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Health Care Cost Analysis in a Population-based Inception Cohort of Inflammatory Bowel Disease Patients in the First Year of Diagnosis

Olga Niewiadomski[a], Corrie Studd[b], Christopher Hair[c], Jarrad Wilson[b], John McNeill[d], Ross Knight[c], Emily Prewett[c], Paul Dabkowski[c], Damian Dowling[c], Sina Alexander[c], Benjamin Allen[c], Mark Tacey[e], William Connell[a], Paul Desmond[a], Sally Bell[a]

[a]Gastroenterology Department, St Vincent's Hospital, Melbourne, VIC, Australia [b]Gastroenterology Department, Royal Hobart Hospital, Hobart, TAS, Australia [c]Gastroenterology Department, University Hospital Geelong, Barwon Health, Geelong, VIC, Australia [d]Department of Epidemiology & Preventive Medicine, Monash University, Alfred Hospital, Melbourne, VIC, Australia [e]Melbourne EpiCentre and Northern Clinical Research Centre, Melbourne Health, Melbourne, VIC, Australia

Corresponding author: Dr Olga Niewiadomski, MBBS, FRACP, University of Melbourne, Gastroenterology Department, St Vincent's Hospital, Fitzroy, VIlC3065, Australia. Email: ola.niewiadomski@svhm.org.au

Abstract

Background: There are limited prospective population-based data on the health care cost of IBD in the post-biologicals era. A prospective registry that included all incident cases of inflammatory bowel disease [IBD] was established to study disease progress and health cost.
Aim: To prospectively assess health care costs in the first year of diagnosis among a well-characterised cohort of newly diagnosed IBD patients.
Method: Incident cases of IBD were prospectively identified in 2007–2008 and 2010–2013 from multiple health care providers, and enrolled into the population-based registry. Health care resource utilisation for each patient was collected through active surveillance of case notes and investigations including specialist visits, diagnostic tests, medications, medical hospitalisation, and surgery.
Results: Off 276 incident cases of IBD, 252 [91%] were recruited to the registry, and health care cost was calculated for 242 (146 Crohn's disease [CD] and 96 ulcerative colitis [UC] patients). The median cost in CD was higher at A$5905 per patient (interquartile range [IQR]: A$1571-$91,324) than in UC at A$4752 [IQR: A$1488-A$58,072]. In CD, outpatient resources made up 55% of all cost, with medications accounting for 32% of total cost [15% aminosalicylates, 15% biological therapy], followed by surgery [31%], and diagnostic testing [21%]. In UC, medications accounted for 39% of total cost [of which 37% was due to 5-aminosalicylates, and diagnostics 29%; outpatient cost contributed 71% to total cost.
Conclusion: In the first year of diagnosis, outpatient resources account for the majority of cost in both CD and UC. Medications are the main cost driver in IBD.

Keywords: Inflammatory bowel disease; health cost analysis; population-based; Crohn's disease; ulcerative colitis

1. Introduction

In this era of escalating health care costs and growing constraints on health care budgets, cost analysis is crucial for planning proper distribution of health care resources and novel therapeutic agents. This is especially so in lifelong incurable diseases such as inflammatory bowel disease [IBD] that have several expensive therapeutic

options available, including anti-tumour necrosis factor [TNF] antibody therapy [biologicals] and resective surgery. The issue is made even more pertinent by the global rise in the incidence of IBD.[1,2,3,4,5,6]

There is limited literature on the health care cost in population-based IBD cohorts, especially since the widespread introduction of biological therapy. The studies that are available have a number of limitations. Frequently patients have been recruited through the use of databases that are dependent on administrative definitions of IBD and, importantly, lack clinical data to compare cost and disease severity.[7,8] Many population-based studies were performed retrospectively, thus introducing bias and difficulties in interpreting disease course and severity.[1,2] Finally, some studies relied on patient-based recall of resource utilisation, which introduces recall bias.[11,12]

With the current escalating medical costs and new advances in therapeutic options, there is a need for more accurate information regarding the health care cost of IBD. This prospective population-based study of a well-characterised inception cohort of patients, with known disease progression, was designed to assess the total health care cost in the first year of diagnosis, from the health care system perspective.

2. Method

2.1. Study population

During a 4-year inclusion period [2007 and 2008, 2010 to 2013], incident cases of IBD from a well-defined area of greater Geelong, Victoria, were recruited to be part of this population-based prospective study. New cases were identified using the multiple source capture methodology as previously described[3,13,14] and enrolled into an IBD registry through the use of an opt-out consent process.

A total of 278 incident cases of IBD were identified during the study period. Of these, 16 [6%] patients were lost to follow up, 8 [3%] were re-diagnosed as not IBD, 1 [0.4%] was not a true incident case, and 1 [0.4%]was not suitable for the study due to an unstable social situation. Thus 252 patients were enrolled into the IBD clinical registry, which was used as a basis to collect outcome data on the natural history, quality of life impact, environmental factors, and health care cost of IBD. Here we publish the health care costs of crohn's disease [CD] and ulcerative colitis [UC] patients [total of 242 patients; 10 cases of indeterminate colitis were excluded].

2.2. Data collection

Patient progress was assessed by the review of specialist case notes, hospital records, and pathology and radiology services, as well as liaison with the treating doctor[s]. For the majority of patients this was done prospectively, and for the smaller group diagnosed in 2007/2008 [*n*=61] this was done retrospectively in 2012. Patients were assessed at diagnosis, 3 and 12 months from diagnosis, and at the end of the study. A minimum of 12 months [+/-3 months] follow-up was required. Audits of case ascertainment and data quality were performed 3-monthly. The clinical data collected included demographics, disease classification, disease activity, medical therapy, surgery, hospitalisation, malignancy, and death.

2.3. Calculation of health care resource utilisation

Health care cost was calculated for each patient for the first 12 months of disease, including cost of diagnosis, from the health care system perspective. This perspective was chosen as providing valid and reliable cost data[4] that can be then extrapolated to other populations, and is least likely to result in the introduction of bias seen with assessment of indirect costs. Cost is reported in Australian dollars [A$]. This was done through active surveillance for the following IBD-related health care resources: diagnostic tests [including pathology, radiology, endoscopy, and capsule endoscopy]; medications based on the treating physician's prescription [topical and oral aminosalicylates, azathioprine, mercaptopurine, methotrexate, adalimumab, infliximab]; outpatient visits to the main treating specialist physician; and medical and surgical hospitalisation. The cost of outpatient visits to other health care professionals such as the general practitioner [GP], surgeon, specialist nurse, or dietitian was not included. Unpublished health economic data from the POCER study in Australia by Wright *et al*. showed that the average cost accrued by a patient visiting the GP for IBD-related problems was 13% of the cost of visiting the specialist. Therefore, this assumption was made to calculate the cost of GP visits in this study.

Any admission that eventuated in a surgical procedure [intestinal and perianal] was classified as a surgical admission [including all elective surgical admissions], and all other hospitalisations were defined as medical admissions.[6] Hospital cost was obtained directly from the relevant hospital for each individual patient. Both private and public hospitals derive their cost based on the Department of Health and Aging Public National Round for the relevant year. In this system, each hospitalisation is assigned a relative cost based on the intensity of resources used. In a public hospital this incorporates physician fees; however, in private hospitals the physician fees are added on separately, based on the Medicare Benefits schedule.

Diagnostic costs were based on the Medicare Benefits schedule, apart from endoscopy, which was collected directly from each of the service providers. For all blood tests an estimate was calculated dependent on the therapy prescribed. Patients on no immunomodulator were predicted to require twice yearly baseline blood tests (full blood examination, electrolytes, liver function tests, and C-reactive protein [CRP]). Those on immunomodulator therapy had a pre-immunosuppression screen added, as well as fortnightly tests for 2 months followed by second-monthly. A similar formula was used for patients on biological therapy.

Medication use was based on what the treating specialist prescribed, including dose and duration. The cost of each medication was calculated from the Pharmaceutical Benefits Scheme [PBS], using the dispensed price for maximum quantity [DPMQ] which was adjusted based on length of treatment. For infliximab, the additional cost of a day procedure at the relevant hospital was added into the cost of the drug.

Outpatient visits to the treating gastroenterologist/specialist were calculated based on the Medicare Benefits schedule.

All efforts were made to adhere to the criteria set out by the Quality of Health Economic Studies [QHES] instrument.[4]

2.4. Statistics

As the health cost was skewed to the right, both median and mean costs per patient were calculated, as median cost is more representative of the outlay in most of the patients without introducing bias from a minority of patients with high cost. However, mean costs are also important for planning future health care budgets as they account for overall expenditure.[7] To further analyse the high-cost outliers, these patients were identified by the statistically verified method [Q3+1.5IQR, where IQR is the interquartile range].[3,8,4,9,5,10]

To determine which clinical variables may predict future high IBD health cost, univariate analysis was done using the Mann-Whitney rank sum because of the skewed distribution of cost. The dependent variable was total cost, with the independent variables being diagnosis, age, gender, disease location, disease behavior, and perianal disease

[CD only], smoking, and steroid/immunomodulator at diagnosis. A threshold of p<0.2 was used to determine which variables would be incorporated into a multivariate [negative binomial] regression analysis, with manual backwards stepwise techniques employed to identify the variables independently associated with cost. Data analysis was performed using STATA version 12.1 [STATA Corporation, College Station, TX]. All statistical tests were two-sided, with $p<0.05$ considered to indicate statistical significance.

Economic guidelines were adhered to in reporting the economic evaluation of disease.[16,17,6,11]

2.5. Ethics

This study was approved by the Barwon Health ethics department and was carried out according to the local regulations.

3. Results

3.1. Cohort characteristics

A total of 242 patients [146 CD and 96 UC] from the IBD registry were included in the cost analysis, with a median follow-up of 18 months. This included 38 paediatric cases [15%, defined as age ≤ 19 years], of whom 25 [65%] had CD, 12 [32%] UC, and 1 IBD unclassified [IBDU] [3%].

Patient demographics as well as disease classification [using the Montreal classification] are listed in Table 1. A more detailed overview of disease progression in this cohort has been described elsewhere.[4,12]

The total expenditure for the 242 patients in the first 12 months from diagnosis was A$2,145,585.00. This included $ 497,767 [23%] on investigations, A$728,897 [34%] on medications, A$321,059 [15%] on medical hospitalisation, A$544,810 [25%] on surgical hospitalisation, and A$53,050 [3%] on gastroenterologist outpatient reviews. The inclusion of GP visits to the latter increased the cost to A$59,240 [3%].

The cost for the first 12 months in the CD cohort [n=146] was A$1,529,750 and for the UC cohort [n=96] it was A$615,835. The median cost per CD patient was A$5905 [range A$1571-91,324] and for a UC patient was $4752 [range $1488-58,072] [Figure 1]. The mean CD cost per patient was significantly higher compared with UC ($p<0.001$, 95% confidence interval [CI] -6686 to 1684], due to higher mean diagnostic [$p<0.001$] and specialist cost [$p<0.001$] [see Table 2].

3.2. Breakdown of total expenditure

The major cost driver in CD were medications at A$491,504 [32%], followed closely by surgery A$473,797 [31%], diagnostic tests A$320,693 [21%], medical hospitalisation A$214, 255 [14%], and lastly outpatient specialist reviews A$29,500 [3%]. The surgical cost includes intestinal resection [A$427,670, 90% of surgical cost] and perianal surgery [A$46,127, 10% of surgical cost]. Figure 2 shows the breakdown of each component of total cost, with a detailed overview of medications used; 5-ASA use accounts for 15% of total cost in CD, and biological therapy for 16%. The bulk of diagnostic testing cost in CD is due to endoscopy, which accounts for 18% of total cost [85% of diagnostic testing], and radiology, pathology, and capsule endoscopy contributed 1% each. The majority of the endoscopy was done at time of diagnosis, with 24 additional colonoscopies [14% of total endoscopy cost] done during follow-up.

In UC patients, medications made up the bulk of the cost at A$237,393 [39%], followed by diagnostic tests at A$177,074 [29%], medical hospitalisation at A$106, 804 [18%], surgery at A$71,013 [12%], and specialist outpatient visits at A$ 23,550 [4%]. Figure 2 illustrates the breakdown of specific medications, with 37% of the total cost stemming from use of 5-ASAs. Biologicals use in UC has not been widely available till recently. Diagnostic cost is mainly due to endoscopy, accounting for 27% of total cost [94% of diagnostic cost], with radiology and pathology contributing 1% each. The majority of the endoscopy was done at diagnosis in UC, with an extra 15 colonoscopies done during follow-up, accounting for 14% of the total endoscopy cost.

Outpatient resources are responsible for the majority of the cost in both CD [55%] and UC [71%], when compared with inpatient resources [hospitalisation and surgery].

Table 1. Patient characteristics and outcomes of 242 incident IBD patients.

	CD	UC
Total no. patients [%]	146 [60%]	96 [40%]
No. of patients diagnosed in 2007/2008	38 [15%]	23 [9%]
Paediatric cases [age ≤ 19 years]	25 [17%]	12 [13%]
Male [%]	68 [47%]	39 [41%]
Female [%]	78 [53%]	57 [59%]
Age at diagnosis [range]	36 [11–82]	40 [11–87]
Median time [months] to diagnosis [range]	6.4 [0.5–79]	3 [0–73]
Current smoker	19 [13%]	5 [5%]
Former smoker	25 [17%]	17 [18%]
Disease extent		
Proctitis	-	31 [32%]
Left-sided colitis	-	31 [32%]
Pancolitis	-	34 [35%]
Disease location		
L1: terminal ileum	49 [32%]	-
L2: colonic	42 [30%]	-
L3: ileocolonic	55 [38%]	-
+L4: upper gastrointestinal	18 [12%]	-
Disease behaviour[a]		
Inflammatory	116 [80%]	-
Stricturing	15 [10%]	-
Penetrating	15 [10%]	-
Perianal	19 [12%]	-
Treatment exposure at 1 year		
No treatment	4 [3%]	0
5-aminosalicylates	82 [56%]	95 [99%]
Steroids	100 [68%]	53 [55%]
Immunomodulators	60 [41%]	9 [9%]
Biological therapy	12 [8%]	1 [1%]
Surgery [intestinal]	20 [14%]	2 [2%]
Surgery [perianal]	11 [8%]	-
Medical hospitalisation	33[23%]	17 [18%]

CD, Crohn's disease; UC, ulcerative colitis; IBDU, inflammatory bowel disease unclassified.

[a]At 12 months. Total health care resource utilization in the first year of diagnosis.

3.3. High-cost outliers

High-cost outliers were identified for both CD and UC; 11% of patients [16 of 146] with CD were defined as outliers [total cost range A$24,321 to A$91,324]. These patients accounted for A$642,325 [42%] of the total cost in CD. The major cost contributors in these patients were surgery [54%] and medications [29%]. Biological therapies contributed 60% to the medication cost. On

more detailed analysis of these 16 patients, there were 5 patients whose cost primarily stemmed from complicated intestinal resections, costing a minimum of A$30,000. This included three patients with a surgical cost of over A$50,000 each due to prolonged admission associated with the surgery [30 days minimum]. There was a delay to salvage therapy or surgery in two of the three patients with severe colonic and ileocolonic disease, respectively. The third was an 80-year-old patient with multiple comorbidities who underwent small bowel resections within 12 months, on no immunomodulator therapy despite predictors of high-risk disease. Of the remaining 11 high-cost CD patients, the major driver to cost was either biological therapy for most of the 1 year, more than one hospitalisation, or the combination of needing both resective or perianal surgery and a biological.

In UC, 10% [10] patients were classified a high-cost outliers [range A$13,426 to A$58,072]. These patients comprised A$ 218,033 [36%] of the total UC cost. Medical hospitalisations accounted for 34%, surgery 33%, and medications 20%. 5-ASAs made up 75% of all the medication cost. There were two patients that had high costs due to a colectomy, with a difference between the two in the cost [A$13,382 vs A$57,631]. This was due to a delay in diagnosis of UC in the higher-cost patient, a young man with a concomitant gastrointestinal infection. Of the remaining high-cost UC patients, the costs of six were due to hospitalisation and of one due to biologicals use.

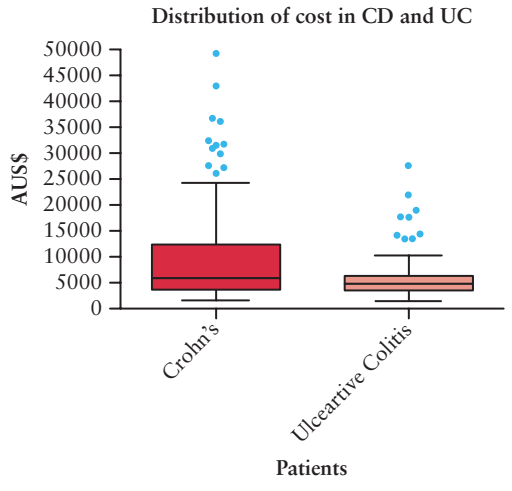

Figure 1. Box and whisker plot [using the Tukey method] illustrating the total distribution of cost in Crohn's and ulcerative colitis patients [the top few outliers excluded here due to very wide distribution].

3.4. Predictors of high cost

In CD, univariate analysis found that the following clinical variables present at diagnosis predicted high cost: perianal disease [p=0.006], colonic and ileocolonic location [p=0.014], complicated disease behaviour [p=0.015], and early immunomodulator [IM] use, defined as within 3 months of diagnosis [p=0.009]. On multivariate regression analysis, colonic (incidence rate ratio [IRR] 1.49, 95% CI: 1.04–2.14) and ileocolonic [IRR 1.84, 95% CI: 1.34–2.52] location and complex disease behaviour [stricturing IRR 1.79, 95% CI: 1.14–2.82, penetrating IRR 2.25, 95% CI 1: 43–3.53, when compared with inflammatory] remained significant [Table 3].

In UC, univariate analysis identified early IM use [p=0.006], extensive disease location [p<0.001], and a high CRP [p=0.013] as predictors of high cost in the first year. On multivariate regression analysis, left-sided colitis [IRR 1.53, 95% CI 1: 12–2.09], pancolitis [IRR 1.76, 95% CI: 1.25–2.47] and a CRP>10 at diagnosis [IRR 1.79, 95% CI: 1.26–2.53] predicted high cost in the first year [see Table 4].

4. Discussion

This cost-analysis of health care in IBD during the first year of disease, including the cost of diagnosis, has identified a number of important findings. First, health care is more expensive in CD than UC. Second, outpatient resources account for more health expenditure when compared with inpatient resources, and medications contribute the largest proportion to total cost. Use of 5-ASAs is not only expensive in UC but also accounts for half the cost of medications

Table 2. Mean and median cost [AUD $] per patient in the first year of disease.

	Crohn's disease [per patient cost A$]	Ulcerative colitis [per patient cost A$]	Mann-Whitney
Total cost			
Mean [SD]	10477 [12737]	6292 [6969]	p=0.003*
Median [IQR]	5905 [3710-12386]	4752 [3202-6338]	
Medical hospitalisation			
Mean [SD]	6493 [2884]	6282 [5276]	p= 0.207
Median [IQR]	5945 [4756-8323]	4756 [2493-8323]	
Surgery			
Mean [SD]	15283 [18656]	35506 [31228]	p = .1837
Median [IQR]	10444 [3494-13382]	35506 [13382-57631]	
Medication			
Mean [SD]	3366 [5912]	2447 [1898]	p =0.1512
Median [IQR]	2165 [207-3280]	2246 [863-3291]	
Diagnostic tests			
Mean [SD]	2196 [956]	1825 [743]	p <0.001*
Median [IQR]	1698 [1401-2749]	1374 [1374-2503]	
Specialist review			
Mean [SD]	258 [34]	242 [37]	p =0.001*
Median [IQR]	282 [226-282]	226 [226-280]	

The Mann-Whitney [rank sum] test was used to compare the two groups
SD, standard deviation; IQR, interquartile range. *Statistically significant.

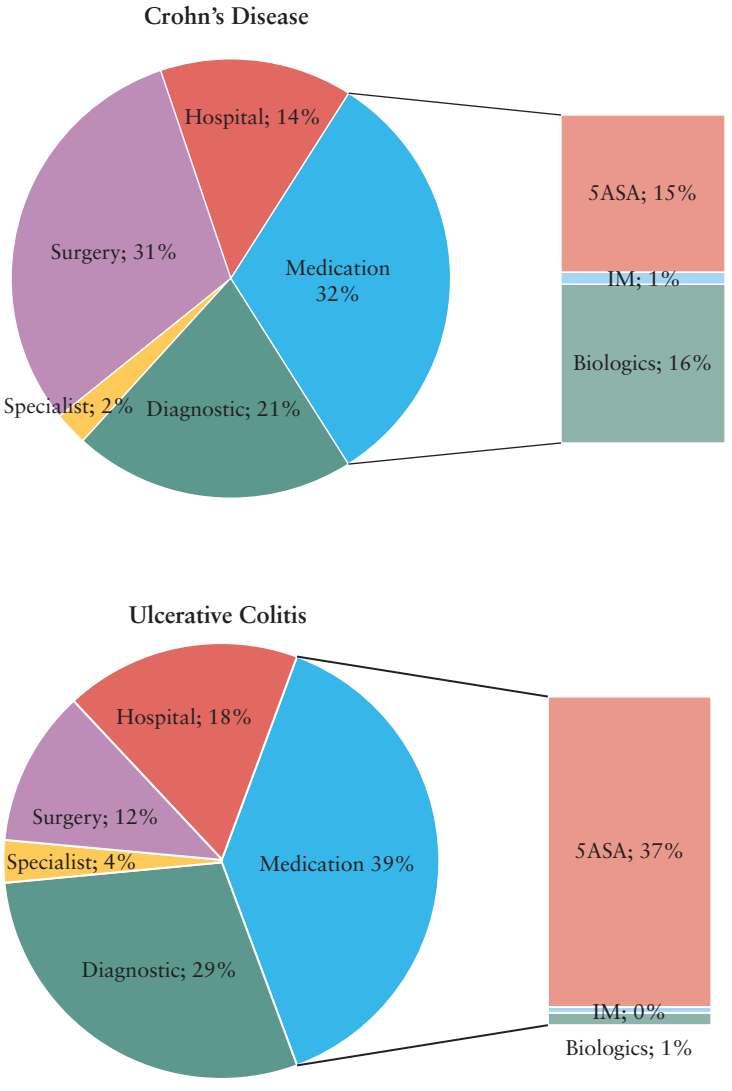

Figure 2. The distribution of costs in Crohn's disease and ulcerative colitis in the first year of disease [% of total].

in CD. Despite the shift to outpatient resources, surgery costs remain high in the first year. Lastly, the distribution of cost is influenced by a small number of 'high-cost outliers'—patients who accumulate a much higher cost in the first year of diagnosis compared with the rest of the cohort.

This prospectively recruited inception cohort of 242 patients has been followed longitudinally to assess disease progression, details of which have been published elsewhere.[7,12] Early disease course was not as aggressive as has previously been reported.[13] Disease behaviour in CD was predominantly inflammatory at 1 year [80%] and, of the CD patients [*n*=38] with 5-year follow up, 75% had non-penetrating non-stricturing disease. Rates of intestinal resection were low in CD [13% at 1 year] and UC [2% at 1 year] compared with the pre-biologicals studies[14,15] but comparable to recent population-based studies from Europe.[16,17,18] Immunomodulator use was frequent [57% at 18 months in CD; 18% in UC], and biological therapy use in CD was common [8% at 1 year; 12% at 18 months]. These rates are very similar to those in Western European countries, described in the recent ECCO-EpiCom cohort,[16] though biological therapy was lower in our cohort, especially in UC. These similarities between cohorts suggest that the health cost data from this study can be extrapolated to other regions, in particular Western Europe.

This study shows a shift from inpatient resources contributing most of the cost in IBD, to outpatient resources. This is due to medications and diagnostic testing contributing a larger percentage of the total cost when compared with historical population-based cohorts.[6,2] This shift has been confirmed in other recent studies.[19,20] It is likely that the gap between inpatient and outpatient resource cost will widen even more after the first year of disease, as surgical and hospitalisation rates continue to decline in later years of disease, as has been shown in recent cohort and health analysis studies [6,8,21,22,23]

In CD the high medication cost is driven equally by biological therapies [50%] and 5-ASAs [49%]. This is one of the first health cost studies to include significant biological therapy [8% at 1 year], as compared with 0.7% at 1 year in the Manitoba cohort[8] and similarly infrequent use in other studies.[1,6] A health cost study in patients with longstanding disease [median 13–16 years] also showed a high number of patients on biological therapy [22%]. In that study, biological therapies accounted for 64% of total cost in CD and 31% in UC,[20] but patient recruitment was hospital based and was through the use of an administrative definition of IBD which may skew to

Table 3. Clinical variables at diagnosis that predict high cost in Crohn's disease patients.

Variable	Count	Mean ± SD	Univariate analysis		Multivariate regression	
			Median [IQR]	p-Value	IRR [95% CI]	*p*-Value
Gender				0.324		
Female	78	10895 ± 13450	6002[3839-12356]			
Male	68	9999 ± 11949	5303[3296-12406]			
Age category [years]				0.564		
<25	53	11766 ± 11510	6719[3697-16410]			
25–45	44	10301 ± 14848	5402[3358-10124]			
>45	49	9243 ± 12069	5281[3875-10340]			
Smoking status				0.915		
Never	49	10531 ± 11381	5572[3697-11450]			
Past smoker	25	8109 ± 6246	6115[2994-13353]			
Current	19	14832 ± 15886	5266[2920-31744]			
Perianal disease				0.006*		
No	127	9447 ± 12041	5281[3697-10620]		1.0	
Yes	19	17365 ± 15313	11450[5572-30056]		1.8[1.21-2.68]	0.003
Location				0.014*		
Ileal	49	8821 ± 10534	4838[3163-10620]		1.0	
Colonic	42	8444 ± 13681	5031[3710-7558]		1.49[1.04-2.14]	0.029
Ileocolonic	55	13507 ± 13411	7039[4890-18804]		1.84[1.34-2.52]	<0.001
Upper GI				0.664		
No	128	10551 ± 13155	5737[3710-12418]			
Yes	18	9954 ± 9518	6473[3821-11305]			
Behaviour				0.015*		
Inflammatory	116	8960 ± 11813	5273[3704-8957]		1.0	
Stricturing	15	13380 ± 9517	12332[6097-20678]		1.79[1.14-2.82]	0.012
Penetrating	15	19310 ± 18217	16410[4125-30056]		2.25[1.43-.53]	<0.001
Steroids at diagnosis				0.514		
No	85	10473 ± 14168	5455[3710-11450]			
Yes	61	10485 ± 10539	6013[3746-12908]			
IM at diagnosis				0.009*		
No	127	8596 ± 11207	4967[3223-8562]			
Yes	19	12259 ± 13874	6719[4125-15032]			

SD, standard deviation; IQR, interquartile range; GI, gastrointestinal.

a more severe disease phenotype and introduce bias, as the definition is used for re-imbursement. As the number of patients using biological therapies in population-based studies increases, it is important to determine if the costly price tag of the therapy will be offset by reduced cost from longer disease remission, as well as less frequent hospitalisation and surgery. There have been studies done with Markov modelling to try to answer this question, one of which concluded that therapy is not cost effective; however, this was on refractory CD patients, and not strictly a population-based cohort.[24] A retrospective analysis of a large IBD registry in Canada found that hospitalisation and surgery rates dropped at 2 and 3 years, respectively, after initiation of infliximab compared with other drug groups in patients who had double the cost of treatment before the initiation of biological therapy—so suggesting that in these patients, biological therapy was cost effective.[25] The ECCO-Epicom group found more frequent anti-TNF α therapy and IM use in the first year of disease in the Western European patients as compared with those in Eastern Europe, but this was not associated with a significant difference in surgery and hospitalisation rates at 3 years,[26] perhaps due to the follow-up not being long enough to demonstrate effect. It is also possible that biological therapies will not be cost saving, as is the case with many health care interventions, but still remain cost effective through impact on quality of life and patient-reported outcomes. Future follow-up of this cohort will include quality of life and disease activity measures that will help determine the cost-effectiveness.

The other cost driver are the 5-ASAs, accounting for 15% of total cost in CD and 37% of total cost in UC. Similar results have been shown before in a US health cost study in which 5-ASAs contributed 29% of the CD cost.[1] In the EC-IBD cohort, mesalamine was more expensive than the cumulative cost of all other drugs.[6] 5-ASAs such as mesalazine are expensive [A$3 per 1g for oral and A$12 for an enema preparation], and are used widely in IBD, with 56% and 99% of CD and UC patients, respectively, being prescribed this medication by the end of the first year from diagnosis in our cohort.[12] Salazopyrin is not as costly but has frequent side effects and is therefore poorly tolerated by patients.[12] The expense of 5-ASAs brings into question the use of these in CD, given the limited evidence for its efficacy in these patients.[27,28,29]

Health care cost from CD has frequently been shown to be more expensive than UC,[2,8,20,30] and we have confirmed this. In our study, this was due to significantly higher cost from diagnostic tests [specifically radiology] and more specialist visits in the CD population compared with UC [see Table 2].

Diagnostic tests are expensive, accounting for 18% and 27% of total cost in CD and UC respectively, and most of this cost is due to endoscopy [>85%]. However, the majority of these procedures are performed during the diagnostic process, so it is reasonable to assume that further follow-up of this cohort will show a significant reduction of endoscopy cost. A potential cost-saving approach would be to reduce the number of follow-up colonoscopies through the use

Table 4. Clinical variables at diagnosis that predict high cost in ulcerative colitis.

Variable	Count	Mean ± SD	Univariate analysis		Multivariate regression	
			Med [IQR]	p-value	IRR [95% CI]	p-value
Gender				0.988		
Female	57	5456 ± 3623	4738 [3370 - 6320]			
Male	39	7485 ± 9911	4770 [2941 - 6265]			
Age category [years]				0.123		
<25	21	8647 ± 11981	5383 [3683 - 8346]			
25–45	39	5337 ± 5210	4233 [2435 - 5858]			
>45	36	6056 ± 4118	5002 [3350 - 6891]			
Smoking status				0.999		
Never	26	6684 ± 10622	4938 [3327 - 5937]			
Past	17	5928 ± 4296	4062 [3444 - 8606]			
Current	5	5886 ± 4223	4845 [3149 - 6176]			
Steroids at diagnosis				0.074		
No	68	5780 ± 7309	4437 [2703 - 6167]			
Yes	29	7496 ± 6046	5383 [3785 - 9187]			
IM at diagnosis				0.006*		
No	78	5867 ± 7291	4243 [2673 - 6045]			
Yes	19	8039 ± 5259	5894 [5037 - 9187]			
Location				<0.001*		
Proctitis	31	3596 ± 1837	3327 [2079 - 4752]		1.0	
Left-sided	31	6531 ± 5061	4817 [3795 - 6101]		1.53 [1.12–2.09]	0.008
Pancolitis	34	8528 ± 10106	5876 [4253 - 8143]		1.76 [1.25–2.47]	0.001
CRP GRP				0.013*		
< 10	28	5931 ± 4788	4662 [3416 - 6386]		1.0	
> 10	23	10354 ± 12038	5830 [3785 - 13551]		1.79 [1.26–2.53]	0.001

IM, immunomodulators; CRP GRP, C reactive protein < 10 and > 10.

of faecal calprotectin to monitor treatment response and mucosal healing, rather than repeat colonoscopy.[33,34,35,36] In this study, 39 follow-up colonoscopies were performed after the initial diagnostic procedure, accounting for A$52,533. If all of these were replaced with a feacal calprotectin [average cost of A$50 each], a 10% saving on total diagnostic testing would be achieved.

There is a right skew in the distribution of cost among the cohort that is further exacerbated by a small number of high-cost outliers contributing a substantial burden of the cost. This has also been found in previous health cost analyses.[7,9,10,12] These high-cost outliers make up 11% and 10% of patients with CD and UC, respectively, and contribute 54% and 36% of the total cost of the cohort. In CD, the cost in this outlier group was driven by surgery and surgical admissions, whereas in UC it was driven by a combination of prolonged complex medical hospitalisations, surgery, and medications. In-depth analysis of the group showed that the three most expensive patients [two CD and one UC] with surgical costs over A$50 0000 each [including hospitalisation at the time of surgery] had experienced delay to either definitive therapy or to diagnosis, underlining the importance of vigilant and active treatment of unwell patients. These outliers must also be considered in future health care planning, as they do consume much of the cost.

Several clinical variables present at diagnosis predicted high cost in the first year of disease. In CD, these were colonic and ileocolonic location and complex disease behaviour. In UC, these were left-sided and pancolitis location as well as an abnormal CRP of >10. These clinical predictors are similar to those predicting a need for surgery and hospitalisation,[21,31] which are both unfavourable clinical outcomes. Patients displaying such clinical variables at diagnosis should be managed aggressively to prevent complex disease behaviour with associated high cost.

There are several limitations to this study. First, we did not include the cost of outpatient visits to other health care providers due to the difficulty of capturing all such visits. However, given the overall low impact specialist visits had on total cost in this study [3%], it is unlikely that the overall cost from these service providers would be significant. Other studies that have included all outpatient visits have shown a low contribution to total cost [20] This should not be interpreted that the outpatient care provided by health professionals is not important, but simply that they are not costly. In fact, the comparative low cost of frequent contact with IBD health professionals suggests cost efficacy, as these visits have a pivotal role in assessing clinical response and achieving treatment to target goals, with a positive effect on patient compliance.[32] The other limitation in this study is the lack of societal and patient cost assessment [indirect costs] including work productivity and absenteeism, as well as out-of-pocket costs.[33] This is because the cost analysis was from a health care system perspective to optimise cost reliability and external validity to other populations. Also, the cost of medications, excluding biological therapy which is monitored strictly, may have been overestimated as non-compliance was not considered [it was based on the doctor's prescription] but, given the low cost of all other medications [apart from 5-ASAs], this is unlikely to be significant. Finally, the use of biological therapies in the UC group was limited due to prescribing restrictions in Australia till recently.

This is one of the only well-characterised inception cohorts of community-based patients with both clinical outcomes and health cost analysis data since the widespread use of biological therapies. This provides real-life health cost data that can be generalised to other populations and used in cost-efficacy assessment of new therapies and in the future planning of allocation of health care resources. Follow-up was excellent [over 90%] reducing risk of bias. Active surveillance was used to capture all resources use, which has the added benefit of thorough and accurate data collection when compared with database-based searches. The study fulfilled the requirements

of a good cost analysis study, therefore providing a basis for cost-utility and cost-effectiveness analysis.[11,34]

This health cost analysis can be extrapolated to other developed countries, given the similarities in cohort characteristics described earlier. One caveat is the dominance of CD over UC in the Australian population, which is similar to North American countries, New Zealand, and France[35,36] but the opposite to other Western and Eastern European countries.[16,17,37] For this reason, total IBD cost may differ [as CD is more expensive than UC] but per patient costs should remain similar. The majority of cost was public systemdriven in this study, and there is no difference between private and public funding for outpatient resources. Additionally, even if there are differences between health care costs between countries, the cost profile should remain the same given the comparable disease progress and treatment strategies used in these countries.

In conclusion, we have shown that health care cost is more expensive for CD than UC patients. There has been a shift in IBD health cost expenditure in the first year of disease, from inpatient driven resources to outpatient driven resources, primarily due to medications such as biological therapy and 5-ASAs. Future longitudinal follow-up of the cohort will help determine which treatment strategies induce sustained low-cost remission in patients and therefore offset the cost of treatment. Quality of life measures will aid in assessing the cost-effectiveness of current strategies.

Conflict of Interest

The authors have no conflict of interest to declare.

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