

# Costs in inflammatory bowel diseases

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Prz Gastroenterol 2016; 11 (1): 6–13

DOI: 10.5114/pg.2016.57883

**Key words:** inflammatory bowel disease, medical economics.

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## Abstract

Variables influencing total direct medical costs in inflammatory bowel diseases include country, diagnosis (generally, patients with Crohn's disease generated higher costs compared with patients with ulcerative colitis), and year since diagnosis. In all studies the mean costs were higher than the median costs, which indicates that a relatively small group of the most severely ill patients significantly affect the total cost of treatment of these diseases. A major component of direct medical costs was attributed to hospitalisation, ranging from 49% to 80% of the total. The costs of surgery constituted 40–61% of inpatient costs. Indirect costs in inflammatory bowel diseases, unappreciated and often underestimated (considered by few authors and as a loss of work), are in fact important and may even exceed direct medical costs.

## Introduction

Ulcerative colitis (UC) and Crohn's disease (CD) belonging to the family of inflammatory bowel diseases and are chronic diseases with a remittent, often severe, course. A multicentre study performed in 1991–1993 in 12 European countries estimated the incidence rates of UC and CD to be 10/100,000 inhabitants and 5/100,000 inhabitants yearly [1]. In many countries, Poland included, an increase in incidence has been observed. Etiopathogenesis of inflammatory bowel diseases is multifactorial and unknown. In a portion of patients with UC and CD perianal disease comprising ulcerations, fissures, abscesses, and fistulas may be diagnosed. Mainly young people, in the most economically productive period of their life, are getting the disease [2]. Aetiology and pathogenesis are multifactorial and complex; genetic, environmental, and immunological factors have been implicated. Ulcerative colitis is characterised by diffuse rectal or colorectal mucosal inflammation and presents with diarrhoea (up to several dozen bowel movements per day) and rectal bleeding. Crohn's disease is characterised by transmural inflammation of the gastrointestinal tract, from the mouth to the perianal area. The majority of patients have abdominal pain and diarrhoea, some develop symptoms of malabsorption syndrome.

Exacerbations followed by periods of remission are typical for both diseases. Both may lead to intestinal complications, including colorectal cancer, and may be associated with extraintestinal manifestations. Patients with inflammatory bowel disease (IBD) have been shown to have decreased quality of life. At the current stage of medical knowledge there is no causal treatment of these diseases, and symptomatic and anti-inflammatory treatment is often necessary for the patient's whole lifespan. During flares, immunosuppressive treatment and antibiotics are used, and many patients require hospitalisation. Fifteen–twenty percent of patients with UC and 70–80% patients with CD will be operated on [3–9].

Although IBDs are relatively rare, and given early onset, generally unchanged compared to overall population mortality, their chronic nature, the need for treatment until the end of life, and hospitalisation and operation rates, one may assume that direct medical costs will be essential. Indirect costs associated with sick leave, reduced employment, and early retirement are also a factor.

The aim of the study is to evaluate costs in inflammatory bowel diseases both from the payer's (direct costs) and societal (indirect costs) perspective on the basis of a review of the literature.

## Cost-of-illness study, terms of cost and outcome in pharmacoeconomic analysis, and types of cost

In pharmacoeconomic analysis the following cost types are defined:

a) direct:

- medical (costs of diagnostic procedures, drug acquisition costs, costs of monitoring therapy, costs of adverse events management, hospitalisation costs, medical staff costs, costs of specialist consultations, administrative costs),
- nonmedical (costs of a special diet or transportation to and from a treatment centre);

b) indirect:

- within the health care sector, i.e. medical costs that may arise during life-years that have been saved,
- outside the health care sector, i.e. loss of productivity,
- intangible, i.e. related to pain, worry, and other distress a patient or their family might suffer.

The categories of costs, which will be taken into account in the calculations, should depend on the selected perspective. If a third-party payer's perspective is chosen, indirect costs and the direct costs, which are not covered by the payer's budget will not be considered. If a societal perspective is chosen, both direct and indirect costs should be taken into account. Units of resources used are identified and then measured. Sensitivity analysis is used to indicate which costs have the greatest impact on total and incremental cost and therefore should be measured and evaluated separately (microcosting method), as well as those for which an overall costs method will be sufficient. There are three alternative ways to monetarily assess units of resources used: use of the list of standard unit costs, use of previously published studies in the field of health economics or local fees schedules, and finally direct calculation.

Currently, the most expensive of all health care services is hospitalisation. The assessment of the cost of hospital care can be made on the basis of the average daily cost of hospital care, the average daily cost of hospital care specific for a department, fares for homogeneous groups of patients (Diagnosis-Related Groups – DRGs), or determination of the value of routine and additional services, the latter having the highest accuracy of those listed.

Indirect costs are often an important component of the total costs. It is recommended that indirect costs be estimated with the use of the human capital method (i.e. calculated as the total value of lost earnings from a certain age to retirement age), and that they are presented separately. Intangible costs due to the lack

of appropriate measurement methods are usually not included in the pharmacoeconomic analysis or alternatively rated as a change in the quality of life.

The outcome is the actual effect of the health programme in natural conditions, which is clinically relevant and takes account of the quality of life of the patient. Randomised clinical trials are usually carried out in highly specialised centres, following a specific protocol, being characterised by limited observation time and homogenous population, and providing mainly intermediate results (surrogates), allowing for evaluation of the efficacy of the drug. A better idea of the value of the drug, however, provides assessment of its effectiveness.

The outcome is provided under natural conditions, the study is carried out in a heterogeneous group of patients, allowing us to answer the question of whether the ultimate goal of treatment, which may be reduced mortality, has been achieved. For example, in a group of patients with hypertension the clinically important outcome will be reduced mortality, and not the exact value by which the pressure has been decreased (surrogate). The outcomes are presented in natural (life-years gained, cure rate, time without disease symptoms, probability of events, quality-adjusted life-years (QALYs)) or monetary units.

Cost-of-illness study is not a pharmacoeconomic analysis – focused on the cost of the disease, it does not take into account the clinical outcome of therapy. It provides information about disease-related financial burden, estimates the cost of diseases belonging to one classification group, allows their mutual comparison, highlights the economic relevance of the diseases, helps to identify research priorities, identifies patients who can benefit most from the treatment, identifies the most significant elements of the costs of the disease, explains the current trends in the cost of the disease, or predicts future costs of the disease based on demographic and epidemiological data, taking into account the development of new medical technologies.

There are two models of cost-of-illness studies:

- 1) based on the prevalence – analyses the costs associated with a given disease incurred in a given year,
- 2) based on the incidence – analyses the cost of disease throughout the whole life of the patients whose disease was diagnosed in a given period [10–13].

## Direct medical costs in inflammatory bowel diseases

There are two main methods for the evaluation of direct medical costs associated with IBD. The first uses the actual data on the consumption of specific resources that is obtained by analysis of the documentation of a sample of patients (for example, databases of in-

surers). The second method is based on modelling, i.e. construction of medical decisions algorithms, assuming a specific sequence of medical interventions, and uses data from the literature regarding the percentage of patients with IBD requiring treatment or intervention [14, 15].

The Swedes Blomqvist and Ekborn conducted a cross-sectional observational study where, in order to evaluate the direct medical costs and indirect 1-year costs related to inflammatory bowel diseases, they used data from the national registers and surveys on ambulatory care, hospital admissions, pharmacotherapy, sick pay, and early retirement. Patients benefited primarily from specialised outpatient care provided by medical specialists in internal medicine (in 1994 there were, respectively, 295/100,000 and 32/100,000 consultations in hospital clinics and primary health care facilities). These figures are expressed in terms of the number of inhabitants – bearing in mind the population of Sweden is 8.8 million, the total number of consultations due to inflammatory bowel diseases in Sweden in 1994 was calculated by the authors of the study to be approximately 29,000. The main component of the direct medical costs was the cost of hospitalisation (58%). About 1/9 patients required admission to hospital, and 2% were taken five or more times, which represented 10% of all admissions. Indirect costs accounted for 68% of the total costs; there have been 59/100,000 sick leave episodes (on average 44 days) and 1.6/100,000 early retirements (on average 14 years before reaching retirement age). Patients with CD benefited from health care 2–4 times more in comparison with UC patients, which is in contrast to the prevalence for both diseases (CD: UC = 1 : 2) [16]. Pinchbeck *et al.* isolated 2430 patients with inflammatory bowel diseases from 1,295,360 people, the population of the Canadian province of Alberta in 1981, and using data from medical records and patient questionnaires, they estimated the impact of IBDs on the health care budget of the province. Direct costs included the salaries of physicians and hospitalisation costs. The average cost of care per patient-year was 1495 CAD in the case of CD and 950 CAD in the case of UC, and it was higher in comparison with the value calculated for the average inhabitant of Alberta (207 CAD). Patients with CD spent, on average, 7.43 days in the hospital over the course of a year, and patients with UC spent 5.3 days in hospital, longer than the average resident of Alberta (1.44 days), which in terms of the monetary units was 2905 CAD and 2070 CAD/patient/year. Seventy-five percent of patients with inflammatory bowel diseases were not hospitalised at all during the year preceding the study, which means that the average time of hospitalisation and the costs

related it were generated primarily by the lower part of the patients, in whom a more severe course of the disease had been observed. Similarly, despite the fact that 50% of patients with CD and 60% of patients with UC were not on sick leave due to IBD, the mean period of temporary incapacity to work was 26.1 and 17.5 days/year, respectively, which was higher than the average for the province (6.3 days per year) [17].

Hay and Hay conducted an analysis of a health insurance claims database (Cigna Corporation, USA) reported over a period of 12 months by patients with established diagnosis of CD or UC. The median costs were lower compared to the mean values: 2681 USD (USD 8727)/patient/year for CD and 1463 USD (USD 5863) for UC. Mean values were in this case skewed and largely remained under the influence of outliers. Two percent of the mostly compromised patients with CD accounted for 28.9% of the total cost, and so the top 2% of patients with UC generated 36.2% of the total cost. Nevertheless, the authors give the limitations of the method. The cost of the disease may have been on the high side, since the patients in remission did not report any claim, just those whose expenses did not exceed the specified amount of their own contribution (deductible). Thus, claims databases do not cover a substantial part of the patients. In addition, patients who have private health insurance are not fully representative of the general population of the disease. Less wealthy patients can tolerate a higher level of severity of the disease before they seek medical help [18]. And so in one study on underinsured children with inflammatory bowel diseases in USA, the underinsured had more than 2.5 times the weight loss of the privately insured patients, longer delay in the months before the diagnosis was made (10.3 vs. 2.7 months), and greater abnormalities in the results of the laboratory tests (level of haemoglobin, erythrocyte sedimentation rate, platelet count) [19].

Feagan *et al.* looked into the claims databases of 50 large US employers. A total of 607 patients with a determined diagnosis of CD were stratified into three groups: I – requiring hospitalisation, II – requiring treatment with glucocorticoids at a dose of > 10 mg/day or immunosuppressive drug therapy for longer than 6 months, and III – everyone else. And there were 117 (19%) patients in group I, 31 (5%) patients in group II, and 459 (76%) patients in group III. The average annual cost of treatment was highest in group I and lower in the other groups: USD 37,135, USD 10,033, and USD 6277 in groups I, II, and III, respectively. The costs of hospitalisation accounted for 57% of all direct medical costs. The average cost of treatment was estimated at USD 12,417 patient/year, which, as in the previous

study, was a much higher value compared to the median (USD 3668), reflecting the fact that the relatively small subgroup of patients with CD generates disproportionate expenses. And indeed, approximately 25% of patients accounted for 80% of the total charges [20].

Similarly, in a 6-month cohort study of 307 patients with UC and 172 patients with CD carried out by Bassi *et al.* in the setting of a university hospital in North East England, 10% of patients accounted for 62% and 59%, respectively, of the direct medical costs of these diseases. This study analysed the costs of hospitalisation, surgery, specialist advice, diagnostic tests, and therapies. Clinical and demographic data was abstracted from the medical records of patients, and individual resource use was attributed to each of the cost categories. Item costs were derived from national and local sources. Individual costs ranged from GBP 73 to GBP 33,254/6 months. Average 6-monthly cost was GBP 1256 for UC and GBP 1652 in the case of CD. Only 14% of patients required hospital admissions, but the costs of hospitalisation accounted for 49% of total costs. Expenditure on drugs accounted for less than 1/4 of total costs. The cost of the treatment of 5-ASA surpassed spending on all other drugs combined. Compared with remission, exacerbation of disease was associated with a 2–3 × increase in cost in the case of patients treated on an outpatient basis and 20 × increase in cost in the case of patients requiring hospitalisation. Hospitalisation, disease severity grade and disease extent correlated positively with cost of illness, but the costs were independent of age or sex [21].

An incidence-based cost analysis model was applied by the European Collaborative Study Group of Inflammatory Bowel Disease. Patients were recruited from local communities and included accordingly to the diagnostic Lennard-Jones criteria enabling the diagnosis of either UC or CD. Then, 896 and 425 patients with CD or UC, respectively, were subject to 10-year follow-up. The study involved 13 centres from eight European countries and Israel. Data on the resources use was based on electronic questionnaires (in 9 languages) addressed directly to patients and an electronic questionnaire (in English) addressed to the doctors. Each of the centres was obliged to provide a list of the standard cost of all resources used for the year 2004 (the end of the 10-year follow-up). Average annual expenditure (out-patient care, diagnostics, hospitalisation, surgery, drug treatment) was 1871 EUR per patient with inflammatory bowel disease and was significantly higher in the case of CD (2548 EUR) compared with UC (1524 EUR). Median costs were lower than the mean values, which is the result of a shift to the right of the latter. This was particularly evident after the breakdown of

patients based on the result of Z score = 3, i.e. the cost of exceeding the average cost for the entire cohort of three standard deviations. Patients with a score of > 3 ( $n = 20$ ) generated much higher costs compared to the rest. The most expensive category of resources was hospitalisation; the cost of hospitalisation accounted for, in CD and UC, respectively, 63% and 45% of the total cost. The average annual rate of medical (at the time only conservative treatment was pursued) and surgical hospitalisations (during which time the patient was operated on) was 1.8 and 0.7 days/patient/year in IBD, 1.4 and 0.4 days/patient/year in UC, and 2.5 and 1.4 days/patient/year in CD. Clearly medical hospitalisations lasted longer than surgical ones, and both types of hospitalisation lasted longer in the case of patients with CD. Total costs and costs of hospitalisation were significantly higher in the first year after diagnosis than in subsequent years. This is due to a number of diagnostic tests performed in order to determine the diagnosis, and aggressive treatment aimed at inducing remission in the first year of the disease. It also suggests reducing the average annual cost of illness per patient as far as increasing study time horizon until patient death. The mean percentage expenditure on the top 5% high-cost patients in the whole cohort was 40.4%, and it was significantly higher in the following few years compared with the first year of diagnosis (41.6% vs. 30.0%), which can be explained by the high costs in the first year for all patients and the lack of their decline in the following years in the case of the most costly. To predict which factors at the time of diagnosis or early in the course of the disease will determine the higher consumption of resources in the future, the logistic regression method was performed, and it showed the importance of the following variables: presence in the top 5% of high-cost patients in the first year of follow-up vs. not being present in that year, gender, age, and diagnosis. The average costs of the disease significantly differed between countries. The highest were in Denmark (3705 EUR/patient/year), while the lowest were in Norway (888 EUR/patient/year). This reflects local differences in the management of inflammatory bowel diseases, in particular with regard to the indications for hospital admission and surgical treatment. This speaks for the need to implement certain standards of conduct, which should result in the reduction of costs. Variables significantly affecting the total cost in IBD have been found to be: country, year since diagnosis (the first year: odds ratio (OR) = 3) and diagnosis (CD: OR = 1.5). Expenditure on 5-ASA derivatives exceeded the total expenditure on all other drugs. This was due to the high acquisition cost of 5-ASA, as well as its frequent use (at the time of the 10-year follow-up patients were pre-

scribed derivatives of 5-ASA over an average of 81.3% of the time) [22].

An example of the use of the modelling method in the evaluation of the direct medical costs of CD is the study by Silverstein *et al.* The population analysed included 174 patients residing within Olmsted County (Minnesota, USA). The observation time was 23 years (1970–1993). Data on the management was obtained retrospectively, also having been based on the medical records of patients. As the clinical spectrum of CD is very broad, ranging from asymptomatic cases to severe, including life threatening situations, it was necessary to define a number of health states (remission, surgical remission, mild disease, moderate, or severe disease, with answer to drugs, moderate or severe disease, with a tolerance to drugs, moderate or severe disease, drug-resistant, operation, death) and to determine the percentage of time spent in the various states of the course of the disease. Assuming that the mortality rate in CD does not differ significantly from that in the general population, the authors estimated the expected survival time for a typical patient at 46.4 years (age at diagnosis 28.1 years). Projected clinical course would include: 11.1 years in remission (without medication), 18.9 years in remission obtained as a result of surgery, 12.7 years taking derivatives of 5-ASA, and 3.2 years of taking oral glucocorticoid and immunosuppressive medications. Data on the fees for treatment were obtained from provincial databases. The cost of illness analysis was carried out from the payer's perspective. The costs were presented as the difference when compared with age- and sex-matched healthy persons. The estimated median cost of the disease throughout the patient's life rated at USD 39,906, what per year gives USD 860. Using the 10-year perspective, the median cost of the disease would be USD 3991/patient/year. Of course, mean values, due to the shift to the right towards the most severe patients, were also significantly higher in this study compared with the median values. Surgery and 5-ASA therapy generated 44% and 29% of the direct medical costs, respectively [23].

Another example of modelling is the study by Hay and Hay. The authors applied both methods, cross-sectional data (study cited above) and theoretical modelling, in order to assess the costs in inflammatory bowel diseases. Similarly to Silverstein *et al.*, they defined a certain number of health states (such as initial diagnosis and treatment, prolonged conservative treatment, hospitalisation and surgery, disease complications). The number of patients residing in the individual states was identified on the basis of a literature search. In a theoretical way they rated costs assigned to each state, taking into account the costs of medical visits, diag-

nostic tests, drug therapies, surgery, parenteral nutrition, hospitalisation, and treatment of complications. The average direct medical costs for CD and UC calculated by this method of modelling were, respectively, USD 6561 and USD 1448, and they were different from the costs calculated on the basis of the cross-sectional data. Hospitalisation and surgery accounted for approximately half of these costs. Expenditure related to pharmacotherapy fluctuated within a limit of 10% of the total cost [24].

### Hospitalisation costs in inflammatory bowel diseases

Studies conducted in the United States and other Western countries clearly show that hospitalisation is the largest single component in the direct medical costs of inflammatory bowel diseases. Bernstein *et al.* determined the costs of hospitalisation of 187 patients with CD and 115 patients with UC admitted to a university-affiliated tertiary care hospital in Manitoba in Canada in the years 1994–1995. Medical records were reviewed in order to verify and determine whether the admission to the hospital was due to IBD. A total of 275 hospital admissions were analysed. Resource use was measured. Monetary assessment of resource units was performed by means of direct calculation. Administrative overheads, facility maintenance, and other non-patient care costs were not included, so the results obtained were directly related to patient care. Hospitalisations were classified as medical or surgical. The calculated average cost of medical hospitalisation for CD and UC was CAD 2571 and CAD 2186, respectively. In surgical cases the average cost of hospitalisation was higher and was estimated at CAD 3427 for CD and CAD 4635 for UC. Median values were for CD and UC, respectively, were CAD 1664 and CAD 1262 in medical cases and CAD 2546 and CAD 3341 in surgical cases. The mean duration of hospital stay was longer in surgical patients compared with medical: appropriately 9.6 and 8 days for CD and 13.2 and 7.3 days for UC, respectively. Surgical treatment cases accounted for 50% of all admissions, 58% of all hospital days, and 61% of all the costs. Only 9.5% of patients required a total parenteral nutrition; however, these patients accounted for 27.1% of the total cost of hospitalisation. Patients receiving total parenteral nutrition stayed longer in hospital and they had a greater number of diagnoses compared with patients who did not use this type of treatment, although the cost of one person-day was comparable in both groups. This means that the total parenteral nutrition identifies a group of patients who require costlier care in every aspect of it, and it was not the cost of nutrition per se that explained the high cost

of hospital treatment of patients receiving parenteral nutrition [25].

Cohen *et al.* analysed the cost of 175 hospitalisations of 147 patients treated at the University Hospital in Chicago (Illinois, USA) over a period of 12 months, in which the main diagnosis was CD. Fifty-seven percent of hospitalisations had a primary surgical procedure. The average length of stay in hospital was 8.7 days: respectively, 7.5 days in medical cases (treated conservatively) and 9.6 days in surgical cases. The average total cost of hospitalisation, excluding physician fees, was USD 12,528: respectively, USD 10,020 in medical cases and USD 14,409 in surgical cases. The average total cost of hospitalisation, including physician fees, was USD 35,378: respectively, USD 20,744 in medical cases and USD 46,354 in surgical cases. The distribution of costs across individual categories was as follows: surgery – 39.6%, drug therapy – 18.6%, laboratory tests – 3.8%, radiology – 2.1%, histopathological examination – 0.8%, endoscopy – 0.3%, and other hospital costs – 34.9%. During hospitalisation patients were given: glucocorticoids (87% of hospitalisations), immunosuppressants (23% of hospitalisations), 5-ASA derivatives (14% of hospitalisations), and total parenteral nutrition (27% of hospitalisations). Total parenteral nutrition accounted for 63% of the total pharmacy cost. Thus, the components with which were associated the highest costs within hospitalisation turned out to be surgery and total parenteral nutrition [26].

### Indirect costs in inflammatory bowel diseases

Indirect costs in inflammatory bowel diseases can be an important component of the cost of illness, mainly because it affects young people in their most economically productive period of life. The majority of studies take into account only the cost of lost productivity due to absence from work, underestimating the same total indirect costs. In this case, the loss of productivity is the result of sick leave, early retirement, unemployment, and early mortality.

Hay and Hay estimated indirect costs due to absence from work to be 15–44% of the total cost of inflammatory bowel diseases. Given that in the United States there are from 380,000 to 480,000 people suffering from CD or UC, the indirect costs would increase each year the burden on the budget by USD 0.4–0.8 billion. The above forecasts are based on the assumption that, on average, in a year 5–10% of patients with IBD will be unable to work and receive a pension [24].

Some of the summaries, such as the number of people receiving disability benefits due to IBD, are provided

by studies examining the natural course of the disease: up to 15% of patients with CD 15 years after diagnosis will be unable to work and will receive a pension [27], 92.8% of patients with UC 10 years after diagnosis will retain the full ability to work [28].

In a study carried out in Germany by Sonneberg, patients with inflammatory bowel diseases receiving of a pension were younger when compared with patients receiving it from other causes [29].

In the previously cited study by Blomqvist and Ekborn the average temporary incapacity to work among Swedish patients with inflammatory bowel disease was long, approximately 6 weeks per year, and the disability pension, although rare, was granted on average of 14 years before reaching retirement age. The authors estimated indirect costs in IBD at 68% of the total cost [16].

In the study of Longobardi *et al.* carried out in the United States, 31.5% of patients with inflammatory bowel diseases, who had experienced symptoms during the 12 months preceding the survey, reported being out of the labour force. The authors estimated that an inflammatory bowel disease that caused the occurrence of symptoms within 12 months, increased the probability of nonparticipation in the professional life of 12.3%. Based on this, the indirect costs attributable to IBD in the United States were calculated for USD 3.6 billion/year or USD 5228/patient/year. It is worth noting that inflammatory bowel disease causing no symptoms in the preceding 12 months did not affect participation in working life. So, according to the authors, not the same diagnosis of the disease, but rather the presence or absence of symptoms implies loss of productivity due to absence from work [30].

The same authors, using the same methodology, conducted a similar study in Canadian conditions and obtained the following results: 28.9% of patients with inflammatory bowel diseases did not participate in working life (compared to 18.5% of respondents without IBD), inflammatory bowel disease increased the probability of nonparticipation in the professional life of 2.9%, and indirect costs attributable to IBD were approximately CAD 104.2 million/year or CAD 868/patient/year [31].

Spanish authors Juan *et al.*, in assessing the cost of CD, used questionnaires addressed to gastroenterologists to obtain clinical data as well as telephone surveys to obtain data on the consumption of drugs. Indirect costs, taking account of nonparticipation in working life, temporary inability to work, and loss of leisure time, were estimated at 4704 EUR/patient/year. Direct medical costs in this study were 2104 EUR/patient/year [32].

The results of the above cited research have been summarised in Table I.

**Table I.** Costs in inflammatory bowel diseases\*

Study	Country	Year of calculation	Study population	Direct medical costs	Hospitalisation costs/direct medical costs in %	Hospitalisation costs/ (surgery costs/ hospitalisation costs in %)	Indirect costs
Blomqvist [16]	Sweden	1994	IBD	3895 USD	58		1390 USD
Pinchbeck [17]	Canada	1985	CD UC	4400 CAD 3020 CAD	66		
Hay [18]	USA	1990	CD UC	8727 USD 5863 USD	55.8		
Feagan [20]	USA	1994	CD	12417 USD	57		
Bassi [21]	UK	2000	CD UC	3304 GBP 2512 GBP**	49		598 GBP 452 GBP**
Odes [22]	8 European countries, Israel	2004	CD UC	2548 EUR 1525 EUR	63		
Silverstein [23]	USA	1995	CD	2944/ 12504 USD***			
Hay [24]	USA	1990	CD UC	6561 USD 1448 USD	80		1174–5225 USD****
Bernstein [25]	Canada	1995	CD  UC			2571 CAD (61) 2186 CAD (61)	
Cohen [26]	USA	1997	CD			35378 USD (39.6)	
Longobardi [30]	USA	1998	IBD				5228 USD
Longobardi [31]	Canada	1999	IBD				868 CAD
Juan [32]	Spain	1997	CD	2104 EUR	69		4704 EUR

\*Costs are given per patient/year, \*\*Multiplied by 2, \*\*\*Patient's lifetime perspective/ perspective of 10 years of follow-up, \*\*\*\*15–44% of total costs.

## Conflict of interest

The authors declare no conflict of interest.

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**Received:** 1.03.2015

**Accepted:** 21.09.2015