Direct Medical Cost of Managing IBD Patients: A Canadian Population-based Study

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Background: This study aimed to quantify the direct medical cost of treating inflammatory bowel disease (IBD) in Manitoba in 2005/2006.

Methods: In all, 7375 individuals with IBD recorded in the University of Manitoba IBD Epidemiology Database were matched on age, gender, and geography to up to 10 non-IBD controls. Data for cases and controls were extracted from Manitoba Health databases in fiscal 2005/2006 for pharmaceutical, physician claims, and hospital abstracts. The mean and median expenditure were computed for the annual cost of pharmaceuticals, hospitalizations (day surgery and inpatient), and physician office visits. We assessed costs based on age, gender, type of IBD, disease duration, and level of care provided.

Results: In 2005/2006 the mean direct cost of an IBD case was $3896 (standard error [SE] = $90) which was twice that of controls ($P < 0.05$). Crohn's disease (CD; $n = 3735$) was significantly more costly on average than ulcerative colitis (UC; $n = 3640$) ($4232; SE = $137 and $3552; SE = $117, respectively, $P < 0.001$). The most costly cases included those within 1 year of diagnosis ($6611; SE = $593), those hospitalized overnight (15%) ($13,495, SE = $416; max = $130,332), those who had a surgical stay (2% of IBD cases) ($18,749, range = $13,413–$125,912), and those using infliximab (0.7%) ($31,440, SE = $2311; max = $96,328). For individuals using infliximab their direct annual average healthcare cost was $9683 (SE = $1745, Max = $55,208) prior to using infliximab.

Conclusions: In Manitoba the direct average annual healthcare cost of CD is greater than UC and that of a patient using infliximab tends to be greater than one incurring a surgical stay.

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Key Words: Crohn's disease, medical cost, population-based study, Canada, ulcerative colitis

There are approximately 200,000 individuals living with inflammatory bowel disease (IBD) in Canada.[1,2] Over 9000 new cases are diagnosed every year; approximately 5000 with Crohn's disease (CD) and 4000 with ulcerative colitis (UC).[1,2] Healthcare utilization is found to be greatest within the first 2 years of diagnosis, and then to plateau over subsequent years to a level higher than age- and gender-matched controls.[3] Although there are episodic flares, at least 65% of patients are in remission at any one time.[4] Disease flares have an impact on quality of life, including the ability to work, and may lead to costly hospitalizations that includes surgery in the most severe cases. Although mortality rates are slightly higher than that of the general population,[5] particularly for CD,[5] patients typically live many years to nearly a full life span with these diseases. Episodic flares spanning a full life suggest a costly lifetime of care. Currently, few population-based datasets have been used to quantify the direct costs of providing healthcare to people with IBD. Understanding these costs is important in making decisions regarding treatment modalities. In particular, these costs could be used to adequately evaluate the cost-effectiveness of novel, expensive biological therapeutics to treat IBD.

The interest in the economics of managing IBD has heightened with the advent of very costly biological agents that to date are still mostly used in a selected minority of IBD patients. The Canadian Agency for Drugs and Technology in Health (CADTH) conducted a health technology assessment of the impact of the anti-tumor necrosis factor alpha (TNF-α) agents (adalimumab, etanercept, and infliximab) compared with conventional therapy and surgery for patients with CD or UC who did not adequately respond to conventional therapy.[6] Based on primary economic evaluations of direct costs, the authors concluded that the cost-effectiveness of adalimumab and infliximab for the treatment of IBD may be considered questionable at best.

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In this study we examined data from the University of Manitoba Inflammatory Bowel Disease Epidemiology Database (UMIBDED), extracted from the provincial administrative health databases, to determine the absolute costs of treating IBD patients in terms of office visits, hospitalization, day surgery, and pharmaceuticals and the relative costs compared to a population-based group of matched controls without IBD. We also examined the association between demographic variables and disease characteristics on costs.

MATERIALS AND METHODS

This study was approved by the University of Manitoba Health Research Ethics Board.

Manitoba is a central Canadian province with a relatively stable population of 1.2 million inhabitants.[7] The population is ethnically diverse and over 60% of the residents live in urban areas. The source of data for this study was the Manitoba Health insurance databases.[8,9] Computerized records of all physician billing claims and hospital discharge abstracts are maintained by Manitoba Health, the province's health insurer. The physician billing claims use a single 3-digit International Classification of Diseases–Clinical Modification (ICD-9-CM) codes to report diagnoses. The hospital records in 2005/2006 use 3- to 7-digit ICD-10-CM codes. In addition, the Drug Programs Information Network (DPIN), an electronic, on-line, point-of-sale prescription drug database is managed by Manitoba Health. Initiated in 1995, it connects Manitoba Health and all retail pharmacies in Manitoba to a central database maintained by Manitoba Health. Manitoba Health also maintains a population registry that is routinely updated with birth and death reports from vital statistics records and coverage updates including the migration of individuals into and out of the province. Since 1984 the population registry has maintained a unique personal health identification number (PHIN) that is included with each physician claim record, hospital discharge abstract, and prescription drug dispensed. This identifier has made it possible to link the registry file with physician, hospital, and prescription drug records and to assemble population-based administrative health data to determine the magnitude of healthcare utilization and associated patterns.

Prior to this study, the hospital, physicians' databases, and the population registry, together with the findings in self-report (via mail-out questionnaire), and chart review in 1995 were used to establish a validated case definition for IBD.[1,10] Using the four databases described above, all healthcare records between the years April 1, 1984 and March 31, 2008 were extracted for IBD cases together with the healthcare records of up to 10 non-IBD controls per case. Controls were matched on age, gender, geography, and whether or not they were covered by Manitoba Health at the time the case person was diagnosed as having IBD. Our subpopulation was identified in all databases and records extracted back to fiscal 1984/1985 to fiscal 2007/2008. Collectively, these records comprise the University of Manitoba IBD Epidemiology Database.

Fiscal 2005 (April 1, 2005 to March 31, 2006) was the focus of our study since it had the most recent records containing cost data. The registry file was initially scanned to identify cases and controls that were covered for at least some portion of the year in question.

Hospitals in Manitoba are funded by global budgets. Each hospitalization is assigned a resource intensity weight (RIW). These are the relative case weights that measure the intensity of resource use (relative cost) associated with different demographic and healthcare characteristics of an individual. RIWs are assigned according to the case mix group to which an individual is assigned as well as their age, health status, and discharge status and are based on micro-costing.[11,12] For surgical procedures that were performed without the need for an overnight stay, a day procedure group weight (DPG_WT) instead of an RIW is assigned. Several records may be generated for one stay. Records were arranged as part of the same episode of care if subsequent records were within 1 day of each other. Stays that were not overnight stays were considered day surgery.

The total weights for all hospital stays were calculated separately for inpatient stays and day surgery for each individual for 2005/2006. Once weights were totaled, the cost per weighted case of $2953.45 was multiplied to the total of the weights. The cost per weighted case is calculated by dividing the total direct inpatient hospital costs for 2005/2006 by the total weighted cases for all cases in 2005/2006. Overhead costs (e.g., hospital administration, human resources, medical records, and physical plant) were not included, nor were building capital costs, as these costs cannot be directly attributed to an individual patient. Similarly, education and research activities at teaching hospitals are excluded from cost estimates. The direct cost of hospitalizations included all direct care costs for nursing, diagnostics and therapeutics, supplies, and drugs. Emergency room and clinic costs are not included, as data are not available to enable costing of these services.

For consistency, all physician costs reported in hospital financial systems are excluded. To include physician fees we first separated them by day surgery or overnight hospitalization. Hospital records were merged with physicians' claims to identify claims that occurred coincident with a hospitalization. By doing so, we separated costs for overnight hospitalization and surgery. The remaining costs for physician fees were considered fees for office visits.

The physician claims data included fee for service claims by physicians in terms of fees for both professional and, where applicable, technical charges. Salaries paid to salaried physicians were not included in these costs. However, since we had no reason to suspect salaried physicians were any more likely to treat IBD cases or controls, we were not concerned that the overall pattern would be affected by neglecting these fees. Moreover, salaried physicians are a very small minority of Manitoba physicians and many of them submit "shadow claims," which are included in the analyses.

Prescription drug costs were those found in the DPIN. This excluded drugs used in hospitals, as these are included in the cost of hospitalization. The DPIN required imputation for 30% of its records. These were records that had nonadjudicated claims. Nonadjudicated claims are for drugs for which the Manitoba government does not have a fiduciary responsibility. This includes drugs not on the benefit list for Manitoba Health, and drugs paid for by other agencies, including federal agencies like Veteran Affairs and Royal Canadian Mounted Police services. Manitoba Health provided us with a dataset of all records with DINs (drug identification numbers) that were missing their unit price in our subset of the DPIN throughout 2005/2006. We found the modal unit price of each DIN in this larger dataset, and merged these into our dataset. If two or more prices had the greatest frequency, their average was taken and assigned as the modal price. Following this process, there still remained 4% of records that did not have a value for their DIN. Appealing to Manitoba Health's dataset once again, the variable PRODG (a grouper for like drugs) was used. The modal price was determined and used to impute the remaining missing unit price. With a complete list of unit prices, unit price was multiplied by metric quantity paid for a total drug cost paid. Excluded from DPIN are dispensing done in hospital pharmacies for inpatients, nursing stations, outpatient visits at Cancer Care Manitoba, and personal care homes that obtain drugs through a hospital pharmacy.

Records were flagged if patients had been hospitalized overnight, if they had an IBD-related surgery, if they had infliximab (identified in the DPIN, adalimumab was not yet available for managing IBD in Canada), and if they used immunomodulators (6-mercaptopurine, methotrexate, azathioprine) or not. IBD-related surgery codes included procedures like colectomy and intestinal resections with a diagnosis code of IBD. Infliximab users were classified by whether they were new users, or if they were annual users. New users had never had infliximab on the DPIN record until their first use in fiscal 2005/2006. Annual users were defined as having had a prescription of infliximab within the first 2 months of April 1, 2005 through to within 2 months of the end of the fiscal year. We accumulated costs for all users, distinguishing between cases and controls, type of IBD (CD or UC), age, gender, and disease duration. We also accumulated costs separately for all annual infliximab users, hospitalized users who did not use infliximab, patients hospitalized having an IBD-related surgery, patients who used an immunomodulator but not infliximab, and those who used none of these drugs. Patients were collapsed, separating fees by overnight hospitalization, outpatient visits, physician office visits, and prescription drugs. In addition, an estimate of the average annual total cost was determined for new infliximab users. This was possible by computing an average daily cost for the days prior to infliximab use, then multiplying this amount by 365.

Costs sorted by disease duration were partitioned by four categories of IBD duration: 0, 1, 2–3, 4+ years with IBD. These categories corresponded to incident cases, 1-year incidence cases with long-standing disease, and those with long-standing disease, respectively.

The z-test was used to test differences in means and proportions, and the Kolmogorov–Smirnov test to test the equality of distributions. Although only one variable was used as the dependent variable when testing for the association between IBD or IBD type and utilization, CD cases tended to be younger and were more likely than UC to be female. To compare medians the Mann–Whitney test of equality of distributions and a nonparametric two-sample test on the equality of medians was used. Since age and gender are known to be correlated with utilization, controls for age and gender were introduced to regressions on CD versus UC to restrict confounding.

All estimates were weighted by person years. We compared costs in 2005/2006 with 1998/1999 which was one of the final years before biological therapy was approved for use. We adopted the term "users" to refer to cases or controls who utilized outpatient or inpatient services, or who had surgery. Costs are given to the nearest Canadian dollar. Despite the skewed nature of cost data, it is desirable to report mean patient costs, as overall total costs can then be calculated. The mean patient costs per year are reported with standard error (SE) estimated using nonparametric bootstrap sampling. Two thousand samples were taken for each SE and bias corrected. The statistical significance of differences in mean costs between IBD and non-IBD controls and between CD and UC were computed with P-values < 0.05 reported. The analysis was completed using both SAS 10 (Cary, NC) and STATA SE 10.1 (Statsoft, Tulsa, OK).

RESULTS

In 2005/2006 there were 7375 IBD cases, of which 3735 had CD and 3640 had UC and there were 71,682 matched controls. Females represented 55% of all IBD cases, 58% of CD cases and 52% of UC cases. The duration of disease was <1 year in 5% of IBD cases, 1 year in 4%, 2–3 years in 9% and 4+ years in 81%. The overall costs by component and disease duration for IBD and non-IBD control populations are shown in Table 1. Overall, the mean and median costs were more than double among IBD patients than among non-IBD controls ($3896 vs. $1826 for mean and $1562 vs. $448 for median), with higher mean costs for those with CD than those with UC. Interestingly, the distribution of costs by component were similar between IBD and non-IBD populations, with the largest component of costs being for inpatient hospital costs (39% of costs in IBD vs. 40% in non-IBD) and prescription drugs (42% in IBD vs. 37% in non-IBD). Costs were greatest in the first year of diagnosis for both CD and UC, with a greater decrement between the first year of diagnosis and through year 3 in UC than for CD.

The costs by component, stratified by gender and for hospitalized and surgical cases only, are shown in Table 2.

TABLE 1. Total Healthcare Costs for Inflammatory Bowel Disease (IBD) and Non-IBD Populations By Component, Disease Type, and Disease Duration

	IBD	Non-IBD	CD	UC
All Subjects				
Sample Size *(n)*	7375	71,682	3735	3640
Mean Cost (SE) ($)	$3896 ($90)	$1826 ($20)[a]	$4232 ($137)	$3552 ($117)[a]
1st Quartile Cost ($)	$535	$104	$502	$570
Median Cost ($)	$1562	$448[b]	$1538	$1574
3rd Quartile Cost ($)	$3782	$1545	$4108	$3533
Max Cost ($)	$130,332	$373,457	$130,332	$125,912
Hospital Outpatient (%)	6%	6%	5%	7%
Hospital Inpatient (%)	39%	40%	39%	39%
Physician Office Visits (%)	13%	17%	12%	14%
Drugs (%)	42%	37%	44%	40%
Duration 0 yrs				
Sample Size *(n)*	402	3994	196	206
Mean Cost (SE) ($)	$6611 ($593)	$1329 ($58)[a]	$6570 ($686)	$6650 ($958)
1st Quartile Cost ($)	$1352	$76	$1439	$1328
Median Cost ($)	$2981	$316[b]	$3190	$2858
3rd Quartile Cost ($)	$6356	$1170	$6848	$5761
Max Cost ($)	$125,912	$101,833	$68,901	$125,912
Hospital Outpatient (%)	6%	7%	7%	5%
Hospital Inpatient (%)	63%	33%	63%	63%
Physician Office Visits (%)	11%	21%	11%	10%
Drugs (%)	20%	39%	19%	21%
Duration 1 yr				
Sample Size *(n)*	313	3149	137	176
Mean Cost (SE) ($)	$4319 ($432)	$1902 ($108)[a]	$5460 ($871)	$3430 ($349)[c]
1st Quartile Cost ($)	$686	$88	$686	$714
Median Cost ($)	$2019	$386[b]	$2223	$1940
3rd Quartile Cost ($)	$4497	$1448	$5600	$3599
Max Cost ($)	$79,226	$122,179	$72,669	$27,323
Hospital Outpatient (%)	9%	5%	6%	6%
Hospital Inpatient (%)	56%	47%	44%	35%
Physician Office Visits (%)	13%	15%	9%	15%
Drugs (%)	42%	32%	40%	44%
Duration 2-3 yrs				
Sample Size *(n)*	680	6915	311	369
Mean Cost (SE) ($)	$4521 ($312)	$1634 ($54)[a]	$5339 ($521)	$3832 ($369)[c]
1st Quartile Cost ($)	$758	$82	$627	$839
Median Cost ($)	$1741	$375[b]	$1727	$1792
3rd Quartile Cost ($)	$4329	$1386	$5100	$3766
Max Cost ($)	$68,227	$88,428	$68,227	$62,625
Hospital Outpatient (%)	6%	6%	4%	6%
Hospital Inpatient (%)	40%	40%	40%	40%
Physician Office Visits (%)	12%	18%	10%	15%
Drugs (%)	43%	36%	46%	39%
Duration 4+ yrs				
Sample Size *(n)*	5980	57,624	3091	2889
Mean Cost (SE) ($)	$3621 ($94)	$1880 ($23)[a]	$3918 ($145)	$3303 ($119)[a]
1st Quartile Cost ($)	$484	$110	$462	$510
Median Cost ($)	$1417	$473[b]	$1409	$1425
3rd Quartile Cost ($)	$3543	$1600	$3698	$3315
Max Cost ($)	$130,332	$373,457	$130,332	$103,988
Hospital Outpatient (%)	6%	6%	5%	7%
Hospital Inpatient (%)	35%	40%	35%	36%
Physician Office Visits (%)	14%	17%	13%	14%
Drugs (%)	45%	37%	47%	43%

[a] $P < 0.001$ comparing IBD vs. non-IBD or CD vs. UC.
[b] $P < 0.001$ comparing IBD vs. non-IBD or CD vs. UC.
[c] $P = 0.02$ comparing IBD vs. non-IBD or CD vs. UC.

TABLE 2. Healthcare Costs for Inflammatory Bowel Disease (IBD) and Non-IBD Controls in Manitoba, by Disease Type and Cost Component, Manitoba, 2005/2006

	IBD	Non-IBD	CD	UC
Male[d]				
Sample Size *(n)*	3317	31,872	1568	1749
Mean Cost (SE) ($)	$3738 ($128)	$1675 ($33)[a]	$3989 ($202)	$3513 ($161)
1st Quartile Cost ($)	$396	$49	$312	$488
Median Cost ($)	$1371	$269[b]	$1282	$1438
3rd Quartile Cost ($)	$3588	$1246	$3836	$3430
Max Cost ($)	$103,988	$373,457	$96,328	$103,988
Hospital Outpatient (%)	5%	6%	5%	6%
Hospital Inpatient (%)	38%	43%	37%	40%
Physician Office Visits (%)	12%	15%	11%	13%
Drugs (%)	44%	36%	46%	42%
Female				
Sample Size *(n)*	4058	39,810	2167	1891
Mean Cost (SE) ($)	$4026 ($126)	$1948 ($26)[a]	$4407 ($185)	$3588 ($168)[a]
1st Quartile Cost ($)	$645	$187	$646	$644
Median Cost ($)	$1712	$590[b]	$1726	$1694
3rd Quartile Cost ($)	$3914	$1758	$4221	$3602
Max Cost ($)	$130,332	$168,315	$130,332	$125,912
Hospital Outpatient (%)	6%	6%	5%	8%
Hospital Inpatient (%)	39%	38%	39%	38%
Physician Office Visits (%)	14%	19%	13%	15%
Drugs (%)	41%	37%	42%	39%
Hospitalized Cases Only				
Sample Size *(n)* (% of total)	1089 (15%)	5278 (7%)	603 (16%)	486 (13%)
Mean Cost (SE) ($)	$13,495 ($416)	$12,607 ($200)	$12,940 ($542)	$14,183 ($644)
1st Quartile Cost ($)	$5512	$4474	$5116	$5827
Median Cost ($)	$9038	$7810[c]	$8647	$9963[c]
3rd Quartile Cost ($)	$16,532	$14,367	$15,225	$17,678
Max Cost ($)	$130,332	$219,652	$130,332	$125,912
Hospital Outpatient (%)	3%	2%	3%	3%
Hospital Inpatient (%)	73%	79%	73%	73%
Physician Office Visits (%)	6%	6%	7%	6%
Drugs (%)	17%	13%	17%	17%
Surgical Cases Only				
Sample Size *(n)* (% of total)	161 (2%)	222 (0.3%)	104 (3%)	57 (2%)
Mean Cost (SE) ($)	$18,749 ($1245)	$18,041 ($1403)	$18,194 ($1309)	$19,763 ($2592)
1st Quartile Cost ($)	$9756	$5117	$9769	$9628
Median Cost ($)	$13,413	$11,752	$13,555	$13,198
3rd Quartile Cost ($)	$23,594	$22,020	$23,724	$22,953
Max Cost ($)	$125,912	$168,315	$72,669	$125,912
Hospital Outpatient (%)	2%	3%	3%	3%
Hospital Inpatient (%)	87%	86%	85%	87%
Physician Office Visits (%)	4%	4%	4%	4%
Drugs (%)	7%	7%	8%	6%

[a] $P < 0.001$ comparing mean cost IBD vs. non-IBD or CD (Crohn's disease) vs. UC (ulcerative colitis).
[b] $P < 0.001$ comparing median cost IBD vs. non-IBD or CD vs. UC.
[c] $P < 0.05$ comparing median cost IBD vs. non-IBD or CD vs. UC.
[d] $P < 0.001$ comparing males and females in distribution and their median costs.

Overall, mean and median costs were somewhat higher for females than males with IBD ($4026 vs. $3738 for mean and $1712 vs. $1371 for median), with these differences being due to higher costs among females with CD. The distribution of costs among healthcare components differed little between males and females.

There were 1089 subjects who were hospitalized in 2005/2006. The mean costs for these subjects was $13,495 (median = $9038). This was not substantially different than the mean cost for non-IBD subjects who were hospitalized ($12,607, median = $7810). However, only 7% of non-IBD controls were hospitalized compared to 15% of IBD subjects. While 71% of this hospitalized cohort had at least 4 years of disease, 14% were within the first year of diagnosis, 5% had 1 year, and 10% had 2–3 years of disease. Two percent of all IBD subjects underwent surgery in 2005/2006 and the average cost incurred by these subjects was $18,749 (median = $13,413). Costs were comparable between CD and UC in this cohort. Hospital inpatient costs accounted for 87% of costs. Disease duration was at least 4 years in 65%, 16% were within the first year of diagnosis, 9% had at least 1 year, and 10% had 2–3 years of disease.

Table 3 shows the distribution of costs by different age cohorts. While the highest mean (and median) costs were incurred among the elderly, the most significant differences between costs for cases versus controls were in the very young with a steadily narrowing differential between cases and controls as age increased.

Table 4 shows the healthcare costs for IBD patients by primary therapy: infliximab, other immunosuppressives, no infliximab or other immunosuppressives, and surgery. Overall, while 1.5% of Manitobans with IBD used infliximab, less than 1% of patients were primarily treated for the entire year with infliximab, and their mean costs ($31,440) were substantially higher than patients on other immunosuppressives ($5155) or neither immunosuppressives nor infliximab ($3361). Similarly, those with surgical therapy ($18,749) had substantially higher costs than non-infliximab users, but still substantially less than infliximab users ($P < 0.01$ for comparison between mean costs and $P < 0.001$ for comparison between median costs). Not surprisingly, the large majority of costs (91%) for infliximab users were due to drug costs. Even though infliximab patients represented a very small proportion of all IBD patients, they accounted for a total of approximately $2 million in drug costs in 2005/2006, which represented approximately half of all prescription drug costs for IBD patients.

The disease duration was at least 4 years in 82% of these infliximab users. Interestingly, prior to using infliximab the estimate of the annual total mean cost was $9683 for those individuals who ultimately received infliximab, which is substantially higher than others without surgical treatment.

Controlling for age, gender, duration of disease, and year, IBD cases are 6.9 (95% confidence interval [CI], 5.7–8.3) times as likely as controls to incur healthcare costs; 5.1 (95% CI: 4.4–5.9) times as likely to have an office visit; 3.3 (95% CI: 3.0–3.6) times as likely to have a hospital inpatient stay; 4.4 (95% CI: 4.1–4.8) times as likely to have had an outpatient visit to hospital; and 5.6 (95% CI: 5.1–6.3) times as likely to have used prescription drugs. Whether an individual had CD or UC was not a predictor of cost, nor was year; however, disease duration, age, and gender were.

The cost distribution was right-skewed with the most costly 2% of IBD cases accumulating 23% of costs (33% for controls). Eleven percent of IBD cases and 10% of controls were considered statistical outliers (applying the rule of 1.5 × IQR), comprising 56% and 65% of total costs, respectively.

We assessed the proportion of cases hospitalized or hospitalized with surgery in 1998/1999 compared to 2005/2006 and it did not change significantly over time. While the difference in costs of patients who had been hospitalized or hospitalized with surgery was greater in IBD cases than hospitalized controls in 1998/1999, it was not statistically different from hospitalized controls in 2005/2006. Since we used RIW to estimate costs for hospitalizations and these were based more on U.S. data in 1998/1999 and Canadian data in 2005/2006 (and since U.S. costs are much higher than Canadian costs), it is possible that the 2005/2006 data more likely reflect the true situation for Canada.

Controlling for disease duration, UC cases were no more likely than CD cases to incur costs (odds ratio [OR] = 1.2; 95% CI: 1.0–1.5). UC cases were no more likely to incur costs due to office visits (OR = 1.1; 95% CI: 0.9–1.3) or prescription drugs (OR = 1.0; 95% CI: 0.9–1.2). However, CD cases were more likely to incur costs due to overnight hospitalization (OR = 1.4; 95% CI: 1.3–1.5) while UC cases (OR = 1.3; 95% CI: 1.2–1.5) were more likely to incur costs as a result of outpatient visit to a hospital (note that in Manitoba much endoscopy is undertaken in hospital outpatient procedure areas, which may account for the increased likelihood evident in UC). But overall, the type of IBD did not influence overall likelihood of incurring cost. Incurring cost is different than the magnitude of costs (which are greater in CD than UC).

DISCUSSION

There were a number of important findings in our study. The breakdown of drivers of costs of care was similar for IBD cases and population-based matched controls for outpatient visits (6% for both), and inpatient stays (39 and 40%, respectively), but diverged at outpatient pharmaceuticals, where a greater percentage of cost was borne in the IBD cohort (42%) compared with controls (37%) and

TABLE 3. Healthcare Costs for Inflammatory Bowel Disease (IBD) and Non-IBD Controls in Manitoba, by Age, Disease Type, and Cost Component, Manitoba, 2005/2006

	IBD	Non-IBD	CD	UC
Age: 0-18 Years				
Sample Size *(n)*	151	1283	89	62
Mean Cost (SE) ($)	$3842 ($606)	$333 ($32)[a]	$4174 ($915)	$3364 ($678)
1st Quartile Cost ($)	$574	$33	$601	$543
Median Cost ($)	$1457	$109[b]	$1816	$1320
3rd Quartile Cost ($)	$4059	$284	$4322	$3183
Max Cost ($)	$70,612	$32,153	$70,612	$27,959
Hospital Outpatient (%)	6%	6%	5%	7%
Hospital Inpatient (%)	47%	27%	40%	59%
Physician Office Visits (%)	12%	40%	10%	14%
Drugs (%)	35%	27%	44%	20%
Age: 19-34 Years				
Sample Size *(n)*	1321	11,880	790	531
Mean Cost (SE) ($)	$3234 ($199)	$740 ($24)[a]	$3805 ($302)	$2383 ($201)[a]
1st Quartile Cost ($)	$287	$32	$257	$333
Median Cost ($)	$1014	$173[b]	$989	$1035
3rd Quartile Cost ($)	$2767	$508	$2949	$2555
Max Cost ($)	$96,328	$122,179	$96,328	$44,027
Hospital Outpatient (%)	5%	7%	5%	7%
Hospital Inpatient (%)	35%	40%	35%	35%
Physician Office Visits (%)	12%	26%	10%	16%
Drugs (%)	47%	27%	50%	42%
Age: 35-44 Years				
Sample Size *(n)*	1575	14,825	863	712
Mean Cost (SE) ($)	$2976 ($147)	$924 ($24)[a]	$3579 ($231)	$2244 ($161)[a]
1st Quartile Cost ($)	$350	$54	$371	$319
Median Cost ($)	$1045	$230[b]	$1145	$967
3rd Quartile Cost ($)	$2632	$717	$3398	$2161
Max Cost ($)	$62,564	$112,963	$62,564	$41,922
Hospital Outpatient (%)	7%	8%	6%	10%
Hospital Inpatient (%)	30%	27%	30%	29%
Physician Office Visits (%)	15%	25%	13%	17%
Drugs (%)	49%	40%	51%	44%
Age: 45-54 Years				
Sample Size *(n)*	1743	16,482	860	883
Mean Cost (SE) ($)	$3264 ($154)	$1320 ($38)[a]	$3790 ($248)	$2753 ($183)[a]
1st Quartile Cost ($)	$485	$94	$511	$468
Median Cost ($)	$1376	$371[b]	$1498	$1280[b]
3rd Quartile Cost ($)	$3252	$1114	$3795	$2800
Max Cost ($)	$72,669	$373,457	$72,669	$62,625
Hospital Outpatient (%)	7%	7%	6%	9%
Hospital Inpatient (%)	31%	27%	34%	26%
Physician Office Visits (%)	15%	21%	14%	16%
Drugs (%)	47%	45%	46%	49%
Age: 55-64 Years				
Sample Size *(n)*	1169	12,279	581	588

(*Continued*)

TABLE 3. (*Continued*)

	IBD	Non-IBD	CD	UC
Mean Cost (SE) ($)	$4029 ($236)	$1952 ($44)[a]	$4538 ($373)	$3527 ($291)[a]
1st Quartile Cost ($)	$739	$197	$739	$745
Median Cost ($)	$1884	$727[b]	$1917	$1832
3rd Quartile Cost ($)	$4022	$1848	$4403	$3640
Max Cost ($)	$130,332	$168,315	$130,332	$125,912
Hospital Outpatient (%)	7%	6%	5%	9%
Hospital Inpatient (%)	36%	32%	38%	32%
Physician Office Visits (%)	14%	18%	13%	15%
Drugs (%)	43%	44%	43%	43%
Age: 65-79 Years				
Sample Size *(n)*	1019	10,493	402	617
Mean Cost (SE) ($)	$5298 ($266)	$3537 ($72)[a]	$5442 ($448)	$5204 ($331)
1st Quartile Cost ($)	$1326	$593	$1239	$1395
Median Cost ($)	$2838	$1511[b]	$2593	$2962
3rd Quartile Cost ($)	$5417	$3305	$5245	$5430
Max Cost ($)	$105,578	$131,805	$78,431	$105,578
Hospital Outpatient (%)	6%	6%	5%	7%
Hospital Inpatient (%)	44%	45%	47%	42%
Physician Office Visits (%)	13%	14%	13%	13%
Drugs (%)	37%	35%	35%	39%
Age: 80-102 Years				
Sample Size *(n)*	397	4440	150	247
Mean Cost (SE) ($)	$8560 ($694)	$5663 ($167)[a]	$8372	$8675
1st Quartile Cost ($)	$1721	$994	$1754	$1611
Median Cost ($)	$3816	$2264[b]	$3997	$3755
3rd Quartile Cost ($)	$8067	$5059	$7687	$9006
Max Cost ($)	$103,988	$219,652	$103,564	$103,988
Hospital Outpatient (%)	2%	3%	3%	2%
Hospital Inpatient (%)	64%	61%	63%	64%
Physician Office Visits (%)	9%	10%	9%	8%
Drugs (%)	26%	26%	25%	26%

[a]$p<0.001$ comparing mean cost IBD vs non-IBD, or CD (Crohn's disease) vs UC (ulcerative colitis).
[b]$p<0.001$ comparing median cost IBD vs non-IBD, or CD vs UC.

office visits were a lesser driver in IBD (13%) versus controls (17%). In 2005/2006, the mean direct cost of an IBD case was $3896 (SE $90) (median cost of an IBD case = $3782). The mean cost associated with an IBD case was twice that of controls in 2005/2006 ($P < 0.05$). The variables that were significantly associated with cost included disease diagnosis (CD mean cost = $4232 ± 137 vs. $3552 ± 117 for UC, $P < 0.0001$), being within 1 year of diagnosis ($6611 ± $593, vs. all others, $P < 0.0001$), an overnight hospital stay ($13,495 ± $416), patients with a surgical stay ($18,749 ± $13,413), and use of infliximab ($31,440 ± $2311). It should be noted that while the mean costs for managing CD were significantly higher than for managing UC, the median costs were comparable at all disease durations, implying that there were more outliers in the CD cohort generating higher costs contributing to higher mean costs. We also found that the difference in costs between cases and controls lessened with increasing age. Even though with age the mean and median costs increased for managing both cases and controls, the greatest differences between cases and controls were in children, with the next greatest difference in those under age 35. While the variables we found associated with costs are consistent with previously published literature from other countries on cost of caring for IBD, perhaps the aspect with the most potential impact on health policy would be the comparison between costs for hospitalizations and surgery vis-à-vis the cost for prescribing infliximab.

TABLE 4. Healthcare Costs for Inflammatory Bowel Disease Patients Based on Primary Therapy Received, Manitoba, 2005/2006

	Infliximab Users	Immunosuppressives	No Immunosuppressives or Infliximab	Surgery
Sample size *(n)* (% of total)	49[a] (0.7%)	821 (11%)	6440 (87%)	161 (2%)
Mean Cost (SE) ($)	$31,440 ($2311)	$5155 ($267)[b]	$3361 ($87)[b]	$18,749 ($1245)[b]
1st Quartile Cost ($)	$22,114	$1680	$450	$9756
Median Cost ($)	$27,739	$2952[c]	$1328[c]	$13,413[c]
3rd Quartile Cost ($)	$35,692	$5819	$3305	$23,594
Max Cost ($)	$96,328	$125,912	$130,332	$125,912
Hospital Outpatient (%)	2%	6%	6%	2%
Hospital Inpatient (%)	5%	41%	42%	87%
Physician Office Visits (%)	2%	12%	14%	4%
Drugs (%)	91%	41%	37%	7%

[a]Of the 114 IBD cases that use infliximab, 49 cases use infliximab throughout the year; defined as using infliximab within the first 3 months to within the last 3 months.
[b]$P < 0.01$ comparing mean cost to infliximab users.
[c]$P < 0.001$ comparing median costs to infliximab users.

Feagan et al[13] assessed a prescription drug and medical claims database from employees of 50 of the largest employers in the U.S. for 1994 for charges of managing the 607 subjects with a diagnosis of CD. The mean (median) charges for that one year was $12,417 ($3668), for those hospitalized at least once were $37,135 ($21,617), for those on chronic immunosuppressives or steroids were $6277 ($2703). It is unknown how charges translated into actual costs but a noteworthy finding from this study was that 25% of subjects accounted for 80% of charges. The average charges for prescription drugs for those receiving immunosuppressives was $444. The costs may have also been inflated by a bias of only including subjects who made claims with the exclusion of the many well CD subjects in that year who would not have made claims, whose mean annual costs would have surely reduced the overall mean but who were not included. Rubinstein et al[14] reported on mean charges, reimbursements, and costs for hospitalized patients with CD at the University of Chicago in 1996–1997. Surgery accounted for 40% of all costs and drugs for 19%. This study also does not estimate the costs of managing a broad cohort of CD patients but rather a select group of hospitalized patients at a tertiary specialized IBD referral center.

Silverstein et al[4] undertook an assessment of costs in a population-based cohort of CD from 1970–1993 in Olmsted County, Minnesota. Among the important findings of this report was that 2% accounted for 34% of total costs of CD. The mean annual costs for 1987–1994 were $4308/patient/year where surgery accounted for 44% of lifetime costs. Further, 65% of the course of CD was spent in medical or surgical remission, underscoring the importance of including these periods in the overall costs estimates of managing patients with IBD. More recently, Kappelman et al[15] assessed the costs data from 2003–2004 in 9056 subjects with CD and 10,364 subjects with UC enrolled in 87 health plans across 33 states. The mean (median) annual cost was $8265 ($3203) for CD and $5066 ($1963) for UC. This study is also biased by inclusion of only those who submitted claims for that year, and hence may have overestimated the overall average costs for managing CD and UC since many subjects may have not accessed the healthcare system at all, or alternatively excluded those costs that were accessed by the subjects outside of the health plans covered. It was noteworthy, though, that in 2003–2004 the drivers of cost in CD were hospitalizations 31%, outpatient care 33%, and pharmacy costs 35%, with pharmacy costs accounting for 27% in UC. Hence, the shift toward drugs accounting for a greater share of costs was evident.

The costs of care for IBD have varied widely from European studies.[16–18] Some themes are constant, such as a minority accounting for a majority of cost (the 10% most costly accounting for 59% of CD and 62% of UC in a UK study,[16] or the increased costs within the first year from diagnosis in a German study).[17,18] A recent Spanish study has identified the much higher costs per patient in the post-infliximab era than when those same patients were treated prior to the infliximab era by a factor of 2.4, even though hospitalization and surgical costs dropped once infliximab was initiated in those subjects.[19]

We have also recently reported on healthcare utilization in our population-based sample of IBD patients.[20] We showed that after infliximab initiation outpatient doctor

visits eventually return to baseline prior to infliximab use in those same infliximab users, but never decrease to a level of IBD patients who are well enough to not be using any of anti-TNF agents or immunosuppressives. We also showed that infliximab users do not have a reduction in surgery rates to that seen with other cohorts such as users of immunosuppressives, or those who do not require any acute courses of steroids, immunosuppressives, or infliximab. Infliximab users are generally more ill. These subjects in our study also had greater mean costs prior to starting infliximab compared to other IBD subjects, attesting to their greater requirements for healthcare resources. While earlier use of infliximab may prevent complicated disease that may lead to the very high costs that were evident in some of the CD patients in our study who were outliers with very high costs, it remains to be seen if that would positively impact overall costs, since these subjects will have to use infliximab annually, at high costs indefinitely. Collectively, our data in the context of the other available literature suggest that from a pure cost perspective it will be difficult to show a cost benefit of anti-TNF use, especially since it is not just a 1-year expense, but rather an indefinite expense, at least with the current approach to therapy. The benefit of anti-TNF is not in question but it is a benefit that might be better measured against quality of life and disease activity rather than cost.

Our study has several advantages over other studies. Our sample is population-based and accounts for all Manitobans with IBD, including those who are in remission and who may be accessing the healthcare system either not at all or even very little. While we are estimating costs for 2005/2006, we can account for persons still living in Manitoba with IBD who have been diagnosed as far back as 1984. Further, we are able to account for drug costs versus hospitalization costs. We have presented costs both as mean and median values and we are able to estimate actual costs and not charges. A limitation of our dataset is that we cannot account for costs by severity of disease, although one can infer disease severity based on hospitalization, surgery, or use of infliximab. Further, we did not have an ability to estimate costs of accessing the Emergency Departments (we do not have data as to how often or how long subjects may have spent in the Emergency Departments across the province). We also do not have reliable data on outpatient laboratory (i.e., blood and stool) testing. Hence, our data may underestimate actual mean and maximal costs. We validated our administrative definition of IBD in 1995 and we have no reason to believe the administrative definition would be any less valid in 2005/2006. While rates of surgery have declined over time in both CD and UC,[21,22] the incidence rates of either form of IBD have remained relatively constant (data not shown).

In conclusion, we have estimated that in 2005/2006 in Manitoba the mean cost of managing an IBD patient was \$3896 (SE = \$90), which was twice that of controls ($P < 0.05$). It was more costly to manage CD than UC patients within 1 year of diagnosis than all others, those hospitalized than those not hospitalized, those undergoing surgery versus those who did not, and the most costly of patients were those using infliximab.

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