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Group-Based Trajectory Modeling of Healthcare Financial Charges in Inflammatory Bowel Disease: A Comprehensive Phenotype

Jianfei Jiang, PhD[1,2,5], Benjamin Click, MD[3,5], Alyce M. Anderson, BS[3], Ioannis E. Koutroubakis, MD, PhD[3], Claudia R.amos Rivers, MD[3], Jana G. Hashash, MD[3], Michael A. Dunn, MD[3], Marc Schwartz, MD[3], Jason Swoger, MD[3], Arthur Barrie, MD, PhD[3], Miguel Regueiro, MD[3], Chung-Chou H. Chang, PhD[1,4] and David G. Binion, MD[3]

OBJECTIVES: Inflammatory bowel disease (IBD) is a heterogeneous group of chronic inflammatory gastrointestinal conditions with variable disease courses often requiring significant healthcare expenditures. We aimed to identify disease trajectory patterns based on longitudinal financial expenditures and to assess the association of classic disease activity parameters with financial charges.

METHODS: This was an analysis of a consented, prospective, natural history IBD registry (2009–2013) from a tertiary IBD center of 2,203 patients and their associated medical charges excluding pharmacy expenses. We applied group-based trajectory modeling to longitudinal healthcare financial charges to determine patterns of charges. We assessed the association between charge patterns and disease activity, quality of life, healthcare utilization, and medication requirement.

RESULTS: The final model included 1,600 IBD patients with 5-year charges. We identified six distinct trajectories over the study period. Consistently High charges were associated with Crohn's disease (66.0% Consistently High patients, $P<0.01$), perianal involvement (22.6%, $P<0.01$), ulcerative colitis extent (89.7% extensive, $P=0.01$), prior IBD surgery (52.5%, $P<0.01$), and depression/anxiety (36.2%, $P<0.01$). Compared with other trajectories, Consistently High charges had higher 5-year disease activity indices (Harvey–Bradshaw $P<0.01$; ulcerative colitis activity index $P<0.01$), elevated C-reactive protein rates (72.3%, $P<0.01$), IBD surgery (64.5%, $P<0.01$), hospitalization (97.2%, $P<0.01$), corticosteroid (70.9%, $P<0.01$) and antitumor necrosis factor requirement (50.4%, $P<0.01$), and worse quality of life ($P<0.01$). Annual trends in parameters were reflected in temporal changes in financial charges. The majority of financial burden stemmed from inpatient care.

CONCLUSIONS: Healthcare financial charges represent a novel phenotype in IBD that reflect trends in classic disease activity parameters and allow for subgroup identification of temporal disease trajectories.

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INTRODUCTION

Inflammatory bowel disease (IBD) is a heterogeneous group of chronic inflammatory disorders affecting the gastrointestinal tract resulting from genetic variations, environmental influences, intestinal microbiota alterations, and disturbances in the innate and adaptive immune response.[1,2] IBD and its subgroups ulcerative colitis (UC) and Crohn's disease (CD) often experience variable disease courses of remission and active disease. Response to treatment is largely unpredictable. Consequently, the majority of IBD patients require hospitalization and surgery at some point in their life, resulting in a large financial burden.[3,4] Recent estimates place the total cost of CD in the United States as high at $15.5 billion[5] and UC as high as $14.9 billion annually.[6] Small groups of patients contribute disproportionately to healthcare expenditures.[7] These patients often require repeat admissions and surgeries for refractory inflammation, complications of IBD, chronic pain, or psychosomatic issues.[8]

Unfortunately, attempts to date at prognostication of disease trajectory and treatment response have largely failed. Furthermore, research and clinical care in IBD has been hampered by the lack of a uniform severity metric that encompasses the longitudinal pattern of disease. Most disease activity measures and endoscopic scores only capture a single point in time. To bypass this lack of a standardized severity measure, clinicians have relied upon a combination of patient-reported symptoms, which can correlate poorly with other activity parameters, along with endoscopic and radiographic activity, and inflammatory biomarkers

[1]Department of Biostatistics, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania, USA; [2]Department of Environmental and Occupational Health, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania, USA; [3]Division of Gastroenterology, Hepatology and Nutrition, University of Pittsburgh School of Medicine, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA and [4]Division of General Internal Medicine, Department of Medicine, School of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, USA
Correspondence: David G. Binion, MD, Division of Gastroenterology, Hepatology and Nutrition, University of Pittsburgh School of Medicine, University of Pittsburgh Medical Center, 200 Lothrop Street, PUH Mezzanine Level, C Wing, Pittsburgh, Pennsylvania 15213, USA. E-mail: binion@pitt.edu
[5]These authors are co-first authors.
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to define disease activity.[9] These latter measures capture only direct results of gastrointestinal inflammation and fail to account for non inflammatory processes and consequences of IBD (e.g., autonomic dysfunction, functional abdominal pain). Consequently, researchers have used measures of healthcare utilization including hospitalizations, emergency department visits, surgical requirement, and requirement of advanced medical therapy as surrogate markers of disease severity. Although these measures are routinely available and comparable across institutions, they fail to differentiate in severity across patients when activity is measured in counts or proportions of patients.

Thus, we propose a unique phenotypic metric—healthcare financial charges—to define distinct subgroups of IBD patients. We hypothesized that financial charges would be a comprehensive, accurate reflection of clinical and biochemical disease severity parameters in a large cohort of IBD patients.

METHODS

Study population. IBD patients who were prospectively recruited to participate in a consented, natural history registry of adult (≥18 years) IBD patients maintained at UPMC were used for this study. The IBD registry encompasses highly detailed, prospectively collected, demographic, phenotypic, clinical, and biochemical data on over 2,500 IBD patients. Both established and new patients were eligible for study inclusion. Patients were eligible for inclusion if they were seen in the outpatient clinic between the years 2009 and 2013 with at least one outpatient clinical visit annually, and were diagnosed with IBD (CD, UC, or IBD unclassified) based on standard endoscopic, radiographic, and clinical findings. Patients were excluded if the diagnosis of IBD was uncertain, did not have complete follow-up data, did not have financial charge data available, or had missing financial charges in 2009.

Baseline patient demographics were collected at the initial clinical encounter during the study period and included age, gender, body mass index, smoking status, and medical comorbidities (psychiatric disease (anxiety and/or depression), hypertension, hyperlipidemia, coronary artery disease, diabetes mellitus). Comorbidities were defined by ICD-9 (International Classification of Diseases, Ninth Revision) code or electronic medical record (EMR) problem list. Disease characteristics determined at the first clinical, endoscopic, and/or radiographic encounter included disease type (CD, UC, IBD unclassified), duration of disease, anatomic location and behavior according to the Montreal Classification,[10] and history of IBD surgery before 2009.

Disease activity was prospectively assessed at each outpatient clinical encounter using the Harvey–Bradshaw Index (HBI) for CD[11] and UC activity index (UCAI) for UC,[12] as well as high-sensitivity C-reactive protein (CRP) elevation defined by UPMC laboratory normal values (CRP $\geq$ 0.74 mg/dl). Mean annual values were calculated for disease activity indices and any elevated biochemical inflammatory marker during a year was dichotomized as abnormal for the year. Health-related quality of life was also prospectively collected at each clinical encounter using the published short inflammatory bowel disease questionnaire (SIBDQ).[13,14] Healthcare utilization parameters included emergency department use, hospital admission for any indication, IBD-related surgery verified by manual review of operative reports, IBD clinic visits, telephone encounters to IBD clinic, and computed tomography (CT) scans. Annual medication exposures were evaluated by electronic prescriptions for corticosteroids, antitumor necrosis factor agents (infliximab, adalimumab, and certolizumab pegol), immunomodulators (methotrexate, azathioprine, 6-mercaptopurine), 5-aminosalicylate medications, antidepressants (selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, tricyclic antidepressants), and opiate pain medications.

Financial charge data. Financial charge data for IBD registry patients for the years 2009–2013 were obtained through the Center for Assistance in Research using the EMR, an information technology support group at UPMC. Charge data were obtained for all healthcare services (i.e., not limited to gastrointestinal care) including inpatient and outpatient services at UPMC ($>$20 hospitals, $>$500 outpatient clinics) for all patients in the IBD registry. If a patient had missing charges for a year, but had charges in the previous and following years, the missing charges were assumed to be zero. Charges missing for more than one consecutive year or missing data occurred on the initial or last year of the study period, the data were left as missing and these patients were excluded. Charges were organized by total annual charge amounts for each year (from 2009 to 2013). Outpatient medications including biologic agents and pharmacy charges (e.g., total parenteral nutrition) were not included in the charge data obtained as these were independent of the UPMC healthcare system. All charges are reported as USD and were indexed to base year 2009 using Consumer Price Index (http://www.bls.gov/data/inflation_calculator.htm).

Statistical analysis. Baseline patient characteristics were summarized using descriptive statistics. Categorical variables were presented as proportions and were compared among different financial charge groups by χ^2 or Fisher's exact test as appropriate. Continuous variables were presented as medians and interquartile ranges and were compared using the Wilcoxon's rank-sum test.

Group-based trajectory modeling was designed to identify distinct trajectory patterns of longitudinally measured variables. We applied this modeling approach to the 5-year financial charge data and followed a two-stage model selection process[15] to select the final model based on both the Bayesian Information Criteria and clinical judgment.[16] The aim was to choose the model with the fewest groups that provided the most information. Adequacy of the final model was assessed using average posterior probability and odds of correct classification, calculated for each trajectory group.[15] An average posterior probability = 1 indicated absolute certainty that each individual belonged in that group. The minimum allowable average posterior probability was at least 0.7 by conventional standards. An odds of correct classification $>$5.0 for all groups indicated high model assignment accuracy. We used the SAS 9.4 software (SAS Institute, Cary,

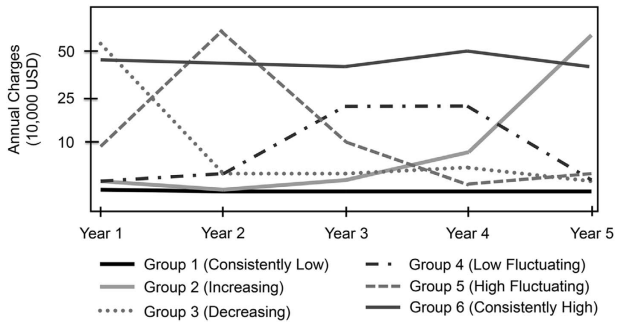

Figure 1 Five-year trends in annual healthcare financial charges by trajectory group.

NC) and the SAS macro *Proc Traj* (http://www.andrew.cmu.edu/user/bjones/).

Using the trajectory model output, we compared baseline demographics, 5-year healthcare utilization, disease activity, medication exposure, and quality of life measures by trajectory group assignment. Additionally, we graphically estimated the temporal approximation of trends in these outcome parameters by trajectory group. To identify the major contributor to financial expenditures, we compared the contributions of charge sources (e.g., inpatient, procedures) by trajectory assignment.

Ethical considerations. Enrollment in and use of the IBD registry (protocol no. 0309054) and this study (protocol no. 15050428) were approved by the Institutional Review Board at the University of Pittsburgh.

RESULTS

Study cohort and model selection. Of patients in the IBD registry, 2,203 had financial charge data available and 1,600 patients met the inclusion criteria and formed the study cohort. Excluded patients were significantly younger (median age 40 years (interquartile range (IQR) 22) excluded patients vs. 45 years (IQR 25) included; $P<0.001$) and male (53% vs. 47%; $P=0.01$). The included patients amassed $183.2 million (median $20,346; IQR $97,809) in total financial healthcare charges over the years 2009–2013. Both total charges over the 5 years and annual charges were highly skewed (Supplementary Figure 1 online). Given the lack of normality of charge data, we converted charges into 41 categorical groups allowing the use of zero-inflated Poisson model (Supplementary Table 1 online). After model selection, the final model identified six distinct trajectory groups (Figure 1). The final model had a single zero-order trajectory financial charge trajectory for Group 1 ("Consistently Low" charges), one quadratic order for Group 2 ("Increasing"), three cubic orders for Groups 3 ("Decreasing"), 4 ("Low Fluctuating"), 5 ("High Fluctuating"), and a linear order for Group 6 ("Consistently High" charges). The majority of patients (52.1%) was assigned to the Consistently Low trajectory, 8.1% to Increasing, 9.3% to Decreasing, 12.1% to Low Fluctuating, 9.4% to High Fluctuating, and 9.0% to Consistently High. The lowest average posterior probability value for groups was 0.950, and the lowest value for the odds of correct classification was 59.2, indicating very high certainty of model trajectory group assignment (Supplementary Table 2 online).

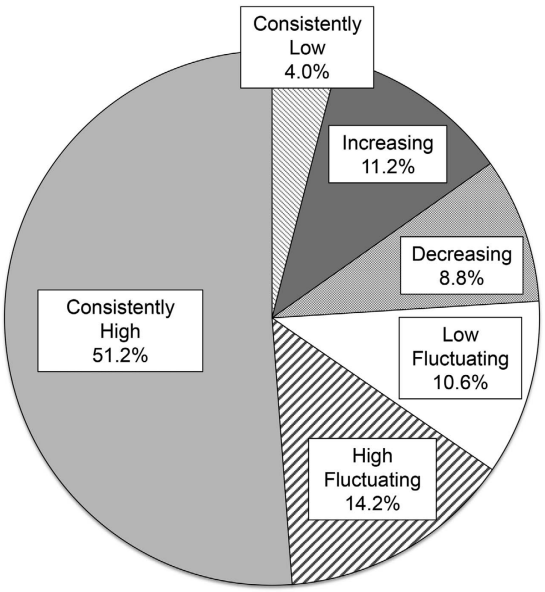

Figure 2 Distribution of cumulative 5-year financial charges by charge trajectory.

Consistently High trajectory accounted for the majority (51.2%, $89.5 million) of 5-year cumulative financial charges followed by High Fluctuating (14.2%, $24.9 million), Increasing (11.2%, $19.5 million), Low Fluctuating (10.6%, $18.5 million), Decreasing (8.8%, $15.4 million), and Consistently Low (4.0%, $6.9 million) (Figure 2).

Extensive clinical data was available for 96.1% ($n=1,537$) of the study population. There was significantly more comorbid anxiety and/or depression ($P<0.01$), diabetes mellitus ($P<0.01$), and hypertension ($P<0.01$) in the Consistently High and High Fluctuating cohorts compared with other groups (Table 1). The Consistently High and High Fluctuating trajectories also had significantly higher proportion of CD ($P<0.01$), perianal disease ($P<0.01$), and more extensive involvement of UC ($P<0.01$) compared with the other groups. Patients in the Consistently High trajectory also had significantly higher rates of prior IBD surgery ($P<0.01$). There was significant variation in the proportion of unemployed patients across trajectories, with Consistently High (26.7%) and Decreasing (28.3%) having the high rates of unemployment ($P<0.01$).

Disease activity and quality of life. The Consistently High charge trajectory had significantly higher 5-year rates of elevated CRP compared with other trajectories (72.3%) while the Consistently Low trajectory had the lowest rates of elevated CRP (24.7%, $P<0.01$) (Table 2). Annual patterns of elevated CRP mirrored trajectory patterns of financial charge fluctuation over the 5-year period (Figure 3a). The Consistently High charge trajectory had the most years with the highest proportion of patients with elevated CRP compared with the other trajectories. Examining groups with fluctuation

Table 1 Study cohort baseline demographics, comorbid conditions, and disease characteristics in inflammatory bowel disease patients[a]

	1 Consistently Low	2 Increasing	3 Decreasing	4 Low Fluctuating	5 High Fluctuating	6 Consistently High	*P*-value
No. (%)	794 (51.7)	121 (7.9)	146 (9.5)	186 (12.1)	149 (9.7)	141 (9.2)	—
Female gender (%)	50.4	51.2	54.8	58.1	61.1	56.7	0.11
Age, median (IQR)	46 (24)	46 (25)	43.5 (27)	43.5 (24)	46 (23)	46 (27)	0.95
BMI, median (IQR)	25.6 (6.3)	25.9 (8.4)	24.8 (6.8)	26.5 (8.6)	25.7 (7.5)	26.2 (8.2)	0.38
Smoking status (%)							0.08
Never	74.0	79.2	75.0	70.9	70.1	61.2	
Former	19.1	15.8	19.3	24.2	24.5	29.5	
Current	6.9	5.0	5.7	5.0	5.4	9.4	
Comorbid (%)							
Psych	20.2	20.7	24.7	26.3	38.3	36.2	<0.01
DM	4.3	5.8	5.5	5.9	11.4	11.3	<0.01
HLD	10.2	9.9	13.7	11.8	13.4	14.9	0.45
HTN	17.4	19.0	17.8	23.7	30.2	33.3	<0.01
CAD	1.4	0.8	2.7	1.6	4.0	4.3	0.09
Thyroid disorder	6.4	5.0	10.3	2.7	6.7	7.1	0.12
Marital status (%)							0.30
Single	34.8	33.7	37.6	33.8	31.5	36.8	
Married	61.1	59.0	60.0	59.2	63.8	53.5	
Divorced	4.1	7.2	2.4	7.0	4.7	9.7	
Employment status (%)							<0.01
Full time	49.7	44.3	42.1	56.6	51.9	44.2	
Unemployed	13.9	21.5	28.3	16.6	17.3	26.7	
Retired	10.0	9.4	8.6	7.2	12.2	9.7	
Part time	2.7	2.5	2.7	1.6	2.0	2.1	
Student	8.2	6.6	6.2	7.0	7.4	9.2	
Other	16.1	10.0	12.3	5.9	10.7	6.4	
Disease (%)							<0.01
CD	51.0	57.9	59.6	59.1	74.5	66.0	
UC	43.2	38.8	35.6	34.9	22.8	29.8	
IBD-U	5.4	0.8	4.1	4.8	2.7	3.5	
Duration (years), median (IQR)	13.5 (12)	14 (20)	12 (11)	14 (14)	13 (12)	14 (12.5)	0.30
CD location[b] *(%)*							0.55
Ileal	27.1	31.8	25.3	32.4	29.9	28.6	0.82
Colonic	20.5	10.6	22.9	17.6	24.3	15.4	0.22
Ileocolonic	52.1	57.6	51.8	48.0	44.9	56.0	0.79
Upper	4.2	3.0	3.6	3.9	4.7	8.8	0.55
Perianal[c] (%)	17.4	5.8	23.3	17.1	29.1	22.6	<0.01
CD behavior[d] *(%)*							0.27
Inflammatory	45.1	50.8	30.9	45.0	35.6	40.2	0.15
Stricturing	30.4	33.8	37.0	32.0	33.7	32.6	0.70
Penetrating	24.5	15.4	32.1	23.0	30.8	27.2	0.13
UC extent[e] *(%)*							0.01
Proctitis	7.0	9.5	4.2	10.9	4.2	2.6	0.52
Left-sided	36.4	35.7	35.4	41.8	20.8	7.7	<0.01
Extensive	56.6	54.8	60.4	47.3	75.0	89.7	<0.01
Prior IBD surgery (%)	31.9	40.5	34.2	34.4	41.6	52.5	<0.01

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CD, Crohn's disease; DM, diabetes mellitus; HLD, hyperlipidemia; HTN, hypertension; IBD-U, inflammatory bowel disease unclassified; IQR, interquartile range; UC, ulcerative colitis.
[a]With clinical data available ($n=1,537$) by trajectory group of annual healthcare charges.
[b]Location data missing in 47 CD patients.
[c]Perianal disease data missing in 16 CD patients.
[d]Behavior data missing in 79 CD patients.
[e]Extent data missing in 89 UC patients.

in their charge patterns, the timing of charge escalation was reflected in simultaneous elevated CRP rates.

Similarly, the Consistently High trajectory had significantly higher 5-year disease activity metrics scores (median HBI 6.9 vs. 2.1 for Consistently Low, $P<0.01$; median UCAI 5.3 vs. 1.9, $P<0.01$) (Table 2). The Consistently High charge trajectory displayed persistently elevated disease activity indices over the 5 years compared with other groups (Figure 3b,c). Conversely, patients in Consistently Low trajectory had persistently lower annual scores, whereas

Table 2 Five-year healthcare utilization, disease activity, medication exposure, and quality of life measures by trajectory group of annual healthcare charges

	1 Consistently Low ($n=794$)	2 Increasing ($n=121$)	3 Decreasing (n-146)	4 Low Fluctuating ($n=186$)	5 High Fluctuating ($n=149$)	6 Consistently High ($n=141$)	*P*-value
Healthcare utilization							
Hospitalization (%)	5.5	83.5	71.2	76.9	83.9	97.2	<0.01
IBD surgery (%)	2.0	26.4	40.4	31.7	59.1	64.5	<0.01
CT scans (%)	24.8	70.2	54.8	71.0	74.5	90.8	<0.01
Clinic visits, median (IQR)	3.0 (5.0)	5.0 (6.0)	7.0 (9.0)	6.0 (7.0)	8.0 (7.0)	9.0 (14.0)	<0.01
Telephone encounters, median (IQR)	10.4 (12.2)	16.2 (18.2)	19.5 (23.1)	17.5 (18.1)	23.3 (21.9)	34.9 (39.9)	<0.01
Disease activity							
CRP elevation (%)	24.7	57.9	46.6	46.8	54.4	72.3	<0.01
HBI, median (IQR)	2.1 (3.8)	3.9 (5.4)	3.0 (5.5)	3.3 (4.2)	3.8 (6.2)	6.9 (5.5)	<0.01
UCAI, median (IQR)	1.9 (4.0)	5.5 (6.8)	2.7 (4.5)	2.5 (3.4)	4.6 (4.5)	5.3 (6.3)	<0.01
Medication exposure							
Corticosteroid (%)	29.6	47.9	44.5	45.7	47.7	70.9	<0.01
Anti-TNF (%)	25.3	40.5	41.8	33.3	45.6	50.4	<0.01
Immunomodulator[a] (%)	39.4	43.0	46.6	46.8	56.4	55.3	<0.01
5-ASA (%)	39.5	38.0	37.0	41.9	34.9	36.9	0.80
Antidepressant[b] (%)	20.7	32.2	24.7	33.9	38.3	48.2	<0.01
Opiate (%)	15.6	49.6	38.4	41.9	48.3	78.0	<0.01
Quality of life							
SIBDQ, median (IQR)	57.0 (13.8)	51.8 (23.4)	51.0 (16.2)	52.4 (17.0)	50.0 (20.7)	40.3 (17.0)	<0.01

Abbreviations: ASA, aminosalicylate; CT, computed tomography; CRP, C-reactive protein; HBI, Harvey–Bradshaw Index; IBD, inflammatory bowel disease; IQR, interquartile range; SIBDQ, short inflammatory bowel disease questionnaire; TNF, tumor necrosis factor; UCAI, ulcerative colitis activity index.
[a]Immunomodulators included methotrexate, azathioprine, and 6-mercaptopurine.
[b]Antidepressants included selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, and tricyclic antidepressants.

groups with temporal variations in charges were reflected in annual patterns of disease activity indices.

Patients belonging to the Consistently High financial charge group had worse 5-year health-related quality of life measured by SIBDQ (median SIBDQ 40.3 vs. 57.0 for Consistently Low, $P<0.01$) (Table 2). Patterns in charge fluctuation were also mirrored by trends in quality of life (Figure 3d).

Healthcare utilization. The Consistently High trajectory demonstrated significantly higher 5-year rates of hospitalization (97.2%, $P<0.01$), IBD surgery (64.5%, $P<0.01$), CT scans (90.8%, $P<0.01$), number of clinic visits (median 9.0, $P<0.01$), and telephone encounters (median 34.9, $P<0.01$) compared with other trajectories (Table 2). Annuals rates of these healthcare utilization parameters were well reflected by the financial charge group status (Figure 3e and Supplementary Figure 2 online).

Medication exposure. Patients belonging to the Consistently High financial charge trajectory had significantly higher 5-year rates corticosteroid (70.9%, $P<0.01$), anti-TNF (50.4%, $P<0.01$), immunomodulator (55.3%, $P<0.01$) antidepressant (48.2%, $P<0.01$), and prescription opiates (78.0%, $P<0.01$) compared with other trajectories (Table 2). The annual rates of corticosteroid use over the 5-year period also corresponded to charge trajectory membership (Figure 3f), with trends in corticosteroid requirement corresponding to surges in financial charges.

Financial charge components. Over the 5-year study period, the majority of all healthcare charges stemmed from inpatient hospitalizations in all trajectories except Consistently Low (Supplementary Figure 3 online). In this trajectory, 62.1% charges were related to procedures. When examining the annual charge distributions by trajectory, the temporal increases of charges were concurrently met with increases in inpatient hospitalization charges (Figure 4b–f). The Consistently High trajectory had between 87.7% and 91.9% of charges stemming from inpatient admissions every year (Figure 4f).

DISCUSSION

In this registry analysis of IBD patients prospectively followed over a 5-year time period, we have identified through the use of group-based trajectory modeling distinct patterns of healthcare financial charges reflective of variations of disease activity, disease-related quality of life, healthcare utilization, and IBD medication requirement. To our knowledge, this is the first use of group-based trajectory modeling using financial data in an IBD patient population. The described modeling strategy is an accurate reflection of multiple commonly used parameters of disease severity.

In this study, we identified six distinct trajectories of annual healthcare financial charges. The patterns can be summarized as Consistently High, Consistently Low, Increasing, Decreasing, Low Fluctuating, and High Fluctuating. Demographic characteristics with significant variation by charge categories included IBD type (with predominance of CD in higher charge groups), perianal involvement, UC extent (higher proportion of extensive colitis), history of prior IBD surgery, and medical and psychiatric comorbidities, as well as employment status. These demographic and disease

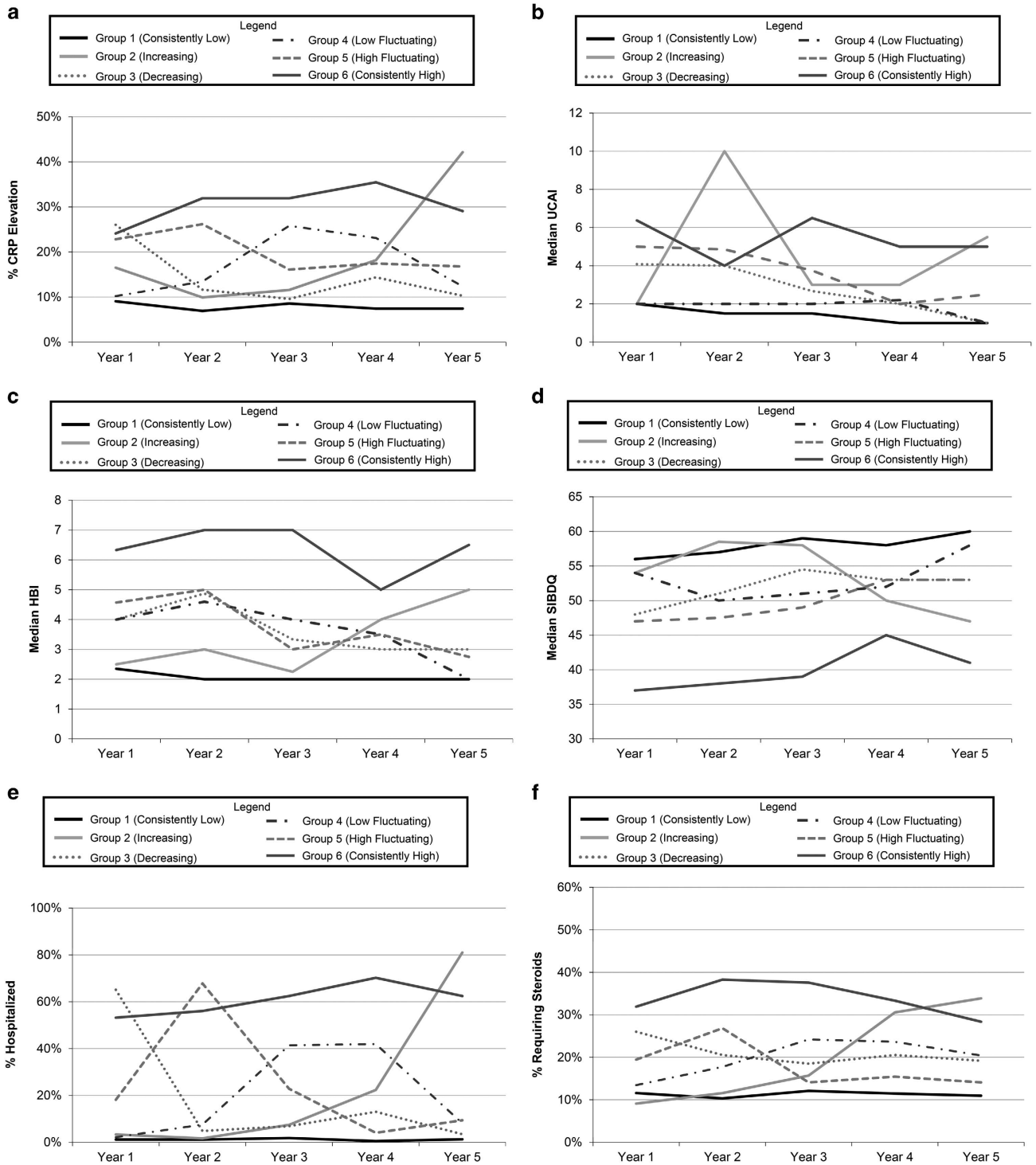

Figure 3 Temporal association of charge trajectories with classic measures of disease activity, quality of life, healthcare utilization and medication requirements. These included C-reactive protein elevation (**a**), ulcerative colitis activity index (**b**), Harvey–Bradshaw Index (**c**), short inflammatory bowel disease questionnaire (**d**), hospitalization (**e**), and corticosteroid prescriptions (**f**) by trajectory group memberships.

associations are not entirely novel. Several studies have demonstrated that CD is, in general, more costly than UC,[5] and that patients with more severe disease (perianal or extensive UC) carry a larger financial burden than those with mild or more limited disease.[4,17,18] Furthermore, unemployment may simply be a reflection of patient disability secondary to severe IBD, thus leading to higher expenses.[19] Similarly, the presence of multiple comorbid conditions has been shown to be associated with patients who use healthcare disproportionately.[20,21]

The majority of patients in this study (51.7%) was grouped in the Consistently Low trajectory, suggesting that most patients

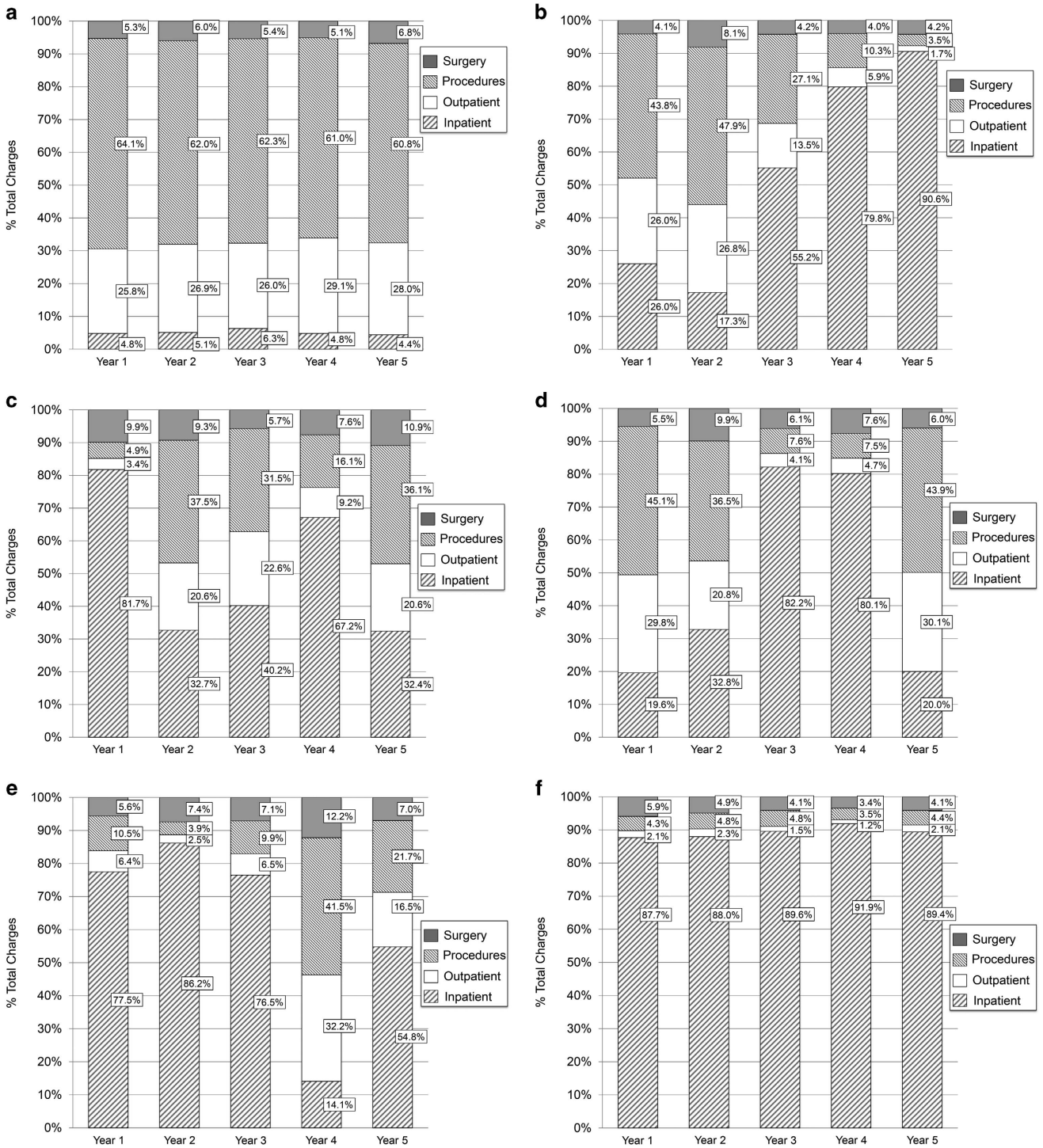

Figure 4 Breakdown of annual total charges for each charge trajectory. Consistently Low (**a**), Increasing (**b**), Decreasing (**c**), Low Fluctuating (**d**), High Fluctuating (**e**), and Consistently High (**f**) charge trajectory. Surgery charge category included professional charges for inflammatory bowel disease-related surgery. Procedures included endoscopy, pathology, radiology, and any other medical procedure (e.g., echocardiogram). Outpatient charges included clinic visit professional charges, labs, and vaccinations. Inpatient charges included inpatient professional services, hospital room and board, inpatient medications, and laboratory testing.

do clinically well and require relatively little healthcare expenditures, mostly in the form of endoscopic and radiographic procedures. Conversely, the majority (51.2%) of cumulative financial charges was generated by the Consistently High trajectory, mostly from hospitalizations. Recognizing the lack of biologic therapy charges in this study, these findings are in concordance with prior studies demonstrating a large financial burden of inpatient care.[3,17]

In this study, we demonstrate that patterns of healthcare spending generated by group-based trajectory modeling are reflective of multiple dimensions of the chronic disease experience. Financial charge patterns reflect acute disease severity, as measured by both patient-reported measures (HBI, UCAI, and SIBDQ) and inflammatory biomarkers (CRP). Perhaps, less surprisingly, patterns in spending echo disease course and healthcare utilization measures such as emergency department use, hospitalization, and surgery. These parameters produce a financial charge inherently, thus association may be partially due to collinearity. The trends in financial charges were also adequately reflective of the need for corticosteroid prescription. Taken together, these trends suggest that financial charges can be an adequate and sensitive comprehensive measure of disease severity, significantly associated with markers of disease impact on the patient, disease burden, and disease course.

There are several limitations to this study. First, the use of observational data limits the data available for collection and analysis. There were a proportion of patients with missing clinical data ($n=63$) as well as missing the Montreal classification characterization (location $n=47$, perianal involvement $n=16$, behavior $n=79$, extent $n=89$). Second, certain variables that temporally vary were only available in a static measure (e.g., smoking). These dynamic changes may have influenced the progression of the disease and largely went unmeasured. Third, the process of enrollment in the IBD registry and backfilling of data to 2009 could allow for bias. If patients were seen in another capacity at UPMC outside of gastroenterological care before registry enrollment, this would result in financial charges and study inclusion while not concurrently receiving targeted IBD care. Perhaps, the largest limitation of this study is the lack of pharmaceutical charges. As charge data was obtained through the hospital system rather than insurer, we were not privy to this financial burden. Consequently, the charges used in this study may not be as reflective of a societal or payer perspective of healthcare expenditures. However, charges stemming from pure healthcare utilization may be a more sensitive measure of acute disease and patient activity rather than large financial burden from expensive, long-term biological therapy. We were also not able to differentiate the specific indication for spending (i.e., for what particular disease or comorbidity a test or procedure was indicated), thus limiting the interpretation of specific disease impact on expenditures. Thus, we sought to categorize charges to give insight into the clinical indication for the charge. Finally, this was a single institutional study at a tertiary referral center using institution-specific financial charges and thus the findings may not be generalizable to other populations or centers. However, we feel that the general patterns and trajectories in healthcare expenditures in a large, longitudinal IBD cohort will be similar across institutions.

There are several strengths to this study. The use of a highly detailed observational natural history registry in a large cohort of IBD patients provides an accurate reflection of real-life clinical care in a tertiary center. This study is a multiyear longitudinal evaluation allowing for temporal variation in disease course. The association of financial charges to classic measures of disease activity, quality of life, healthcare utilization, and medication requirement implies that financial healthcare expenditures are perhaps a comprehensive measure of disease burden (both from an activity standpoint as well as a patient perspective) in IBD. Thus, financial burden can be used as a novel surrogate outcome measure to reflect a general global assessment of patient status.

In conclusion, group-based trajectory modeling of financial charges in IBD patients allows for identification of patient subgroups that mirrors overall disease severity. Financial charges represent a novel and unique means of phenotyping in IBD. Further studies are needed to determine effective interventions for each financial charge trajectory pattern.

CONFLICT OF INTEREST

Guarantor of the article: David G. Binion, MD.
Specific author contributions: study concept and design: D.G.B., C.-C.H.C., B.C., and J.J.; acquisition of data: C.R.R. and B.C.; analysis and interpretation of data: J.J., B.C., and C.-C.H.C.; statistical analysis: J.J., B.C., and C.-C.H.C.; drafting of manuscript: B.C. and J.J.; critical revision of manuscript: A.M.A., I.E.K., J.G.H., M.R., M.A.D., M.S., J.S., A.B., and D.G.B.; final approval of manuscript: all authors.
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Potential competing interests: None.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Prognostication of inflammatory bowel disease (IBD) trajectory and treatment response have largely failed.
- ✓ Research and clinical care in IBD has been hampered by the lack of a uniform severity metric that encompasses the longitudinal pattern of disease.

WHAT IS NEW HERE

- ✓ Healthcare financial charges represent a novel and unique phenotype in IBD that reflect trends in disease activity, quality of life, healthcare utilization, and medication requirement.
- ✓ Healthcare financial charges allow for subgroup identification of temporal disease trajectories.

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