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Drivers of Cost After Surgical and Medical Therapy for Chronic Ulcerative Colitis: A Nested Case-Cohort Study in Olmsted County, Minnesota

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Abstract

Background—We previously reported the costs associated with surgery for chronic ulcerative colitis in the Olmsted County population and found that direct medical costs after surgery were significantly reduced compared with before surgery. However, in that study costs associated with chronic medical therapy for ulcerative colitis were not assessed in non-surgical patients.

Objective—To gain insight into the drivers of costs of treatment for chronic ulcerative colitis, we assessed direct costs after surgical and medical therapy in 120 patients in the Rochester Epidemiology Project database.

Methods—A cohort of 60 patients who recovered from surgery for ulcerative colitis from 1988–2006 were 1:1 matched by age, gender, and referent year to medically-managed patients. Direct healthcare costs were estimated from an institutional database, and observed cost differences over a 2-year period were calculated. Statistical significance was assessed by paired *t*-tests and bootstrapping; mean costs are adjusted 2009 constant dollars.

Results—Two-year direct healthcare costs in the surgical and medical cohorts were \$10,328 vs. \$6,586 (*p*=0.19). In the surgical cohort, Brooke ileostomy patients were observed to have higher costs than patients with ileal pouch-anal anastomosis (Δ\$8,187, *p*=0.04), and after ileal pouch, pouchitis was associated with increased costs (Δ\$12,763, *p*<0.01). In the medical cohort, disease extent (Δ\$6,059, *p*=0.04) but not disease severity was associated with increased costs.

Limitations—Relatively small population size, in county tertiary referral center.

Conclusions—Before the introduction of biologic therapies for ulcerative colitis, patients were observed to have similar healthcare costs after surgical and medical therapy. In medically treated

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patients, disease extent was associated with increased costs, while in surgically-treated patients, permanent ileostomy and pouchitis were observed to be associated with increased costs.

Keywords

Chronic ulcerative colitis; Population-based; Direct costs; Surgery ileal pouch-anal anastomosis

Introduction

An estimated 1.3 million persons in the United States and Canada have inflammatory bowel disease,¹ of which approximately 750,000 suffer from chronic ulcerative colitis (CUC).² Within the United States (US), the economic burden of CUC is approximately \$2.1 billion dollars per year.³ This recrudescence disease of chronic colonic mucosal inflammation is known to be associated with decreased quality of life, and patients suffering from this illness are known to consume significant healthcare resources, incurring both indirect and direct costs (e.g., missed work-sick days and costs of hospitalization, respectively).^{4, 5}

The mainstay of treatment for CUC is medical drug therapy with agents which can both induce and maintain remission, such as 5-aminosalicylate (5-ASA) derivatives, corticosteroids, immunomodulators (e.g. azathioprine or mercaptopurine), and more recently biologic agents (infliximab and others). However, despite this armamentarium of medical therapies, approximately 25-30% of CUC patients will ultimately require surgery during their lifetime, usually for medically-refractory disease or the development of colorectal dysplasia or colorectal cancer.⁶

We previously reported the costs associated with surgery for CUC in the Olmsted County population.⁵ That study found direct medical costs after surgery are significantly reduced as compared with before surgery.⁵ However, costs associated with chronic medical therapy for CUC were not assessed in nonsurgical patients. Thus, in order to gain further insight into the long-term comparative effectiveness of these two treatment strategies, and to identify drivers of costs within these groups, the aim of the present study was to assess total direct costs and healthcare resource utilization in a cohort of CUC patients who had previously undergone surgery compared with a matched cohort undergoing chronic medical therapy in Olmsted County, Minnesota.

Methods

Study Setting

Our study population was located in the north-central region of the United States in Olmsted County, Minnesota. According to the US Census Bureau data, as of 2009, there were approximately 143,962 residents in the county (<http://quickfacts.census.gov>). Although the surrounding area is mostly rural, a majority of residents live within the city of Rochester, with an estimated 2009 population of approximately 96,975 persons. From within this population, a cohort of CUC was identified using the Rochester Epidemiology Project (REP) as previously described.⁵

Rochester Epidemiology Project

The REP (<http://www.rochesterproject.org/>), since its inception in 1966, has been a long-term passive medical-records linkage system that collects, organizes, and provides research access to medical data for the vast majority of healthcare that Olmsted County, Minnesota residents receive within the county by electronically linking and indexing the medical records of almost all providers of medical care to Olmsted County residents (NIH-grant (R01 AG034676 [2010])).⁷ Electronic search of this database allows all county residents who

were given a specific diagnosis during a specific time period to be identified. This allows access to virtually all medical records (including outpatient, clinic, and ER visits, hospitalizations in the county's three hospitals, inpatient and outpatient laboratory results, and correspondence) from all sources of medical care within the county. Melton *et al.* previously reported that >96% of all care provided to Olmsted County residents is provided within the county, and >94% of residents have provided research authorization and research access to their medical records in a population-based manner.⁷ To date, researchers have used the REP to publish approximately 2000 scientific studies on a wide range of diagnoses and conditions.

Olmsted County Healthcare Expenditure and Utilization Database

One of the databases which exist within the framework of the REP is the Olmsted County Healthcare Expenditure and Utilization Database (OCHEUD). This administrative database provides a standardized inflation-adjusted estimate of the costs of each service or procedure provided since 1987 at Mayo Clinic and Olmsted Medical Center (OMC) and their affiliated hospitals and outpatient clinics in constant dollars. Economic costs are estimated for each line item in the billing record, allowing for the aggregation of costs into clinically relevant categories. More specifically, the OCHEUD uses a “bottom-up” costing approach; the database categorizes resource utilization based on the Medicare Part A and B classification scheme. Part A billed charges are adjusted by using hospital cost-to-charge ratios and wage indexes, and Part B physician services are costed using Medicare reimbursement rates. Although the services provided represent the clinical practice patterns of Mayo Clinic and OMC providers, the value of each unit of service has been adjusted to national norms by use of widely accepted valuation techniques.⁸ Services delivered to nonhospitalized patients by Mayo and OMC providers in their outpatient clinics is included, but services that may have been delivered by providers other than Mayo Clinic or OMC (*e.g.*, dental procedures, ambulance services, stoma supplies) and outpatient medications costs are not captured and not included. However, given the robust access to individual medical records, use of outpatient medications and stoma supplies were manually abstracted but not costed.

Study Subjects

After Institutional Review Board approval by Mayo Clinic and OMC, the REP was used to identify two population-based cohorts. The surgical cohort of adult CUC patients who were Olmsted County residents at the time of proctocolectomy was previously identified based on International Classification of Disease revision 9 [ICD-9] codes for CUC (556.X), and colectomy (45.X), or any ileostomy (46.X) between January 1st 1988 and December 31st 2006 in Olmsted County.⁵

The matched medical cohort was derived from the population of Olmsted County using REP resources to perform an electronic search for all Olmsted County patients with a diagnosis of CUC. Patients with any previous diagnosis of Crohn's disease were excluded, as were nonincident cases, those who had ever had surgery for CUC (including during the study period), or those who were diagnosed before 9/1/1971 (earliest date of first diagnosis for a surgical patient). This list was then limited to the maximum and minimum age of the surgical cohort. The resultant list of potential matched subjects included 254 patients. The surgical cohort was then matched in a 1:1 ratio to the medical cohort. Matching criteria included age at diagnosis (± 1 year), gender, and referent year (defined as year of surgery matched to a gastroenterology visit $\pm$ one calendar year). Olmsted County residency status was then verified for the periods of observation to decrease the likelihood of missing economic data. Subjects who were not residents for the entire period of observation were excluded and new matched pairs were used.

The 2-year period of observation (Figure 1) for each cohort was defined as follows: the surgical cohort's period of observation arbitrarily began 180 days after the date of the last planned surgery - either after diverting loop ileostomy closure or Brooke ileostomy construction (*i.e.*, day 181, the day after a six-month recovery period).⁵ We specifically chose this date as after a 6-month recovery period, a point by which most surgical patients be expected to have fully recovered and thus representative of long-term postsurgical costs. A 2-year interval was chosen in the first study mainly to lessen the influence of surgery on the presurgical costs and obtain a more reliable estimate of longer-term costs.

A single exception was an ileal pouch-anal anastomosis (IPAA) patient with refractory pouchitis who underwent pouch excision and conversion to Brooke ileostomy prior to the present study period of observation and was thus included in the Brooke ileostomy subgroup. The 2-year period of observation for the medical cohort began on a referent date. The referent date was defined by identifying a gastroenterology visit within (+/-) one calendar year (referent year) of the surgical date within a matched pair. Time 1 represents the start of the 2-year period and Time 2 represents the end of the 2-year period of observation. Given the matching algorithm, no medical patient had surgery during any part of the study period.

Retrospective chart review was used to verify demographic and treatment-related variables. These included age, gender, body mass index, date of CUC diagnosis, number/types/duration of CUC-related medications, age-adjusted Charlson Comorbidity Index,⁹ and disease severity and extent according to the Montreal classification (medical cohort only).¹⁰ The Montreal Classification classifies CUC based on severity (S0 = clinical remission, S1 = mild CUC, S2 = moderate CUC, S3 = severe CUC) and extent (E1 = proctitis, E2 = left-sided colitis, E3 = extensive colitis). Given the difficulty of retrospective assessment of disease severity and extent, and given the limited size of the population, for the purposes of this study patients were classified as either S0/S1 vs. S2/S3, and E1/E2 vs. E3.

The OCHEUD administrative database was then used to estimate per patient total direct healthcare costs (**primary outcome**) and was reported as mean and median total direct healthcare adjusted constant 2009 US dollars over the 2-year period of observation for each cohort or subgroup. Direct costs, which are reflective of the monetary value required to actually deliver the care, and in the present study does not include outpatient medication and stoma supply costs because they are not accounted for in the OCHEUD database. Indirect costs, such as lost wages or the cost of childcare while ill, are a separate category and not included in this study. The database was also used to estimate several **secondary outcomes** including the mean number of hospital episodes, mean number of hospital days, mean number of lower endoscopies (including flexible colonoscopy, sigmoidoscopy, pouchoscopy, and rigid proctosigmoidoscopy), and mean number of abdominal imaging procedures (including plain radiographs, computed tomography, and magnetic resonance imaging), from the perspective of the payer. Secondary outcome utilization was assessed using Current Procedure Terminology Revision 4 (CPT-4) codes: lower endoscopic procedures (443xy, 453xy), and abdominal imaging (74xyz, 721xy).

Statistical Analysis

The overall statistical approach was a matched-paired design. Given the limited size of the population, descriptive data were presented as median (interquartile range) or frequency (proportion). Descriptive differences in baseline characteristics between the surgical and medical cohorts were assessed using nonparametric tests (Wilcoxon rank-sum test or Fisher exact test) as appropriate.

The **primary analysis** assessed the mean difference in 2-year total estimated direct healthcare cost between the surgical and medical cohorts using paired two-sided *t*-tests and nonparametric bootstrapped 95% confidence intervals.¹¹ Costs were reported as mean (median) $\pm$ standard deviation. All costs were reported in 2009 constant dollars standardized to national norms.

In addition to the primary analysis, subgroup analyses were performed within the surgical cohort (pouchitis vs. never pouchitis, IPAA vs. Brooke ileostomy) and within the medical cohort (severity [S0/S1 vs. S2/S3], and extent [E1/E2 vs. E3]). Differences in the subgroup analyses were compared using two-sided rank sum tests. Bonferroni's correction was applied in cases of multiple comparisons, and *p*-values <0.05 were considered statistically significant. All descriptive and comparative statistical analyses were performed using either JMP version 8.0 for Mac OS X or SAS version 9.1 (SAS Institute Inc., Cary, NC).

Results

From 1988 to 2006, a total of 60 Olmsted County, Minnesota residents underwent surgery for CUC (surgical cohort) and were matched to 60 residents with CUC who never had surgery (medical cohort). Baseline characteristics are presented in Table 1. The two cohorts did not differ with respect to age at diagnosis, gender, duration of CUC, body mass index (BMI), Charlson comorbidity index, or age at referent date. As previously reported, the indication for surgery was medically-refractory disease in 87%, and colorectal neoplasia (dysplasia and cancer) in 13%.⁵

Disease Severity

For the surgical cohort, pouchitis was observed at Time 1 and Time 2 in 11.7% vs. 16.7%, respectively, $p=0.08$; a total of 14 patients (23.3%) had at least one episode of pouchitis. For the medical cohort, the Montreal classification of severity and extent of disease are shown in Table 2. These patients were observed to have more extensive disease at Time 1 than at Time 2 (E3, 48.3% vs. 43.8%, $p<0.0001$), and more were in clinical remission at Time 2 than at Time 1 (85% vs. 48.3%, $p=0.04$).

IBD Medication Usage

Medication usage is summarized in Table 3. For the surgical cohort, median IBD medication usage was zero at both Time 1 and 2 ($p=0.5$), and only 1 patient with pouchitis was noted to be receiving both corticosteroids and immunomodulator treatment for pouchitis, and no biologic-based therapy. In addition, surgical patients were more likely to be on antibiotics (for pouchitis) at Time 2 than at Time 1 (8.3% vs. 5%, $p=0.02$). Among the surgical patients, 11 patients (18.3%) had received any antibiotics for pouchitis in the two-year period.

For the medical cohort, the median number of medications at both Time 1 and 2 was one, but the variability (upper limit of range 3 vs. 2, respectively), resulted in significantly more medication use at Time 1 ($p=0.01$, Bonferroni corrected). At Time 1 more patients were on 5-ASA (61.7% vs. 55%, $p<0.0002$) or steroids (23.3% vs. 8.3%, $p=0.02$), but at Time 2 more were receiving immunomodulator therapy (11.7% vs. 8.3%, $p<0.0002$). In this cohort, only 1 patient was on anti-TNF- α therapy during the period of observation.

Direct Medical Costs

Two-year direct healthcare costs, not including outpatient medication and stoma supply costs, in the surgical and medical cohorts are shown in Table 4. Overall mean costs in the surgical and medical cohorts were \$10,328 vs. \$6,586, for a mean difference of \$3,742, $p=0.19$. In the surgical cohort, Brooke ileostomy patients were noted to consume more costs

than IPAA patients (\$16,332 vs. \$8,145, mean cost difference \$8,187, $p=0.04$), while in the medical cohort, disease extent (pancolitis vs. left-sided colitis or proctitis) at Time 1 was associated with increased costs (\$8,613 vs. \$4,690, mean cost difference \$3,923 ($p=0.04$)). The mean cost difference between patients who had never or ever had pouchitis was not significant (mean cost difference -\$9,689, $p=0.16$), nor was the cost difference between patients in remission or mild disease severity at Time 1 compared with those with moderate-to-severe disease (mean cost difference \$2407, $p=0.83$).

Distribution analysis of the cost data revealed two surgical outliers (\$104,788 [patient required 4-vessel coronary angioplasty during period of observation], and \$95,305 [patient required debridement of superficial wound infection after incisional hernia repair, drainage of tubo-ovarian abscess with total abdominal hysterectomy, varicose veins surgery]) and one medical outlier (\$85,416, multiple comorbidities, adjusted Charlson comorbidity index 7; coronary artery disease, Lewy body dementia, delirium, CUC, hyperlipidemia, impaired glucose, vasomotor rhinitis, snoring, dermatitis, hemifacial spasm & Parkinsonism, thrombocytopenia, incarcerated inguinal hernia [surgical repair], Mallory Weiss tear). These patients, along with their respective matches, were removed and cost analyses were redone but did not lead to a change in statistical significance of any cost analysis (detailed results not shown), with the exception of the extent of disease analysis; removing the single medical outlier changed the p -value from 0.04 to 0.07. Finally, the out-of-pocket costs of ileostomy supplies were estimated for the 2-year period of observation. The mean (median) costs were \$2,704 (\$2,600), range \$1,843 - \$3,795.

Specific Healthcare Resource Utilization

The utilization of specific healthcare resources was shown in Table 5. Overall the postsurgical patients required more hospitalization and more abdominal imaging, but these differences and the cost thereof were not significantly different between the cohorts. Postsurgical patients had a similar number of lower endoscopies, but at a significantly lower cost than the medical cohort (mean cost \$49 vs. \$135, $p=0.002$).

Discussion

Overall, several conclusions can be drawn from the observations made in this population-based study. In the era prior to the biologic therapy, patients with CUC appeared to consume a similar amount of direct healthcare dollars, approximately \$5000 per year, irrespective of whether they had *previously* undergone surgery or if they were receiving medical therapy. However, additional study, or decision-analysis modeling, is needed to help determine if the long-term costs associated with cure of CUC are comparable to, if not reduced, relative to those in patients undergoing long-term maintenance therapy, as suggested by the present study.

More specifically, as the indication for surgery in the surgical cohort was medically-refractory disease in 87%⁵, these represent distinct groups of patients: those with aggressive disease who require colectomy within an average of 4 years, and those with less severe disease who have not yet, or may never, require colectomy, on chronic medical therapy. We previously reported that the costs of surgery plus 180 days of recovery were estimated to be \$50,530 for the 45 IPAA patients and \$39,309 for the 15 Brooke ileostomy patients.⁵ Thus, the data from the present study support and extend those original observations, providing a more complete description of the costs of care for a population of patients with CUC. These observations add significantly to the population-based, and cost-based, literature on CUC.^{1, 5, 12-18}

The observed mean 2-year costs for the IPAA patients without pouchitis was \$5284, or \$2642 per year, slightly higher than current high-deductible insurance plans, and although beyond the scope of this study, likely close to average yearly medical costs for non-CUC patients in Olmsted County. In addition, we observed that IPAA patients had an overall 2-year incidence of pouchitis of 23%, that with time they were more likely to be on antibiotics ($p=0.02$), and that those who have pouchitis consume significantly more direct healthcare dollars (\$12,962 on average) than those who do not. The pouchitis incidence in our study is within the range of 15 – 60% reported in the literature.¹⁹⁻²² Simchuk, *et al.*, in a consecutive series of 114 patients, found a 3-year pouchitis rate of 37%. Although we did not observe an increased incidence of pouchitis over the 2 years ($p=0.08$), other studies have demonstrated that with longer follow-up the incidence of pouchitis continues to rise.^{23, 24} Studies from Mayo Clinic have also documented a progressively rising incidence of pouchitis to > 60%.^{25, 26} More recent population-based (Olmsted County) data indicates the long-term population-based cumulative incidence of pouchitis is approximately 60%.^{27, 28} The etiology of pouchitis remains frustratingly enigmatic,²⁹ with only empirically-proven effective therapies.^{24, 30} These findings emphasize the need to search for and develop lower cost, effective treatments for pouchitis and methods for the prevention of pouchitis (*i.e.*, determine the cause), and to perform decision-analysis modeling based on the data presented herein.

With respect to the medical cohort, our study demonstrated that medical therapy for CUC, prior to the widespread use of biologics, was highly effective and resulted in decreased disease severity and extent with time. Patients with more severe disease at Time 1 did not consume more dollars than those with less mild disease or remission, but those with more extensive disease, as expected, consumed more healthcare dollars. By examining the prescribed medications at Time 1 and Time 2 we found that the cohort migrated from 5-ASA compounds (61.7% to 55%, $p<0.0002$) and steroids (23.3% to 8.3%, $p=0.02$) to immunomodulators (8.3% to 11.7%, $p<0.0002$). These findings reinforce those of a meta-analysis which found that azathioprine may be effective for patients intolerant of 5-ASA products or those on corticosteroids.³¹ However, in terms of costs, a more granular analysis would be necessary to definitely conclude that any difference, or lack of difference, in costs within the medical subgroups was due to increased costs of the medications (e.g., certain proprietary 5-ASA compounds may be more expensive than immunomodulators), and is beyond the scope of the present study. That being said, the mean cost difference between the unadjusted and adjusted medical groups was roughly \$4500, emphasizing the importance of consideration of pharmaceutical costs in comparative analyses such as this.

There are several limitations inherent to our study design. The OCHEUD database does not contain outpatient pharmaceutical or ileostomy supply costs and estimations of these costs were not included. In addition, it was beyond the scope of the present study to provide a more granular analysis of disease-attributable costs other than as presented. The size of each cohort is relatively limited; the REP is ideal for studying common diseases (such as diabetes, obesity, asthma, or coronary artery disease), but the size of the overall population (145,000 persons currently) limits the statistical power for analyses of less common diseases such as CUC. Thus, the present study may be underpowered to detect economically significant differences. However, economic analyses frequently do not use *a priori* power calculations, because cost as an endpoint represents real dollars and the value is relative based on perspective of the payor.³² A difference of \$1000 dollars may be valued differently by a single patient, the head of a household, the hospital, the insurance company, or the government, for example. Thus, the use of the bootstrapping technique and 95% confidence interval for this typically skewed data is preferred and presented in this paper.¹¹ With respect to the costs of medical therapy, the majority of patients were studied before FDA approved infliximab for CUC (67% of surgical patients and 76% medical patients had their

two year period of observation end before September 15th, 2005); therefore, we are limited in our ability to comment on the effect of this relatively expensive medication on the cost difference between medical and surgical therapy. Additional research is needed to assess the cost-effectiveness of biologic therapy to avoid colectomy.

Finally, due to our chosen study design, the ability to directly compare the effectiveness of surgical and medical therapy in this study is limited by the confounder of disease severity (i.e., patients with more active disease are more likely to undergo colectomy). Although we can describe the observed lack of difference in costs between the two groups, one may argue that surgical therapy is inherently effective for those who require it, as medical therapy has been demonstrated to be by this and other studies for those whose disease is relatively mild. Thus, conclusions drawn from results within each cohort may provide more meaningful insights than the primary analysis. Nonetheless, our observations are population-based, and are not subject to the typical biases associated with retrospective studies and thus are high quality despite the above mentioned limitations, and will form the basis for a planned Markov model to help further understand implication of potential cost differences in these patients.

In summary, CUC patients were observed to have similar healthcare costs after surgical and medical therapy. The principle drivers of costs in CUC patients were disease extent, presence of Brooke ileostomy, and pouchitis. Strategies which prevent extensive colitis and prevent pouchitis may result in cost-savings. Prospective assessment of treatment for CUC, including the costs and efficacy of newer treatment modalities such as laparoscopy and biologic therapy, are needed to more fully understand the comparative effectiveness of these respective treatments in the 21st century.

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Figure 1.
Schematic representation of the periods of observation.

Table 1

Baseline characteristics of Olmsted County, Minnesota, residents with CUC.

Variable	Surgical Cohort (n=60)	Medical Cohort (n=60)	<i>p</i>
Age at diagnosis, years	32 (24 – 43.3)	33 (24 – 45)	0.59
Male gender, n (%)	40 (67%)	40 (67%)	1.0
Duration of CUC, years [†]	4 (1 – 11)	6 (3 – 10)	0.2
Age at the event, years [*]	42 (31.3 – 50.5)	42 (34 – 52)	0.59
BMI (kg/m ²)	26.2 (23.8 – 28.7)	26.8 (24.6 – 29.4)	0.34
Age-adjusted Charlson comorbidity index	0 (0 – 2)	0 (0 – 1.75)	0.65

Values represent median (interquartile range).

CUC, chronic ulcerative colitis; BMI, body mass index.

^{*} Event represents surgical intervention for surgical cohort and gastroenterologist visit for medical cohort[†] Before the start of the time frame

Table 2

Montreal classification of disease extent and severity throughout the 2-year period of observation for medical patients.

Variable		Time 1 Medical cohort (n=60)	Time 2 Medical cohort (n=60)	<i>p</i>
Extent of CUC	Ulcerative Proctitis (E1)	11 (18.3%)	11 (18.3%)	<0.0001
	Left Sided-UC (E2)	20 (33.3%)	23 (38.3%)	
	Extensive-UC (E3)	29 (48.3%)	26 (43.8%)	
Severity of CUC	Clinical remission (S0)	29 (48.3%)	51 (85%)	0.02
	Mild-UC (S1)	14 (23.3%)	5 (8.3%)	
	Moderate-UC (S2)	14 (23.3%)	4 (6.7%)	
	Severe-UC (S3)	3 (5%)	-	

CUC, chronic ulcerative colitis. “E” represents Montreal Classification Extent, and “S” represents Montreal Classification Severity.

Table 3
Medication usage in CUC surgical and medical cohorts from Olmsted County, Minnesota.

	Time 1 Surgical Cohort (n=60)	Time 2 Surgical Cohort (n=60)	p-value	Time 1 Medical Cohort (n=60)	Time 2 Medical Cohort (n=60)	p
No. of CUC drugs, median	0 (0 - 1) [†]	0 (0 - 2) [†]	0.5	1 (0 - 3) [†]	1 (0 - 2) [†]	0.01
5-ASA compounds	-	-	--	37 (61.7%)	33 (55%)	<0.0002
Antibiotics	3 (5%)	5 (8.3%)	0.02	-	-	--
Steroids	3 (5%) *	3 (5%) **	0.86	14 (23.3%)	5 (8.3%)	0.02
Immunomodulators	-	2 (3.3%) ^{††}	--	5 (8.3%)	7 (11.7%)	<0.0002
Anti TNF- α -Ab	-	-	--	1 (1.7%)	-	--

CUC, chronic ulcerative colitis; 5-ASA, 5-aminosalicylates; TNF- α -Ab, tumor necrosis factor- α antibodies.

* Inflammatory arthritis (2), steroid withdrawal (1)

** Inflammatory arthritis (2), pouchitis (1)

[†] Range, not interquartile range

^{††} Rheumatoid arthritis (1), pouchitis (1, same patient as **)

Table 4
Two-year direct healthcare costs after surgical and medical therapy for CUC*

Cohort	Subgroup	Mean total cost ^{*,†}	Mean cost Difference (95% C.I.) [§]	<i>p</i>
Both Cohorts (n=120)	Surgical cohort (n=60)	\$10,328 (\$4,292) ± 18,585	\$3,742 (-\$1,171 to \$9,897)	0.19 [‡]
	Medical cohort (n=60)	\$6,586 (\$2,483) ± 12,641		
Surgical Cohort (n=60)	IPAA (n=44)	\$8,145 (\$2,713) ± 16,578	-\$8,187 (-\$20,477 to \$1,888)	0.04 ^{**}
	Brooke ileostomy (n=16)	\$16,332 (\$11,650) ± 22,766		
IPAA Cohort (n=44)	Never pouchitis (n=31)	\$5,283 (\$2,418) ± 7,360	-\$9,689 (-\$27,357 to \$1,270)	0.16 ^{**}
	Ever pouchitis (n=13)	\$14,972 (\$8,177) ± 27,887		
Medical Cohort (n=60)	S0 or S1 at Time 1 (n=43)	\$7,268 (\$2,537) ± 14,286	\$2,407 (-\$2,547 to \$8,031)	0.83 ^{**}
	S3 or S4 at Time 1 (n=17)	\$4,861 (\$2,006) ± 7,004		
Medical Cohort (n=60)	E1 or E2 at Time 1 (n= 31)	\$4,690 (\$1,629) ± 8,112	-\$3,923 (-\$11,630 to \$1,551)	0.04 ^{**}
	E3 at Time 1 (n= 29)	\$8,613 (\$3,667) ± 16,062		

IPAA, ileal pouch-anal anastomosis.

* Estimated costs per patient are reported in 2009 constant dollars.

† Values are presented as mean (median) ± standard deviation.

§ Bootstrap 95% Confidence Interval (C.I.) using the percentile method.

** Rank-sum test

‡ Paired *t*-test

Table 5
Hospital Admissions and Procedures and Associated Costs*

Variable	No.		p	Costs		p
	Surgical Cohort (n=60) ‡	Medical Cohort (n=60) ‡		Surgical Cohort (n=60) ‡	Medical Cohort (n=60) ‡	
Total hospital days	2.45 (0 – 4ss0)	1.77 (0 – 36)	~1.0	\$6,006 (\$0) ± 17,846	\$2,936 (\$0) ±10,149	0.75
Hospital admissions	0.45 (0 – 4)	0.28 (0 – 4)	~1.0			
Lower endoscopies	0.53 (0 – 3)	0.58 (0 – 3)	~1.0	\$49 (\$0) ± 76	\$135 (\$0) ± 170	0.002
Abdominal imaging	1.48 (0 – 18)	0.67 (0 – 9)	0.38	\$288 (\$0) ± 786	\$152 (\$0) ± 393	0.70

* Estimated costs per patient are reported in 2009 constant dollars.

‡ Values are presented as mean (range)

§ Values are presented as mean (median) ± standard deviation

** Paired t-test, Bonferroni correction