

Introduction

- Crohn’s disease (CD) is a chronic inflammatory bowel disease marked by immune dysregulation in a genetically predisposed individual.
 - The disease is often progressive, and complications frequently require hospitalization and surgical intervention.
- CD is increasingly being treated with biologic therapies as many patients fail to achieve lasting, side-effect-free remission with conventional therapy (i.e., corticosteroids and immunomodulators).
- Although therapeutic costs have steadily risen over the last decade due to the increased uptake of costly biologics, hospitalizations still account for about half of direct CD-related costs.
 - Direct costs paid by US health plans are estimated to be \$18,637 per member per year.

Research Objectives

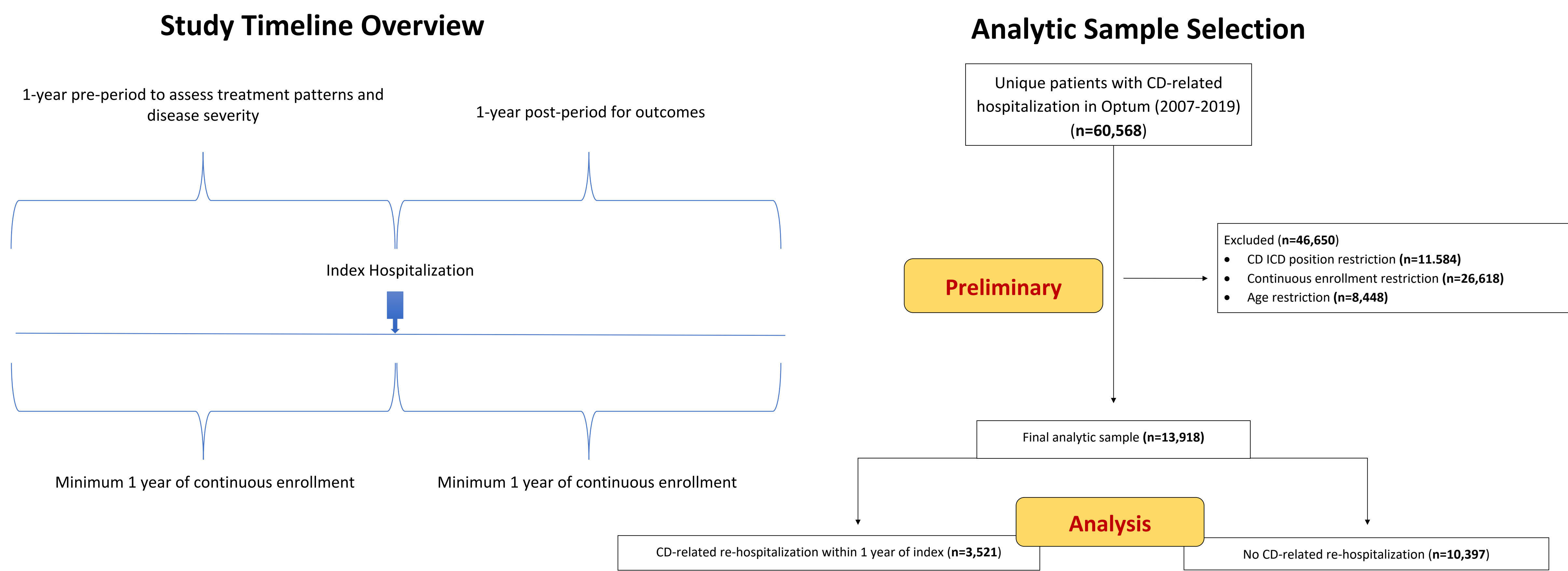
The objectives of this study were to:

- Characterize sociodemographic characteristics, healthcare resource utilization, and health outcomes in patients initially hospitalized for CD
- Analyze the association between CD-related rehospitalization, healthcare resource utilization, clinical comorbidities, and sociodemographic characteristics
- Assess the potential of CD severity confounding the causal effect of biologic therapies on health outcomes

Methods

- This retrospective observational study identified a cohort of hospitalized CD patients using de-identified administrative claims from the Optum Clinformatics® Data Mart (2007-2019).
- Included patients were aged 18-64, had an index inpatient claim with a primary or secondary CD ICD code, and were continuously enrolled for 1 year pre- and post-index hospitalization. The earliest claim that satisfies each of the above criteria was considered the patient’s “index hospitalization.”
- All characteristics were compared across the primary health outcome: CD-related rehospitalization within 1 year of discharge from index hospitalization.
 - Differences were tested via t test for continuous variables and Pearson χ^2 test for categorical variables.
- Sociodemographic controls: age, year of index, gender, education, income, geography, race, and insurance type.
- Baseline healthcare resource utilization characteristics were categorized into index hospitalization (admission type, admission origin, length of stay, transfer of care during stay, total cost) or within 1 year prior to start of index hospitalization (biologic use and count, other therapy use, CD-related procedures, gastroenterologist visits, CD-related hospitalization or emergency department visits, and CD-related costs).
- CD-related comorbidities were included based on clinician recommendation and were measured in the year prior to index.
- CD-related health outcomes and resource utilization at index were compared across presence of biologic use in the pre-period.

Methods (continued...)



Results

Variable†	Re-hospitalized (n=3521)	Not Re-hospitalized (n=10397)	P Value‡
Age at index, mean (SD, min-max)	40.1 (13.4, 18-64)	43.2 (12.8, 18-64)	<0.0001
Year of index, No. (%)			
2008	491 (13.9)	1,174 (11.3)	
2009	352 (10.0)	1,038 (9.9)	
2010	338 (9.6)	1,010 (9.7)	
2011	325 (9.2)	1,050 (10.2)	
2012	320 (9.1)	1,000 (9.7)	
2013	300 (8.5)	863 (8.3)	0.004
2014	271 (7.7)	865 (8.3)	
2015	244 (6.9)	821 (7.9)	
2016	283 (8.0)	802 (7.7)	
2017	309 (8.8)	881 (8.5)	
2018	298 (8.5)	892 (8.6)	
Education, No. (%)			
HS diploma or less	843 (23.9)	2,392 (23.0)	
Some college	2,995 (86.7)	9,809 (95.9)	0.16
Bachelor's or more	672 (19.3)	2,185 (20.8)	
Unknown	11 (0.3)	31 (0.3)	
Household income, No. (%)			
<\$50k	843 (23.9)	2,299 (22.0)	
\$50k-\$74k	510 (14.5)	1,529 (14.7)	
\$75k-\$99k	478 (13.6)	1,554 (15.0)	0.001
\$100k+	2,009 (58.1)	5,766 (56.2)	
Unknown	490 (13.9)	1,295 (12.3)	
Race, No. (%)			
White	2,768 (78.6)	8,067 (77.6)	
Black	385 (10.9)	1,082 (10.2)	0.009
Hispanic	236 (6.7)	761 (7.3)	
Asian	48 (1.4)	231 (2.2)	
Unknown	84 (2.4)	276 (2.7)	
Division, No. (%)			
New England	148 (4.2)	431 (4.2)	
Middle Atlantic	245 (7.0)	864 (8.3)	
East North Central	370 (10.2)	1,223 (11.6)	
West North Central	459 (13.0)	1,321 (12.8)	
South Atlantic	355 (9.9)	1,047 (10.0)	0.09
East South Central	336 (9.5)	995 (9.6)	
West South Central	432 (12.3)	1,276 (12.3)	
Mountain	278 (7.7)	804 (7.7)	
Pacific	220 (6.3)	719 (6.9)	
Unknown	6 (0.2)	7 (0.1)	
Female, No. (%)	2,009 (57.1)	5,834 (56.3)	
Unknown	1 (0.0)	1 (0.0)	0.44
Insurance type, No. (%)			
Medicaid	2,119 (60.2)	6,490 (62.4)	
Medicare	569 (16.2)	1,801 (17.4)	0.06
Private	855 (24.1)	2,564 (24.8)	
Other	238 (6.8)	830 (8.0)	
Unknown	240 (6.8)	610 (5.9)	
CDH, No. (%)			
CDH	233 (6.6)	708 (6.8)	
HS	325 (9.2)	1,099 (10.5)	0.007
None	232 (6.6)	697 (6.7)	
Unknown	815 (23.2)	2,438 (23.5)	
Insurance plan switched in year pre-index, No. (%)	355 (10.1)	776 (7.5)	0.66

Variable, No. (%)	Re-hospitalized (n=3521)	Not Re-hospitalized (n=10397)	P Value‡
CD-related			
Rectal bleed	420 (11.9)	899 (8.7)	<0.0001
Abscess	351 (10.0)	586 (5.6)	<0.0001
Anemia	1,107 (31.4)	2,122 (20.4)	<0.0001
Bowel obstruction	699 (19.9)	1,273 (12.3)	<0.0001
Nausea and vomiting	882 (25.1)	1,693 (16.3)	<0.0001
Nausea	1,193 (33.9)	2,242 (21.5)	<0.0001
Vomiting	1,022 (29.0)	1,989 (19.1)	<0.0001
Weightloss	419 (11.9)	698 (6.7)	<0.0001
Malnutrition	283 (8.0)	413 (4.0)	<0.0001
Fistula	393 (11.2)	596 (5.7)	<0.0001
C. difficile infection	96 (2.7)	170 (1.6)	<0.0001
Abdominal pain	2,364 (67.1)	5,439 (52.3)	<0.0001
GI hemorrhage	242 (6.9)	503 (4.8)	<0.0001
Sepsis	169 (5.2)	271 (2.6)	<0.0001
Diarrhea	1,374 (39.0)	2,900 (27.9)	<0.0001
Intestinal perforation	47 (1.3)	93 (0.9)	0.02

Variable†	Re-hospitalized (n=3521)	Not Re-hospitalized (n=10397)	P Value‡
Index Hospitalization			
Admission type, No. (%)			
Emergency	2,019 (57.4)	5,402 (52.0)	
Urgent	534 (15.2)	1,484 (14.3)	<0.0001
Elective	578 (16.4)	2,397 (23.0)	
Other	5 (0.1)	28 (0.3)	
Unknown	385 (10.9)	1,086 (10.4)	
Admission origin, No. (%)			
Physician Referral	2,155 (61.2)	6,533 (62.8)	
Clinic Referral	314 (8.9)	1,013 (9.7)	0.03
Emergency Room	590 (16.8)	1,525 (14.7)	
Other	87 (2.5)	250 (2.4)	
Unknown	375 (10.6)	1,076 (10.4)	
Length of stay, mean days (SD, min-max)	6.6 (15.8, 0-427)	5.6 (9.2, 0-289)	0.0001
Transfer of care during stay, No. (%)	89 (2.5)	233 (2.2)	0.33
Within 1 Year Prior to Start of Index Hospitalization			
Any biologic, No. (%)	1,184 (33.6)	2,091 (20.1)	<0.0001
TNF inhibitor	1,117 (31.3)	1,991 (19.2)	<0.0001
Infliximab	531 (15.1)	1,039 (10.0)	<0.0001
Biosimilar	28 (0.8)	33 (0.3)	0.0002
Adalimumab	459 (12.8)	813 (7.8)	<0.0001
Certolizumab pegol	208 (5.9)	292 (2.8)	<0.0001
Non-TNF inhibitor	109 (3.1)	150 (1.4)	<0.0001
Vedolizumab	76 (2.2)	115 (1.1)	<0.0001
Ustekinumab	42 (1.2)	42 (0.4)	<0.0001
Biologic count, No. (%)			
0	2,337 (66.4)	8,306 (79.9)	<0.0001
1	1,024 (29.1)	1,896 (18.2)	
2	150 (4.2)	180 (1.7)	
3	10 (0.3)	15 (0.2)	
Any steroid, No. (%)	1,786 (50.7)	3,780 (36.4)	<0.0001
Oral	1,619 (46.0)	3,285 (31.6)	<0.0001
Intravenous	117 (3.3)	117 (1.1)	<0.0001
Any immunomodulator, No. (%)	304 (8.6)	612 (5.9)	<0.0001
Thiopurine	266 (7.6)	551 (5.3)	0.004
Methotrexate	38 (1.1)	63 (0.6)	
ASA, No. (%)	391 (11.1)	504 (4.9)	0.27
Colectomy, No. (%)	67 (1.9)	175 (1.7)	0.39
Small bowel resection, No. (%)	41 (1.2)	87 (0.8)	0.08
Exam under anesthesia, No. (%)	30 (0.9)	36 (0.4)	0.0002
Incision and drainage, No. (%)	175 (5.0)	327 (3.2)	<0.0001
PICC insertion, No. (%)	104 (3.0)	115 (1.1)	<0.0001
Fistula-related procedure, No. (%)	60 (1.7)	77 (0.7)	<0.0001
Ileostomy, No. (%)	58 (1.7)	109 (1.1)	0.005
Colostomy, No. (%)	19 (0.5)	54 (0.5)	0.89
Colonoscopy/sigmoidoscopy, No. (%)	1,400 (39.8)	3,239 (31.2)	<0.0001
EGD, No. (%)	153 (4.4)	227 (2.2)	<0.0001
Feeding tube placement, No. (%)	40 (1.1)	64 (0.6)	0.002
Total parenteral nutrition, No. (%)	109 (3.1)	141 (1.4)	<0.0001
Gastroenterologist visit, No. (%)	2,958 (73.8)	5,912 (56.9)	<0.0001
Unique gastroenterologists, No. (%)			
0	923 (26.2)	448 (4.3)	
1	1,577 (44.8)	3,990 (38.4)	<0.0001
2	545 (15.5)	1,199 (11.5)	
>2	476 (13.5)	723 (7.0)	
CD hospitalization, No. (%)	508 (14.4)	401 (3.9)	<0.0001
CD hospitalization count, No. (%)			
0	3,013 (86.6)	9,996 (96.1)	<0.0001
1	276 (7.8)	309 (3.0)	
2-3	170 (4.8)	97 (1.0)	
>3	62 (1.8)	11 (0.1)	
CD ED visit, No. (%)	274 (7.8)	415 (4.0)	<0.0001
CD ED visit count, No. (%)			
0	3,247 (92.2)	9,982 (96.0)	<0.0001
1	165 (4.7)	309 (3.0)	
2-3	88 (2.3)	81 (0.8)	
>3	29 (0.8)	25 (0.2)	

* Patients are considered “re-hospitalized” if a CD-related hospitalization occurred within 1 year post index hospitalization.
 † Mean, standard deviation, minimum and maximum reported for continuous variables. Frequencies and percentages reported for categorical variables.
 ‡ Differences between groups were tested via t test for continuous variables and Pearson χ^2 test for categorical variables.
 ASA: aminosalicylic acid; CD: Crohn’s disease; ED: emergency department; EGD: esophagogastroduodenoscopy; PICC: peripherally inserted central catheter; TNF: tumor necrosis factor

Results (continued...)

- Mean age at index hospitalization differed significantly between re-hospitalized and not re-hospitalized patients (respectively 40.1 and 43.2, $P<0.001$).
- Lower income and black race were associated with rehospitalization.
- Most CD-related comorbidities and procedures were strongly associated ($P<0.001$) with re-hospitalization.
- Any biologic use in the pre-index period was strongly associated with rehospitalization (33.6% vs 20.1%, $P<0.001$)
 - This strong association was consistent across biologic type (TNF inhibitor vs. other).
- Biologic use in the pre-period was strongly associated with presence of CD-related comorbidities (e.g., fistula) and procedures (e.g., small bowel resection, colectomy, ileostomy) at index hospitalization.

Conclusions

- Clinical and utilization variables are strongly associated with CD rehospitalization and may prove to be useful for predictive modeling.
- Isolating the effect of biologics on health outcomes is challenging due to confounding by unobserved disease severity.
- Analyses that identify the causal impact of biologics on health outcomes and resource utilization are needed.

Limitations

- Objective markers of disease severity (e.g., biomarker labs and diagnostic results) that may have significant associative power were not available.
- Patient treatment history and disease activity prior to presence in Optum data is unknown.
- Historical SES data is not kept by Optum; values are from the recent past and may not reflect actual values present on the index date.

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