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Relationship between disease severity and quality of life and assessment of health care utilization and cost for ulcerative colitis in Australia: A cross-sectional, observational study☆

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Abbreviations: 5-ASAs, 5-aminosalicylic acids; AMA, Australian Medical Association; AQoL-8D, Assessment of Quality of Life–8-dimension; AUD, Australian dollars; CI, confidence interval; DPMQ, Dispensed Price for maximum Quantity; ED, emergency department; EQ-5D-5L, Euro Quality of Life–5-dimension, 5-level; IBD, inflammatory bowel disease; IBDQ, Inflammatory Bowel Disease Questionnaire; IQR, interquartile range; MID, minimally important difference; PBS, Pharmaceutical Benefits Scheme; pMayo, Partial Mayo Score; Q, quartile; QoL, quality of life; SD, standard deviation; UC, ulcerative colitis; WPAI, Work Productivity and Activity Impairment; WPAI–UC, Work Productivity and Activity Impairment Questionnaire–Ulcerative Colitis.

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KEYWORDS
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Abstract

Background & aims: The burden of ulcerative colitis (UC) in relation to disease severity is not well documented. This study quantitatively evaluated the relationship between disease activity and quality of life (QoL), as well as health care utilization, cost, and work-related impairment associated with UC in an Australian population.
Methods: A cross-sectional, noninterventional, observational study was performed in patients with a wide range of disease severity recruited during routine specialist consultations. Evaluations included the Assessment of Quality of Life–8-dimension (AQoL-8D), EuroQol 5-dimension, 5-level (EQ-5D-5L), the disease-specific Inflammatory Bowel Disease Questionnaire (IBDQ), and the Work Productivity and Activity Impairment (WPAI) instrument. The 3-item Partial Mayo Score was used to assess disease severity. Health care resource utilization was assessed by chart review and patient questionnaires.
Results: In 175 patients, mean (SD) AQoL-8D and EQ-5D-5L scores were greater for patients in remission (0.80 [0.19] and 0.81 [0.18], respectively) than for patients with active disease (0.70 [0.20] and 0.72 [0.19], respectively, both Ps < 0.001). IBDQ correlated with both AQoL-8D ($r = 0.73$; $P < 0.0001$) and EQ-5D-5L (0.69; $P < 0.0001$). Mean 3-month UC-related health care cost per patient was AUD $2914 (SD = $3447 [mean for patients in remission = $1970; mild disease = $3736; moderate/severe disease = $4162]). Patients in remission had the least work and activity impairment.
Conclusions: More severe UC disease was associated with poorer QoL. Substantial health care utilization, costs, and work productivity impairments were found in this sample of patients with UC. Moreover, greater disease activity was associated with greater health care costs and impairment in work productivity and daily activities.

1. Introduction

Ulcerative colitis (UC) is a global disease, the incidence and prevalence of which have increased with time throughout different regions around the world.[1] The prevalence of UC in an Australian sample has recently been reported in a preliminary communication to be 136/100,000.[2] Although UC is less common than some other chronic disorders, the impact of UC on quality of life (QoL) is particularly relevant because of the young age of disease onset, the severity of symptoms, and the unpredictability of disease flares.[3–5] Symptoms of active UC include diarrhea, fecal urgency, rectal bleeding, and fatigue, all of which may severely affect a patient's QoL.[4–7] The disease is not "curable" except by surgery, which may result in postoperative complications, continued abnormal bowel function, and no discernible improvement in QoL for some patients.[6]

Although some patients are well controlled with conventional therapies, the clinical course of UC is characterized by unpredictable periods of relapse and remission, and many patients do not maintain a durable remission. All health care systems operate within a limited budget, and the costs of surgery and other medical management options for these patients with more severe disease must be weighed against the benefits provided. In Australia, cost-utility analyses are used by the government to make funding decisions across various therapeutic areas, evaluating the incremental effectiveness of different treatment options (their utility) relative to their incremental cost. For evaluation of treatments for inflammatory bowel diseases, improvements in QoL are the most relevant way to measure utility to assess the "value-for-money" of different treatment options.[8] One approach is to use multiattribute utility, health-related QoL instruments that weight responses by the relative importance, or preference, of each attribute to the patient. A previous study confirmed the validity of a multiattribute utility QoL instrument across a spectrum of disease severity in patients with Crohn's disease.[8] Similar data quantifying the relationship between QoL and disease severity in patients with UC are currently lacking.

Therefore, the primary objective of this study was to assess the quantitative relationship between disease activity

and health-related QoL (utility) in patients with UC in Australia. We also evaluated UC-related health care utilization and costs in this sample, and explored the relationships between disease severity, health care costs, and UC-related work productivity impairment.

2. Materials and methods

2.1. Study design and patients

SOLUTION UC was a cross-sectional, noninterventional, observational study conducted at 13 sites in Australia from July through October 2011. An identical study was conducted in the United Kingdom, and the data will be reported separately. Data were collected by patient questionnaires and clinician assessments at 1 patient visit and by contemporaneous, retrospective chart reviews.

Patients were recruited while attending routine outpatient specialist consultations in either public or private health care settings. They were actively recruited across all levels of disease activity (purposive sampling) so that a range of severity would be represented in the total population. Each site began the study with a target number of patients who could be recruited. During the recruitment period, several sites had their targets increased to make up for sites that had low enrollment. The protocol defined maximum limits on enrollment in each disease severity category. These limits, however, were not reached.

Patients were under routine medical management, and participation in the study did not influence care. Men or women $\geq$18 years of age with diagnosed UC that was confirmed by a gastroenterologist were eligible to participate. Patients were excluded if they had participated in any clinical trials within the previous 12 months, had a colectomy, or had any other condition or life event unrelated to UC that investigators believed could affect health-related QoL during the study.

Independent ethics committees approved this study at each site. Participants provided written informed consent at enrollment.

2.2. Assessments and data collected

Patients completed several questionnaires and underwent a clinician assessment for disease severity using the 3-item Partial Mayo Score (pMayo), the validity of which relative to the full Mayo instrument has been confirmed.[9] pMayo scores categorized patients as either being in remission (score of 0–2) or having active disease (score of $\geq$3). For some analyses, active disease scores were further divided into mild disease (pMayo of 3 or 4) or moderate/severe disease (pMayo of $\geq$5).

Quality of life was measured by the Assessment of Quality of Life–8-dimension (AQoL-8D),[10] the Euro Quality of Life–5-dimension, 5-level (EQ-5D-5L),[11] and the Inflammatory Bowel Disease Questionnaire (IBDQ).[12] Both the AQoL-8D and the EQ-5D-5L are generic, multiattribute utility, preference-based, health-related QoL instruments. The IBDQ measures disease-specific QoL in adults with IBD.

Perceived impact of UC on work and daily activities was measured by the Work Productivity and Activity Impairment Questionnaire–Ulcerative Colitis (WPAI–UC).[13] The questionnaire measures impairment in work productivity, absenteeism, and impairment in ability to perform daily activities other than work (e.g., shopping, housework, child care, exercising, and studying) in the past 7 days.

UC-related health care resource utilization was assessed by chart review. Utilization was assessed for the previous 3 months, with the exception of hospitalization, which was assessed for the previous 12 months. UC-related health care resources that were extracted from chart review were:

- Number and type of consultations with gastroenterologists or other medical specialists for reasons related to UC, excluding the visit at which the patient questionnaire was administered;
- Other visits for investigations related to UC (e.g., blood tests, medical imaging, and pathology tests);
- Emergency department (ED) visits;
- Hospital day admissions (reasons for hospitalization, including treatment versus investigations, were collected and used to calculate costs associated with resource utilization);
- Hospital stays greater than 1 day; and
- Current prescription medicine use related to UC.

Information was also collected from patient questionnaires to capture health care utilization that may have occurred external to the study site that would not be in the medical chart. Patient-reported data for the past year included visits to primary care providers and other allied providers for UC-related care, ED visits (when not admitted and only for hospitals other than at the study site), and current over-the-counter and complementary medicine use.

The data from chart review and patient reports were combined to calculate the total number of ED visits over a 12-month period. To describe a patient's ED visits in the past year, the 3-month value from the chart extraction was multiplied by 4 before being added to the 12-month result from the patient questionnaire.

Total medication use was calculated from the combination of data from chart review and patient reports. Health care resource costs were calculated by using a combination of frequency (from patient questionnaire and chart review, as described above) and price of each type of resource (assigned based on unit costs derived from several Australian health care sources). Hospitalization costs were derived from the Department of Health and Aging Public National Cost Round 13 (2008–09). Costs associated with investigative and diagnostic procedures were calculated using the December 2009 version of the Department of Health and Aging Manual of Resource Items and their Associated Costs. Consultation and investigation fees were derived from the 2011 Australian Medical Association (AMA) list of medical services and fees booklet.[14] Drug prices were calculated as a per-mg cost using the Dispensed Price for Maximum Quantity (DPMQ) and the mg per pack (mg per dose multiplied by total doses per pack) as listed on the Pharmaceutical Benefits Scheme (PBS). The unit cost was inclusive of the government subsidy and patient's contribution.

The total UC-related cost included all cost components identified from patients' medical charts and reported health care resource utilization from patient questionnaires. To ensure that the estimate of total UC-related cost was based on a consistent time horizon, variables collected for 12 months (i.e., hospitalizations from chart review and health resource utilization variables from patient questionnaires) were divided by 4. The resulting 3-month estimated costs for UC-related hospitalizations and currently prescribed medications were added to the other cost components to generate an estimate of the total 3-month UC-related cost.

2.3. Statistical analysis

The sample size was derived using a power of 80%, 5% level of significance, and the ability to detect a 0.10 difference in mean utility score between remission and non-remission patient groups, assuming a 1:1 recruitment ratio of remission and non-remission patients. Statistical analyses were performed using SAS version 9.2 (Cary, NC).

The primary analysis was of the relationships between UC disease severity category (remission or non-remission) and the 2 patient QoL measures (AQoL-8D score and EQ-5D-5L score). These were evaluated with Kruskal–Wallis tests because the data were not normally distributed according to a Shapiro–Wilk statistic. Statistical significance was set at the 5% level. Secondary analyses included the relationships between subcategories of disease severity (remission, mild disease, and moderate/severe disease, defined by pMayo scores of 0–2, 3 or 4, and ≥5, respectively) and mean QoL scores (measured by both multiattribute instruments, AQoL-8D and EQ-5D-5L), which were analyzed with Kruskal–Wallis tests. The relationships between IBDQ and patient QoL (AQoL-8D and EQ-5D-5L) were examined with Spearman's rank correlations. Health care utilization, health care costs, and the impact of UC on work productivity were analyzed descriptively. Descriptive statistics were also used to analyze patient demographics and disease characteristics.

3. Results

Of the 181 patients who were enrolled in the study, 175 were included in the final analysis (Fig. 1). Two patients were excluded because of ineligibility (1 had Crohn's disease and the other was participating in a clinical trial). Four patients were excluded because they did not return the questionnaires. Of the enrolled patients, 74% were seen at a public facility and 26% at a private facility.

Demographic and disease characteristics are shown in Table 1. Patients ranged in age from 18 to 88 years with a mean age of 42 (standard deviation [SD] = 15) years. A total of 53.7% (94/175) of patients were in remission (pMayo 0–2), 16.6% (29/175) had mild disease (pMayo 3–4) and 29.7% (52/175) had moderate/severe disease (pMayo ≥5).

3.1. Relationships between disease activity and QoL measures

Mean AQoL-8D scores were greater for patients in remission (mean = 0.80; SD = 0.19) than for patients who had active

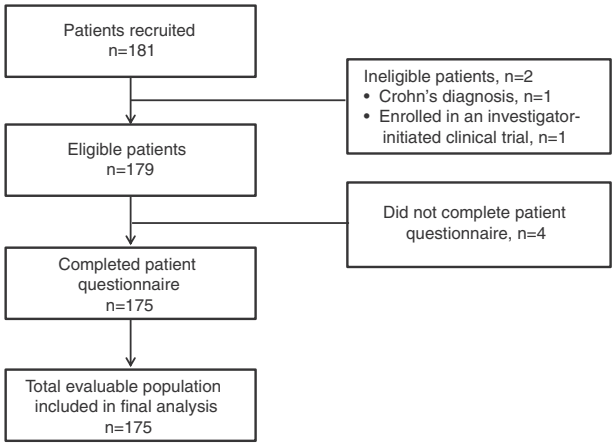

Figure 1 Patient enrollment flow chart.

Table 1 Patient demographic and disease characteristics.

Characteristic	All patients (N = 175)
Age (years), mean (SD)	41.7 (15.1)
Gender, %	
Male	47.4
Female	52.6
Current work status, %	
Full-time	50.3
Part-time	14.9
Unemployed: seeking work	2.3
Unemployed: unable to seek work due to my UC	4.0
Working in home/home duties	8.6
Retired	10.3
Student	2.3
Other	7.4
Years since UC diagnosis, mean (SD)	9.6 (8.8)
pMayo score	
Mean (SD)	2.8 (2.8)
Median	2.0
pMayo disease severity subgroups, n (%)	
Remission (pMayo <3)	94 (53.7)
Mild (pMayo = 3 or 4)	29 (16.6)
Moderate/severe (pMayo ≥5)	52 (29.7)
IBDQ score, mean (SD)	
All patients	149.2 (41.7)
Patients in pMayo remission	172.2 (33.5)
Patients with pMayo mild disease	147.0 (29.0)
Patients with pMayo moderate/severe disease	109.4 (29.1)
Patients reporting each number of acute exacerbations in the past 12 months, %	
All the time	12.6
>6 episodes	9.7
4–6 episodes	12.0
2–3 episodes	29.1
≤1 episodes	36.6

IBDQ, Inflammatory Bowel Disease Questionnaire; pMayo, Partial Mayo Score; SD, standard deviation; UC, ulcerative colitis.
Note: Percentages may not sum to 100% because of rounding error.

disease (mean = 0.70; SD = 0.20), $P = 0.0004$. Of those with active disease, lower scores were seen in patients with mild disease vs moderate/severe disease (means 0.76 [SD = 0.18] vs 0.66 [SD = 0.20], respectively). For comparison, an overall Australian population norm for the AQoL-8D is 0.81 (SD = 0.22; 95% confidence interval: 0.81–0.82).[15]

Mean EQ-5D-5L scores were also greater for patients in remission (n = 94; mean = 0.81; SD = 0.18) than for patients who had active disease (mean = 0.72; SD = 0.19), $P < 0.0001$. Of those with active disease, lower scores were seen in patients with mild disease vs moderate/severe disease (means 0.78 [SD = 0.18] vs 0.68 [SD = 0.19], respectively); Supplementary Table 1 shows a similar pattern for EQ visual analog scale scores. The mean minimally important difference (MID) for the EQ-5D, based on 8 longitudinal studies, is 0.074.[16]

Both of the multiattribute QoL measures were positively correlated with the disease-specific QoL measure, the IBDQ, as demonstrated by Spearman rank correlations of 0.73 ($P < 0.0001$) between AQoL-8D and IBDQ, and of 0.69 ($P < 0.0001$) between EQ-5D-5L and IBDQ.

3.2. Health care utilization

General practitioners were the most commonly visited health care provider for UC-related care in the year prior to the study visit (Fig. 2A). Almost three-quarters of patients visited their general practitioner for UC-related care at least once in the past 12 months, and almost half reported 3 or more such visits.

At least 1 visit to a gastroenterologist in the past 3 months (apart from the recruitment visit) was recorded for 79.5% of patients. Other specialists and nurses were seen much less often (Fig. 2B).

In the past 12 months, 43.5% of the cohort was hospitalized at least once, and 25.8% of patients had at least 1 hospital admission that lasted longer than 1 day. In addition, 16% of patients had UC-related visits to the ED that did not result in hospital admission (Fig. 3). The reasons for the 1-day hospitalizations were reported as follows: 52% were for treatments (infliximab, iron, cyclosporine infusions), 44% were for investigations (colonoscopy, sigmoidoscopy, endoscopy), and 4% were for other clinical evaluations.

A total of 90.9% of patients had a current UC prescription medication. For these patients, the most common prescriptions were for 5-aminosalicylic acids (5-ASAs) (80.0%), immunomodulators (40.6%), corticosteroids (33.1%), and anti-tumor necrosis factor agents (6.9%, reflecting the teaching hospital bias in this cohort because these are not generally subsidized for UC in Australia). Use of over-the-counter medication for UC was reported by 89.7% of patients.

3.3. Health care costs

For the overall cohort (N = 175), the mean 3-month cost per patient for UC-related health care resources was Australian dollars (AUD) $2914 (SD = $3447) (Table 2). As is typical of cost data, the distributions were positively skewed, and median cost was lower, at AUD $1688 (interquartile range [IQR] = $655–$3680).

The breakdown of the various contributors to UC-related health care costs is in Table 2. Across all patients, the

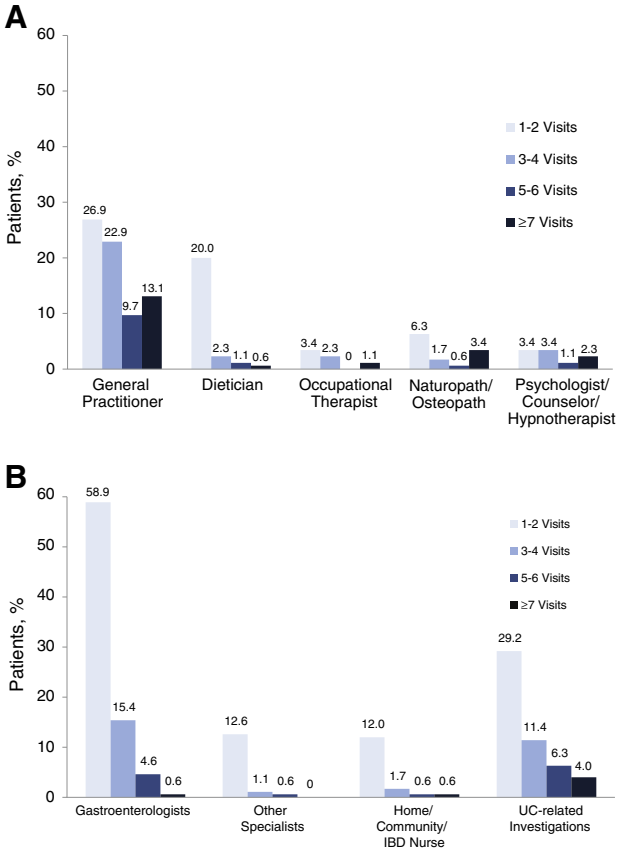

Figure 2 A) Percentage of patients with each frequency of visits to health care providers for UC-related health care in the past 12 months. Data collected from patient survey (N = 175). B) Percentage of patients who reported each frequency of visits to health care providers for UC-related health care in the past 3 months. Data collected from chart review (N = 175). IBD, inflammatory bowel disease; UC, ulcerative colitis.

estimated 3-month mean cost per patient for day admissions was AUD $310 (SD = $576) and for hospitalizations >1 day was AUD $1182 (SD = $2660). Hospitalizations that lasted >1 day accounted for 40.6% of total mean costs. Because

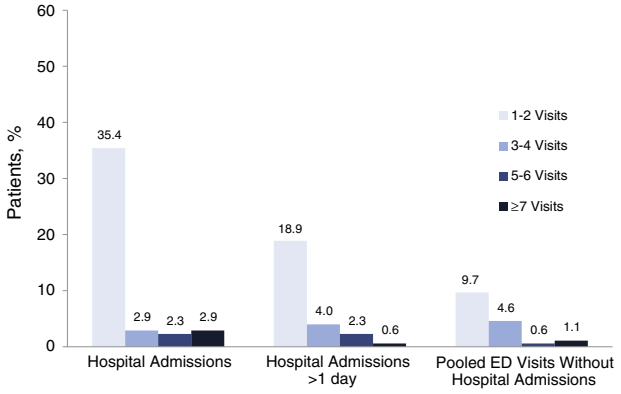

Figure 3 Percentage of patients with each frequency of hospital admissions and emergency department (ED) visits in the past 12 months.

Table 2 Per-patient 3-month costs of UC-related health care resources (N = 175).

Type of health care resource [a]	UC-related health care costs ($AUD)		
	Mean (SD)	95% CI	Median (Q1, Q3)
Total cost of UC-related health care resources	2914 (3447)	2399, 3428	1688 (655, 3680)
Hospital day admissions (estimated from 12-month cost of $1241)	310 (576)	224, 396	0 (0,0)
Hospitalizations >1 day stay (estimated from 12-month cost of $4728)	1182 (2660)	785, 1579	0 (0,0)
Current prescription medications	1166 (1909)	881, 1451	668 (244, 1412)
Gastroenterologists consultations	83 (77)	71, 94	53 (0, 106)
Home/community/IBD nurse visits	21 (69)	11, 32	0 (0,0)
Other specialists consultations	18 (55)	10, 26	0 (0,0)
Other UC-related investigations	124 (265)	85, 164	39 (0, 140)
Emergency/casualty admissions at study site (without admission)	9 (62)	0, 19	0 (0,0)

AUD, Australian dollars; CI, confidence interval; IBD, inflammatory bowel disease; Q, quartile; SD, standard deviation; UC, ulcerative colitis.
[a] UC-related health care resource utilization data were extracted from chart review for the previous 3 months except for hospitalizations, which were calculated from 12-month data.

less than half of patients were ever hospitalized, the mean hospitalization costs did not represent the typical patient; median costs of both categories of hospitalization were $0. Total mean 3-month health care costs for patients who were hospitalized (n = 80) vs not hospitalized (n = 95) were AUD $4284 (SD = $4077) and AUD $1760 (SD = $2253), respectively. Median costs for these groups were AUD $2509 (IQR = $1539–$6748) and AUD $847 (IQR = $274–$1956), respectively.

Prescription medications (mean $1166, median $668) accounted for 40.0% of total mean health care costs. This cost did not include inpatient medications, which were counted as part of hospital costs. The costs associated with all other categories of UC-related care were very small in comparison with the hospitalization and prescription medication costs (Table 2).

Although the study was not designed to analyze the relationship between health care costs and disease severity, a post hoc analysis found much greater costs for patients with greater pMayo disease severity (Table 3). Mean 3-month total health care costs were AUD $1970, $3736, and $4162 for patients in remission, with mild disease, and with moderate/severe disease, respectively (median costs were AUD $843, $1698, and $2399, respectively).

Table 3 Per-patient 3-month costs of total UC-related health care resources by disease severity category (N = 175).

pMayo category	3-Month total UC-related health care costs ($AUD)		
	Mean (SD)	95% CI	Median (Q1, Q3)
Remission	1970 (2635)	1430, 2509	843 (355, 2282)
Mild	3736 (4323)	2092, 5380	1698 (917, 5423)
Moderate/ Severe	4162 (3742)	3120, 5204	2399 (1356, 6231)

AUD, Australian dollars; CI, confidence interval; pMayo, Partial Mayo Score; Q, quartile; SD, standard deviation; UC, ulcerative colitis.

3.4. Work impairment

Patients reported substantial UC-related impairment on all 4 of the work and activity items of the WPAI (Fig. 4A). Overall, the greatest level of impairment (30.9%) was in daily activities other than work. As shown in Fig. 4B, patients in remission and with mild disease had much less impairment than patients with moderate/severe disease for every type of work and activity impairment.

4. Discussion

To ensure that informed decisions are made regarding allocation of health care funding, it is important to have good measures of utility of treatments in relation to their cost. In UC, a chronic illness that substantially disrupts daily life in relapsing and remitting cycles, QoL measures are important for evaluating new treatments. In the present study of UC in an Australian population, QoL was inversely related to disease activity. Patients in remission had significantly higher QoL scores than those with active disease (3–4% higher than patients with mild disease and 13–14% higher than patients with severe disease). Both QoL measures yielded similar results and had high correlations with the well-established IBDQ, lending validity to the usefulness of these QoL measures as utility weights. Overall, the data will be useful in future cost-utility analyses for UC.

Although the economic burden of IBD has been shown to be substantial in studies across several countries,[17–20] the current study is the first to report actual health care utilization for patients with UC in the Australian population. In 2005, the financial cost of IBD in Australia, including both UC and Crohn's disease, was estimated at AUD $496.8 million, with productivity losses accounting for 55% and health system costs accounting for 16% of the total cost.[21] However, these costs were derived from estimates of disease prevalence that were then used to calculate estimated health care utilization and costs based on a national database of health services utilization and expenditures for specific diseases. The current study provides much more direct evidence of the burden of UC in Australia by direct assessment of health

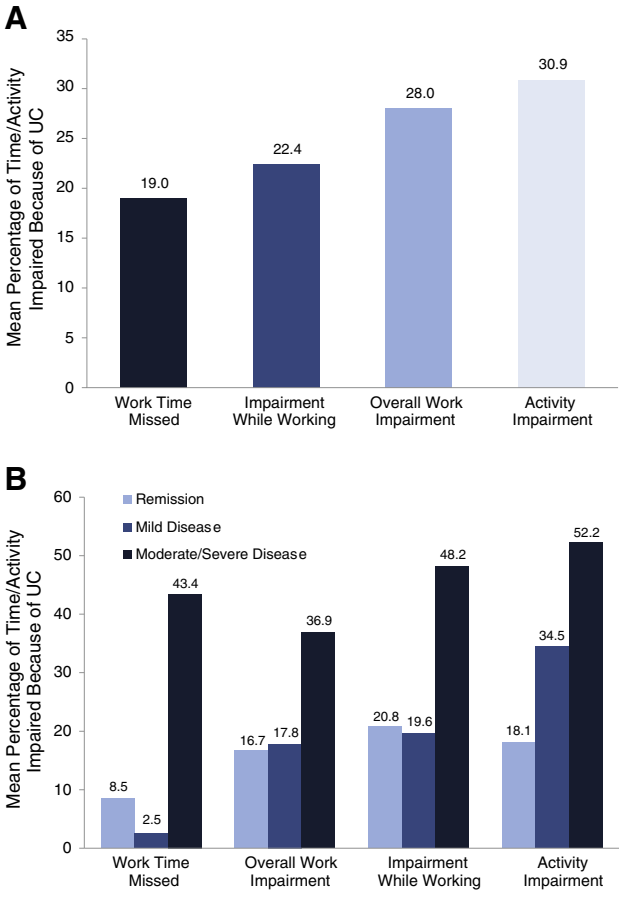

Figure 4 A) Patient-reported percentage of impairment in work productivity and daily activities because of UC (N = 175). B). Patient-reported percentage of impairment in work productivity and daily activities because of UC by pMayo category. pMayo, Partial Mayo Score; UC, ulcerative colitis.

care utilization and work productivity. Patients reported that UC had a substantial negative effect on their productivity at work and in daily non-work activities, and these impairments were larger for patients with active disease.

The average cost of UC-related health care resources in this Australian sample was AUD $2914 over a 3-month period. More than 80% of the cost was contributed by two sources: hospitalizations that lasted longer than 1 day (40.6%) and current prescription medication (40.0%). Although hospitalizations that lasted longer than 1 day accounted for a large proportion of the total cost, only one-quarter of the study sample experienced this type of hospitalization. As might be anticipated for a chronic disease for which maintenance therapy is recommended, 9 out of 10 patients in the study population had at least one current UC-related medication prescription, with the most common drug being 5-ASA.

The deliberate over-sampling of patients with severe disease in the current study makes comparison with other published UC cost studies somewhat problematic. Nevertheless, it does appear that our Australian patient population has annual health care utilization and costs that are comparable with those reported elsewhere.

A recent systematic review of UC costs reported that the annual per-patient direct medical costs of ulcerative colitis in Western countries ranged from US $6217 to US $11 477 in the United States and from €8949 to €10 395 in Europe (2008 currency).[22] However, these studies employ different recruitment and data collection methods from those used in the SOLUTION UC study. In a United Kingdom study of health care utilization that used similar methods and recruitment strategies as our Australian study, per-patient health care costs (mean £1211 [SD = £1588], median £783) were similar to our Australian data.[23] Furthermore, the annual costs reported here are similar to those obtained for Australian patients with any form of Crohn's disease, and in those specifically with fistulizing Crohn's disease (means AUD $8119 and AUD $10 647, respectively, in 2006 costs)[8].

One strength of our study is its generalizability to the Australian health care setting. Patients were recruited across 4 states or territories of Australia, where administration and funding of health care related to hospitalization varies. The proportion of patients treated in public or private settings was similar to that for Australian health care delivery more generally, where 79% and 21%, respectively, are seen at public and private facilities,[24] compared with 74% and 26% of the patients in the present study. All levels of disease severity were represented among patients recruited. Indeed, disease severity in this population may have been more evenly distributed than in other UC samples because efforts were made to actively recruit patients across the range of disease severity to allow for the planned analyses of disease severity and health-related QoL. The high rate of hospitalization in this study suggests a greater level of disease severity in this population than a general population with UC.

Because this is a retrospective, observational study, it is subject to various challenges in data collection that may have led to over- or underestimation of resource utilization. For example, the portion of health care utilization data that were collected through patient reports over the past year may have been affected by poor recall. Resource utilization data collected directly from medical charts were not subject to such problems; however, it is likely that not all costs associated with health care for UC were captured in this study. In addition, some patients may not have utilized certain specialists or home/community/IBD nurses simply because they did not have access to such resources. Because the visit at which the patient questionnaire was administered was not counted as a specialist visit (even though it was a routine care visit), it may also be argued that costs and utilization are underestimated by one visit per enrolled subject. In addition, patients who had colectomy, a high-cost group, were excluded from the study. On the other hand, cost estimates for consultation and test fees may have been lower if Australian Medicare fees had been used for costing rather than AMA fees. Finally, the 3-month period assessed for ED visits via chart review may not have been typical for the patient in terms of disease activity, resulting in potential under- or overestimation of such visits over the course of a year.

In an exploratory post-hoc analysis of the current study, patients with mild and moderate/severe disease had median health care costs that were 2.0- and 2.8-fold higher, respectively, than patients who were in remission at the time of assessment (median costs AUD $843, $1698, and $2399 for remission, mild, and moderate/severe disease,

respectively). This relationship between disease severity and health care utilization is important and warrants further study. Although the results may seem intuitively obvious, the methods used in the current study were not optimal for careful examination of this relationship. UC typically has a relapsing and remitting course, with disease severity fluctuating over time. The optimal study design would have assessed disease severity multiple times during the period for which health care costs were calculated. However, this was a retrospective study, and such a design was not possible. Therefore, although these data are suggestive of a relationship between disease severity and costs, future studies should more carefully address the relationship between disease severity and health care costs over time.

In summary, more severe UC disease was associated with poorer QoL, as measured by the AQoL-8D and the EQ-5D-5L. These data will aid in cost utility analyses for UC treatments, which are vital to effective and efficient use of health care resources. In this Australian population, substantial health care utilization, health care costs, and work productivity impairments were found. Moreover, greater disease activity was associated with greater health care costs and greater impairment in work productivity and daily activities. Future work should further evaluate the relationships among disease severity, health care utilization, and cost.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.crohns.2013.11.017.

Conflict of interest

The authors wish to disclose the following:

- PR Gibson has received consulting fees from Ferring Pharmaceuticals, Abbott, Janssen, Schering-Plough, and Merck; research support from Falk Pharma Gmb, Norgine, Orphan Australia, Fresenius Kabi, Shire, and Abbott; and payments for lectures from Abbott, Merck, Janssen, and Fresenius Kabi.
- C Vaizey has received consulting fees from Movetis and payment for lectures from Movetis, Shire, and Schering Plough.
- C Black and T Fan are employees of Merck.
- R Nicholls and AR Weston are employees of OptumInsight who were contracted by Merck & Co. to develop the study protocol, provide operational support, and perform statistical analyses, in conjunction with the other authors.
- P Bampton has received consulting fees from Ferring Pharmaceuticals, Abbott, Janssen, and Schering Plough; payment for lectures by Abbott and Schering Plough; and research support from Nycomed and Abbott.
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- IC Lawrance has received consulting fees from Ferring Pharmaceuticals, Abbott, AbbVie, Janssen, Schering-Plough, and Merck; research support from Abbott and Ferring Pharmaceuticals; and payments for lectures from Ferring Pharmaceuticals, Abbott, Schering-Plough, and Janssen.
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- FA Macrae is a member of the Janssen Medical Advisory Board and has received research support from Abbott Australasia, Amgen, BMS, Centocor, CSIRO, Genentech, Millennium Pharmaceuticals, Osiris Therapeutics, and Pfizer; consulting fees from CSIRO (Australia), S.L.A Pharma AG, and Endogen Pty Ltd.; and has served as director for the International Society for Gastrointestinal Hereditary Tumors Inc., and for Genetic Health Services Victoria.
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Statement of authorship: PG, CV, TF, AWeston, and RN designed the study; PG, PB, MS, IL, WS, JA, AWalsh, DH, FM, GM, MW, and RL recruited patients and collected data; CB analyzed the data; all authors were responsible for interpreting data, providing feedback on several drafts of the manuscript, and approving the final version of the manuscript for submission.

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