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ORIGINAL RESEARCH ARTICLE

Identifying Measures of Suboptimal Healthcare Interaction (SOHI) to Develop a Claims-Based Model for Predicting Patients with Inflammatory Bowel Disease at Risk for SOHI

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Abstract

Background Understanding the demographic and clinical characteristics of patients with Inflammatory Bowel Disease (IBD) who are likely to experience poor disease outcomes may allow early interventions that can improve health outcomes.

Objectives To describe demographic and clinical characteristics of patients with ulcerative colitis (UC) and Crohn's disease (CD) with the presence of at least one Suboptimal Healthcare Interaction (SOHI) event, which can inform the development of a model to predict SOHI in members with IBD based on insurance claims, with the goal of offering these patients some additional intervention.

Methods We identified commercially insured individuals with IBD between 01 January 2019 and 31 December 2019 using Optum Labs' administrative claims database. The primary cohort was stratified on the presence or absence of ≥ 1 SOHI event (a SOHI-defining data point or characteristic at a specific time point) during the baseline observation period. SOHI was deployed as the basis for the development of a model to predict which individuals with IBD were most likely to continue to have SOHI within a 1-year timeframe (follow-up SOHI) using insurance claims data. All baseline characteristics were analyzed descriptively. Multivariable logistic regression was used to examine the association of follow-up SOHI with baseline characteristics.

Results Of 19,824 individuals, 6872 (34.7%) were found to have follow-up SOHI. Individuals with follow-up SOHI were more likely to have had similar SOHI events in the baseline period than those with non-SOHI. A significantly greater proportion of individuals with SOHI had ≥ 1 claims-based C-reactive protein (CRP) test order and ≥ 1 CRP lab results compared with non-SOHI. Individuals with follow-up SOHI were more likely to incur higher healthcare expenditures and resource utilization as compared with non-SOHI individuals. A few of the most important variables used to predict follow-up SOHI included baseline mesalamine use, count of baseline opioid fills, count of baseline oral corticosteroid fills, baseline extraintestinal manifestations of disease, proxy for baseline SOHI, and index IBD provider specialty.

Conclusion Individuals with SOHI are likely to have higher expenditures, higher healthcare resource utilization, uncontrolled disease, and higher CRP lab results as compared with non-SOHI members. Distinguishing SOHI and non-SOHI patients in a dataset could efficiently identify potential cases of poor future IBD outcomes.

Plain Language Summary

We have developed a model for identifying suboptimal healthcare interactions (SOHI) at follow-up and used it to predict the individuals with inflammatory bowel disease (IBD) who are likely to suffer poor healthcare outcomes. Our study showed that the SOHI and non-SOHI cohorts had notable differences in clinical baseline characteristics. Compared with non-SOHI members, individuals with SOHI experienced poor IBD outcomes and incurred higher healthcare resource utilization and costs. Understanding baseline characteristics of patients with SOHI to predict follow-up SOHI can improve health outcomes

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by early identification of patients with IBD who are likely to experience it. This can help in targeting efforts toward additional care, resulting in greater chances of a well-managed disease.

Key Points

By understanding the demographic and clinical characteristics of patients with inflammatory bowel disease (IBD) who are likely to experience poor disease outcomes, it may be possible to provide them with early and targeted interventions, which could result in improved healthcare outcomes. Therefore, we developed a predictive model for identifying follow-up suboptimal healthcare interactions (SOHI) in commercially insured individuals with IBD using claims data.

Our study showed that individuals with SOHI experienced poor IBD outcomes, higher C-reactive protein (CRP) levels, and incurred higher expenditures and healthcare resource utilization costs as compared with non-SOHI members. Based on the final model, some of the most important variables used to predict follow-up SOHI included baseline mesalamine use, baseline targeted immunomodulator use, count of baseline opioid fills, count of baseline oral corticosteroid fills, baseline extraintestinal manifestations of disease, a proxy for baseline SOHI, and index provider specialty.

The application of this model is to timely identify the patients with IBD who are likely to have SOHI and, thereby, maximize patient outcomes effectively by targeting efforts toward additional care. This can result in greater chances of a well-managed disease.

1 Introduction

Inflammatory bowel disease (IBD) including ulcerative colitis (UC) and Crohn's disease (CD), are chronic gastrointestinal disorders characterized by discontinuous phases of remission and relapse of active inflammation [1, 2]. IBD affects around 6.8 million people globally [3]. In the USA, an estimated $30 billion is spent annually [4] for the management of IBD with per member annual costs approaching almost $30,000 [5]. A recent report suggests that the total cost of care for IBD has increased in the last 5 years, and patients with IBD are incurring higher costs associated with healthcare utilization, out-of-pocket expenditures, and workplace productivity losses as compared with non-IBD controls [5].

Advances in therapeutic options for IBD have led to an improvement in the quality of life for individuals with IBD, as well as a reduction in the number of surgeries and hospitalizations [6]. However, many continue to experience poor outcomes and cycle through periods of flares and remissions, with 25–50% of patients expected to relapse within a year [7–11]. Poor IBD outcomes are likely due to a complex series of factors, including individual compliance with provider visits and prescribed therapy, the ability of individuals to access specialty providers, provider adherence to recommended diagnostic and treatment guidelines, and other factors that cannot be directly observed.

If patients who experience suboptimal healthcare interactions (SOHI) can be predicted using insurance claims, then early identification is possible, and intervention can occur, which could lead to better patient outcomes. Therefore, we aimed at describing demographic and clinical characteristics of patients with UC and CD with the presence of at least one SOHI event to inform the development of a model to predict SOHI in members with IBD, based on insurance claims, with the goal of offering these patients some type of additional intervention.

2 Methods

2.1 Definitions

2.1.1 Baseline SOHI (or SOHI)

SOHI was defined operationally as the presence of certain factors available in the claims database that are known or were believed to be relevant, in describing SOHI during baseline observation period.

2.1.2 Follow-up SOHI

Refers to 1 year after baseline period for individuals who would likely experience poor IBD outcomes.

2.1.3 SOHI Event

The term is used broadly as the presence of a SOHI-defining data point or characteristic at a specific point in time. A SOHI event was defined as any one of the following:

I. ≥ 3 all-cause emergency room (ER) visits on different service dates during the follow-up period
II. ≥ 4 oral corticosteroid prescription fills on different dates during the follow-up period
III. ≥ 3 opioid prescription fills on different dates during the follow-up period

IV. ≥ 1 medical claim with a Current Procedural Terminology (CPT) code associated with GI tract surgery during the follow-up period
V. ≥ 1 medical claim with a diagnosis code for extraintestinal manifestations of IBD in any position during the follow-up period
VI. Evidence of anemia of chronic disease
VII. For CD patients: ≥ 1 pharmacy claim associated with mesalamine during the follow-up period.

2.2 Study Design and Patient Selection

This observational retrospective claims-based analysis identified commercially insured individuals with IBD between 01 January 2019 and 31 December 2019 (identification period; Fig. 1).

For the study, individuals were considered to have IBD if there was evidence of at least two medical claims on distinct service dates with a diagnosis of IBD (any billable ICD-10 code underneath K51 that was defined as UC and K50 that was defined as CD) in any position during the identification period. The date of the second diagnosis claim for IBD was set as the index date.

To be included in the final analytic study population, individuals were required to have continuous insurance coverage with medical and pharmacy benefits from 12 months before the index date (baseline period) to 12 months after (and including) the index date (follow-up period). In addition, individuals were also required to have no missing demographic information (age, gender, and region) as of the index date.

2.3 Data Source

Data were extracted from Optum Labs' administrative claims database. The database contains medical, pharmacy, and laboratory claims data with linked enrollment information. Medical claims include services from all venues, including in-patient (IP), outpatient, emergency room (ER), and physician offices. Both medical and pharmacy claims have amounts allowed by both healthcare insurers and patients.

2.4 Ethics Approval

The data were fully de-identified before access by the research team and were used in compliance with the Health Insurance Portability and Accountability Act regulations. This observational study used only previously collected data and did not impose any form of intervention; thus no formal consent to release information or institutional review board approval was required.

2.5 Development of SOHI

We classified individuals at the index date as either having or not having evidence of SOHI based on the definition described above.

In this study, based on clinical expertise and known risk factors for disease severity, a measure termed "SOHI" was developed as a classifier predictive of poor IBD outcomes, identified through higher than expected utilization of services and/or prescription medications. Once developed, SOHI was deployed as the basis for the development of a model to predict which individuals with IBD were most likely to continue to have SOHI within a 1-year timeframe using insurance claims data. Factors were added or subtracted based on early experimentation with the model.

The primary cohort of interest was based on the presence of at least one SOHI event during the baseline observation period (12 months prior to index date). Members were categorized into 2 cohorts based on the presence of ≥ 1 SOHI event(s) or absence of SOHI events (non-SOHI).

2.6 Baseline Characteristics

Baseline demographics (age, gender, region, and provider specialty) were extracted from the first IBD medical claim during the identification period. Patients were recorded as having UC, CD, or both based on the first two medical claims with IBD diagnoses in the identification period on distinct dates. The Quan–Charlson comorbidity index (CCI) was measured during the baseline period using diagnosis codes from medical claims. The following list of procedures,

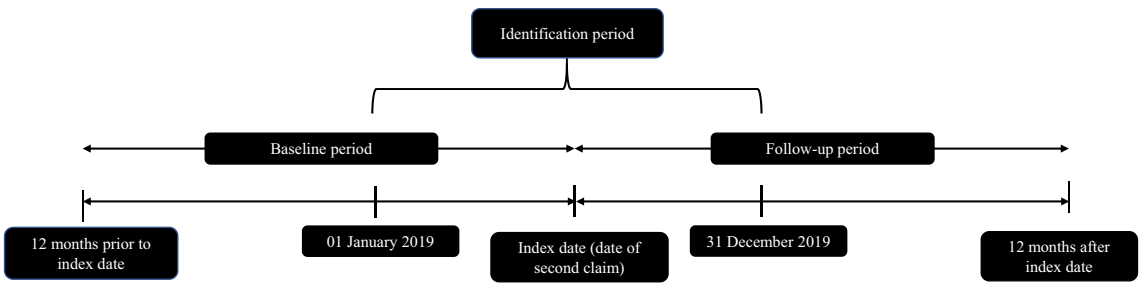

Fig. 1 Study design

diagnoses, and diagnostics was also captured during the baseline period as indicator variables: colonoscopy, anxiety, depression, maintenance medication use, iron deficiency, and C-reactive protein (CRP) lab test orders. Further, all the SOHI components outlined previously were also assessed during the baseline period for use as a predictor of follow-up SOHI occurrence. Both all-cause and IBD-related healthcare utilization and costs were captured during the baseline period, as well as the ratio of ER to IP admission utilization.

2.7 Statistical Analysis

All baseline characteristics were analyzed descriptively. Counts and percentages were provided for categorical variables; means and standard deviations were provided for continuous variables. Testing for differences was completed using chi-squared tests for categorical variables and *t*-test for continuous variables.

Multivariable logistic regression was used to examine the association of follow-up SOHI with baseline characteristics. Variable selection was conducted using all baseline variables with non-missing responses in a stepwise selection logistic regression. Those variables remaining after the forward stepwise selection process had been completed were included in the final logistic regression model. The final model was retained for the potential use in predicting the probability of a member having follow-up SOHI.

3 Results

3.1 Patient Attrition

A total of 86,603 individuals were identified as having commercial insurance coverage and had at least two diagnosis codes for IBD during 2019 (Fig. 2). Of these, 19,824 individuals had sufficient continuous enrollment with both medical and pharmacy benefits and no missing demographics. Of these 19,824 individuals, 9347 (47.1%) had a diagnosis of UC, and 9601 (48.4%) had a diagnosis of CD. A total of 876 (4.4%) individuals had diagnoses of both, UC and CD, on their index date. After applying the SOHI logic to the final analytic population, about one-third ($n = 6872$; 34.7%) of the individuals were found to have follow-up SOHI (Fig. 2).
CD Crohn's disease, *ER* emergency room, *GI* gastrointestinal, *IBD* inflammatory bowel disease, *OCS* oral corticosteroid, *SOHI* suboptimal healthcare interaction, *UC* ulcerative colitis

3.2 Demographic and Clinical Characteristics

Table 1 provides demographics and baseline clinical characteristics of individuals stratified by SOHI status. The individuals with SOHI were < 1 year older (47.1 years versus 46.3 years), more likely to be female (52.9% versus 48.9%), and more likely to have an index diagnosis of CD (55.9% versus 44.5%) than non-SOHI individuals. The individuals in the SOHI cohort were more likely to have

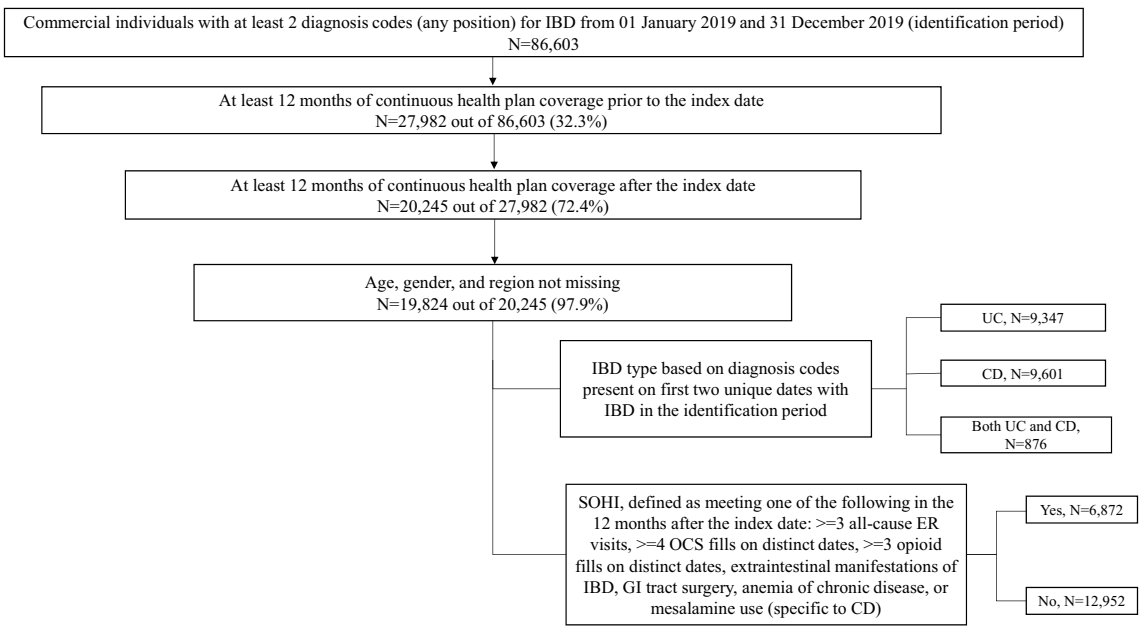

Fig. 2 Patient Attrition

Table 1 Demographic and baseline characteristics

Category	Index demographics		Non-SOHI	SOHI	*p*-Value
Age	Age (continuous)	*N*	12,952	6872	
		Mean (SD)	46.3 (15.8)	47.1 (15.4)	< 0.001
Gender	Female	*N* (%)	6336 (48.9)	3638 (52.9)	< 0.001
	Male	*N* (%)	6616 (51.1)	3234 (47.1)	< 0.001
Index diagnosis	CD	*N* (%)	5762 (44.5)	3839 (55.9)	< 0.001
	UC	*N* (%)	6819 (52.7)	2528 (36.8)	< 0.001
	Both	*N* (%)	371 (2.9)	505 (7.4)	< 0.001
Index provider (not mutually exclusive)[a]	Gastroenterology	*N* (%)	4990 (38.5)	2439 (35.5)	< 0.001
	Rheumatology	*N* (%)	175 (1.4)	176 (2.6)	< 0.001
	Surgery	*N* (%)	177 (1.4)	219 (3.2)	< 0.001
Baseline SOHI	Baseline SOHI (proxy definition)	*N* (%)	3350 (25.9)	4837 (70.4)	< 0.001
	Anemia (based on diagnosis code, not ACD)	*N* (%)	1928 (14.9)	1755 (25.5)	< 0.001
	≥ 3 ER visits	*N* (%)	227 (1.8)	403 (5.9)	< 0.001
	≥ 4 OCS fills	*N* (%)	551 (4.3)	1116 (16.2)	< 0.001
	≥ 3 opioid fills	*N* (%)	365 (2.8)	1201 (17.5)	< 0.001
	Extraintestinal manifestation of IBD	*N* (%)	232 (1.8)	661 (9.6)	< 0.001
	GI tract surgery	*N* (%)	548 (4.2)	599 (8.7)	< 0.001
	Mesalamine (if CD)	*N* (%)	311 (2.4)	1640 (23.9)	< 0.001
Colonoscopies	≥ 1 colonoscopy	*N* (%)	3913 (30.2)	2539 (37.0)	< 0.001
	Colonoscopy events (among members with ≥ 1)	Mean (SD)	1.1 (0.4)	1.1 (0.3)	0.003
Mental health	Anxiety	*N* (%)	1053 (8.1)	732 (10.7)	< 0.001
	Depression	*N* (%)	924 (7.1)	785 (11.4)	< 0.001
TIM use[b]	≥ 1 maintenance (TIM) medication fill	*N* (%)	4787 (37.0)	2381 (34.7)	0.001
	Pharmacy claim	*N* (%)	2203 (17.0)	1265 (18.4)	0.014
	Medical claim	*N* (%)	2744 (21.2)	1291 (18.8)	< 0.001
		N (%)			
IBD visits	≥ 1 IBD visit	*N* (%)	12,913 (99.7)	6872 (100.0)	< 0.001
	Count of IBD visits (among members with ≥ 1)	N	12,913	6872	
		Mean (SD)	5.1 (7.9)	6.9 (14.4)	< 0.001
CCI score	CCI score	*N*	12,952	6872	
		Mean (SD)	0.4 (0.9)	0.6 (1.2)	< 0.001
	0	*N* (%)	10,298 (79.5)	4734 (68.9)	< 0.001
	1–2	*N* (%)	2225 (17.2)	1680 (24.5)	< 0.001
	3–4	*N* (%)	314 (2.4)	326 (4.7)	< 0.001
	5+	*N* (%)	115 (0.9)	132 (1.9)	< 0.001
CRP lab presence	≥ 1 CRP test order	*N* (%)	5407 (41.8)	3330 (48.5)	< 0.001
	≥ 1 CRP lab result	*N* (%)	2678 (20.7)	1712 (24.9)	< 0.001
	Count of CRP labs (among those with ≥ 1 lab)	*N*	2678	1712	
		Mean (SD)	1.8 (1.6)	1.9 (1.7)	0.222
Average CRP results (among those with ≥ 1 lab)	Average CRP lab result (mg/l)	*N*	2678	1712	
		Mean (SD)	6.5 (15.0)	11.1 (25.1)	< 0.001
	CRP result > 10 mg/l	*N* (%)	410 (15.3)	428 (25.0)	< 0.001
	CRP result ≤ 10 mg/l	*N* (%)	2268 (84.7)	1284 (75.0)	< 0.001
Max CRP results (among those with ≥ 1 lab)	Max CRP lab result (mg/l)	*N*	2678	1712	
		Mean (SD)	8.4 (20.4)	13.8 (29.1)	< 0.001
	CRP result > 10 mg/l	*N* (%)	507 (18.9)	485 (28.3)	< 0.001
	CRP result ≤ 10 mg/l	*N* (%)	2171 (81.1)	1227 (71.7)	< 0.001

ACD anemia of chronic disease, *CCI* Charlson comorbidity index, *CD* Crohn's disease, *CRP* C-reactive protein, *ER* emergency room, *GI* gastrointestinal, *IBD* inflammatory bowel disease, *OCS* oral corticosteroid, *SD* standard deviation, *SOHI* suboptimal healthcare interaction, *TIM* targeted immunomodulator medication, *UC* ulcerative colitis

[a]Based on all claims with an IBD-diagnosis code on the index date

[b]Immunomodulator medications included adalimumab, golimumab, cetrolizumab pegol, natalizumab, infliximab, ustekinumab, vedolizumab, and tofacitinib

seen a rheumatologist (2.6% versus 1.4%; $P < 0.001$) or surgeon (3.2% versus 1.4%; $P < 0.001$) than a gastroenterologist (35.5% versus 38.5%; $P < 0.001$) on their index date.

The individuals with follow-up SOHI were more likely to have had similar SOHI events in the baseline period than those with non-SOHI (70.4% versus 25.9%; $p < 0.001$). All the individual components of SOHI (anemia, ≥ 3 ER visits, ≥ 4 oral corticosteroids [OCS] fills, ≥ 3 opioid fills, extraintestinal manifestations of IBD, GI tract surgery, and use of mesalamine in case of CD) that make up the SOHI proxy in the baseline period were more common in members who had follow-up SOHI compared with individuals who do not have follow-up SOHI (Table 1). Individuals with follow-up SOHI were more likely to undergo a baseline colonoscopy, have a baseline diagnosis of anxiety, and baseline diagnosis of depression, as compared with individuals without follow-up SOHI.

A greater proportion of individuals with SOHI had ≥ 1 claims-based CRP test orders (48.5% versus 41.8%; $p < 0.001$) and ≥ 1 CRP lab results (24.9% versus 20.7%; $p < 0.001$) compared with the proportion of individuals with non-SOHI (Table 1). Among individuals with available CRP lab results, the mean (SD) for average CRP results for members with SOHI compared with non-SOHI was 11.1 (25.1) versus 6.5 (15.0) mg/l, respectively; $p < 0.001$. The CRP lab results were further stratified by the index diagnosis group (for UC and CD) and are presented in Table 2.

3.3 Baseline All-Cause Cost and Utilization

Baseline all-cause utilization and all-cause costs are reported for IBD patients and by follow-up SOHI status. By definition, all individuals had at least one healthcare interaction in the baseline period, with the follow-up SOHI cohort having an average of 21.6 ambulatory visits in the baseline period compared to 15.8 for the non-SOHI cohort ($p < 0.001$) (Table 3). While this may include recurring infusion treatment visits, this represents high utilization among the studied IBD population. Among individuals with at least one IP stay, the ratio of ER visits to IP stays was 1.1 and 0.7 for the SOHI and non-SOHI cohorts, respectively ($p < 0.001$); this indicates that individuals with follow-up SOHI were more likely to have ER visits than IP stays during the baseline period (Table 3).

The total average all-cause costs for the SOHI and non-SOHI cohorts were $50,052 and $36,335, respectively ($p < 0.001$). The biggest difference in the absolute costs across cohorts appears to be medical costs—driven by IP stay costs—followed by pharmacy costs (Table 4). The same

Table 2 CRP values stratified by index diagnosis (ulcerative colitis and Crohn's disease)

Category	Baseline laboratory results		UC index diagnosis		UC	Crohn's index diagnosis		Crohn's
			Non-SOHI	SOHI	*p*-Value	Non-SOHI	SOHI	*p*-Value
CRP lab presence	≥ 1 CRP test order	*N*	2414	1129		2833	1945	
		%	35.4	44.7	< 0.001	49.2	50.7	0.151
	≥ 1 CRP lab result	*N*	1267	574		1329	1008	
		%	18.6	22.7	< 0.001	23.1	26.3	< 0.001
	Count of CRP labs (*among those with ≥ 1 lab*)	*N*	1267	574		1329	1008	
		Mean	1.7	1.9	0.0584	2.0	1.9	0.440
		SD	1.4	1.6		1.7	1.7	
Average CRP results (*among those with ≥ 1 lab*)	Average CRP lab result (mg/l)	*N*	1267	574		1329	1008	
		Mean	5.5	10.3	< 0.001	7.4	10.8	< 0.001
		SD	11.4	21.7		17.9	24.6	
	CRP result > 10 mg/l	*N*	172	151		226	239	
		%	13.6	26.3	< 0.001	17.1	23.7	< 0.001
	CRP result ≤ 10 mg/l	*N*	1095	423		1,103	769	
		%	86.4	73.7	< 0.001	83.0	76.3	< 0.001
Max CRP results (*among those with ≥ 1 lab*)	Max CRP lab result (mg/l)	*N*	1267	574		1329	1008	
		Mean	7.2	13.1	< 0.001	9.7	13.4	< 0.001
		SD	16.1	25.5		24.1	28.5	
	CRP result > 10 mg/l	*N*	222	165		272	274	
		%	17.5	28.8	< 0.001	20.5	27.2	< 0.001
	CRP result ≤ 10 mg/l	*N*	1045	409		1057	734	
		%	82.5	71.3	< 0.001	79.5	72.8	< 0.001

CRP C-reactive protein, *CD* Crohn's disease, *SD* standard deviation, *SOHI* suboptimal healthcare interaction, *UC* ulcerative colitis

Table 3 Baseline all-cause utilization

Baseline all cause utilization	Non-SOHI	SOHI	*p*-Value
≥ 1 IP stay, *N* (%)			
N (%)	1224 (9.5)	1121 (16.3)	< 0.001
≥ 1 ER visit, *N* (%)			
N (%)	2497 (19.3)	2130 (31.0)	< 0.001
≥ 1 AMB visit, *N* (%)			
N (%)	12,899 (99.6)	6864 (99.9)	< 0.001
Count of IP stays			
N	12,952	6872	
Mean (SD)	0.1 (0.5)	0.3 (0.9)	< 0.001
Count of ER visits			
N	12,952	6872	
Mean (SD)	0.3 (0.7)	0.6 (2.5)	< 0.001
Count of AMB visits			
N	12,952	6872	
Mean (SD)	15.8 (16.1)	21.6 (23.0)	< 0.001
Ratio of ER:IP visits (among individuals with ≥ 1 IP stay)[a]			
N	1224	1121	
Mean (SD)	0.7 (1.0)	1.1 (3.1)	< 0.001

AMB ambulatory, *ER* emergency room, *IP* in-patient, *SD* standard deviation

[a] < 1 indicates more IP stays than ER visits, > 1 indicates more ER visits than IP stays

Table 4 Baseline all-cause costs

Baseline all-cause cost	Non-SOHI (*N* = 12,952)	SOHI (*N* = 6872)	*p*-Value
Total costs			
Mean	$36,335	$50,052	< 0.001
SD	$49,215	$78,068	
Pharmacy costs			
Mean	$15,247	$19,276	< 0.001
SD	$30,557	$38,890	
Medical costs			
Mean	$21,088	$30,776	< 0.001
SD	$40,993	$66,956	
IP costs			
Mean	$3445	$9127	< 0.001
SD	$23,099	$47,799	
ER costs			
Mean	$563	$1427	< 0.001
SD	$1874	$6309	
AMB costs			
Mean	$17,080	$20,222	< 0.001
SD	$31,744	$39,461	

AMB ambulatory, *ER* emergency room, *IP* in-patient, *SD* standard deviation, *SOHI* suboptimal healthcare interaction

cost variables were also stratified by UC and CD index diagnosis and presented in Supplementary Table S1. In addition, we also analyzed the baseline healthcare utilization and costs stratified by SOHI and non-SOHI cohorts specific to IBD, which are presented in detail in Supplementary Tables S2 and S3. The average IBD-related total costs for the SOHI and non-SOHI cohorts were $30,461 and $26,902, respectively, representing 60.9% and 74.0% of all-cause costs.

3.4 Predicting Follow-up SOHI

Based on the final model laid out for predicting follow-up SOHI, some of the most important variables used to predict follow-up SOHI included baseline mesalamine use, baseline targeted immunomodulator use, count of baseline opioid fills, count of baseline oral corticosteroid fills, baseline extraintestinal manifestations of disease, a proxy for baseline SOHI, and index providers (Fig. 3). The odds of follow-up SOHI in individuals with CD who used mesalamine were approximately eight times higher than in those with no mesalamine use (Odds ratio [OR]: 7.93 [95% confidence interval {CI} 6.74–9.34]; $p < 0.0001$). Similarly, the odds of follow-up SOHI in individuals with baseline extraintestinal manifestation of disease impacts are four times higher than the odds of follow-up SOHI in individuals without baseline extraintestinal manifestation of the disease (OR: 4.0 [95% CI 3.36 –4.77]; $p < 0.0001$) (Fig. 3). Because the purpose of this model was for the prediction of SOHI, note that there may be multicollinearity (independent variables that are highly correlated) present that influences the parameter estimates discussed above.* $p < 0.05$. To predict *SOHI*, all the baseline variables with non-missing responses were included in a stepwise selection logistic regression. Those variables remaining after the stepwise selection process had completed were included in the final logistic regression model. *CD* Crohn's disease, *OCS* oral corticosteroid, *SOHI* suboptimal healthcare interaction, *UC* ulcerative colitis

The above model resulted in a *c*-statistic of 0.806, indicating that the model was a good fit for correctly classifying individuals as having follow-up SOHI. By running this final logistic regression model on the population of interest, unique individuals were scored by outputting linear log odds based on their baseline characteristics, which was transformed into a probability measure of follow-up SOHI (Supplementary Table S4).

4 Discussion

This retrospective observational cohort study in commercially insured individuals with IBD is an effort to define and predict SOHI to enable capturing poor patient outcomes using claims data. We first defined SOHI and then

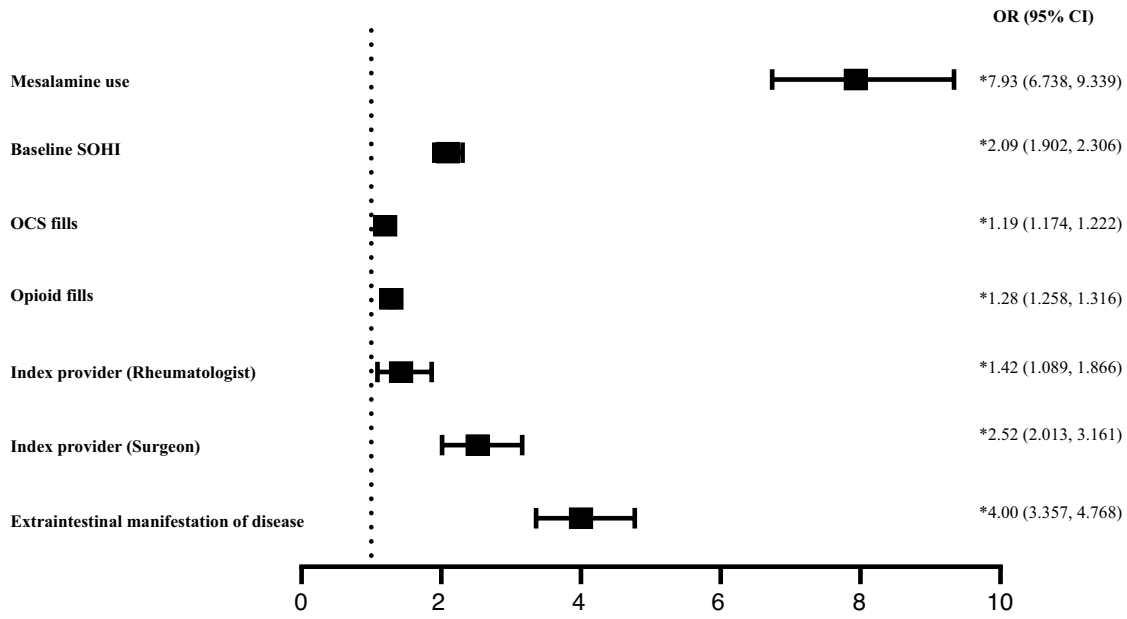

Fig. 3 Final logistic regression model variables for predicting SOHI (selective variables)

used member baseline and disease characteristics to evaluate associations between these variables and follow-up SOHI. Our study showed that the SOHI and non-SOHI cohorts presented with notable differences in baseline characteristics, many of which were found to be statistically as well as clinically significant. The individuals with follow-up SOHI were more likely to undergo a baseline colonoscopy, have a baseline diagnosis of anxiety, and baseline diagnosis of depression, as compared with individuals without follow-up SOHI.

Noteworthy is that the odds of follow-up SOHI in individuals with CD who used mesalamine were approximately eight times higher than in those with no mesalamine use (OR: 7.93 [95% CI 6.74–9.34]; $p < 0.0001$). The effectiveness of 5-ASAs in ulcerative colitis is clear; however, studies have shown little benefit for induction or maintenance treatment of CD [12]. Inappropriate use of corticosteroids, opioids, and mesalamine are proxies for poor guideline adherence, which could be a factor in suboptimal outcomes. It is also noteworthy that we observed significantly higher baseline use of targeted immunomodulators in the non-SOHI cohort versus SOHI, suggesting that early intervention with biologics might be associated with better health outcomes. Literature suggests that early and aggressive biologic therapy in IBD can contribute to mucosal healing, prevent progression to structural bowel damage, and lead to decreased complications, surgery, and hospitalization rates [13].

It is worth noting that, although many demographic and provider variables showed a statistically significant difference of < 0.05 between the SOHI and non-SOHI cohorts, not all were clinically meaningful. The SOHI cohort had higher healthcare utilization and comorbidities in the baseline period with a higher average Charlson score, increased rate of common comorbidities, and more inflammation assessed by higher CRP lab values. CRP was found to be uniformly high in individuals with UC and CD in SOHI. This demonstrates that CRP laboratory results are equally relevant in UC and CD patients. Finding clinically significant CRP values in individuals with UC in the SOHI cohort may be an indication that measuring CRP in such patients is warranted. For both all-cause and IBD-related, the SOHI cohort had higher utilization and costs compared with the non-SOHI cohort, suggesting the SOHI cohort was using more resources for achieving adequate control of all their conditions.

Given these clinical and utilization differences observed between SOHI and non-SOHI members, we utilized this definition as leverage to identify follow-up SOHI through a predictive model. The stepwise logistic regression model performed well with a *c*-statistic of 0.806, which meant it performed well in predicting which members were part of the SOHI and non-SOHI cohorts. The simplicity of this model's drivers and the factors that influence future SOHI suggest that the SOHI concept could be utilized in other claims sets or even non-claim settings, such as the clinician's office. Because the model development may be prone to overfitting, further model validation using data held out of the training process or through evaluation of the deployed model is recommended, and performance, as measured by the *c*-statistic, is expected to be lower than reported.

The treatment of uncontrolled IBD is expensive, and if the disease remains uncontrolled for a substantial period of time, it leads to a significant reduction in quality of life, lost productivity in work or school, and escalation in care either in the acute setting of the ER or through prolonged hospitalization [14]. Although expensive treatments account for a large portion of IBD costs, inappropriate therapies, lack of adherence, and suboptimal care have led to estimates of the total IBD cost burden reaching between $14.6 billion and $31.6 billion in 2014 in the USA [15]. Therefore, understanding risk factors for SOHI is critical for individuals with IBD.

To the best of our knowledge, there are no existing outcomes in claims-based metrics that could predict the follow-up outcomes. This is the first retrospective cohort study to develop a model for predicting follow-up SOHI in individuals with IBD using claims data. Understanding and predicting SOHI effectively can better position care providers to optimize patient outcomes and remain engaged in producing high-value, reliable healthcare for the future. The SOHI tool can facilitate healthcare providers and payers in the timely identification of patients with IBD having SOHI. It can also guide physicians to target efforts toward additional care if the current IBD treatment path is not working, thereby resulting in greater chances of a well-managed disease.

The results of this study must be interpreted in light of a few limitations. The study population contained commercially insured individuals and not individuals enrolled in Medicare or Medicaid plans who are systematically different from commercially insured individuals. Furthermore, commercial insurance claims available for analysis are a subset of the overall commercially insured population. All events and comorbidities were limited to members seeking care and subsequently billing through insurance. Although we used forward stepwise logistic regression to select covariates to include in our final predictive model with an entry criterion of 5% and exit criterion of 10%, the prediction model was not tested to further improve generalizability.

Additionally, history was limited for individuals who were not continuously enrolled during the baseline period; hence, these individuals were excluded from our study. Pharmacy claims were limited to medications covered by insurance; therefore, the medication-class flags were missing for individuals who may have cash-pay fills. Additionally, the presence of a drug fill did not guarantee an individual's adherence to the medication regimen.

Current data sources do not provide insight into in-hospital medications or treatment regimens. A drug's indication must be assumed since diagnosis codes were not present for pharmacy claims. Determination of clinically significant events was limited with claims data, as we could not review detailed clinical notes on an individual from electronic medical records or chart notes. This was pertinent to our investigative factors, which sought to identify people who were not adequately controlled for their disease; our claims definition identified individuals, but we were unable to determine the reliability of these findings without a more detailed individual history. The study period overlapped with the COVID-19 pandemic, a time when standard clinical care was interrupted, and approaches to care may have been modified. The final model was not controlled for the index month to test if pandemic exposure systematically affected SOHI for members during the 12-month follow-up period.

5 Conclusions

In summary, our results suggest that individuals with SOHI are likely to have uncontrolled disease, higher expenditures, higher healthcare resource utilization, and higher CRP lab results as compared with non-SOHI members, which could be due to insurance coverage differences such as with co-payments, deductibles, supplementary insurance, their index IBD provider speciality, or currently siloed care processes. Being able to distinguish SOHI and non-SOHI patients in a dataset may be a way to efficiently identify individuals at higher risk for poor IBD outcomes. The accuracy of the SOHI definition and model should be validated in a real-world setting. Further research in future IBD studies to validate these findings and extend the scope of the research to earlier time points along the IBD diagnosis journey care are warranted.

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Declarations

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Conflicts of interest Ms Korrer is an employee of UnitedHealth Group. Drs Naegeli and Gottlieb are employees and stockholders of Eli Lilly and Company. Drs Etemad and Johnson are employees and stockholders of UnitedHealth Group.

Availability of data material All the data from this study are presented in this manuscript, including in the supplementary material. The datasets analyzed during the current study are not publicly available due to data owner's policy. Any request for accessing the data pertaining to this study should be routed through corresponding author.

Ethics approval The data were fully de-identified before access by the research team and were used in compliance with the Health Insurance Portability and Accountability Act regulations. This observational study used only previously collected data and did not impose any form

of intervention; thus no formal consent to release information or institutional review board approval was required.

Consent to participate Consent was not obtained, as the data used by the research team were de-identified.

Consent to publication Not applicable to this study owing to its design.

Code availability Not applicable.

Author contributions The authors confirm their contributions to the study as follows: Naegeli, Etemad, Johnson, and Gottlieb contributed to the conception of the study. Korrer, Naegeli, Etemad, Johnson, and Gottlieb designed the study. Korrer collected the data; Korrer and Gottlieb analyzed the data. Korrer, Naegeli, Etemad, Johnson, and Gottlieb contributed to the interpretation of the data; Korrer and Johnson drafted the manuscript; Korrer, Naegeli, Etemad, Johnson, and Gottlieb contributed to the critical revision of the paper for important intellectual content. All authors reviewed the results, and confirm that they have read and approved the final version of the manuscript.

References

1. Ford AC, Sandborn WJ, Khan KJ, Hanauer SB, Talley NJ, Moayyedi P. Efficacy of biological therapies in inflammatory bowel disease: systematic review and meta-analysis. Am J Gastroenterol. 2011;106(4):644–59 (**quiz 60**).
2. Rosen MJ, Dhawan A, Saeed SA. Inflammatory bowel disease in children and adolescents. JAMA Pediatr. 2015;169(11):1053–60.
3. Alatab S, Sepanlou SG, Ikuta K, Vahedi H, Bisignano C, Safiri S, et al. The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol. 2020;5(1):17–30.
4. Beard JA, Franco DL, Click BH. The burden of cost in inflammatory bowel disease: a medical economic perspective and the future of value-based care. Curr Gastroenterol Rep. 2020;22(2):6.
5. Park KT, Ehrlich OG, Allen JI, Meadows P, Szigethy EM, Henrichsen K, et al. The cost of inflammatory bowel disease: an initiative from the Crohn's & Colitis Foundation. Inflamm Bowel Dis. 2020;26(1):1–10.
6. Roda G, Jharap B, Neeraj N, Colombel J-F. Loss of response to anti-TNFs: definition, epidemiology, and management. Clin Transl Gastroenterol. 2016;7(1): e135.
7. Sewitch MJ, Abrahamowicz M, Bitton A, Daly D, Wild GE, Cohen A, et al. Psychological distress, social support, and disease activity in patients with inflammatory bowel disease. Am J Gastroenterol. 2001;96(5):1470–9.
8. Husain A, Triadafilopoulos G. Communicating with patients with inflammatory bowel disease. Inflamm Bowel Dis. 2004;10(4):444–50 (**discussion 51**).
9. Summers RW, Switz DM, Sessions JT Jr, Becktel JM, Best WR, Kern F Jr, et al. National Cooperative Crohn's Disease Study: results of drug treatment. Gastroenterology. 1979;77(4 Pt 2):847–69.
10. Riley SA, Mani V, Goodman MJ, Lucas S. Why do patients with ulcerative colitis relapse? Gut. 1990;31(2):179–83.
11. Ghosh S, Mitchell R. Impact of inflammatory bowel disease on quality of life: results of the European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) patient survey. J Crohns Colitis. 2007;1(1):10–20.
12. Noureldin M, Cohen-Mekelburg S, Mahmood A, Stidham R, Higgins PDR, Govani S, et al. Trends of 5-aminosalicylate medication use in patients with Crohn disease. Inflamm Bowel Dis. 2021;27(4):516–21.
13. Berg DR, Colombel JF, Ungaro R. The role of early biologic therapy in inflammatory bowel disease. Inflamm Bowel Dis. 2019;25(12):1896–905.
14. Egberg MD, Gulati AS, Gellad ZF, Melmed GY, Kappelman MD. Improving quality in the care of patients with inflammatory bowel diseases. Inflamm Bowel Dis. 2018;24(8):1660–9.
15. Mehta F. Report: economic implications of inflammatory bowel disease and its management. Am J Manage Care. 2016;22(3 Suppl):s51-60.