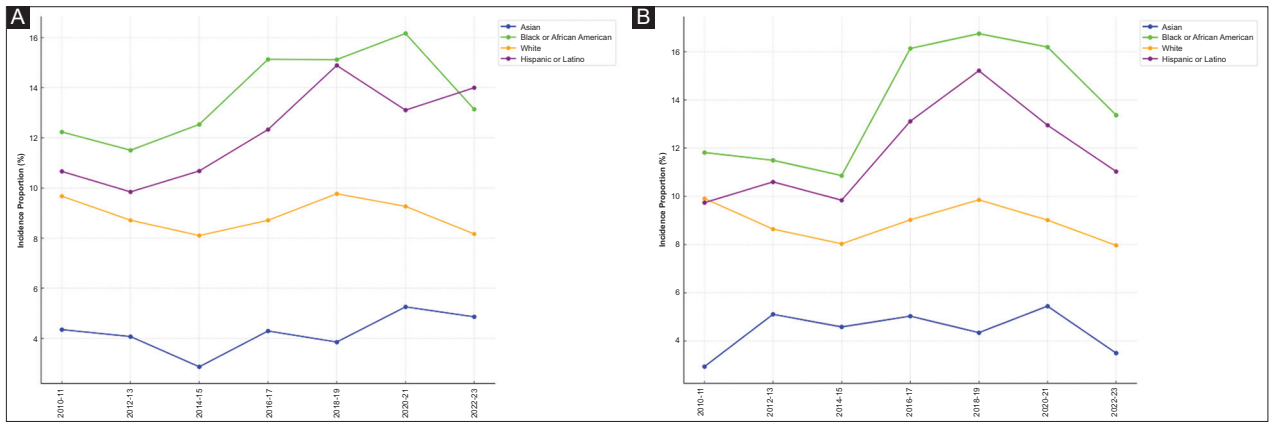
- From 2010-2023, one-third of patients with ulcerative colitis (UC) and Crohn's disease (CD) met the criteria for MetS
- MetS prevalence rises steeply with age, is higher in men, and is greatest among Black, Hispanic and American Indian patients; Asian patients have the lowest prevalence
- MetS clusters with more extensive/severe IBD phenotypes (pancolitis, acute severe UC, stricturing CD, prior CD surgery); advanced-therapy use is not associated with higher MetS prevalence (and is lower than 5-aminosalicylic acid use in UC)
- After propensity matching, MetS is associated with greater systemic steroid exposure and higher surgery/colectomy rates, while stricture and fistula risks are similar

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Supplementary material



Supplementary Figure 1 Incidence proportion of obesity based on race in patients with (A) ulcerative colitis and (B) Crohn's disease from 2010-2023

Supplementary Table 1 ICD-10-CM, Rxnorm and/or CPT codes utilized in the identification of different variables in the UC and CD cohort

Variable	Term	ICD-10-CM or Rxnorm or CPT code
Pancolitis	Ulcerative (chronic) pancolitis	K51.0
Left sided colitis	Left sided colitis	K51.5
Ulcerative proctosigmoiditis	Ulcerative (chronic) rectosigmoiditis	K51.3
Ulcerative proctitis	Ulcerative (chronic) proctitis	K51.2
5-ASA	Mesalamine	52582
	Sulfasalazine	9524
	Balsalazide	18747
	Olsalazine	32385
Advanced therapy	Infliximab	191831
	Adalimumab	327361
	Golimumab	819300
	Certolizumab	709271
	Vedolizumab	1538097
	Ustekinumab	847083
	Tofacitinib	1357536
	Upadacitinib	2196092
	Ozanimod	2288236
	Risankizumab	2166040
Acute severe ulcerative colitis	Intravenous methylprednisolone	6902
	Intravenous hydrocortisone	5492
IPAA	Colectomy, total, abdominal, with proctectomy; with ileoanal anastomosis, includes loop ileostomy, and rectal mucosectomy, when performed	44157
	Colectomy, total, abdominal, with proctectomy; with ileoanal anastomosis, creation of ileal reservoir (S or J), includes loop ileostomy, and rectal mucosectomy, when performed	44158
	Laparoscopy, surgical; colectomy, total abdominal, with proctectomy, with ileoanal anastomosis, creation of ileal reservoir (S or J), with loop ileostomy, includes rectal mucosectomy, when performed	44211
	Proctectomy, partial, with rectal mucosectomy, ileoanal anastomosis, creation of ileal reservoir (S or J), with or without loop ileostomy	45113
	Colectomy, total, abdominal, with proctectomy	1007468
	Colectomy, total, abdominal, with proctectomy; with ileostomy	44155
	Colectomy, total, abdominal, with proctectomy; with continent ileostomy	44156
	Laparoscopy, surgical; colectomy, total, abdominal, with proctectomy, with ileostomy	44212
	Laparoscopy, surgical, closure of enterostomy, large or small intestine, with resection and anastomosis	44227
	Closure of enterostomy, large or small intestine, with resection and anastomosis other than colorectal	44625
	Closure of enterostomy, large or small intestine	44620

ICD-10-CM, International Classification of Disease, Tenth Revision, Clinical Modification; CPT, current procedural terminology; UC, ulcerative colitis; CD, Crohn's disease; 5-ASA, 5-aminosalicylic acid; IPAA, ileal pouch-anal anastomosis

Supplementary Table 2 ICD-10-CM, Rxnorm and/or CPT codes utilized in the identification of different variables in the CD cohort

Variable	Term	ICD-10-CM or Rxnorm or CPT code
Small bowel disease	Crohn's disease of small intestine	K50.0
Large bowel disease	Crohn's disease of large intestine	K50.1
Small and large bowel disease	Crohn's disease of both small and large intestine	K50.8
Stricturing disease	Other and unspecified intestine obstruction	K56.6
	Crohn's disease of both small and large intestine with intestinal obstruction	K50.812
	Crohn's disease of large intestine with intestinal obstruction	K50.112
	Crohn's disease of small intestine with intestinal obstruction	K50.012
	Gastrointestinal System/Dilation/Sigmoid colon	0D7N
	Gastrointestinal System/Dilation/Anus	0D7Q
	Gastrointestinal System/Dilation/Descending colon	0D7M
	Gastrointestinal System/Dilation/Rectum	0D7P
	Gastrointestinal System/Dilation/Transverse Colon	0D7L
	Gastrointestinal System/Dilation/Small intestine	0D78
	Gastrointestinal System/Dilation/Ascending colon	0D7K
	Gastrointestinal System/Dilation/Jejunum	0D7A
	Gastrointestinal System/Dilation/Cecum	0D7H
	Gastrointestinal System/Dilation/Duodenum	0D79
	Gastrointestinal System/Dilation/Ileum	0D7B
	Gastrointestinal System/Dilation/Ileocecal Valve	0D7C
	Gastrointestinal System/Dilation/Large Intestine	0D7E
	Gastrointestinal System/Dilation/Large intestine, Right	0D7F
	Gastrointestinal System/Dilation/Large intestine, Left	0D7G
	Gastrointestinal System/Dilation/Ileocecal valve	0D7C
	Sigmoidoscopy, flexible; with transendoscopic balloon dilation	45386
	Colonoscopy, flexible; with transendoscopic balloon dilation	45386
Fistulizing disease	Crohn's disease of both small and large intestine with fistula	K50.813
	Crohn's disease of large intestine with fistula	K50.113
	Crohn's disease of small intestine with fistula	K50.013
	Vesicointestinal fistula	N32.1
	Anorectal fistula	K60.5
	Rectal fistula	K60.4
	Anal fistula	K60.3
	Fistula of vagina to small intestine	N82.2
	Fistula of vagina to large intestine	N82.3
	Fistula of stomach and duodenum	K31.6
	Fistula of intestine	K63.2
Surgery	Enterectomy, resection of small intestine	1007438
	Colectomy, partial	1007455
	Colectomy, total, abdominal, without proctectomy	1007463
	Colectomy, total, abdominal, with proctectomy	1007468
	Colectomy, partial, with removal of terminal ileum with ileocolostomy	44160

(Contd...)

Supplementary Table 2 (*Continued*)

Variable	Term	ICD-10-CM or Rxnorm or CPT code
	Laparoscopic Excision Procedures on the Intestines	1007479
	Gastrointestinal System/Excision or Resection/Small intestine	0DB8, 0DT8
	Gastrointestinal System/Excision or Resection/Duodenum	0DB9, 0DT9
	Gastrointestinal System/Excision or Resection/Jejunum	0DBA, 0DTA
	Gastrointestinal System/Excision or Resection/Ileum	0DBB, 0DTB
	Gastrointestinal System/Excision or Resection/Ileocecal valve	0DBC, 0DTC
	Gastrointestinal System/Excision or Resection/Large intestine	0DBE, 0DTE
	Gastrointestinal System/Excision or Resection/Large intestine, Right	0DBF, 0DTF
	Gastrointestinal System/Excision or Resection/Large intestine, Left	0DBG, 0DTG
	Gastrointestinal System/Excision or Resection/Cecum	0DBH, 0DTH
	Gastrointestinal System/Excision or Resection/Ascending Colon	0DBK, 0DTK
	Gastrointestinal System/Excision or Resection/Transverse Colon	0DBL, 0DTL
	Gastrointestinal System/Excision or Resection/Descending Colon	0DBM, 0DTM
	Gastrointestinal System/Excision or Resection/Sigmoid Colon	0DBN, 0DTN
	Gastrointestinal System/Excision or Resection/Rectum	0DBP, 0DTP

ICD-10-CM, *International Classification of Disease, Tenth Revision, Clinical Modification*; CPT, *current procedural terminology*; UC, *ulcerative colitis*; 5-ASA, *5-aminosalicylic acid*; IPAA, *ileal pouch-anal anastomosis*

Supplementary Table 3 Incidence proportion, prevalence and incidence rate (cases per 1000 person years) of obesity by sex and race in patients with ulcerative colitis and Crohn's disease

Ulcerative colitis							
Incidence proportion % (N)							
Sex	2010-11	2012-13	2014-15	2016-17	2018-19	2020-21	2022-23
Female	9.769% (1685)	9.075% (1694)	8.282% (1635)	9.163% (1831)	10.245% (2001)	9.795% (1752)	8.542% (1316)
Male	9.624% (1382)	8.994% (1426)	8.339% (1421)	8.856% (1546)	9.854% (1717)	9.502% (1537)	8.334% (1167)
Race	2010-11	2012-13	2014-15	2016-17	2018-19	2020-21	2022-23
Asian	4.342% (33)	4.065% (35)	2.857% (28)	4.287% (46)	3.846% (43)	5.249% (60)	4.853% (51)
Black or African American	12.233% (298)	11.503% (287)	12.534% (321)	15.131% (376)	15.121% (362)	16.164% (343)	13.138% (224)
White	9.669% (2473)	8.709% (2412)	8.096% (2389)	8.706% (2610)	9.765% (2864)	9.262% (2496)	8.161% (1901)
Hispanic or Latino	10.658% (141)	9.84% (148)	10.676% (177)	12.329% (207)	14.887% (244)	13.103% (190)	13.998% (167)
Prevalence % (N)							
Sex	2010-11	2012-13	2014-15	2016-17	2018-19	2020-21	2022-23
Female	18.752% (3592)	23.645% (5256)	27.271% (6789)	31.785% (8458)	37.281% (10420)	42.066% (11715)	46.291% (12145)
Male	17.705% (2792)	22.471% (4182)	26.025% (5495)	30.123% (6859)	35.084% (8489)	39.587% (9592)	43.692% (9960)
Race	2010-11	2012-13	2014-15	2016-17	2018-19	2020-21	2022-23
American Indian or Alaska Native	27.397% (20)	30% (27)	33.333% (35)	40.179% (45)	42.735% (50)	45.045% (50)	49.057% (52)
Asian	8.207% (65)	10.799% (100)	11.606% (125)	13.987% (167)	16.731% (216)	19.896% (269)	23.313% (304)
Black or African American	21.339% (580)	28.078% (862)	34.253% (1167)	41.805% (1515)	48.15% (1887)	54.779% (2155)	59.995% (2221)
Native Hawaiian or Pacific Islander	26.667% (12)	26.531% (13)	31.579% (18)	34.426% (21)	37.313% (25)	39.394% (26)	40.299% (27)
White	18.129% (5116)	22.828% (7479)	26.362% (9709)	30.572% (12051)	35.86% (14796)	40.417% (16588)	44.527% (17171)
Hispanic or Latino	17.803% (256)	22.823% (401)	27.65% (566)	33.902% (755)	41.607% (994)	47.258% (1129)	53.172% (1165)
Incidence rate (cases per 1000 person-years)							
Sex	2010-11	2012-13	2014-15	2016-17	2018-19	2020-21	2022-23
Female	57.34	51.87	47.48	58.44	56.98	54.42	51.5
Male	56.98	52.23	48.21	56.98	55.52	53.33	51.14
Race	2010-11	2012-13	2014-15	2016-17	2018-19	2020-21	2022-23
Asian	24.47	22.65	16.07	27.03	20.82	29.22	28.12
Black or African American	73.05	66.11	73.05	100.08	88.39	94.23	77.8
White	56.98	49.67	46.39	55.52	54.42	51.5	49.31
Hispanic or Latino	63.19	58.81	62.46	81.09	88.03	78.16	86.39

(Contd...)

Supplementary Table 3 (Continued)

Crohn's disease											
Incidence proportion % (N)											
Sex		2010-11	2012-13	2014-15	2016-17	2018-19	2020-21	2022-23			
Female		10.677% (1764)	10.022% (1776)	8.899% (1638)	10.352% (1923)	11.273% (1998)	10.49% (1675)	9.166% (1246)			
Male		9.089% (1167)	8.155% (1153)	7.602% (1154)	8.608% (1336)	9.344% (1420)	8.611% (1208)	7.403% (900)			
Race		2010-11	2012-13	2014-15	2016-17	2018-19	2020-21	2022-23			
Asian		2.941% (13)	5.108% (26)	4.584% (27)	5.032% (31)	4.348% (29)	5.446% (36)	3.5% (21)			
Black or African American		11.81% (308)	11.49% (313)	10.856% (302)	16.123% (450)	16.738% (429)	16.183% (357)	13.364% (234)			
White		9.908% (2371)	8.637% (2211)	8.031% (2170)	9.023% (2475)	9.851% (2593)	9.011% (2160)	7.965% (1646)			
Hispanic or Latino		9.733% (91)	10.595% (114)	9.836% (114)	13.108% (151)	15.201% (166)	12.944% (124)	11.028% (88)			
Prevalence % (N)											
Sex		2010-11	2012-13	2014-15	2016-17	2018-19	2020-21	2022-23			
Female		20.785% (3872)	26.013% (5606)	29.854% (7137)	34.749% (8869)	40.705% (10795)	45.637% (11999)	50.063% (12378)			
Male		16.705% (2341)	21.053% (3463)	24.432% (4535)	28.767% (5728)	33.98% (7091)	38.205% (7926)	41.93% (8129)			
Race		2010-11	2012-13	2014-15	2016-17	2018-19	2020-21	2022-23			
American Indian or Alaska Native		24.176% (22)	31.429% (33)	35.537% (43)	37.984% (49)	46.377% (64)	53.333% (72)	57.813% (74)			
Asian		6.332% (29)	10.223% (55)	12.733% (82)	16.069% (112)	18.205% (142)	21.973% (176)	24.215% (185)			
Black or African American		20.635% (598)	27.292% (905)	32.554% (1197)	40.839% (1616)	48.935% (2045)	55.691% (2324)	60.932% (2366)			
Native Hawaiian or Pacific Islander		33.333% (10)	29.73% (11)	35.897% (14)	36.585% (15)	47.619% (20)	45.238% (19)	50% (21)			
White		18.838% (5004)	23.428% (7156)	26.95% (9168)	31.307% (11374)	36.88% (13865)	41.324% (15360)	45.432% (15835)			
Hispanic or Latino		17.092% (174)	22.793% (284)	27.481% (396)	34.788% (534)	42.945% (697)	48.487% (785)	52.635% (789)			
Incidence rate (cases per 1000 person-years)											
Sex		2010-11	2012-13	2014-15	2016-17	2018-19	2020-21	2022-23			
Female		63.19	57.71	51.14	66.48	63.19	58.81	55.15			
Male		53.69	46.75	43.46	55.15	52.23	48.21	44.93			
Race		2010-11	2012-13	2014-15	2016-17	2018-19	2020-21	2022-23			
Asian		17.17	28.85	26.3	31.05	24.11	29.95	20.09			
Black or African American		69.76	66.11	62.46	108.48	98.62	95.7	79.62			
White		58.44	49.31	45.66	57.71	54.79	50.04	47.48			
Hispanic or Latino		57.34	63.19	56.61	86.2	88.76	75.61	67.94			