


Original research

Direct costs of inflammatory bowel diseases in a Finnish tertiary-level clinic

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Received 13 March 2020
Revised 31 May 2020
Accepted 4 June 2020
Published Online First 26 June 2020

ABSTRACT

Background Inflammatory bowel disease (IBD), Crohn's disease (CD) and ulcerative colitis (UC) are chronic diseases associated with a high and continuous economic burden. The introduction of biologics has changed the distribution of costs over the past two decades, and there are no recent studies on direct costs in Finland. This study aimed to estimate the direct healthcare costs of these diseases in a tertiary-level clinic.

Methods The data were collected during a 1-year period of patients with IBD visiting Turku University Hospital. Patients were included if they lived in the hospital district area and were over 18 years old. This comprised an IBD group of 2208 patients, including 794 cases of CD and 1414 cases of UC. A sex-matched and age-matched control group was collected for comparison. Direct costs were collected during a 1-year study period from the hospital records.

Results Total direct costs per patient with IBD in a tertiary-level clinic were €4223 annually. IBD-generated direct costs were estimated to total €3981 per patient annually. Patients with IBD who were given infliximab had €9157 higher direct healthcare costs per patient annually than patients with IBD with no infliximab medication. Direct healthcare costs generated in a tertiary-level gastroenterological clinic averaged €1652 per patient with IBD annually. On average, patients with CD had €1111 higher direct healthcare costs annually than patients with UC.

Conclusions The direct healthcare costs of IBD were significant, almost 17-fold higher compared with a control group. Patients with IBD administered with biologics had significantly higher costs. Patients with CD had higher annual infliximab costs than patients with UC.

INTRODUCTION

Inflammatory bowel disease (IBD) consists of two major disorders: Crohn's disease (CD) and ulcerative colitis (UC). They are

Key messages**What is already known on this topic**

- ▶ Treating inflammatory bowel disease (IBD) causes substantial expenses.
- ▶ Introduction of biological treatment has changed the cost distribution from surgery to medication.

What this study adds

- ▶ The mean incremental cost of IBD compared to the general population was €3981 per patient-year.
- ▶ Biological treatment was administered to a small patient population.

characterised by chronic relapsing intestinal inflammation. At the moment, no curative treatment is available. Patients may thus need life-long treatment and surveillance, or even surgery.¹⁻⁴

The peak age of onset for IBD is 16–35, although the disease can be diagnosed at any age.³⁻⁵ The incidence and prevalence have been estimated to continuously rise, especially in southern Europe, Asia and in most low-income countries.^{3 6 7} The prevalence of CD was 124/100 000 and UC 291/100 000 in a Finnish study from 2010. The annual incidence per 100 000 was 19.6 in UC and 9.4 in CD.⁸

As chronic diseases, CD and UC are associated with a high and continuous economic burden.^{3 4} Due to early onset, IBD may affect work productivity and thus cause productivity losses resulting from work disability and sick leave.⁹⁻¹¹ With biologics introduced to the treatment, a more cost-effective approach to improve quality of life is needed.^{9 12}

There are previous European studies on the overall costs of IBD.⁹⁻¹³ However, during some of these studies, biologics were not used in treating IBD on a regular



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To cite: Rankala R, Kosonen J, Mattila K, *et al.* *Frontline Gastroenterology* 2021;**12**:385–389.

basis.^{9–11} In a recent Dutch study (2014), the direct healthcare costs for UC and CD were €2380 and €6501, respectively.¹² These were annual costs extrapolated from a 3-month period.¹² Total costs were stable over 2 years of follow-up, with annual total costs of €3600 in UC and €7835 in CD.¹⁴ Bassi *et al* conducted a UK single-centre study regarding IBD cost of illness, in which the extrapolated annual mean costs per patient were €2806 for UC and €3692 for CD.⁹

Up to the early 2000s, hospitalisation and surgery accounted for the vast majority of overall costs of the treatment of patients with IBD.^{3 13 15} However, the development of antitumour necrosis factor alfa (TNF α) therapy has shifted the cost distribution from hospitalisation and surgery to medication without increasing the overall treatment costs.^{12 14 15} Meanwhile, the total IBD costs have remained stable.^{3 12 14}

The aim of this study was to estimate the direct costs of IBD in a tertiary-level clinic, comparing the costs between CD and UC and to estimate the costs of biologics.

To our knowledge, there are no previous studies on the direct healthcare costs of IBD in Finland.

PATIENTS AND METHODS

Patient selection

Data collection was carried out in the Turku University Hospital (TUH), and it was done retrospectively from the hospital records. Patients with IBD were identified using the ICD-10 (International Classification of Diseases V.10) system, K50 for CD and K51 for CU. We excluded patients younger than 18 years, as well as patients who had died or who lived outside the hospital district area covering a population of 470 000 people. The study group was identified during a 1-year period, 1 September 2015–31 August 2016. This produced a sample of 2208 patients.

A control group was collected from patients who had visited the emergency department to represent the general population. The control group, with the same exclusion criteria, was matched to the IBD group by age and sex. This produced a control group of 2208 patients. The control group was chosen over a 2-year period (1 September 2014–31 August 2016). The costs considered were within the same time frame as the study group.

Costs

All cost estimates were based on the cost level of 2016. Hospital charges were recorded based on diagnosis-related group codes. All costs were recorded, whether generated by the initial visit or subsequent treatment. They were registered and represented the true costs used to charge the final payer. The user only pays a nominal fee for a visit to the emergency care or, if admitted to the hospital, a predetermined sum per day spent hospitalised. This cost is not affected by the medical treatment received, and all patients pay the

same amount. The costs analysed for both groups were collected from a 1-year period, between 1 September 2015 and 31 August 2016. All direct healthcare costs generated were considered as accurately as possible with the help of hospital records and accounting.

Costs can be divided into direct and non-direct costs. This study focused only on direct costs, which can be further divided into medical and non-medical costs. Direct healthcare costs were collected from all the hospitals' clinics. Medical costs considered consisted of the following: outpatient and emergency department visits, imaging (X-rays, CT, MRI and positron emission tomography–CT), diagnostic procedures (such as gastroscopy, colonoscopy and capsule endoscopy) and therapy, medical equipment, blood and other laboratory work, pathology, medical staff, consultations, day hospital visits and hospitalisation. Medications given during hospitalisation or outpatient visits (including infliximab or corresponding biosimilar) were accounted for in this study, whereas medications patients used at home were not. Non-medical costs, such as transport services for outpatient visits to the hospital, are not paid by the university hospital, so they generate no costs to the hospital. All costs are estimates that the hospital has provided, and they include staff services, equipment and property costs.

Statistics

The statistical evaluation of the data was based on the χ^2 test for proportions and on the Student t-test for means. The Pearson coefficients of correlation were used to examine the degree of relationship between two continuous variables. Linear regression models were used to study how different background factors affected the variation in treatment cost estimates. The distribution of overall treatment costs was skewed so the data were converted to close to a normal distribution by natural logarithmic transformation and used as a dependent variable.

RESULTS

Patient characteristics

The IBD group of 2208 patients comprised 794 patients with CD and 1414 with UC. The patients with UC were predominantly men, whereas patients with CD had a higher percentage of women. The IBD and the control group had similar patient characteristics (table 1). Sex and age did not affect the total costs in patients with IBD, UC or CD in a linear regression model of the total costs (R^2 0.001–0.002) ($p=0.4$).

Infliximab

Infliximab (Remicade and Inflectra included) treatment was given to 197 patients with IBD, and the mean annual cost of this treatment was €6880 per patient receiving biologics. This group consisted of 84 patients with CD (10% of patients with CD) and 113 patients with UC (8% of patients with UC). Infliximab treatment

Table 1 Mean age, sex distribution and total annual healthcare costs (€) of the IBD and control group in a tertiary-level clinic

	IBD (n=2208)	Control (n=2208)
Male	1139 (51.6%)	1139 (51.6%)
Age (years)	48.4	47.3
Total costs	4223 (7570)	243* (635)

SD presented in parentheses.

*P<0.001, otherwise no statistically significant difference.

IBD, inflammatory bowel disease.

accounted for 14.7% of the mean total annual direct healthcare costs of the study sample. The mean difference in total annual healthcare costs between patients with IBD with infliximab treatment and patients with IBD with no infliximab treatment was €9157. Patients with infliximab treatment had statistically significantly higher costs in outpatient visits, surgery and laboratory work (p<0.001) (table 2). On average, patients with CD had higher annual costs (€861) of infliximab than patients with UC (€474) (p<0.002).

IBD versus control

The difference in mean total annual direct healthcare costs generated in a tertiary-level clinic between a patient with IBD and a control patient was €3981 (p < 0.001) (table 1).

CD versus UC

The mean total annual direct cost of treatment of patients with CD in a tertiary-level clinic was significantly higher than that of patients with UC. The mean annual direct healthcare cost difference was €1111 (table 3). Patients with CD had statistically significantly higher costs in the gastroenterology department. When gastroenterology was viewed more closely, a statistically significant difference was seen in

Table 2 Mean annual total healthcare costs (€) of patients with IBD with infliximab (Remicade and Inflectra included) treatment compared with patients with IBD without infliximab treatment in a tertiary-level clinic

	Infliximab (n=197)	No infliximab (n=2011)
Infliximab	6880 (4999)	0
Outpatient clinic	1795 (1034)	942* (1241)
Hospitalisation	629 (1837)	509 (2083)
Surgery	1378 (3754)	478* (2169)
Emergency department	335 (826)	325 (1223)
Imaging	186 (308)	172 (315)
Laboratory	694 (472)	301* (760)
Diagnostic procedures	803 (1893)	782 (1955)
Total costs	12563 (7366)	3406* (7082)

SD presented in parentheses.

*P<0.001, otherwise no statistically significant difference.

IBD, inflammatory bowel disease.

Table 3 Mean age, sex distribution and total annual healthcare costs (€) of the patients with CD and UC

	CD (n=794)	UC (n=1414)
Male	371 (46.7%)	768 (54.3%)
Age	48.3	48.5
Gastroenterology	2118 (3577)	1390* (2678)
Internal medicine	364 (2306)	279 (1435)
Surgery	537 (2002)	570 (2550)
Emergency department	394 (1582)	287 (902)
Other clinics	1522 (6047)	1298 (3972)
Total costs	4934 (9391)	3823† (6291)

SD presented in parentheses.

*P<0.001.

†P<0.05, otherwise no statistically significant difference.

CD, Crohn's disease; UC, ulcerative colitis.

imaging, outpatient clinic, medication and procedures performed to patients (table 4).

DISCUSSION

Inflammatory bowel diseases (IBDs) create significant overall treatment costs to a tertiary-level clinic and eventually to taxpayers. In the present study, the costs generated by the study group were significantly higher, almost 17-fold, compared with the costs generated by the age-matched and sex-matched control group during the same period. In this study, all costs are based on true costs collected from registers used to charge the final payer. These include all direct costs from the study period regarding patients both recently diagnosed with IBD and those diagnosed earlier. The present study findings of total costs in both UC and CD are consistent with the data from earlier studies, although there are major differences between these studies.^{9–11 13 16 17} The costs considered vary between studies, and costs have been extrapolated to an annual

Table 4 Annual mean costs (€) of treating patients with CD and UC in the gastroenterological clinic

	CD (n=794)	UC (n=1414)
Intensive care unit	5 (109)	11 (191)
Hospitalisation	86 (508)	80 (485)
Imaging	88 (167)	35* (129)
PET imaging	0	1 (42)
Outpatient clinic	537 (517)	402* (479)
Medication	750 (2658)	394† (1736)
Pathology	26 (50)	27 (42)
Diagnostic procedures	195 (387)	156‡ (255)
Total gastroenterological clinic costs	2118 (3577)	1390* (2678)

SD presented in parentheses.

*P<0.001.

†P<0.01.

‡P<0.05, otherwise no statistically significant difference.

CD, Crohn's disease; PET, positron emission tomography; UC, ulcerative colitis.

level.^{9 11 12 18} In this study, the local diagnosis-related group costs were used to estimate the costs of treatment. As DRGs are not a constant figure, the costs are not directly comparable to other countries. Thus, the comparison with the present study and direct costs involved may be problematic. Furthermore, the introduction of biologics in treatment may have affected the treatment modalities and shifted the cost profile from surgery and hospitalisation towards anti-TNF α treatment without increasing the total costs.^{12 14 15}

One of the major strengths of this study was the age-matched and sex-matched control group for reference of costs. The control group consisted of people who visited the emergency ward, received medical care and were possibly admitted to the hospital. It was estimated that this would produce a feasible representation of the general population in the healthcare setting. Conditions of patients visiting tertiary-level clinics range from mild to debilitating. Indeed, the control group patient material likely exhibits more severe health problems compared with the average healthcare user. Thus, the present study costs of IBD are likely not exaggerated. Recent studies on the direct costs of IBD have not used control groups for a more accurate estimation of costs.

According to a study conducted by van der Valk *et al*, anti-TNF α therapy has shifted the cost distribution from hospitalisation and surgery to medication without increasing the overall treatment costs.¹² In a 2-year follow-up study, total costs remained stable, but the proportion of costs of biologics increased.¹⁴ This was also underlined by Feagan *et al*.¹⁹ Surgery and hospitalisation rates seem to have decreased in the postbiological era.⁵ Early treatment of CD with immunomodulators and biologics was associated with reduced risk of developing bowel stenosis in a Swiss study; however, anti-TNF treatment was not associated with reduced risk of undergoing new intestinal surgery.²⁰ The Social Insurance Institution of Finland reimburses biologics administered subcutaneously at home by patients themselves. This may result in a decreased use of biologics administered in the hospital and during outpatient visits, explaining the lower costs generated by biologics in this study. Outpatient visits are included in the costs of a tertiary-level clinic but do not include medication administered by the patients themselves at home in Finland. In the present study, however, patients with IBD treated with infliximab had higher outpatient visits, surgery and laboratory costs. In Finland, anti-TNF α therapy is mainly used on severe, relapsing forms of CD and UC when other treatment methods have been insufficient. Thus, it is probable that patients with IBD receiving infliximab treatment have a more severe illness than the average patient with IBD. This might also affect the costs generated by biologics in this study and may lead to higher costs in a tertiary-level clinic.

Biologic treatments administered to patients with IBD in TUH also include vedolizumab. However, due to a flaw in the hospital medical records at the time of the data collection, vedolizumab was included in the same category as infliximab in the hospital records. The anti-TNF α agent Remicade was changed to Inflectra by TUH in spring 2016. The reason for this change was that the cost of Remicade was almost threefold compared with Inflectra. This might have led to exaggerated infliximab treatment costs in this study. Later, Remicade has again become cheaper than Inflectra. Lower costs of biologics may result in lower biological treatment costs to a tertiary-level clinic per treated patient with IBD in the future.

In this study, the mean direct costs per patient was €4934 for CD and €3823 for UC annually. The present study included all the direct costs generated by patients with IBD in a tertiary-level clinic. Our study methods did not allow analysis of total medication costs, as only information of the costs of medications given during hospitalisation or outpatient visits was available.

Manninen *et al* reported that both the incidence and prevalence of IBDs in Finland have been on the rise.⁸ Their data are consistent with other studies, although the incidence of IBD varies greatly worldwide. However, if biologics alongside with biosimilars continue to modify the treatment modalities of IBD, this might further decrease hospitalisation and surgery rates. Thus, direct costs of IBD may decrease in the future.

IBD seems to generate more direct annual healthcare costs in a Finnish tertiary-level clinic when compared with other chronic diseases, such as type 1 diabetes or psoriasis.^{21 22} In the present study, the annual average direct healthcare costs of treating patients with IBD in a tertiary-level clinic totalled €4223. Direct healthcare costs generated in a tertiary-level gastroenterological clinic averaged €1652 per patient with IBD annually. Honkasalo *et al* estimated that the average annual cost of treating patients with type 1 diabetes in a tertiary-level clinic was €344 (fixed in 2016 price level).²¹ They included the costs of visits and treatment periods related to type 1 diabetes or diabetes-related diseases. Non-diabetes-related treatment episodes were excluded.²¹ Mustonen *et al* estimated the average annual healthcare cost of treating patients with psoriasis or psoriatic arthritis to be €1550 (fixed in 2016 price level). These costs included all medications, medical equipment, time used by doctors and other medical staff members, as well as other expenses of the tertiary-level clinic, such as outpatient visits, phototherapy or hospitalisation.²² The significant difference in annual costs can partly be explained by procedures, such as gastroscopy and colonoscopy, and partly by surgeries, which are still a significant part of IBD diagnosis, control and treatment. Furthermore, treating patients with IBD with costly biological agents makes a notable difference in annual costs, especially between

IBD and diabetes patients. On average, patients with IBD might have more hospitalisation periods than psoriatics or diabetics because of the relapses in IBD.

This study aimed to estimate the direct costs of patients with IBD compared with a control group in a tertiary-level clinic; thus, no indirect costs were considered. The impact of biological treatment was also of interest. An aspect this study did not consider was self-administered medications at home, which patients themselves bought from the pharmacy. This might have led to decreased estimates of the total direct costs. Both healthcare and social security systems vary between countries, which naturally affects how the total direct costs of IBD are distributed. Hospitalisation still generates big expenditure for some patients, and if this could be reduced, it would result in lower healthcare costs. Also, infliximab accounted for almost 15% of the total costs of IBD, while only a small proportion of patients are treated with it. Patients with IBD generate a significant economic burden to a tertiary-level hospital. Thus, it is essential to assess the costs and cost-effectiveness of treatments. Gradually, when biosimilars become more available, they could reduce the total costs of biologics administered. IBD is still generally a costly disease, but with better treatment options, costs could be reduced. However, to fully determine how these factors are affected by IBD, further studies are needed.

CONCLUSIONS

This study estimated the IBD-generated annual direct healthcare costs to a tertiary-level clinic to total €3981. A patient with IBD treated with infliximab had €9157 higher annual direct healthcare costs than a patient with IBD with no infliximab. The direct healthcare costs generated by CD were higher than those generated by UC.

Contributors Conception and design: RR, JK, AM, KM, MV and RT. Acquisition of data: RR, JK, AM and KM. Analysis and interpretation of data: RR, JK, AM and KM. Drafting of the manuscript: RR and JK. Critical revision: AM, KM, MV and RT. Final approval: RR, JK, AM, KM, MV and RT.

Funding This study was supported by grants from the Hospital District of Southwest Finland.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study was approved by the ethics committee of the Hospital District of Southwest Finland.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. All data relevant to the study are included in the article or uploaded as supplementary information. Data relevant to the study are included in the article. Raw data may be obtained from Kliininen tietopalvelu, atp(at)tyks.fi.

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