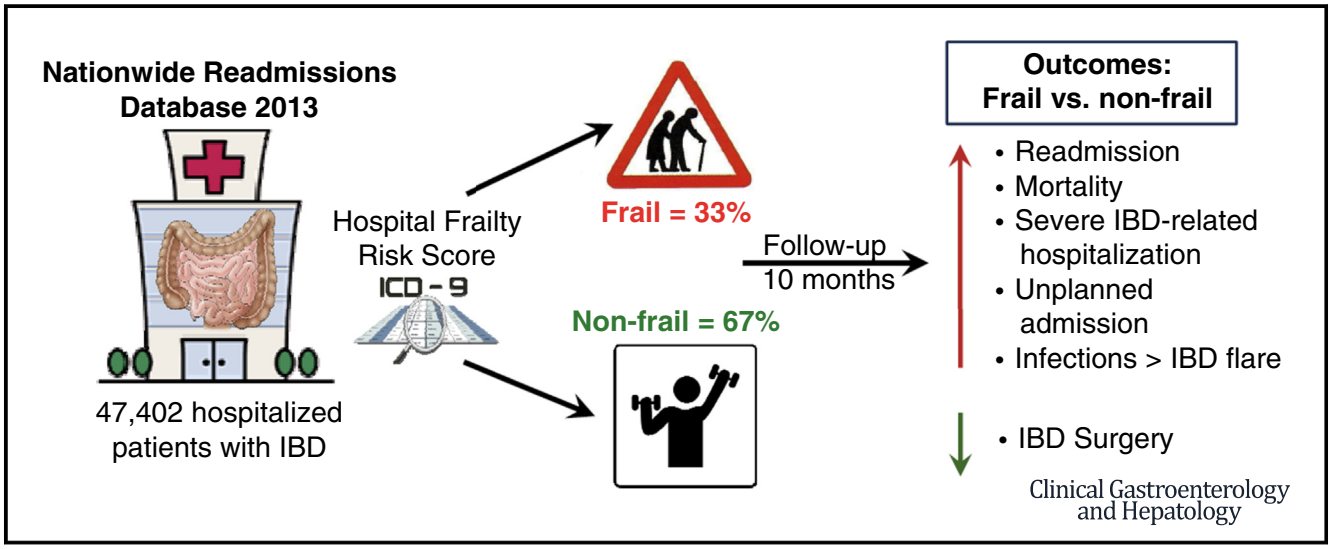
Frailty Is Independently Associated with Mortality and Readmission in Hospitalized Patients with Inflammatory Bowel Diseases

Alexander S. Qian,[*,a] Nghia H. Nguyen,[*,a] Jessica Elia,[‡] Lucila Ohno-Machado,[§] William J. Sandborn,[*] and Siddharth Singh[*,§]

[*]Division of Gastroenterology, Department of Medicine, University of California San Diego; [‡]Expert Rehabilitation Services and [§]Division of Biomedical Informatics, Department of Medicine, University of California San Diego, La Jolla, California



BACKGROUND & AIMS: Old age must be considered in weighing the risks of complications vs benefits of treatment for patients with inflammatory bowel diseases (IBD). We conducted a nationally representative cohort study to estimate the independent effects of frailty on burden, costs, and causes for hospitalization in patients with IBD.

METHODS: We searched the Nationwide Readmissions Database to identify 47,402 patients with IBD, hospitalized from January through June 2013 and followed for readmission through December 31, 2013. Based on a validated hospital frailty risk scoring system, 15,507 patients were considered frail and 31,895 were considered non-frail at index admission. We evaluated the independent effect of frailty on longitudinal burden and costs of hospitalization, inpatient mortality, risk of readmission and surgery, and reasons for readmission.

RESULTS: Over a median follow-up time of 10 months, adjusting for age, sex, income, comorbidity index, depression, obesity, severity, and indication for index hospitalization, frailty was independently associated with 57% higher risk of mortality (adjusted hazard ratio [aHR], 1.57; 95% CI, 1.34–1.83), 21% higher risk of all-cause readmission (adjusted hazard ratio [HR], 1.21; 95% CI, 1.17–1.25), and 22% higher risk of readmission for severe IBD (aHR, 1.22; 95% CI, 1.16–1.29). Frail patients with IBD spent more days in the hospital annually (median 9 days; interquartile range, 4–18 days vs median 5 days for non-frail patients; interquartile range, 3–10 days; $P < .01$)

[a]Authors share co-first authorship.

Abbreviations used in this paper: aHR, adjusted hazard ratio; CCI, Charlson Comorbidity Index; CCS, Clinical Classifications Software; HCUP, Healthcare Cost and Utilization Project; IBD, inflammatory bowel disease; ICD-9-CM, International Classification of Diseases, 9th Revision-Clinical Modification; NRD, Nationwide Readmissions Database.

1542-3565/$36.00
https://doi.org/10.1016/j.cgh.2020.08.010

with higher costs of hospitalization ($17,791; interquartile range, $8368–$38,942 vs $10,924 for non-frail patients, interquartile range, $5571–$22,632; $P < .01$). Infections, rather than IBD, were the leading cause of hospitalization for frail patients.

CONCLUSIONS: **Frailty is independently associated with higher mortality and burden of hospitalization in patients with IBD; infections are the leading cause of hospitalization. Frailty should be considered in treatment approach, especially in older patients with IBD.**

Keywords: Ageing; Prognostic; Infection; Crohn's Disease; Colitis.

The incidence and prevalence of inflammatory bowel disease (IBD) in older adults are rising; approximately 10%–15% of new IBD diagnoses occur in individuals older than 60 years, with incidence rates as high as 18.9 per 100,000.[1–3] In addition, it is expected that within the next decade, more than one-third of patients with IBD will be older patients.[4] Older patients with IBD represent a vulnerable population with higher rates of hospitalization, inpatient mortality, serious infections, and longer length of stay and higher costs of hospitalization.[5–8] Although there has been considerable emphasis on identifying patients at high risk for disease-related complications to inform early use of biologic therapy, there has been limited evaluation of factors that inform risk of treatment-related or extraintestinal non-IBD complications that may be more relevant to older patients.[9–11] Age is an inadequate metric to ascertain risk-benefit tradeoffs of different therapies based on underlying risks of disease and treatment complications. As a result, there is considerable practice variability in managing older patients with IBD, with a preponderance of long-term corticosteroid use and limited use of steroid-sparing therapies.[12,13]

Beyond age, a more comprehensive assessment of biologic reserve and functional status may be more predictive of overall risks of adverse health outcomes. Frailty represents a dynamic state with vulnerability to external and internal stressors and has been associated with increased risk of hospitalization and mortality in several diseases, although there has been limited assessment of frailty in IBD.[14] Recently, Kochar et al[15] identified frailty, measured by using the Hospital Frailty Risk Score, as an independent predictor of serious infections in biologic-treated patients with IBD.

To further understand the impact of frailty on risk of unplanned healthcare utilization in patients with IBD, we conducted a retrospective cohort study in hospitalized adults with IBD. We used the Nationwide Readmissions Database (NRD) 2013, a longitudinal, nationally representative sample of all-payer hospital inpatient stays from 21 state inpatient databases developed as part of the family of databases developed by Healthcare Cost and Utilization Project (HCUP), to estimate and compare the hospitalization-related burden, costs, and causes of hospitalization in frail vs non-frail patients with IBD.[16,17] The presence of frailty was determined by using the Hospital Frailty Risk Score, a validated, administrative claims-based frailty risk score for hospitalized patients.[18]

Methods

Data Source

The NRD 2013 is a nationally representative longitudinal database developed and maintained by HCUP as a partnership among federal, state, and industry stakeholders and sponsored by Agency for Healthcare Research and Quality.[16,17] The database tracks patients from 21 state inpatient databases around the country and accounts for 49.3% of the US population, capturing demographic, clinical, and nonclinical variables from community, public, and academic medical centers. The databases track patients hospitalized within a state over the course of any single year, and after adjusting for missing patient linkage numbers and overlapping inpatient stays, they capture 85% of all discharges. Using this database, we created a retrospective cohort study to compare clinical outcomes between frail vs non-frail patients hospitalized with IBD.

This study was deemed exempt from Institutional Review Board because the NRD is a publicly available database that contains de-identified patient information. Overall study design with cohort selection, exposure assignment, and outcome ascertainment has been summarized in Supplementary Figure 1.

Study Population

We included all adults (age $\geq$18 years) admitted with a primary or secondary discharge diagnosis of IBD between January and June 2013 at time of index hospitalization. After the first admission with a discharge diagnosis of IBD, patients were deemed to be "at-risk" for hospitalization and contributed to follow-up time until December 31, 2013 or death. We used the Clinical Classifications Software (CCS) for International Classification of Diseases, 9th Revision-Clinical Modification (ICD-9-CM), developed by HCUP, to identify patients with IBD (CCS code 144).[19] The CCS for ICD-9-CM, developed by HCUP, is a categorization scheme for diagnoses and procedures that collapses ICD-9-CM's extensive codes into smaller number of categories that are both clinically meaningful and more useful for presenting descriptive statistics (Supplementary Methods).

We excluded patients with (1) age <18 at time of index hospitalization, (2) index hospitalization between

July and December 2013, (3) initial hospitalization for elective surgery (to allow assessment of impact of frailty in medically treated patients with IBD), (4) transferred from another hospital, (5) missing data for length of hospital stay, or (6) missing data on hospital charges for a given admission.

Exposure Assessment

At the time of first hospitalization, patients' frailty risk score was calculated by using the Hospital Frailty Risk Score.[18] This frailty score was developed and validated in 1.04 million hospitalized older adults ≥75 years to screen for frailty and identify a group of patients who are at greater risk of adverse outcomes (mortality, readmission, length of stay). This low-cost score is based on International Classification of Diseases and Related Health Problems, Tenth Revision codes, can be readily implemented in hospital information systems, and performs as well as existing frailty and risk stratification tools. We translated the International Classification of Diseases and Related Health Problems, Tenth Revision codes used in the study to corresponding ICD-9-CM codes (Supplementary Table 1) and used them to assign patients into a low frailty risk (frailty risk score <5) (or non-frail patients), medium frailty risk (score 5–15), and high frailty risk (score >15). Although the Hospital Frailty Risk Score ranges from 0 to 99, the original validation study defined these cutoffs to create categories that discriminated most strongly between individuals with different outcomes. Because high frailty risk population accounted for only 3.1% of the cohort, we combined medium and high frailty risk patients into one exposure category, classified as frail.

Patient and Hospital Characteristics

For each patient, we examined their age, sex, primary expected payment source (Medicare, Medicaid, private insurance, self-pay, and other insurance types), income quartile based on household income of the patient's zip code, and relevant comorbidities to calculate Charlson Comorbidity Index (CCI) (Supplementary Table 2). For each hospitalization, we captured procedures (gastrointestinal or hepatic procedures such as endoscopy, colonoscopy, paracentesis, etc, and IBD-related procedures), gastrointestinal surgeries (colostomy, ileostomy, small bowel resection, colorectal resection, local excision of large intestine lesion, etc), and clinical events (blood transfusions and parenteral or enteral nutrition) (Supplementary Table 3). For each hospital, we examined hospital location, teaching status, and bed size (small, medium, large).

Outcomes

Our co-primary outcomes of interest were risk of inpatient mortality and readmission after discharge from index hospitalization. Secondary outcomes of interest included (1) annual burden of hospitalization (total number of days spent in hospital in 2013), (2) annual costs of hospitalization (total costs of hospitalization in 2013, calculated by multiplying charges for each hospitalization with the cost-to-charge ratios for each hospital for 2013), (3) need for IBD-related surgery, (4) severe IBD-related readmission (length of stay >7 days or need for IBD-related surgery), (5) unplanned hospitalization, and (6) preventable admission. Preventable hospital admissions were characterized by using ICD-9 codes for Prevention Quality Indicators, which are a set of measures, developed by Agency for Healthcare Research and Quality, that can be used with hospital inpatient discharge data as a "screening tool" to identify ambulatory conditions for which high-quality, community-based outpatient care can potentially prevent hospitalization, complications, or more severe disease (Supplementary Table 4).

In addition, we categorized causes for hospitalizations as cardiac, cerebrovascular, respiratory, infections, genitourinary, gastrointestinal (divided into IBD-related vs non-IBD gastrointestinal causes), endocrine/metabolic, neuropsychiatric, malignancies, fractures, thromboembolism, inflammatory bowel disease specific, and others based on primary CCS diagnosis codes (Supplementary Tables 5 and 6).

Statistical Analysis

We used descriptive statistics to compare patient demographics, admission characteristics, and hospital characteristics for the index hospitalization for frail vs non-frail patients with IBD. We used Pearson χ^2 test to

What You Need to Know

Background

Age is an inadequate metric to ascertain risks vs benefits of treatments for inflammatory bowel diseases (IBD). Assessment of biologic reserve and functional status might be better for determining overall risk of adverse outcome.

Findings

In a nationally representative cohort study of 47,402 hospitalized patients with IBD (33% frail), frailty, measured using a validated hospital frailty risk score, was associated with a higher subsequent risk of mortality, readmission, and annual burden and costs of hospitalization. Infections, rather than IBD, were the leading cause of hospitalization in frail patients.

Implications for patient care

Frailty is an important prognostic factor for patients with IBD and should be considered in selection of treatment.

Table 1. Patient, Hospital, and Hospitalization Characteristics of Frail vs Non-frail Patients With IBD at Time of Index Hospitalization

Characteristics at time of index hospitalization	Non-frail patients (N = 31,895)	Frail patients (N = 15,507)	*P* value
Age, *y* (mean ± standard deviation)	49.2 ± 18.5	61.9 ± 18.2	<.01
Age by categories (%)			
• Age <40	36.1	14.1	
• Age 40–64	39.5	35.4	<.01
• Age >64	24.4	50.5	
Female (%)	55.7	60.0	<.01
Urban (%)	92.4	91.5	<.01
Primary expected payer (%)			
1. Medicare/Medicaid	43.6	69.2	
2. Private insurance	45.6	24.0	<.01
3. Self-pay	5.5	3.49	
4. No charge/others	5.3	3.29	
Median household income (%)			
1. 0–25th percentile ($1–$37,999)	21.9	23.4	
2. 26th to 50th percentile ($38,000–$47,999)	24.9	26.5	<.01
3. 51st to 75th percentile ($48,000–$63,999)	26.3	25.4	
4. 76th to 100th percentile ($64,000 or more)	27.0	24.8	
Teaching status (%)			
1. Metropolitan non-teaching	39.6	43.6	
2. Metropolitan teaching	52.8	47.9	<.01
3. Non-metropolitan	7.6	8.5	
Bed size (%)			
1. Small	10.4	10.6	
2. Medium	23.3	23.8	.28
3. Large	67.3	65.6	
Deyo-Charlson Comorbidity Index (%)			
• 0	69.1	41.8	
• 1	17.6	20.3	<.01
• 2 or more	13.3	37.9	
IBD-related procedures (%)	34.3	30.4	<.01
IBD-related surgery (%)	0	0	
Length of stay (unadjusted by month of follow-up)			
• Median	3	5	<.01
• IQR	2–5	3–9	
Proportion with severe IBD hospitalization (LOS >7 days or surgery) (%)	11.6	32.3	<.01
Unplanned hospitalization (%)	77.8	91.1	<.01
Preventable hospitalization (%)	5.3	11.7	<.01

IBD, inflammatory bowel disease; IQR, interquartile range; LOS, length of stay.

analyze categorical variables and Student *t* test for continuous variables. Categorical variables are expressed as percentages and continuous variables as median with an interquartile range. All hypothesis testing was performed by using a two-sided *P* value with a statistical significance threshold <.05. To evaluate the effect of independent effect of frailty on longitudinal outcomes, we performed multivariable Cox proportional hazard analysis using backward variable selection, adjusting for age, sex, obesity, household income, and CCI score (based on smoking, obesity, anemia, congestive heart failure, chronic lung disease, depression, diabetes, hypertension, coagulation disorder, liver disorder, electrolyte abnormalities, peripheral vascular disease, psychoses, chronic pain, and renal failure).[20] In addition, we performed analysis stratified by patients without any significant comorbidities (CCI score 0) and patients with comorbidities (CCI 1 or more). Post hoc, on the basis of reviewers' comments, we updated the multivariable analysis, also adjusting for length of stay at index admission, and reason for index admission (IBD-related vs non-IBD related). All statistical analyses were performed with Stata MP (2015, Stata Statistical Software: Release 14; StataCorp, College Station, TX).

Results

Out of 14,325,172 discharge records analyzed in NRD 2013, 94,498 records were identified for analysis, representing 47,402 unique patients with index hospitalizations between January and June 2013 with a primary or secondary discharge diagnosis of IBD. Of these, 31,895 patients (67.2%) were classified as non-frail, and 15,507 patients (32.7%) were classified as frail (14,027 patients classified as having medium and 1480 as high frailty risk). As compared with non-frail patients, patients with frailty were older, female, and had higher burden of comorbidities and longer length of stay at time of index hospitalization (when their frailty status was assessed) (Table 1). Claims codes within the hospital frailty risk score that were most frequently represented in our cohort were "disorders of fluid electrolyte and acid-base

Table 2. Longitudinal Hospitalization-Related Outcomes in Patients With IBD, Based on Frailty Risk Score

Outcomes during follow-up	Non-frail patients (N = 31,895)	Frail patients (N = 15,507)	*P* value
Outcomes within 6 months of index hospitalization			
Readmission (%)	33.2	41.2	<.01
Inpatient mortality (%)	0.70	2.60	<.01
Severe hospitalization (length of stay >7 days or need for IBD-related surgery) (%)	10.4	15.4	<.01
Unplanned hospitalization (%)	28.3	37.6	<.01
Preventable hospitalization (%)	3.6	7.7	<.01
IBD-related procedures (%)	14.1	13.5	.106
IBD-related surgery (%)	2.02	1.04	<.01
Annual burden and costs of hospitalization			
Total follow-up time (*months*), median (IQR)	10 (7–11)	10 (8–11)	<.01
Annual days spent in the hospital (including during index hospitalization), median (IQR)	5 (3–10)	9 (4–18)	<.01
Annual costs across all hospitalizations (in dollars), median (IQR)	10,924 (5571–22,632)	17,791 (8368–38,942)	<.01

IBD, inflammatory bowel disease; IQR, interquartile range.

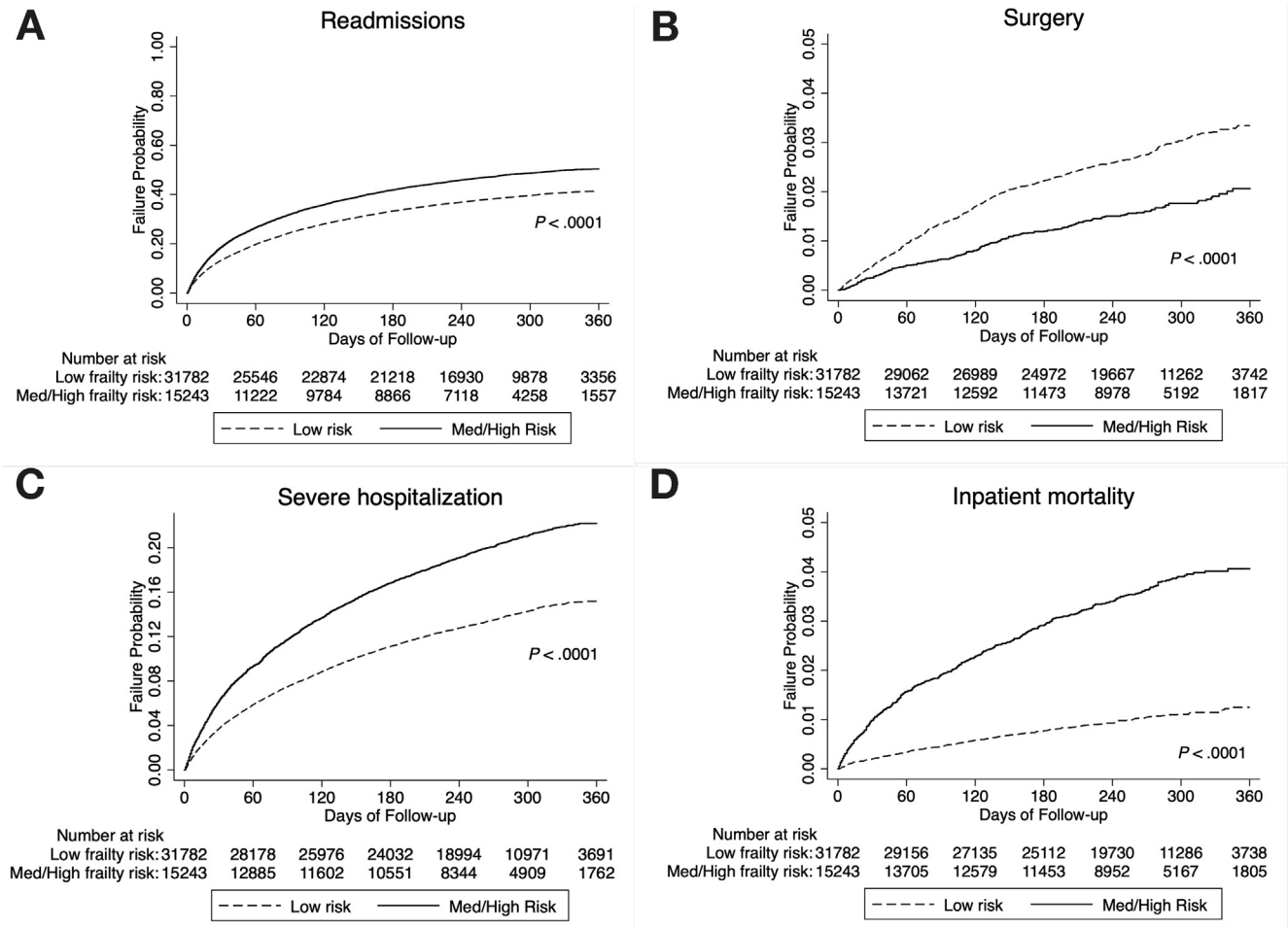


Figure 1. Longitudinal outcomes in frail vs non-frail patients with IBD after index hospitalization: (*A*) readmission, (*B*) inpatient mortality, (*C*) severe hospitalization (length of stay >7 days or need for IBD-related surgery), and (*D*) IBD-related surgery. IBD, inflammatory bowel disease.

Table 3. Cox Proportional Hazard Analysis Evaluating Risk of Readmission by Frailty Risk Score

Variable	Hazard ratio (95% confidence interval)	*P* value
Frailty risk score (moderate/high vs low)	1.21 (1.17–1.25)	<.01
Age (per 1-y increase)	0.99 (0.99–0.99)	<.01
Charlson Comorbidity Index (reference group: 0)		
• 1	1.24 (1.20–1.30)	<.01
• 2 or more	1.66 (1.60–1.72)	<.01
Length of stay at index hospitalization (per 1-day increase)	1.01 (1.00–1.01)	<.01
Gender (women vs men)	0.98 (0.95–1.01)	.16
Obese (yes vs no)	0.95 (0.91–1.00)	.06
Depression (yes vs no)	1.19 (1.14–1.24)	<.01
Median household income (per quartile increase)	0.96 (0.94–0.97)	<.01
Reason for index hospitalization (IBD vs non-IBD)	1.18 (1.14–1.22)	<.01

IBD, inflammatory bowel disease.

Table 4. Cox Proportional Hazard Analysis Evaluating Risk of Inpatient Mortality by Frailty Risk Score

Variable	Hazard ratio (95% confidence interval)	*P* value
Frailty risk score (moderate/high vs low)	1.57 (1.34–1.83)	<.01
Age (per 1-y increase)	1.02 (1.02–1.03)	<.01
Charlson Comorbidity Index (reference group: 0)		
• 1	2.71 (2.09–3.53)	<.01
• 2 or more	7.86 (6.30–9.81)	<.01
Length of stay (per 1-day increase)	1.02 (1.01–1.02)	<.01
Gender (women vs men)	0.89 (0.77–1.02)	.11
Obese (yes vs no)	0.70 (0.52–0.92)	.01
Depression (yes vs no)	0.70 (0.55–0.88)	<.01
Median household income (per quartile increase)	1.05 (0.98–1.12)	.14

NOTE. Reason for index hospitalization (IBD-related vs non-IBD-related) was removed because of $P > .2$.

balance" (47.8% of patients), "Other and unspecified anemias" (24.7% of patients), "Personal history of certain other diseases" (13.4% of patients), "Acute renal failure" (11.5% of patients), and "Chronic kidney disease" (9.4% of patients).

Longitudinal Outcomes in Frail vs Non-Frail Patients

Patients were followed over median of 10 months after index hospitalization. Patients with IBD with frailty had significantly higher rate of readmission within 6 months (41.2% vs 33.2%, $P < .01$), inpatient mortality (2.6% vs 0.7%, $P < .01$), risk of severe hospitalizations (15.4% vs 10.4%, $P < .01$), and unplanned hospitalization (37.6% vs 28.3%, $P < .01$), as compared with non-frail IBD patients (Table 2). Frail patients were also less likely to undergo IBD-related surgery (1.04% vs 2.02%, $P < .01$), although no differences were observed in risk of IBD-related procedures (13.5% vs 14.1%, $P = .11$), as compared with non-frail patients. Frail patients also had a shorter time to readmission, inpatient mortality, and severe hospitalization as compared with non-frail patients (Figure 1*A–C*).

On multivariable analysis, adjusting for age, sex, household income, CCI score, obesity, depression, length of stay, and reason for index admission, frailty was independently associated with 21% higher risk of readmission (adjusted hazard ratio [aHR], 1.21; 95% confidence interval, 1.17–1.25) (Table 3), 57% higher risk of mortality (aHR, 1.57 [1.34–1.83]) (Table 4), and 22% higher risk of IBD-related severe hospitalization (aHR, 1.22 [1.16–1.29]). Frailty was also independently associated with 22% lower risk of IBD-related surgery (aHR, 0.78 [0.66–0.91]) (Supplementary Table 7). This independent impact of frailty on risk of readmission, inpatient mortality, and severe hospitalization was observed on several stratified analyses: patients with vs without significant comorbidities (CCI 1 or more vs CCI = 0), patients with severe vs non-severe index hospitalization, and patients with index hospitalization due to IBD vs not related to IBD (Supplementary Table 8).

Annual Burden and Costs of Hospitalization by Frailty Status

Patients with IBD with frailty spent more days in the hospital annually as compared with non-frail patients (median [interquartile range]: 9 days [4–18] vs 5 days [3–10], $P < .01$) and had higher annual costs of hospitalization ($17,791 [$8368–$38,942] vs $10,924 [$5571–$22,632], $P < .01$) (Table 2). Averaged over total follow-up time, frail patients spent more days in hospital per month (0.9 days/month [0.44–1.9] vs 0.5 days/month [0.27–1.0], $P < .01$), with higher monthly cost of

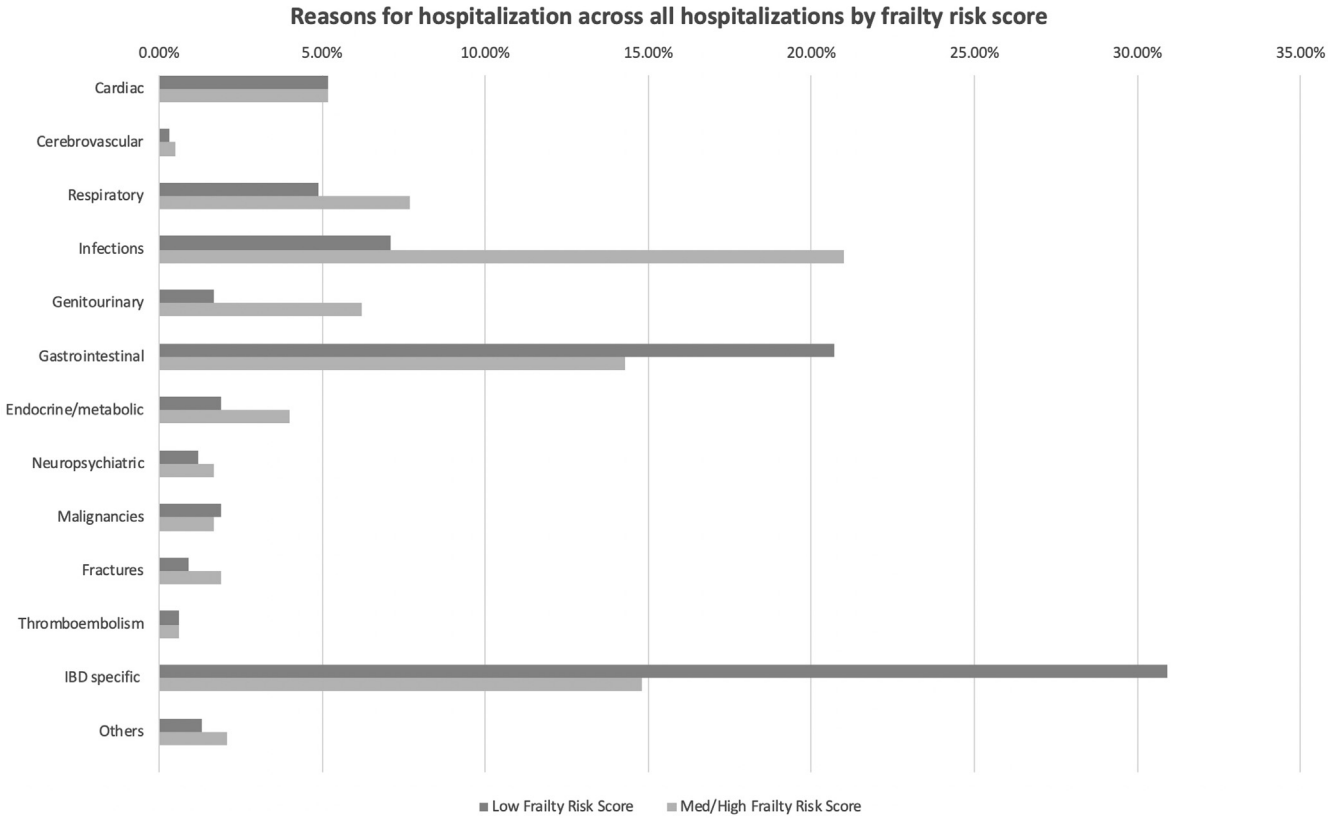


Figure 2. Causes for hospitalization in frail vs non-frail patients with IBD. IBD, inflammatory bowel disease.

hospitalization ($1882/month [$886–$4008] vs $1158/month [$595–$2376]).

Reasons for Hospitalization by Frailty Status

Across all hospitalizations, frail patients with IBD were significantly less likely to be hospitalized primarily for gastrointestinal symptoms (14.3% vs 20.7%, $P < .01$) or specifically for IBD flare (14.8% vs 30.9%, $P < .01$). However, frail patients were significantly more likely to be hospitalized for serious infections (21.0% vs 7.1%, $P < .01$) and for respiratory causes (7.7% vs 4.9%, $P < .01$) or fractures (1.9% vs 0.9%, $P < .01$) (Figure 2). Overall, frail patients with IBD were significantly more likely than non-frail IBD patients to experience preventable admissions (27.5% vs 14%, $P < .01$).

Discussion

As the prevalence of IBD increases in older patients, treatment options improve patient longevity, and extra-intestinal manifestations compromise overall health status, it is imperative to identify patients who may be at high risk of disease-related vs treatment-related complication risks. In this nationally representative longitudinal study using NRD, which captures more than 85% of all hospital discharges in 21 states, and the validated Hospital Frailty Risk Score, we made several key observations regarding the prognostic impact of frailty in hospitalized adults with IBD. First, we observed approximately one-third of hospitalized adults with IBD may be classified as frail. As anticipated, frail patients were older and had a higher burden of comorbidities. However, approximately half the patients classified as frail were younger than 65 years, and 42% did not have any significant comorbidities. This helps to highlight a distinct profile of frail patients. Second, we observed that frailty was independently associated with a significantly higher burden and costs of hospitalization, risk of readmission, and inpatient mortality, even after adjustment for age, comorbidities, and severity and indication for index admission. Third, the most common reason for readmission in frail patients with IBD was infection-related or related to cardiorespiratory compromise, in contrast to a higher burden of IBD-related hospitalization in non-frail patients with IBD. Frail patients were also likely to undergo IBD-related surgery, although no differences were observed in rates of IBD-related endoscopic procedures. Overall, these findings suggest higher burden of hospitalization and mortality in frail patients with IBD that may be driven by treatment-related or non–IBD-related complications. Frailty can serve as an important prognostic factor in risk-stratifying patients with IBD and inform optimal treatment approach.

Several studies have identified that older age is independently associated with higher risk of serious infections, hospitalization, and intolerance to immunosuppressive agents in patients with IBD.[5–8,21] Yet, other

studies have suggested that selective use of an algorithmic treatment step-up strategy in older patients with suboptimal disease control may be safe and effective in decreasing treatment disutility and avoid persistence on chronic corticosteroids.[22] This suggests that chronological age is not an ideal metric to inform treatment approach. On the other hand, frailty, characterized by a decline in functioning across multiple physiological systems, accompanied by an increased vulnerability to stressors, has been more consistently associated with adverse health outcomes across a spectrum of conditions. Frailty has been associated with higher mortality, hospitalization, and disability in the general population and specifically with adverse outcomes after kidney and liver transplantation and elective and emergency surgery.[14,23–27] Frailty has not been well-studied in patients with IBD to date. In a systematic review, Asscher et al[28] highlighted that comprehensive geriatric assessment, including frailty assessment, was often not performed in older patients with IBD. In a recent electronic health record-based study in immunosuppressive-treated patients with IBD, Kochar et al[15] observed that pretreatment frailty assessed using a similar code-based algorithm was present in ~12% patients and was associated with 1.8- to 2.0-fold higher risk of serious infections in these patients. The prevalence of frailty rates was higher in our cohort, which may be due to differences in patient population; we focused only on hospitalized adults with IBD. Nonetheless, we confirmed their observation that frail patients with IBD are more likely to be hospitalized for serious infections rather than for direct disease-related complications.

We focused on relatively short-term outcomes after a diagnosis of frailty. This was, in part, a limitation inherent to the database, which only tracks patients longitudinally within a calendar year. However, it is also important to recognize that frailty is a dynamic state, arising because of dysregulated, often interconnected, stress response, across immune, endocrine, and energy response systems, and may occur even in absence of a clear disease state or because of failure to rebound after illness or hospitalization. Frailty may be mitigated or possibly prevented through targeted interventions such as precise physical rehabilitation strategies, nutritional counseling and supplementation, and cognitive training.[29,30] Hence, attributing long-term adverse health outcomes after a one-time diagnosis of "frailty" may be challenging and better analyzed through repeated measures of frailty.

The strengths of our study include (1) innovative use of a nationally representative database, which was designed for the study of readmission risk and hospital-related outcomes, (2) comprehensive implementation of validated code-based frailty risk score algorithm to identify patients at low, medium, and high risk of frailty, (3) thorough evaluation of multiple adverse health outcomes around unplanned healthcare utilization, adjusting for important confounders, and (4) assessment of reasons for hospitalizations, including preventable and nonpreventable admissions. Although our study draws its strength from a large sample of patients who were longitudinally followed over the course of a year, it has some limitations. First, all analyses are based on administrative codes and CCS, which have inherent limitations with regard to misclassification of IBD diagnosis (especially in older patients), as well as with regard to causes of admissions. Second, in using the Hospital Frailty Risk Score, we combined patients at medium to high risk of frailty and classified them as frail. Frailty status was determined cross-sectionally at a single time point. Frailty is a dynamic, multidomain concept, encompassing somatic, mental, functional, and social status, that extends along a spectrum rather than being binary.[31] Future prospective studies would focus on examining all these domains of frailty, repeatedly over time, and evaluate its evolution and impact on adverse health outcomes in patients with IBD. Third, our analyses only focused on hospitalized patients, without details of outpatient clinic visits, medication use, and subjective and objective disease activity assessment, which may more comprehensively explain the differential outcomes observed between frail and non-frail IBD patients. Fourth, causes of readmissions were based on primary discharge diagnoses and grouped by system for ease of interpretation, which could result in potential misclassification and be somewhat biased because of reimbursement practices. Fifth, although the frailty risk scoring codes include physical function components such as hemiplegia, abnormal gait, fracture, and care involving rehabilitation procedures, no objective physical performance measures were assessed. Finally, NRD is inherently limited because it captures admissions only within state boundaries, is limited to 1 calendar year, and does not capture out-of-hospital mortality.

In summary, we observed that frailty is prevalent in approximately one-third of hospitalized adults with IBD. Frail patients have significantly higher burden and costs of hospitalization, higher risk of unplanned and preventable hospitalizations, and higher in-hospital mortality. Infections, rather than IBD-related causes, are the leading cause of hospitalization in frail patients. Future prospective studies incorporating routine assessment of multiple domains of frailty using validated scales, objective sarcopenia and physical function measurement, and eventual rehabilitation intervention to prevent or treat frailty are warranted to better inform the impact of frailty and its treatment in the management of patients with IBD.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2020.08.010.

References

1. Gisbert JP, Chaparro M. Systematic review with meta-analysis: inflammatory bowel disease in the elderly. Aliment Pharmacol Ther 2014;39:459–477.
2. Singh S, Underwood F, Loftus EV, et al. Worldwide incidence of older-onset inflammatory bowel diseases in the 21st century: a systematic review of population-based studies. Gastroenterology 2019;156:S394–S395.
3. Global Burden of Diseases Collaborators. 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;5:17–30.
4. Coward S, Clement F, Benchimol EI, et al. Past and future burden of inflammatory bowel diseases based on modeling of population-based data. Gastroenterology 2019;156:1345–1353.
5. Ananthakrishnan AN, McGinley EL, Binion DG. Inflammatory bowel disease in the elderly is associated with worse outcomes: a national study of hospitalizations. Inflamm Bowel Dis 2009; 15:182–189.
6. Brassard P, Bitton A, Suissa A, et al. Oral corticosteroids and the risk of serious infections in patients with elderly-onset inflammatory bowel diseases. Am J Gastroenterol 2014; 109:1795–1802.
7. Cottone M, Kohn A, Daperno M, et al. Advanced age is an independent risk factor for severe infections and mortality in patients given anti-tumor necrosis factor therapy for inflammatory bowel disease. Clin Gastroenterol Hepatol 2011;9:30–35.
8. Nguyen NH, Ohno-Machado L, Sandborn WJ, et al. Infections and cardiovascular complications are common causes for hospitalization in older patients with inflammatory bowel diseases. Inflamm Bowel Dis 2018;24:916–923.
9. Ha CY, Katz S. Clinical implications of ageing for the management of IBD. Nat Rev Gastroenterol Hepatol 2014;11:128–138.
10. Singh S, Picardo S, Seow CH. Management of inflammatory bowel diseases in special populations: obese, old, or obstetric. Clin Gastroenterol Hepatol 2020;18:1367–1380.
11. Ananthakrishnan AN, Donaldson T, Lasch K, et al. Management of inflammatory bowel disease in the elderly patient: challenges and opportunities. Inflamm Bowel Dis 2017;23:882–893.
12. Benchimol EI, Cook SF, Erichsen R, et al. International variation in medication prescription rates among elderly patients with inflammatory bowel disease. J Crohns Colitis 2013;7:878–889.
13. Waljee AK, Wiitala WL, Govani S, et al. Corticosteroid use and complications in a US inflammatory bowel disease cohort. PLoS One 2016;11:e0158017.
14. Hoogendijk EO, Afilalo J, Ensrud KE, et al. Frailty: implications for clinical practice and public health. Lancet 2019; 394:1365–1375.
15. Kochar B, Cai W, Cagan A, et al. Pre-treatment frailty is independently associated with increased risk of infections after immunosuppression in patients with inflammatory bowel diseases. Gastroenterology 2020;158:2104–2111.
16. Overview H. Healthcare Cost and Utilization Project (HCUP). Rockville, MD: Agency for Healthcare Research and Quality, 2016.
17. Overview N. Healthcare Cost and Utilization Project (HCUP). Rockville, MD: Agency for Healthcare Research and Quality, 2015.
18. Gilbert T, Neuburger J, Kraindler J, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. Lancet 2018;391:1775–1782.
19. Elixhauser APL. Clinical Classifications Software (CCS): Agency for Healthcare Research and Quality. vol 2017. Rockville, MD: Agency for Healthcare Research and Quality, 2015.
20. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–383.
21. Borren NZ, Ananthakrishnan AN. Safety of biologic therapy in older patients with immune-mediated diseases: a systematic review and meta-analysis. Clin Gastroenterol Hepatol 2019; 17:1736–1743.
22. Singh S, Stitt LW, Zou G, et al. Early combined immunosuppression may be effective and safe in older patients with Crohn's disease: post hoc analysis of REACT. Aliment Pharmacol Ther 2019;49:1188–1194.
23. Handforth C, Clegg A, Young C, et al. The prevalence and outcomes of frailty in older cancer patients: a systematic review. Ann Oncol 2015;26:1091–1101.
24. Hewitt J, Long S, Carter B, et al. The prevalence of frailty and its association with clinical outcomes in general surgery: a systematic review and meta-analysis. Age Ageing 2018; 47:793–800.
25. Kallenberg MH, Kleinveld HA, Dekker FW, et al. Functional and cognitive impairment, frailty, and adverse health outcomes in older patients reaching ESRD: a systematic review. Clin J Am Soc Nephrol 2016;11:1624–1639.
26. Kim DH, Kim CA, Placide S, et al. Preoperative frailty assessment and outcomes at 6 months or later in older adults undergoing cardiac surgical procedures: a systematic review. Ann Intern Med 2016;165:650–660.
27. Kobashigawa J, Dadhania D, Bhorade S, et al. Report from the American Society of Transplantation on frailty in solid organ transplantation. Am J Transplant 2019;19:984–994.
28. Asscher VER, Lee-Kong FVY, Kort ED, et al. Systematic review: components of a comprehensive geriatric assessment in inflammatory bowel disease—a potentially promising but often neglected risk stratification. J Crohns Colitis 2019; 13:1418–1432.
29. Dent E, Martin FC, Bergman H, et al. Management of frailty: opportunities, challenges, and future directions. Lancet 2019; 394:1376–1386.
30. Negm AM, Kennedy CC, Thabane L, et al. Management of frailty: a systematic review and network meta-analysis of randomized controlled trials. J Am Med Dir Assoc 2019; 20:1190–1198.
31. Asscher V, Jong AVM, Mooijaart S. The challenges of managing inflammatory bowel diseases in older patients. Clin Gastroenterol Hepatol 2020;18:1648–1649.

Reprint requests
Address requests for reprints to: Siddharth Singh, MD, MS, Division of Gastroenterology, University of California San Diego, 9452 Medical Center Drive, ACTRI 1W501, La Jolla, California 92093. e-mail: sis040@ucsd.edu; fax: (858) 657-7259.

CRediT Authorship Contributions
■■■

Conflicts of interest
These authors disclose the following: JE has been Team Leader of the Inflammatory Bowel Disease, Physical Therapy, and Exercise Clinical Practice Guideline Team. WJS has received research grants from Atlantic Healthcare Limited, Amgen, Genentech, Gilead Sciences, AbbVie, Janssen, Takeda, Lilly, Celgene/Receptos, Pfizer, Prometheus Laboratories (now Prometheus Biosciences); consulting fees from AbbVie, Allergan, Amgen, Arena Pharmaceuticals, Avexegen Therapeutics, BeiGene, Boehringer Ingelheim, Celgene,

Celltrion, Conatus, Cosmo, Escalier Biosciences, Ferring, Forbion, Genentech, Gilead Sciences, Gossamer Bio, Incyte, Janssen, Kyowa Kirin Pharmaceutical Research, Landos Biopharma, Lilly, Oppilan Pharma, Otsuka, Pfizer, Progenity, Prometheus Biosciences (merger of Precision IBD and Prometheus Laboratories), Reistone, Ritter Pharmaceuticals, Robarts Clinical Trials (owned by Health Academic Research Trust, HART), Series Therapeutics, Shire, Sienna Biopharmaceuticals, Sigmoid Biotechnologies, Sterna Biologicals, Sublimity Therapeutics, Takeda, Theravance Biopharma, Tigenix, Tillotts Pharma, UCB Pharma, Ventyx Biosciences, Vimalan Biosciences, and Vivelix Pharmaceuticals; and stock or stock options from BeiGene, Escalier Biosciences, Gossamer Bio, Oppilan Pharma, Prometheus Biosciences (merger of Precision IBD and Prometheus Laboratories), Progenity, Ritter Pharmaceuticals, Ventyx Biosciences, Vimalan Biosciences. His spouse has received the following: Opthotech - consultant, stock options; Progenity - consultant, stock; Oppilan Pharma - employee, stock options; Escalier Biosciences - employee, stock options; Prometheus Biosciences (merger of Precision IBD and Prometheus Laboratories) - employee, stock options; Ventyx Biosciences – employee, stock options; and Vimalan Biosciences – employee, stock options. SS has received research grants from AbbVie and Janssen. The remaining authors disclose no conflicts.

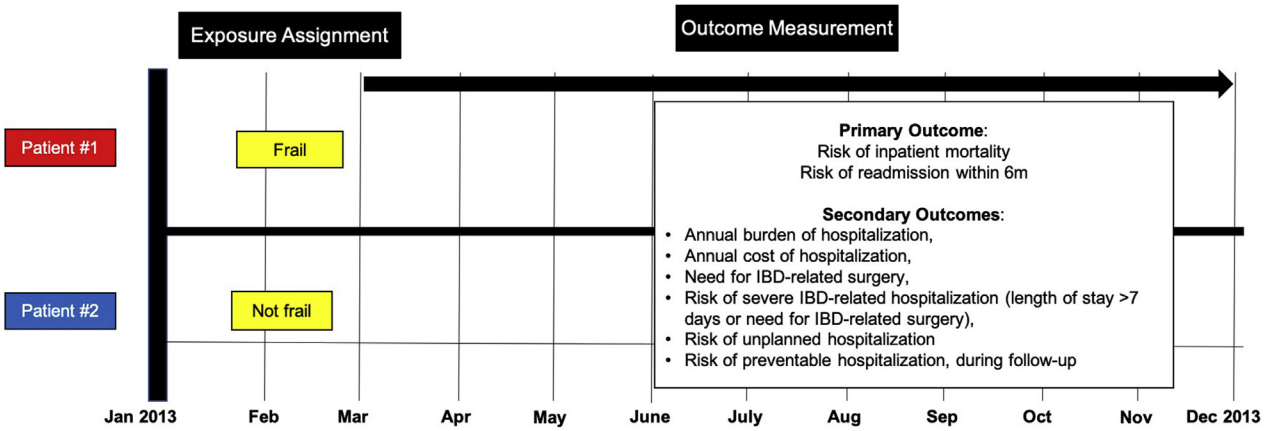
Funding

Dr Nguyen is supported by NIH/NIDDK (T32DK007202). Dr Sandborn is partially supported by NIDDK-funded San Diego Digestive Diseases Research Center (P30 DK120515). Dr Singh is supported by NIH/NIDDK (K23DK117058), IOIBD Operating Grant 2019, and the Crohn's and Colitis Foundation Career Development Award (#404614).

Supplementary Methods

Clinical Classifications Software Codes

The single level CCS code for IBD (144) is based on ICD-9 codes for Crohn's disease and ulcerative colitis (555.0, 555.1, 555.2, 555.9, 556.0, 556.1, 556.2, 556.3, 556.4, 556.5, 556.6, 556.8, and 556.9). CCS has been used in managed care plans to rank hospitalizations by type of condition, by insurers to develop clinically based utilization profiles, by researchers to explore the types of conditions and procedures that are most frequent in their study populations or to compare alternative treatments for similar conditions, and in risk adjustment models and as a way to predict future health resource utilization.



web 4C/FPO

Supplementary Figure 1. Study design with cohort selection, exposure assignment, and outcome ascertainment. IBD, inflammatory bowel disease.

Supplementary Table 1. ICD-9 Revision Codes Used to Identify Frailty Risk Score

ICD 9 codes	ICD-9 condition	Points
2900	Senile dementia, uncomplicated	7.1
2941	Dementia in conditions classified elsewhere	7.1
342	Hemiplegia	4.4
3310	Alzheimer's disease	4
438	Late effects of cerebrovascular disease	3.7
V1588	History of fall	3.6
788	Symptoms involving urinary system	3.2
6256	Stress incontinence, female	3.2
5990	Urinary tract infection	3.2
2930	Delirium due to conditions classified elsewhere	3.2
E8889	Unspecified fall	3.2
920	Contusion of face, scalp, and neck except eye(s)	3.2
921	Contusion of eye and adnexa	3.2
5997	Hematuria	3
041	Bacterial infection in conditions classified elsewhere and of unspecified site	2.9
482	Other bacterial pneumonia	2.9
483	Pneumonia due to other specified organism	2.9
78097	Altered mental status	2.7
7812	Abnormality of gait	2.6
437	Other and ill-defined cerebrovascular disease	2.6
7803	Convulsions	2.6
7800	Alterations of consciousness	2.5
99676	Other complications due to genitourinary device, implant, and graft	2.4
850	Concussion	2.4
851	Cerebral laceration and contusion	2.4
852	Subarachnoid subdural and extradural hemorrhage following injury	2.4
853	Other and unspecified intracranial hemorrhage following injury	2.4
854	Intracranial injury of other and unspecified nature	2.4
810	Fracture of clavicle	2.3
811	Fracture of scapula	2.3
812	Fracture of humerus	2.3
818	Ill-defined fractures of upper limb	2.3
276	Disorders of fluid electrolyte and acid-base balance	2.3
719	Other and unspecified disorders of joint	2.3
797	Senility without mention of psychosis	2.2
V57	Care involving use of rehabilitation procedures	2.1
2909	Unspecified senile psychotic condition	2.1
V63	Unavailability of other medical facilities for care	2

Supplementary Table 1. Continued

ICD 9 codes	ICD-9 condition	Points
2904	Vascular dementia	2
924	Contusion of lower limb and of other and unspecified sites	2
682	Other cellulitis and abscess	2
369	Blindness and low vision	1.9
266	Deficiency of b-complex components	1.9
V62	Other psychosocial circumstances	1.8
332	Parkinson's disease	1.8
7802	Syncope and collapse	1.8
807	Fracture of rib(s) sternum larynx and trachea	1.8
564	Functional digestive disorders not elsewhere classified	1.8
584	Acute renal failure	1.8
7070	Pressure ulcer	1.7
7072	Pressure ulcer stages	1.7
V02	Carrier of infectious disease	1.7
7071	Ulcer of lower limbs, except decubitus ulcer	1.6
7801	Hallucinations	1.6
532	Duodenal ulcer	1.6
458	Hypotension	1.6
586	Unspecified renal failure	1.6
99591	Sepsis	1.6
038	Septicemia	1.6
V12	Personal history of certain other diseases	1.5
5188	Other diseases of lung	1.5
715	Osteoarthrosis and allied disorders	1.5
345	Epilepsy and recurrent seizures	1.5
7330	Osteoporosis	1.4
821	Fracture of other parts of femur	1.4
820	Fracture of neck of femur	1.4
808	Fracture of pelvis	1.4
805	Fracture of vertebral column without mention of spinal cord injury	1.4
251	Other disorders of pancreatic internal secretion	1.4
794	Abnormal results of function studies	1.4
585	Chronic kidney disease	1.4
7882	Retention of urine	1.3
7999	Other unknown and unspecified cause of morbidity and mortality	1.3
593	Other disorders of kidney and ureter	1.3
78830	Urinary incontinence, unspecified	1.2
3311-3319	Other cerebral degenerations (excluding Alzheimer's)	1.2
9590	Other and unspecified injury to head face and neck	1.2

Supplementary Table 1. Continued

ICD 9 codes	ICD-9 condition	Points
7992	Nervousness	1.2
435	Transient cerebral ischemia	1.2
V6089	Other specified housing or economic circumstances	1.1
729	Other disorders of soft tissues	1.1
E8844	Accidental fall from bed	1.1
873	Other open wound of head	1.1
008	Intestinal infections due to other organisms	1.1
009	Infectious colitis, enteritis, and gastroenteritis	1.1
486	Pneumonia, organism unspecified	1.1
485	Bronchopneumonia, organism unspecified	1.1
481	Pneumococcal pneumonia	1.1
507	Pneumonitis due to solids and liquids	1
7845	Other speech disturbance	1
268	Vitamin D deficiency	1
V44	Artificial opening status	1
7854	Gangrene	1
783	Symptoms concerning nutrition metabolism and development	0.9
3898	Other specified forms of hearing loss	0.9
E880	Accidental fall on or from stairs or steps	0.9
E885	Fall on same level from slipping, tripping and stumbling	0.9
242	Thyrotoxicosis with or without goiter	0.9
7373	Kyphoscoliosis and scoliosis	0.9
7872	Dysphagia	0.8
V468	Dependence on other enabling machines	0.8
V097	Infection with microorganisms resistant to other specified antimycobacterial agents	0.8
7331	Pathologic fracture	0.8
578	Gastrointestinal hemorrhage	0.8
538	Gastrointestinal mucositis (ulcerative)	0.8
56989	Other specified disorders of intestine	0.8
5699	Unspecified disorder of intestine	0.8
43401	Cerebral thrombosis with cerebral infarction	0.8
43411	Cerebral embolism with cerebral infarction	0.8
43491	Cerebral artery occlusion, unspecified with cerebral infarction	0.8
592	Calculus of kidney and ureter	0.7
303	Alcohol dependence syndrome	0.7
3050	Nondependent alcohol abuse	0.7
879	Other procedures without mention of misadventure at the time of procedure as the cause of abnormal reaction of patient or of later complication	0.7

Supplementary Table 1. Continued

ICD 9 codes	ICD-9 condition	Points
7850	Tachycardia, unspecified	0.7
7851	Palpitations	0.7
7853	Other abnormal heart sounds	0.7
5198	Other diseases of respiratory system, not elsewhere classified	0.7
V69	Problems related to lifestyle	0.6
7906	Other abnormal findings of blood chemistry	0.6
V15	Other personal history presenting hazards to health	0.5
881	Open wound of elbow forearm and wrist	0.5
2962	Major depressive disorder single episode	0.5
2963	Major depressive disorder recurrent episode	0.5
7240	Spinal stenosis other than cervical	0.5
7230	Spinal stenosis in cervical region	0.5
275	Disorders of mineral metabolism	0.4
6868	Other specified local infections of skin and subcutaneous tissue (approximate match)	0.4
285	Other and unspecified anemias	0.4
686	Other local infections of skin and subcutaneous tissue	0.4
7870	Nausea and vomiting	0.3
558	Other and unspecified noninfectious gastroenteritis and colitis	0.3
7806	Fever and other physiologic disturbances of temperature regulation	0.1

ICD-9, International Classification of Diseases, 9th Revision.

Supplementary Table 2. ICD-9-CM Coding Algorithm for Charlson Comorbidity Index

Comorbidities	Charlson's ICD-9-CM	Weight
Myocardial infarction	410.x, 412.x	1
Congestive heart failure	428.x	1
Peripheral vascular disease	443.9, 441.x, 785.4, V43.4. Procedure 38.48	1
Cerebrovascular disease	430.x-438.x	1
Dementia	290.x	1
Chronic pulmonary disease	490.x-505.x, 506.4	1
Rheumatic disease	710.0, 710.1, 710.4, 714.0-714.2, 714.81, 725.x	1
Peptic ulcer disease	531.x-534.x	1
Mild liver disease	571.2, 571.4-571.6	1
Diabetes without chronic complication	250.0-250.3, 250.7	1
Diabetes with chronic complication	250.4-250.6	1
Hemiplegia or paraplegia	344.1, 342.x	2
Renal disease	582.x, 583-583.7, 585.x, 586.x, 588.x	2
Any malignancy, including lymphoma and leukemia, except malignant neoplasm of skin	140.x-172.x, 174.x-195.8, 200.x-208.x	2
Moderate or severe liver disease	456.0-456.21, 572.2-572.8	2
Metastatic solid tumor	196.x-199.1	6
AIDS/HIV	042.x-044.x	6

AIDS/HIV, acquired immune deficiency syndrome/human immunodeficiency virus; ICD-9-CM, International Classification of Diseases, 9th Revision-Clinical Modification.

Supplementary Table 3. Diagnosis and Procedure Codes, ICD-9-CM and CCS, Used in Classifying Patients

Diagnoses/procedures	PRCCS (CCS codes for procedures) DXCCS (CCS codes for diagnoses)	Description of corresponding CCS codes
Procedures		
Gastrointestinal or hepatic procedures	68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 87, 88, 89, 90, 92, 93, 94, 95, 96, 97, 98, 99, 221	68 – Injection or ligation of esophageal varices 69 – Esophageal dilatation 70 – Upper gastrointestinal endoscopy, biopsy 71 – Gastrostomy, temporary and permanent 72 – Colostomy, temporary and permanent 73 – Ileostomy and other enterostomy 74 – Gastrectomy, partial and total 75 – Small bowel resection 76 – Colonoscopy and biopsy 77 – Proctoscopy and anorectal biopsy 78 – Colorectal resection 79 – Local excision of large intestine lesion (not endoscopy) 80 – Appendectomy 81 – Hemorrhoid procedures 82 – Endoscopic retrograde cannulation of pancreas (ERCP) 83 - Biopsy of liver 84 - Cholecystectomy and common duct exploration 87 – Laparoscopy 88 - Abdominal paracentesis 89 - Exploratory laparotomy 90 - Excision, lysis peritoneal adhesions 92 - Other bowel diagnostic procedures 93 - Other non-OR upper GI therapeutic procedures 94 – Other OR upper GI therapeutic procedures 95 – Other non-OR upper GI therapeutic procedures 96 – Other OR lower GI therapeutic procedures 97 – Other gastrointestinal diagnostic procedures 98 – Other non-OR gastrointestinal therapeutic procedures 99 – Other OR gastrointestinal therapeutic procedures 221 – Nasogastric tube
Gastrointestinal surgeries	72, 73, 75, 78, 79, 89, 90	72 – Colostomy, temporary and permanent 73 – Ileostomy and other enterostomy 75 – Small bowel resection 78 – Colorectal resection 79 – Local excision of large intestine lesion (not endoscopic) 89 – Exploratory laparotomy 90 – Excision, lysis peritoneal adhesions
Blood transfusions	222	
Parenteral or enteral nutrition	223	

Supplementary Table 3. Continued

Diagnoses/procedures	PRCCS (CCS codes for procedures) DXCCS (CCS codes for diagnoses)	Description of corresponding CCS codes
Inflammatory bowel related procedures	70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 81, 87, 89, 92, 93, 94, 95, 96, 97, 98, 99	70 – Upper gastrointestinal endoscopy, biopsy 71 – Gastrostomy, temporary and permanent 72 – Colostomy, temporary and permanent 73 – Ileostomy and other enterostomy 74 – Gastrectomy, partial and total 75 – Small bowel resection 76 – Colonoscopy and biopsy 77 – Proctoscopy and anorectal biopsy 78 – Colorectal resection 79 – Local excision of large intestine lesion (not endoscopy) 81 – Hemorrhoid procedures 87 – Laparoscopy 89 - Exploratory laparotomy 92 - Other bowel diagnostic procedures 93 - Other non-OR upper GI therapeutic procedures 94 – Other OR upper GI therapeutic procedures 95 – Other non-OR upper GI therapeutic procedures 96 – Other OR lower GI therapeutic procedures 97 – Other gastrointestinal diagnostic procedures 98 – Other non-OR gastrointestinal therapeutic procedures 99 – Other OR gastrointestinal therapeutic procedures
Surgeries		
Colostomy	72	
Ileostomy	73	
Small bowel resection	75	
Colorectal resection	78	
Local excision of large intestine lesion	79	
Exploratory laparotomy	89	
Excision, lysis peritoneal adhesions	90	

CCS, Clinical Classifications Software; GI, gastrointestinal; ICD-9-CM, International Classification of Diseases, 9th Revision-Clinical Modification.

FLA 5.6.0 DTD ■ YJCGH57424_proof ■ 27 October 2020 ■ 4:38 am ■ ce CLR

Supplementary Table 4. ICD-9-CM Coding For Agency for Healthcare Research and Quality Preventive Quality Indicators[a]

PQI number	Preventive Quality Indicator	Definition[a]	ICD-9 codes
1	Diabetes short-term complications	Discharges with principal ICD-9-CM diagnosis for diabetes short-term complications (ketoacidosis, hyperosmolarity, or coma)	250.10, 250.11, 250.12, 250.13, 250.20, 250.21, 250.22, 250.23, 250.30, 250.31, 250.32, 250.33
2	Perforated appendix	Discharges with any listed ICD-9-CM diagnosis codes for perforations or abscesses of appendix	540.0, 540.1, 540.9, 541
3	Diabetes long-term complications	Discharges with principal ICD-9-CM diagnosis code for diabetes with long-term complications (renal, eye, neurological, circulatory, or complications not otherwise specified)	250.40, 250.41, 250.42, 250.43, 250.50, 250.51, 250.52, 250.53, 250.60, 250.61, 250.62, 250.63, 250.70, 250.71, 250.72, 250.73, 250.80, 250.81, 250.82, 250.83, 250.90, 250.91, 250.92, 250.93
5	Chronic obstructive pulmonary disease or asthma in older adults	Discharges with principal ICD-9-CM diagnosis code for COPD or asthma Excluded cases Any listed ICD-9-CM codes for cystic fibrosis and anomalies of the respiratory system	COPD (excluding acute bronchitis) 491.0, 491.1, 491.20, 491.21, 491.22, 491.8, 491.9, 492.0, 492.8, 494, 494.0, 494.1, 496 Asthma 493.00, 493.01, 493.02, 493.10, 493.11, 493.12, 493.20, 493.21, 493.22, 493.81, 493.82, 493.90, 493.91, 493.92 Excluded cases 277.0, 277.01, 277.02, 277.03, 277.09, 516.61, 516.62, 516.63, 516.64, 516.69, 747.21, 748.3, 748.4, 748.5, 748.60, 748.61, 748.69, 748.8, 748.9, 750.3, 759.3, 770.7

Supplementary Table 4. Continued

PQI number	Preventive Quality Indicator	Definition[a]	ICD-9 codes
7	Hypertension	Discharges with principal ICD-9-CM diagnosis code for hypertension Excluded cases With any listed ICD-9-CM procedure codes for cardiac procedure or any listed ICD-9-CM diagnosis codes for Stage I-IV kidney disease, only if accompanied by any listed ICD-9-CM procedure codes for dialysis access	401.0, 401.9, 402.00, 402.10, 402.90, 403.00, 403.10, 403.90, 404.00, 404.10, 404.90 Excluded cases 403.00, 403.10, 404.00, 404.10, 404.90 Procedure codes 00.50, 00.51, 00.52, 00.53, 00.54, 00.56, 00.57, 00.66, 17.51, 17.52, 17.55, 35.00, 35.01, 35.02, 35.03, 35.04, 35.05, 35.06, 35.07, 35.08, 35.09, 35.10, 35.11, 35.12, 35.13, 35.14, 35.20, 35.22, 35.23, 35.24, 35.25, 35.26, 35.27, 35.28, 35.31, 35.32, 35.33, 35.34, 35.35, 35.39, 35.41, 35.42, 35.35, 35.39, 35.41, 35.42, 35.50, 35.51, 35.52, 35.53, 35.54, 35.55, 35.60, 35.61, 35.62, 35.63, 35.70, 35.71, 35.72, 35.73, 35.81, 35.82, 35.83, 35.84 ,35.91, 35.92, 35.93, 35.94, 35.95, 35.96, 35.97, 35.98, 35.99, 36.01, 36.02, 36.03, 36.04, 36.05, 36.06, 36.07, 36.09 , 36.10, 36.11, 36.12, 36.13, 36.14, 36.15, 36.16, 36.17, 36.19, 362, 363, 3631, 36.32, 36.33, 36.34, 36.39, 36.91, 36.99, 37.31, 37.32, 37.33, 37.34, 37.35, 37.36, 37.37, 37.41, 375, 37.51, 37.52, 37.53, 37.54, 37.55, 37.60 37.61, 37.62, 37.63, 37.64, 37.65, 37.66, 37.70, 37.71, 37.72, 37.73, 37.74, 37.75, 37.76, 37.77, 37.78, 37.79, 37.80, 37.81, 37.82, 37.83, 37.85, 37.86, 37.87, 37.89, 37.94, 37.95, 37.96, 37.97, 37.98, 38.26 38.95, 39.27, 39.29, 39.42, 39.43, 39.93, 39.94
8	Congestive heart failure	Discharges with principal ICD-9-CM diagnosis code for heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428.0, 428.1, 428.20, 428.21, 428.22, 428.23, 428.30, 428.31, 428.32, 428.33, 428.40, 428.41, 428.42, 428.43, 428.9
10	Dehydration	Discharges with either principal ICD-9-CM diagnosis code for dehydration or any secondary ICD-9-CM diagnosis codes for dehydration and principal ICD-9-CM diagnosis code for hyperosmolality and/or hypernatremia, gastroenteritis, or acute kidney injury Excluded cases Any listed ICD-9-CM diagnosis codes for chronic renal failure	276.5, 276.50, 276.51, 276,52, 276.0, 008.61, 008.62, 008.63, 008.64, 008.65, 008.66, 008.67, 008.69, 008.8, 009.0, 009.1, 009.2, 009.3, 558.9, 584.5, 584.6, 584.7, 584.8, 584.9, 586, 997.5 Exclude cases 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 585.5, 585.6

Supplementary Table 4. Continued

PQI number	Preventive Quality Indicator	Definition[a]	ICD-9 codes
11	Bacterial pneumonia	Discharges with principal ICD-9-CM diagnosis code for bacterial pneumonia Excluded cases Any listed ICD-9CM diagnosis codes for sickle cell anemia or HB-S disease. Any listed ICD-9-CM diagnosis codes or any listed ICD-9-CM procedure codes for immunocompromised state	481, 4822, 48230, 48231, 48232, 48239, 48240, 48241, 48242, 48249, 4829, 4830, 4831, 4838, 485, 486 Excluded cases 42, 136.3, 199.2, 238.73, 238.76, 238.77, 238.79, 260, 261, 262, 279.00, 279.01, 279.02, 279.03, 279.04, 279.05, 279.06, 279.09, 279.10, 279.11, 279.12, 279.13, 279.19, 279.2, 279.3, 279.4, 27941, 279.50, 279.51, 27952, 279.53, 279.8, 279.9, 284.09, 284.1, 284.11, 284.1, 284.19, 288.0, 288.00, 288.01, 288.02, 288.03, 288.09, 288.1, 288.2, 288.4, 288.50, 288.51, 288.59, 289.53, 289.83, 403.01, 403.11, 439.1, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 579.3, 585, 585.5, 585.6, 996.8, 996.80, 996.81, 996.82, 996.83, 996.84, 996.85, 996.86, 996.87, 996.88, 996.89, V420, V421, V426, V427, V428, V4281, V428.2, V428.3, V4284, V4289, V451, V451.1, V560, V561, V562 Procedure codes 00.18, 33.5, 33.50, 33.51, 33.52, 33.6, 37.5, 37.51, 41.0, 41.00, 41.01, 41.02, 41.03, 41.04, 41.05, 41.06, 41.07, 41.08, 41.09, 4697, 50.51, 50.59, 52.80, 52.81, 52.82, 52.83, 52.85, 52.86, 55.69
12	Urinary tract infection	Discharges with principal ICD-9-CM diagnosis code for urinary tract infection Excluded cases With any listed ICD-9-CM diagnosis codes for kidney/urinary tract disorder. With any listed ICD-9-CM diagnosis codes or any listed ICD-9-CM procedure codes for immunocompromised state	590.10, 590.11, 590.2, 590.3, 590.80, 590.81, 590.9, 595.0, 595.9, 599.0 Excluded cases 590.00, 590.01, 593.70, 593.71, 593.72, 593.73, 753.0, 753.10, 753.11, 753.12, 753.13, 753.14, 753.15, 753.16, 753.17, 753.19, 753.20, 753.21, 753.22, 753.23, 753.29, 753.3, 753.4, 753.5, 753.6, 753.8, 753.9
13	Angina without procedure	Discharges with principal diagnosis code for angina Excluded cases With any listed ICD-9-CM procedure codes for cardiac procedure	411.81, 411.89, 413.0, 413.1, 413.9
14	Uncontrolled diabetes	Discharges with principal diagnosis code for uncontrolled diabetes without mention of short-term or long-term complication	250.02, 250.03

Supplementary Table 4. Continued

PQI number	Preventive Quality Indicator	Definition[a]	ICD-9 codes
15	Asthma in younger adults	Discharges with principal ICD-9-CM diagnosis code for asthma Excluded cases With any listed ICD-9 diagnosis codes for cystic fibrosis and anomalies of the respiratory system	493.00, 493.01, 493.02, 493.10, 493.11, 493.12, 493.20, 493.21, 493.22, 493.81, 493.82 493.90, 493.91, 493.92
16	Lower-extremity amputation among diabetics	Any listed ICD-9-CM procedure codes for lower-extremity amputation and any listed ICD-9-CM diagnosis codes for diabetes Excluded cases 89.50, 89.51, 89.60, 89.61, 89.62, 89.63, 89.70, 89.71, 89.72, 89.73, 89.72, 89.73, 89.74, 89.75, 89.76, 89.77	Procedure codes 84.10, 84.12, 84.13, 84.14, 84.15, 84.16, 84.17, 84.18, 84.19 Diagnosis codes 250.00, 250.01, 250.02, 250.03, 250.10, 250.11, 250.12, 250.13, 250.20, 250.21, 250.22, 250.23, 250.30, 250.31, 250.32, 250.33, 250.40, 250.41, 250.42, 250.43, 250.50, 250.51, 250.52, 250.53, 250.60, 250.61, 250.62, 250.63, 250.70, 250.71, 250.72, 250.73, 250.80, 250.81, 250.82, 250.83, 250.90, 250.91, 250.92, 250.93

COPD, chronic obstructive pulmonary disease; HB-S disease, hemoglobin SS disease; ICD-9-CM, International Classification of Diseases, 9th Revision-Clinical Modification; PQI, Prevention Quality Indicator.
[a]ICD-9 codes for Prevention Quality Indicators, which are a set of measures that can be used with hospital inpatient discharge data to identify quality of care for ambulatory conditions for which good outpatient care can potentially prevent hospitalization, complications, or more severe disease. PQIs were developed by the Agency for Healthcare Research and Quality.

Supplementary Table 5. Diagnosis Codes Used in Grouping Causes of Admission in Patients With IBD

Diagnoses/procedures	DXCCS (CCS codes for diagnoses)
Cardiac	96, 97, 100, 101, 102, 104, 105, 106, 107, 108
Cerebrovascular	109, 110, 111, 112
Respiratory	122, 125, 127, 128, 129, 130, 131, 132, 133, 134
Infections	1, 2, 3, 4, 7, 8, 76, 77, 123, 124, 126, 135, 159, 197, 201, 246
Genitourinary	156, 157, 158, 160, 161, 162, 163, 165, 166
Gastrointestinal	14, 15, 60, 137, 138, 139, 140, 141, 142, 143, 145, 146, 147, 148, 149, 151, 152, 153, 154, 155, 250, 251
Endocrine/metabolic	48, 49, 50, 51, 52, 53, 54, 55
Neuropsychiatric	83, 84, 85, 93, 95, 65, 66, 67, 68, 69, 70, 71, 72
Malignancies	11, 12, 13, 16, 17, 18, 19, 20, 21, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44
Fractures	226, 229, 230, 231
Thromboembolism	116, 118
Inflammatory bowel disease specific	144
Others	150, 199, 204, 209, 211, 252, 253, 254, 257, 233, 235, 239, 242, 244, 259

CCS, Clinical Classifications Software; IBD, inflammatory bowel disease.

Supplementary Table 6. Specific Diagnosis Codes for Readmissions

Diagnoses/procedures	ICD-9 codes
Serious infections	
Meningitis	320.x, 321.x, 049.x
Encephalitis	323.x, 054.x, 062.x
Endocarditis	421.x
Pneumonia	481.x, 482.x
Pyelonephritis	590.x
Septic arthritis, Osteomyelitis	711.0x, 730.0x, 730.1x, 730.2x
Septicemia or bacteremia	038.x, 790.7
Clostridium difficile	008.45
Opportunistic infections	
Pulmonary tuberculosis	011.x
Atypical mycobacteria	031.x
Cryptococcosis, Aspergillosis, Histoplasmosis	117.5, 117.3, 115.x
Listeriosis	027.0
Leishmaniasis	085.x
Pneumocystis jiroveci pneumonia	136.3
Cardiac	
Acute myocardial infarction	410.xx (except 410.x2)
Heart failure	402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428.xx
Unstable angina	411.xx
Arrhythmia	427.xx (except 427.5)
Cardiac arrest	427.5

ICD-9, International Classification of Diseases, 9th Revision.

Supplementary Table 7. Cox Proportional Hazard Analysis Evaluating Risk of IBD-Related Surgery Within 6 Months by Frailty Risk Score, Adjusting for Age, Sex, Obesity, Household Income, and Charlson Comorbidity Index Score

Variable	Hazard ratio (95% confidence interval)	*P* value
Frailty risk score (moderate/high vs low)	0.80 (0.69–0.94)	.01
Age (per 1-y increase)	0.98 (0.98–0.99)	<.01
Charlson Comorbidity Index (reference group: 0)		
• 1	0.67 (0.56–0.82)	<.01
• 2 or more	0.50 (0.40–0.63)	<.01
Gender (women vs men)	0.86 (0.76–0.97)	.02
Median household income (reference group: 0 to 25th percentile ($1–$37,999))		
• 26th to 50th percentile ($38,000–$47,999)	1.25 (1.08–1.45)	<.01
• 76th to 100th percentile ($64,000 or more)	1.12 (0.96–1.30)	.15

NOTE. Inclusive of depression, obesity, and 51st to 75th percentile ($48,000–$63,999).

Supplementary Table 8. Stratified Analysis: Cox Proportional Hazard Analysis Evaluating Longitudinal Outcomes by Frailty Risk Score in Patients With vs Without Significant Comorbidities (CCI 1 or More vs CCI = 0), Patients With Severe vs Non-Severe Index Hospitalization, and Patients With Index Hospitalization due to IBD vs Not Related to IBD

Frail vs non-frail (adjusted hazard ratio, with 95% CI)	Readmission	Inpatient mortality	Readmission with severe hospitalization	IBD-related surgery
Comorbidity index				
CCI 0	1.37 (1.31–1.43)	2.80 (1.89–4.15)	1.54 (1.43–1.67)	0.85 (0.71–1.03)
CCI 1 or more	1.15 (1.10–1.20)	1.75 (1.49–2.06)	1.38 (1.28–1.48)	0.68 (0.51–0.91)
Severity of index hospitalization				
Severe	1.30 (1.22–1.39)	1.85 (1.37–2.49)	1.23 (1.12–1.35)	N/A
Non-severe	1.11 (1.07–1.15)	1.34 (1.11–1.62)	1.08 (1.01–1.15)	0.67 (0.55–0.81)
Reason for index hospitalization				
IBD-related	1.11 (1.04–1.17)	1.58 (1.10–2.28)	1.08 (0.98–1.19)	0.71 (0.56–0.90)
Non–IBD-related	1.25 (1.21–1.31)	1.54 (1.30–1.83)	1.27 (1.19–1.36)	0.82 (0.66–1.03)

NOTE. All analyses were adjusted for age, sex, income, obesity, depression, Charlson Comorbidity Index score, and severity and reason for admission.
CCI, Charlson Comorbidity Index; CI, confidence interval; IBD, inflammatory bowel disease.