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Health Care Costs and Resource Utilization Among Patients With Crohn's Disease With and Without Perianal Fistula

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Background: Perianal fistula (PAF), a complication of Crohn's disease (CD), is associated with substantial economic costs and poor prognosis. We determined prevalence of PAF CD in the United States and compared costs and health care resource utilization (HRU) of PAF CD patients with matched non-PAF CD patients.

Methods: This was a retrospective cohort study of claims data from the IBM MarketScan Commercial Database from October 1, 2015, to September 30, 2018. Eligible patients were aged 18 to 89 years with ≥2 CD diagnoses. Patients with PAF CD had ≥1 PAF diagnosis or procedure code and were matched with non-PAF CD patients. Cumulative prevalence of PAF CD in the US population was calculated across total patients in MarketScan. All-cause and gastrointestinal (GI)-related costs and HRU were compared between groups using a generalized linear model (GLM).

Results: Cumulative 3-year prevalence of PAF was 7.70% of patients with CD (N = 81,862) and 0.01% of the US population. Among PAF CD (n = 1218) and matched non-PAF CD (n = 4095) patients, most all-cause costs and HRU were GI-related. Mean total all-cause and GI-related health care costs per patient and per year for PAF CD were $85,233 and $71,612, respectively, vs $40,526 and $29,458 for non-PAF CD ($P$ < .0001). Among PAF CD vs non-PAF CD patients, GLM-adjusted proportions of patients with GI-related inpatient, outpatient, or pharmacy visits, mean GI-related inpatient length of stay, and mean GI-related surgeries were higher (P < .0001 for all comparisons).

Conclusions: Costs and HRU are significantly higher for patients with PAF CD vs non-PAF CD patients, highlighting the economic burden of the disease.

Key Words: Crohn's disease; perianal fistula; resource utilization; health care costs

Introduction

Crohn's disease (CD), a form of inflammatory bowel disease (IBD), is a relapsing-remitting systemic inflammatory disease that mainly affects the gastrointestinal (GI) tract and causes symptoms that include abdominal pain, diarrhea, weight loss, and rectal bleeding.[1,2] The 2015 National Health Interview Survey estimated that 1.3% of adults in the United States have received a diagnosis of IBD at some point (CD or ulcerative colitis).[3] Estimates of the prevalence of CD range from 16.7 to 318.5 per 100,000 in North America and from 0.6 to 322 per 100,000 in Europe, thus affecting up to 0.3% of the population in both North America and Europe.[4] One population-based study has estimated that approximately 785,000 people in the United States have CD.[5]

Among patients with CD, the development of perianal abscesses and fistulas is a common complication arising from the ongoing inflammatory process of the disease.[6,7] A perianal fistula (PAF) is an abnormal tubular tract that opens between the intestine and the nearby skin or adjacent organ and can cause drainage, bleeding, pain, swelling, and abscess formation.[2,6] Perianal fistula is an indicator of greater disease severity in CD and is associated with poor prognosis, with 1 study reporting that 71% of PAFs were treated surgically.[8,9] In a long-term analysis of 169 US patients with CD, the cumulative risk of experiencing a PAF was 12% after 1 year, 15% after 5 years, 21% after 10 years, and 26% after 20 years.[9] Similarly, a population-based study in the Netherlands found that the overall cumulative probability of developing PAF was 8% after 1 year, 12% after 5 years, and 16% after 10 years.[10] A recent analysis from a large US claims database estimated that 8% of US patients with CD have a PAF at any given time point.[7]

Patients with CD who develop PAF commonly experience symptoms such as fecal incontinence and anal pain, which significantly impact patients' quality of life.[11] One study found that IBD patients with perianal disease experienced worse physical functioning, fatigue, emotional well-being, and social functioning and reported more limitations due to physical health and emotional problems compared with patients who did not have perianal disease.[12] Patients with CD often require treatment with biologics or immunomodulators to control their luminal disease.[13] For patients with PAF CD, control of the underlying luminal disease is essential to obtaining maximum fistula response.[13] Recent guidelines discussing

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PAF CD recommend medical management with anti-tumor necrosis factor (TNF) agents, antibiotics, and/or immunosuppressants; surgery is used to control sepsis or manage complicated or poorly controlled cases.[6,13–15] Unfortunately, a large proportion of CD patients with complex PAF (defined here as involving the upper part of the sphincter complex, connecting to another organ such as the vagina, having multiple tracts, or involving perianal abscess) experience inadequate response to treatment or treatment failure, exacerbating the burden of the disease.[16]

There has been little research on the economic costs of PAF CD on the health care system. In a claims database analysis of US patients with a CD diagnosis from 2000 to 2005, median annual costs were higher for patients with fistulizing CD ($10,863) than for those with nonfistulizing CD ($6268); mean costs were $35,373 for fistulizing CD and $15,564 for nonfistulizing CD. The costs of fistulizing CD were largely driven by hospitalization and surgery.[2] Among 97 adult patients in Spain with CD and complex PAF (defined here as involving high fistula, multiple external orifices, perianal abscess, anal stenosis, or active rectal disease), the mean annual cost of care was $9657, with 75% of this amount spent for pharmacologic treatment.[17] The use of opioids among patients with IBD is also associated with higher costs,[18] and the amount of opioid use following anal fistulotomy is higher on average than opioid use after other common anorectal operations.[19]

To date, limited real-world evidence is available on the cumulative prevalence, clinical characteristics, and economic impact of PAF CD in the US population. We aimed to determine US-specific estimates of the cumulative prevalence of PAF CD and examine the economic impact of the disease by comparing the economic outcomes (costs and health care resource utilization [HRU]) of patients with PAF CD with those of matched patients with non-PAF CD.

Materials and Methods

Study Design and Patients

This is a retrospective cohort study of claims data from the IBM MarketScan Commercial database from October 1, 2015, to September 30, 2018 (study period; Figure 1). The IBM MarketScan Database contains longitudinal, de-identified, patient-level medical and pharmacy administrative claims from commercial plans across the United States. It is one of the largest claims data sources that contains employer-sponsored insurance claims. In the most recent 5 years of IBM MarketScan data, nearly 29 million patients had ≥12 months of continuous enrollment.

Patients with CD included those with ≥2 diagnoses of CD (International Classification of Disease [ICD]-9-Clinical Modification [CM]: 555.xx; ICD-10-CM: K50.xxx) ≥30 days apart during the study period. Patients with PAF CD were CD patients with ≥1 ICD-9/10-CM or Current Procedural Terminology (CPT) code for a PAF diagnosis or procedure (Supplementary Data Content 1) between October 1, 2016, and September 30, 2017 (identification period; Figure 1). The index date was the first claim date for a PAF diagnosis or procedure at any time during the identification period. The baseline period was the 12 months before the index date, and the follow-up period was the 12 months postindex date.

Patients with non-PAF CD had no PAF diagnosis or procedure during the study period. Non-PAF CD patients were matched to PAF CD patients based on birth year (±2 years) and sex. The same index date of the matched PAF CD patients was assigned to the non-PAF CD patients. Further matching was based on the presence or absence of a CD diagnosis during the baseline period, the location of CD in the body, and duration of the follow-up period (in months). The location of CD was incorporated into the matching process as follows: Among patients with the presence of CD during the baseline period, the disease location at the first CD diagnosis during the baseline period was considered and matched. Among patients with absence of CD during the baseline period, the disease location at the first CD diagnosis during the follow-up period was considered and matched. Each PAF CD patient was matched to up to 4 non-PAF CD patients. The PAF CD patients for whom a matched non-PAF CD patient could not be identified were excluded from the analysis.

Patients with CD included in the analysis were 18 to 89 years of age at index date and had continuous health plan enrollment for ≥12 months before and after the index date. Patients were excluded if they had a diagnosis for ankylosing spondylitis, psoriasis, psoriatic arthritis, or rheumatoid arthritis during the study period. Patient data were assessed until the earliest of either disenrollment or study end.

Study End Points

Cumulative prevalence of PAF CD among patients with CD in the US population was assessed as follows: Prevalent cases of

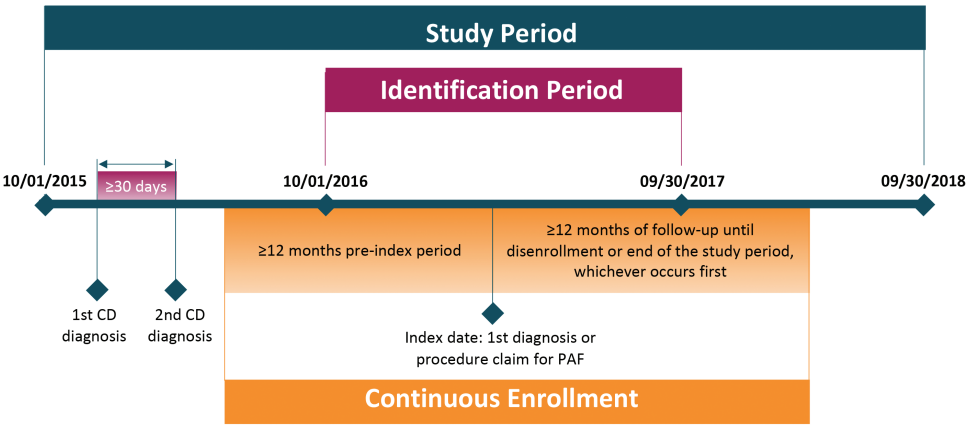

Figure 1. Study design. Abbreviations: CD, Crohn's disease; PAF, perianal fistula.

CD were identified by screening for ≥2 claims 30 days apart with CD-related ICD-9/10-CM codes during the 3-year study period. Patients with PAF were identified using ICD-9/10-CM and CPT codes (including relevant surgical codes; Supplementary Data Content 1) during the same 3-year study period. To calculate the prevalence of PAF CD in the CD patient population, the denominator was patients diagnosed with CD. To calculate the prevalence of PAF CD in the US population, the denominator was the total number of patients enrolled in the IBM MarketScan database during the same 3-year study period.

Demographic and clinical characteristics retrieved from patient records included age, sex, Quan-Charlson Comorbidity Index score, comorbidities (cardiac complications, diabetes mellitus, liver disease, renal disease, or chronic obstructive pulmonary disease), and the location of CD. Claims were considered GI-related if they contained a diagnosis of a GI condition at any position in the claim during the follow-up period. Gastrointestinal-related pharmacy costs included costs for any GI-related therapies.

All-cause and GI-related health care costs were computed during the 12-month follow-up period and reported as per patient per year (PPPY) for the following services: inpatient hospitalization costs, outpatient costs, pharmacy costs, total medical (inpatient + outpatient) costs, and total (medical + pharmacy) costs. Costs were adjusted to 2018 US dollars using the annual medical care and drug cost components of the Consumer Price Index to reflect inflation.

All-cause and GI-related HRU was computed during the follow-up period and reported as the proportion of patients receiving the following services: ≥1 inpatient hospitalization, ≥1 outpatient visit (office visit, emergency department visit, other visit), or ≥1 pharmacy visit, and PPPY length of hospitalization (days), number of inpatient stays, number of outpatient visits, and number of pharmacy visits. The number of GI-related surgeries was also reported as PPPY. Claims were considered GI-related surgery if the patient had any GI-related surgical CPT code in any position on the medical claim for IBD-related surgery, CD-related surgery, or PAF-related surgery.

To assess costs related to postsurgical opioid use, PAF CD patients who had PAF-related surgical procedures identified by ICD or CPT procedure codes during the follow-up period were identified. Of these, patients with at least 1 claim for opioid use during the first 7 days after the index date or with at least 1 claim for opioid use after the first 7 days after the index date were identified.

Statistical Analyses

For all statistical analyses, SAS 9.4 for Windows (SAS Institute, Cary, NC) was used. Numbers and percentages were reported for dichotomous and polychotomous variables. Means and standard deviations were reported for continuous variables. Cost outcomes were reported as PPPY and calculated as total cost/(follow-up length/365). For between-group comparisons of descriptive cost and HRU findings, P values were calculated using χ^2 tests for dichotomous and polychotomous variables and Student t tests for continuous variables.

Generalized linear models (GLMs) were used to adjust for multiple covariates to estimate HRU and costs. The dependent variables included patients with CD-related HRU. Independent variables included all baseline demographic and clinical characteristics. In addition, the number of health care visits per patient was estimated using the negative binomial model. The dependent variable was the number of GI-related health care visits. To estimate GI-related health care costs, log-transformation and GLMs were applied, depending on the distribution and presence of heteroscedasticity. In these models, the dependent variables were GI-related health care costs. Independent variables included all baseline demographic and clinical characteristics. For the cost data, gamma variance with a log link function was used in GLMs. For the HRU data reporting HRU percentage, binomial distribution with a logit link function was used. For the HRU data reporting the quantity of HRU (eg, number of visits), negative binomial distribution was used. A P value of $< .05$ was considered to be statistically significant.

Ethical Considerations

Because this study did not involve the collection, use, or transmittal of individual identifiable data, institutional review board approval was not required. All data security measures met the requirements of the Health Insurance Portability and Accountability Act (HIPAA) of 1996.

Results

PAF CD Prevalence and Patient Characteristics

The cumulative prevalence of PAF CD among patients with CD was calculated at 7.70%, based on 6303 patients diagnosed with PAF CD during the 3-year study period of 81,862 CD patients. Cumulative prevalence of PAF CD in the US population was estimated at 0.01%, based on 6303 patients with PAF CD among a total of 47,121,092 patients in the data set.

Among 81,862 patients with ≥2 diagnoses of CD during the study period, 2968 patients were identified as having a PAF diagnosis or procedure during the identification period (Figure 2). Of these, 1218 patients with PAF CD met additional inclusion criteria and did not meet exclusion criteria; these patients composed the PAF CD group. Of the original 81,862 patients with CD, 4095 patients without PAF were selected as matched non-PAF CD control patients (see Figure 2).

Patients with PAF CD had a mean age of 42.41 years, and 48% were female (Table 1). Matched patients with non-PAF CD had a mean age of 43.39 years, and 49% were female; the 2 groups were thus well matched on age and sex. The 2 groups were also well matched on other baseline characteristics, with the exception of slightly higher rates of comorbidities among patients with PAF CD. The majority of patients had health care coverage under preferred provider organizations (PPOs).

Health Care Costs

Most all-cause costs and HRU in both cohorts (PAF CD and non-PAF CD) were GI-related. In the GLM analysis, mean PPPY total all-cause costs were $85,233 for patients with PAF CD and $40,526 for non-PAF CD patients ($P < .0001$; Figure 3; Supplementary Data Content 2). Mean all-cause pharmacy costs were $28,635 for patients with PAF CD and $17,756 for patients with non-PAF CD ($P < .0001$). During follow-up, 65.8% of PAF and 42.3% of non-PAF patients were treated with >1 biologic agent. In the 30 days postindex, 31.9% of PAF patients were treated with biologics, with this percentage increasing over time; steroid use also remained high

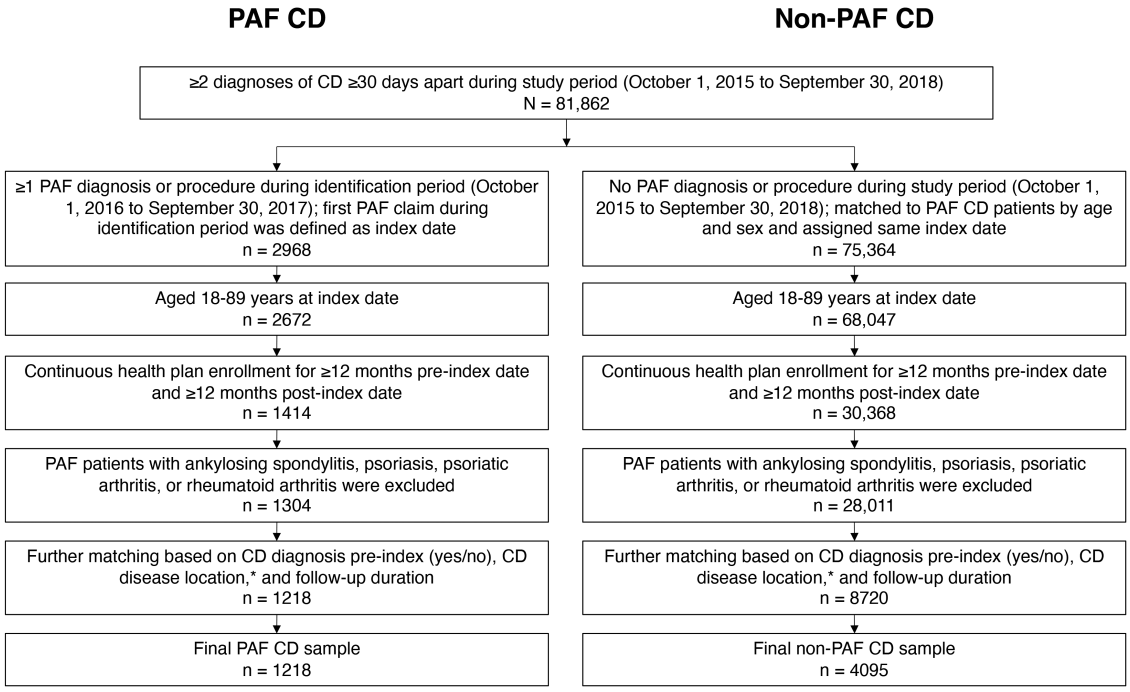

Figure 2. Selection of patients with PAF CD and matched patients with non-PAF CD from among patients in the IBM MarketScan database. Among patients with a presence of CD during the 12-month baseline period, the CD location of the first CD diagnosis during the baseline period was considered and matched. Among patients with an absence of CD during the baseline period, the CD location of the first CD diagnosis location during the follow-up period was considered and matched. Abbreviations: CD, Crohn's disease; PAF, perianal fistula.

(Figure 4). Mean GI-related health care costs were also greater for patients with PAF CD ($71,612) than for non-PAF CD patients ($29,458; $P < .0001$). Of the total GI-related costs for patients with PAF CD, $26,821 was attributed to outpatient care, $25,204 to pharmacy costs, and $18,505 to inpatient care.

Mean costs for GI-related inpatient stays were much higher among patients with PAF CD ($18,505) than among patients with non-PAF CD ($2138). For both all-cause and GI-related costs, inpatient, outpatient, and pharmacy costs were greater among PAF CD patients than among non-PAF CD patients (all between-group comparisons, $P < .0001$; Figure 3). The same pattern was observed in analyses based on descriptive findings for mean costs (Supplementary Data Content 2).

Health Care Resource Utilization

The GLM-adjusted proportions of PAF CD patients with at least 1 GI-related inpatient, outpatient, or pharmacy visit were 46%, 100%, and 91%, respectively, compared with 12%, 97%, and 82% of non-PAF CD patients ($P < .0001$; Figure 5; Supplementary Data Content 3).

The mean GI-related inpatient length of stay in days (PPPY) was 3.98 and 0.53 ($P < .0001$) for PAF CD and non-PAF CD patients, respectively. Overall surgery utilization was higher in the PAF group (Figure 6; Table, Supplementary Data Content 4), and almost all surgeries reflect fistula surgeries and procedures (7.16 vs 0 PAF-related surgeries) rather than intestinal resection (0.06 vs 0.01 for CD-related surgeries). Mean (PPPY) IBD-related surgeries in PAF CD and non-PAF CD patients were 1.51 and 0.06 ($P < .0001$), respectively.

Health Care Costs Associated With Opioid Use

Among patients who had any opioid drug use after PAF-related surgery, mean PPPY GI-related health care costs were $50,605 and $53,984, respectively, for patients who had 1 and >1 opioid use during the first 7 days after surgery (Figure 7; Supplementary Data Content 5). Gastrointestinal-related costs were higher—$82,973 ($P = 0.0194$) and $92,375 ($P < .0001$), respectively—among patients with 1 and >1 opioid use after the first 7 days following surgery (statistical comparisons were made to patients with 1 opioid use during the first 7 days).

Among PAF CD patients, mean PPPY total GI-related health care costs were $77,430 and $53,119 ($P < .0001$) for patients with and without opioid use, respectively. The higher cost for patients with opioid use is largely driven by costs associated with inpatient stays ($23,591 for patients with opioid use and $5012 for patients without opioid use; $P < .0001$).

Discussion

Based on an analysis of 81,862 patients with CD, the prevalence of PAF CD over a 3-year period was calculated at 7.70% of patients with CD and 0.01% of the US population. Our estimates of prevalence of PAF CD are consistent with previous studies, which have estimated that 8% of patients with CD have a PAF at any given time and that the cumulative risk of PAF is 12% to 15% after 5 years and 16% to 21% after 10 years.[7,9,10] Of note, one population-based cohort study found that the cumulative risk of PAF or rectovaginal fistula (RVF) in patients with CD had significantly decreased over time, with a 10-year cumulative risk for PAF or RVF of 24% among patients diagnosed with CD before 1998 (the prebiologic era) vs those diagnosed during or after 1998 (the biologic era), suggesting that earlier use of biologics may protect against the development of perianal CD.[20]

Table 1. Patient characteristics at baseline.

Characteristic	PAF CD (n = 1218)	Non-PAF CD[a] (n = 4095)
Age, years, mean (SD)	42.41 (13.97)	43.39 (13.90)
Age group, years, n (%)		
18–34	380 (31)	1124 (27)
35–44	293 (24)	986 (24)
45–54	270 (22)	979 (24)
55–64	231 (19)	867 (21)
65–80	39 (3)	120 (3)
81–89	5 (0.4)	19 (0.5)
Sex, n (%)		
Female	580 (48)	2012 (49)
Male	638 (52)	2083 (51)
Quan-Charlson Comorbidity Index score, mean (SD)	0.67 (1.34)	0.57 (1.21)
Other individual comorbidities, n (%)		
Cardiac complications	0	1 (0.02)
Diabetes mellitus	90 (7)	318 (8)
Liver disease	107 (9)	255 (6)
Renal disease	64 (5)	115 (3)
COPD	141 (12)	374 (9)
CD disease location, n (%)		
Ileum/colon	190 (16)	626 (15)
Ileum	150 (12)	518 (13)
Colon	210 (17)	707 (17)
Not specified	504 (41)	1832 (45)
None	164 (13)	412 (10)
Health plan type, n (%)		
Health maintenance organization (HMO)	140 (11)	441 (11)
Point of service (POS)	71 (6)	281 (7)
Preferred provider organization (PPO)	688 (56)	2357 (58)
Consumer-driven health plan	165 (14)	480 (12)
Other[b]	154 (13)	536 (13)

[a]Non-PAF CD patients were matched to PAF CD patients by birth year, sex, presence or lack of CD diagnosis during the pre-index period, CD disease location, and duration of follow-up period. Percentages for age group and CD disease location may not total 100 due to rounding.
[b]Other health plan types include indemnity, basic/major medical, comprehensive, high deductible health plan, exclusive provider organization.
Abbreviations: CD, Crohn's disease; COPD, chronic obstructive pulmonary disease; PAF, perianal fistula; SD, standard deviation.

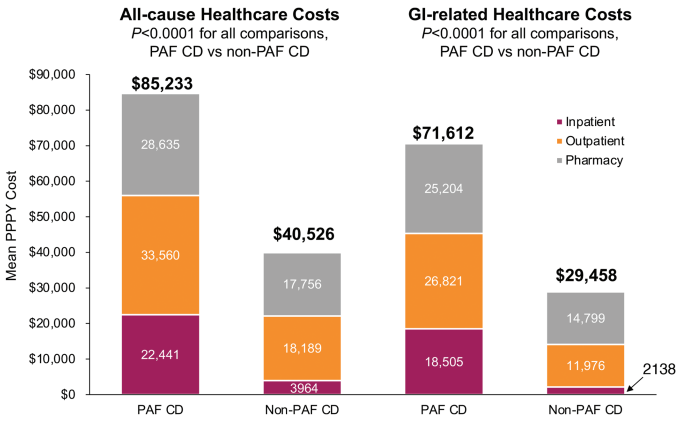

Figure 3. Comparison of mean PPPY health care costs for patients with PAF CD vs non-PAF CD (generalized linear model analysis). See Supplementary Data Content 2 for detailed findings. Abbreviations: CD, Crohn's disease; GI, gastrointestinal; PAF, perianal fistula; PPPY, per patient per year.

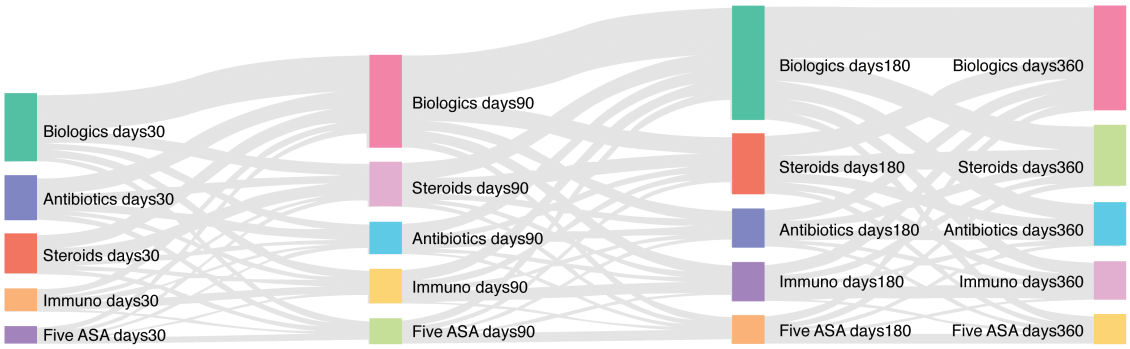

Figure 4. Sankey diagram of prescription medication treatment patterns among the PAF CD cohort. Abbreviations: ASA, aminosalicylic acid; CD, Crohn's disease; PAF, perianal fistula.

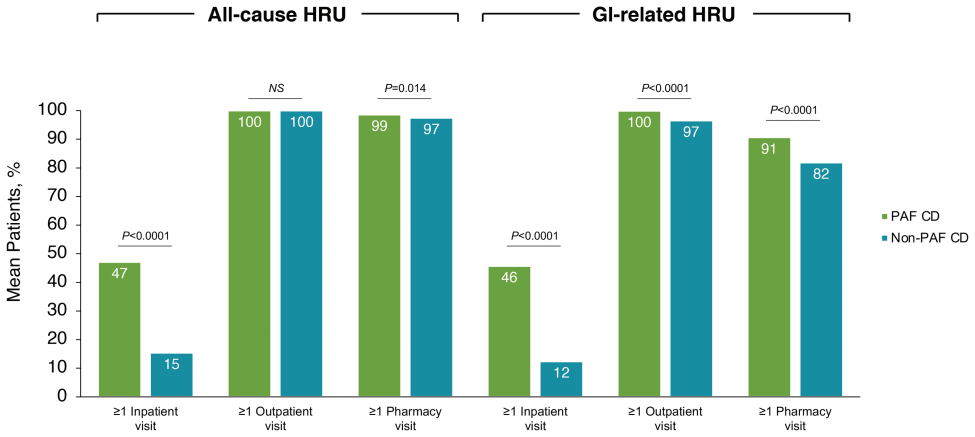

Figure 5. Comparison of HRU for patients with PAF CD vs non-PAF CD (generalized linear model analysis). See Supplementary Data Content 3 for detailed findings. Abbreviations: CD, Crohn's disease; GI, gastrointestinal; HRU, health care resource utilization; NS, nonsignificant; PAF, perianal fistula.

Mean costs among patients with PAF CD in this study were more than twice as high as costs for non-PAF CD patients. Costs for PAF CD were driven primarily by outpatient care and higher pharmacy costs among patients with PAF CD (PAF CD vs non-PAF CD: $P < .0001$ for both outpatient and pharmacy costs), which could be attributable to the higher percentage of these patients having received treatment with biologics (65.8%) compared with the percentage of non-PAF CD patients (42.3%; $P < .0001$). Inpatient care costs were significantly higher among those with PAF CD vs non-PAF CD ($P < .0001$). Health care resource utilization was greater among patients with PAF CD compared with non-PAF CD, particularly regarding the number of outpatient visits and the occurrence, length, and number of inpatient stays. Additionally, although the rate of surgeries was expected to be higher in PAF CD vs non-PAF CD patients, it is interesting to note that penetrating/perforating perianal disease was not associated with a large increase in bowel resections or diverting ostomy surgery.

Similar to previous studies,[2,17,21] we observed high costs associated with the care of PAF CD. In an earlier US-based analysis, the costs of care for fistulizing CD were driven by hospitalization and surgery,[2] whereas in this study, spending for PAF CD primarily went to outpatient visits and pharmacy costs. Similar to our analysis, earlier studies of perianal CD in New Zealand and Spain reported that the largest proportion of costs were attributable to medications.[17,21]

Among PAF CD patients who underwent PAF surgery and received opioids after surgery, costs were highest for those with opioid use after the first 7 days following surgery. Use of opioids immediately after surgery suggests acute pain management related to the surgical procedure. In contrast, opioid use for pain management beyond the perioperative period, as highlighted in this analysis, may suggest more severe disease resulting in increased risk of hospitalizations.[22]

Although claims data are extremely valuable for the efficient and effective examination of health care outcomes, treatment patterns, HRU, and costs, they are collected primarily for administrative purposes rather than for research. Therefore, certain limitations are associated with claims data use, such as the proportion of patients who may change insurance plans and are subsequently lost to follow-up. Additionally, because the IBM MarketScan Research Database contains claims from commercial plans only, the findings may not be generalizable to all patients, including those with public insurance, such as Medicaid or Medicare.

There are no published or validated algorithms for the identification of PAF using claims data. The presence of a diagnosis code on a medical claim does not necessarily indicate a positive presence of disease because the medical record may have been incorrectly coded or included as a rule-out criterion rather than the actual disease. Also, diagnosis codes only signify the presence of the disease and do not detail the characteristics or the nature of the disease (eg, complex vs simple PAF). It is also possible that a patient's admitting diagnosis could be noted as "CD, NOS (not otherwise specified)" by a provider without general GI or GI sur-

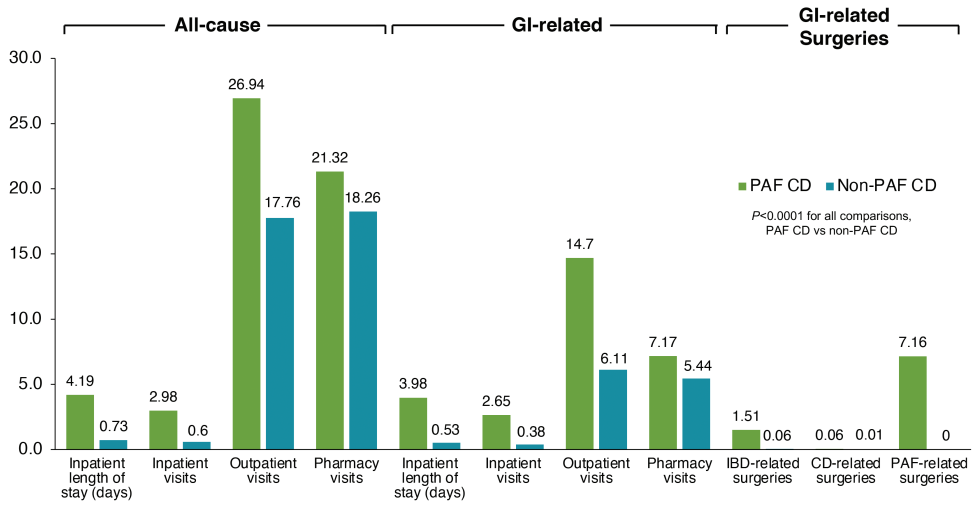

Figure 6. Comparison of PPPY mean length of stay, number of visits, and number of surgeries for patients with PAF CD vs non-PAF CD (generalized linear model analysis). See Supplementary Data Content 4 for detailed findings. Abbreviations: CD, Crohn's disease; GI, gastrointestinal; IBD, inflammatory bowel disease; PAF, perianal fistula, PPPY, per patient per year.

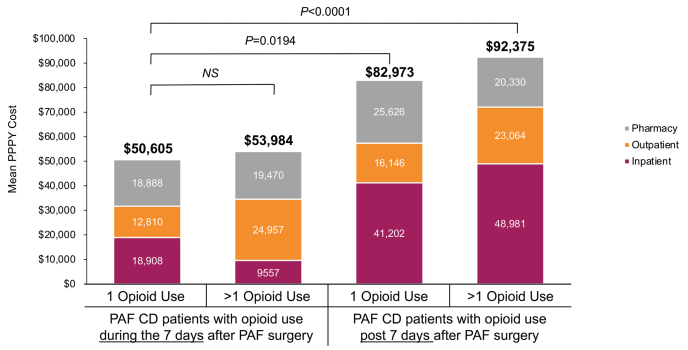

Figure 7. Comparison of mean PPPY gastrointestinal-related health care costs for patients with PAF CD who had PAF-related surgical procedures and ≥1 opioid drug use during and after the 7 days immediately following surgery (descriptive findings; N = 361 patients with surgery and opioid use). All statistical comparisons are relative to patients with 1 opioid use during the 7 days immediately following surgery. *P* values show statistical comparisons for total mean PPPY cost. See Table, Supplementary Data Content 5 for detailed findings. Abbreviations: CD, Crohn's disease; NS, nonsignificant; PAF, perianal fistula; PPPY, per patient per year.

gery expertise. Accordingly, the actual prevalence of PAF may be underestimated. We included ICD-9 and ICD-10 diagnosis codes along with procedure codes to be more comprehensive. In addition to the limitations presented by those who assign diagnostic codes, the 1-year baseline period and 1-year follow-up period may underestimate the number of patients.

The index date is the first diagnosis date or the first procedure claim for PAF. The index date may not necessarily indicate that it was the patient's first PAF episode because we did not exclude patients who had PAF before the identification period. The presence of a claim for a filled prescription does not indicate that the medication was taken as prescribed or at all. Moreover, medications filled over-the-counter or provided as samples by the physician cannot be observed in the claims data. We reported GI-related costs, but we cannot ascertain that these costs are attributable to the GI-related disease.

Certain information that could influence study outcomes and introduce bias is not readily available in claims data, such as clinical and disease-specific parameters. Thus, we were not able to analyze the association between the clinical status of the PAF and HRU and costs. We were unable to capture indirect costs or the cost of any disease-related sequelae. Health care resource utilization results are not necessarily generalizable beyond the insured population. Finally, the limited duration of follow-up does not capture the full costs of the natural course of the disease.

Conclusion

Our findings from this large cohort study of more than 80,000 patients with CD, who had comparable baseline characteristics across the PAF vs non-PAF CD groups, expand on previous studies by demonstrating that PAF is a common feature of this disease and carries a large economic impact. In this real-world analysis, costs for patients with PAF CD were more than twice as high than for CD patients without PAF, and patients with PAF CD were 3 times more likely to be hospitalized.

When matched for age, sex, and potential predictors for CD severity, overall HRU and costs are significantly higher for patients with PAF CD than for non-PAF CD patients, highlighting the economic burden of the disease. More effective management of PAF CD has the potential to reduce the

economic impact of this condition, and a better understanding of the related drivers of cost is essential in developing more cost-efficient treatment strategies for patients with PAF CD.

Supplementary Data

Supplementary data is available at *Inflammatory Bowel Diseases* online.

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Conflicts of Interest

G.C. is a former employee and S.C., Q.R.K., and K.N. are current employees of Takeda Pharmaceuticals U.S.A., Inc. and may have stock or stock options in the company. V.P. is an employee of STATinMED Research, Plano, TX, and is a paid consultant to Takeda Pharmaceuticals U.S.A., Inc. D.A.S. is an employee of Vanderbilt University Medical Center, Nashville, TN, and is a paid consultant to Takeda Pharmaceuticals U.S.A., Inc.

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