



# The Burden of Ulcerative Colitis and Crohn's Disease in Spain

XAVIER CORTÉS<sup>1</sup>, LUIS FERNÁNDEZ-SALAZAR<sup>2</sup>, LUCÍA MÁRQUEZ<sup>3</sup>, LAURA RAMOS<sup>4</sup>,  
CRISTINA DÍAZ RUBIO<sup>5</sup>, LAURA PLANELLAS<sup>6</sup>, DAVID GASCHÉ<sup>6</sup>

<sup>1</sup>Gastroenterology Section, Internal Medicine of Hospital Universitario de Sagunto. University CEU Cardenal Herrera, Department of Medicine, Valencia, <sup>2</sup>Department of Gastroenterology of Hospital Clínico Universitario de Valladolid, <sup>3</sup>Department of Gastroenterology of Hospital del Mar de Barcelona, <sup>4</sup>Department of Gastroenterology of Hospital Universitario de Canarias, <sup>5</sup>Market Access Department, AbbVie, <sup>6</sup>HEOR-RWE, IMS Health.

## Abstract

**Objectives:** Crohn's Disease and Ulcerative Colitis are associated to relevant social and individual impact in Spain due to its chronic nature and its high prevalence. Furthermore, not only healthcare costs due to both diseases are considerable, but also the indirect costs of the illnesses. The aim of the study was to estimate the burden of the illnesses in terms of costs from the Spanish Health System perspective according to the clinical practice in Spain in 2013. Secondary objectives included the estimation of the indirect costs (societal perspective) and comorbidities' costs.

**Methods:** Prevalence methodology was used. Structure of the model and inputs were obtained from a literature review, gaps were covered using data collected from 4 gastroenterologists. Healthcare costs included were those related to drugs, treatment monitoring, medical visits, tests, adverse events management and hospitalizations. Indirect costs were calculated based on the loss of productivity. Costs are presented in 2013 euros.

**Results:** The cost of Ulcerative Colitis and Crohn's Disease for the Health System in 2013 was estimated in 259.199.430 euros and 370.404.727 euros, respectively. From the societal perspective, cost for Ulcerative Colitis was 306.669.407 euros and 400.304.757 euros for Crohn's Disease. Yearly cost per an average patient with Ulcerative Colitis and Crohn's Disease were respectively 5.059 euros and 9.091 euros from the health system perspective, and 5.986 euros and 9.825 euros per patient per year when including indirect costs.

**Conclusions:** The study informs about the significant burden of Crohn's Disease and Ulcerative Colitis for both the Spanish Health System and the society.

**Key words:** burden of illness, ulcerative colitis, crohn's disease, public expenditure.

## INTRODUCCIÓN

Inflammatory bowel disease (IBD) encompasses a group of idiopathic chronic inflammatory conditions, with a considerable impact in Spain at a social and individual level due to its high prevalence (87,45 for Crohn's Disease [CD] and 109,96 for ulcerative colitis [UC] per 100,000 individuals)<sup>1</sup> and incidence (7,6 for CD and 4,8 for UC per 100.000 individuals)<sup>2</sup>. The disease also has a great impact in Spain because of its chronic nature and because the average age at onset is during the second and third decades of a patient's life (the most economically productive)<sup>3</sup>, with one third of cases occurring before 20 years of age.

At present, the main goals of disease management in patients with IBD are to induce and maintain clinical remission and to prevent and reduce the number and duration of relapses in order to decrease its impact on patient quality of life. The recommended treatment protocols in Spain include aminosalicilates, corticosteroids, antibiotics, immunomodulators, and biologic agents as drug therapy, along with nutritional care and surgical treatment<sup>4</sup>.

There are substantial direct healthcare costs associated with the management of patients with IBD, including not only biologic therapies but also medical visits, hospitalizations, and surgeries<sup>5,6</sup>. In addition, the important physical and psychological impact of CD and UC may result in poor quality of life for patients<sup>7</sup>. In turn, this decreases work productivity, which increases the indirect costs of the illness.

## Autor para correspondencia

Cristina Díaz Rubio  
Market Access Department. AbbVie  
Av. Burgos, 91. 28950. Madrid  
Tfno: 914 831 899  
cristina.diazrubioechaide@abbvie.com



Burden of illness studies provide information about the economic impact and risk factors of a disease for a given society, government, or individual. Additionally, because healthcare systems tackle an increasing demand of resources and rising costs in medical care, studies on burden of illness offers the potential to assess the efficiency of resource allocation when managing a specific disease<sup>8</sup>.

To the best of our knowledge, there are currently no published studies that estimate the total direct and indirect costs of IBD in Spain conducted after the popularization of biologics and considering all the available treatments and utilization rates using economic modeling. However, some studies have evaluated the cost of CD<sup>9,10</sup> or UC<sup>11</sup> in subpopulations of patients in Spain.

The aim of this study was to estimate the burden of CD and UC in terms of costs from the Spanish health system (SHS) perspective, according to routine clinical practice in Spain in 2013. The study also aimed to estimate the cost of both pathologies from the societal perspective, as well as the costs of the related comorbidities associated with both diseases.

## MATERIALS AND METHODS

Using prevalence methodology, a study on the burden of CD and UC in 2013 was conducted. In the SHS perspective, only direct costs were evaluated. To achieve the secondary aims of the study, the analysis was performed from a societal point of view; therefore, indirect costs (loss of productivity) and patient copayments were also included. Finally, an additional analysis was conducted to assess the cost of comorbidities related to CD and UC.

The structure of the economic model and the utilization of health resources were determined using a review of the existing literature through PubMed using specific search terms: ("Crohn's disease or CD" or "ulcerative colitis or UC" or "inflammatory bowel disease or IBD") and ("epidemiology" or "natural history" or "burden of disease" or "burden of illness" or "cost" or "health resources" or "management" or "treatment pattern". Information missing in

the literature was completed using data collected through specific questionnaires sent to 4 gastroenterologists. The results were validated with a Delphi panel conducted with these experts.

### Target population

The target population was estimated on the basis of the total Spanish population in 2013 (46.591.857 inhabitants) taken from the Spanish Statistics Institute (INE, *Instituto Nacional de Estadística*), and the prevalence of CD (87,45 per 100.000 inhabitants) and UC (109,96 per 100.000 inhabitants) in Spain<sup>1</sup>. Under the premise that patients with different disease severities would use health resources in a different manner, both target populations were divided into "mild," "moderate," and "severe" according to the severity of the disease. As agreed with the clinical experts, this classification was based on the type of treatment received, considering that patients classified as mild were treated with 5-aminosalicylic acids (5-ASA), patients receiving immunomodulators (azathioprine or methotrexate) were considered moderate, and finally, severe patients were those treated with biological agents, cyclosporine, or tacrolimus. In addition, patients who had disease flare-ups and required a change in therapeutic strategy were also taken into account.

### Health resources associated with disease management

The utilization of health resources by patients with mild, moderate, and severe CD and UC was obtained using a literature review and the opinion of the expert panel. The following resources were included as direct costs: pharmacologic treatments, monitoring of treatments, adverse event management, medical visits, diagnostic tests, and hospitalizations.

Several types of drugs were considered in the analysis of both diseases: salicylates (mesalazine and sulfasalazine), corticosteroids, immunomodulators, biologic agents (adalimumab, infliximab, and certolizumab) and others (antibiotics, apheresis, calcium, vitamin D, heparin, and parenteral nutrition). The use of every type of drug (active substance) according to patient profile was obtained from the Delphi panel,

and the market shares of the different actives substances within each type of drug were obtained from the IMS Health sell out and hospital panels (IMS Health, 2013, unpublished data). The daily dose was established according to the corresponding summary of product characteristics (SmPC). Finally, drug costs were estimated using ex-factory retail or laboratory prices taken from a Spanish database<sup>12</sup>, including deductions according to the Royal Decrees 8/2010 and 9/2011 and the copayment in case of retail drugs<sup>13</sup>. The inclusion of the retail price or the laboratory price depended on whether the drug was a prescription drug or for hospital use only.

The costs to monitor pharmacologic treatments were estimated through medical visits and tests required for monitorization. The number of medical visits and tests were estimated using expert experience; unitary costs were collected from the eSalud database<sup>14</sup>.

Estimation of the management of adverse events was limited to severe adverse events only, assuming that these events would be the most resource-consuming. The percentage of patients with severe adverse events and the cost of these events were obtained from the literature. Otherwise, costs were obtained from the corresponding diagnostic-related groups (DRGs)<sup>14</sup>.

Diagnosis and disease follow-up costs were also considered in the model. The number of medical visits and tests used in daily clinical practice were collected from the expert panel. The number of hospitalizations and surgeries in patients with UC and CD over a 1-year period was also gathered. The costs associated with medical visits and tests used for the diagnosis of the disease were only considered for incidental patients. The unitary cost of each health resource was obtained from the eSalud database<sup>14</sup>.

Indirect costs were calculated based on the loss of productivity through absenteeism from work and presenteeism while at work. Moreover, the productivity loss associated with individuals caring for an inpatient was also taken into account. The costs associated with sick leaves and loss of work hours was determined

using the human capital method, applying the average Spanish wage in 2013<sup>15</sup>, as well as taking into account the average occupancy in the same period according to data published by INE<sup>16</sup>. This cost was divided between the fraction borne by the company and the Ministry of Employment and Social Services according to the in-force legislation in 2013<sup>17</sup>.

Regarding comorbidities, the relevant comorbidities associated with UC and CD, the prevalence among patients, and the costs per year of comorbidities were obtained from the literature when available. Otherwise, the cost was estimated through the corresponding DRG.

Costs prior to 2013 were adjusted to 2013 values using the Consumer Price Index (CPI); therefore, all costs are reported in 2013 euros. The analysis was conducted using Microsoft Excel<sup>®</sup> 2007 (Microsoft Corporation, Bellevue, Washington, USA).

## RESULTS

### Epidemiology results

In 2013, our study estimated that there were 2.236 new cases of UC in Spain. Overall, 51.232 patients had UC; 4.912 patients (10 per cent) had severe disease, 22.612 patients (44 per cent) had moderate disease, and 23.708 patients (46 per cent) had mild disease. The estimated population of patients with CD for 2013 was 40.745 patients, with an incidence of 3.522 new cases. Among patients with CD, 5.774 (14 per cent) had severe disease, 17.798 (44 per cent) had moderate disease, and 17.173 (42 per cent) had mild disease. Hence, in total, 91.977 patients were affected by IBD in 2013, representing 0,2 per cent of the population in Spain. Table 1 shows the epidemiologic results for UC and CD.

Comorbidities associated with UC or CD were generally similar: celiac disease (5 per cent for UC<sup>10</sup> and 14,5 per cent for CD<sup>10</sup>), extraintestinal manifestations (42 per cent for UC and 35 per cent for CD<sup>7</sup>), depression (38 per cent for UC and 33 per cent for CD<sup>7</sup>), and colorectal cancer (0,2 per cent for UC<sup>18</sup> and 1,2 per cent for CD<sup>19</sup>).

The overall cost of IBD for the SHS in 2013 was estimated to be 629.604.157 euros: 259.199.430 euros for patients with UC and 370.404.727



euros for patients with CD. The cost for the SHS per an average patient with UC was 5.059 euros per year. An average patient with severe, moderate, or mild UC cost 9.402 euros, 6.497 euros, and 2.746 euros every year, respectively. The cost of pharmacologic treatment (1.894 euros per patient per year) represented 37 per cent of the overall cost per patient, followed by costs associated with medical visits and tests used for disease follow-up (1.042 euros per patient per year), which represented 21 per cent of the total cost per patient (Table 2). Biologic agents accounted for 66 per cent of the cost of pharmacologic treatment.

**TABLE 1**

PREVALENCE AND INCIDENCE OF ULCERATIVE COLITIS AND CROHN'S DISEASE			
	Ulcerative colitis	Crohn's disease	Reference
Prevalence (number of cases per 100.000 inhabitants)	109,96	87,45	Saro Gismera 2003
<b>Prevalence (number of patients)</b>	<b>51.232</b>	<b>40.745</b>	
Incidence (number of cases per 100,000 inhabitants)	4,8	7,6	Cueto Torreblanca 2014
<b>Incidence (number of patients)</b>	<b>2.236</b>	<b>3.522</b>	

**TABLE 2**

DIRECT ANNUAL COSTS ASSOCIATED WITH UC FROM THE POINT OF VIEW OF THE SHS

Type of cost	Total cost of UC	Severe UC	Moderate UC	Mild UC
<b>Cost per average patient per year</b>				
Sum	5.059€	9.402€	6.497€	2.746€
Pharmacologic treatment	1.894€	2.874€	2.801€	825€
Treatment monitorization	613€	1.110€	742€	387€
Management of adverse events	194€	417€	276€	69€
Medical visits and tests	1.042€	1.675€	1.220€	740€
Hospitalizations	740€	890€	724€	724€
Surgery	578€	2.436€	735€	0€
<b>Total patient population cost per year</b>				
Sum	259.199.430€	46.177.452€	146.905.744€	65.096.434€
Pharmacologic treatment	97.009.552€	14.115.481€	63.324.443€	19.569.628€
Treatment monitorization	31.402.408€	5.452.363€	16.771.417€	9.178.629€
Management of adverse events	9.930.027€	2.046.621€	6.238.354€	1.645.052€
Medical visits and tests	53.361.647€	8.227.293€	27.587.927€	17.546.427€
Hospitalizations	37.891.934€	4.372.164€	16.363.071€	17.156.698€
Surgery	29.603.861€	11.963.529€	16.620.532€	0€

UC: Ulcerative colitis.

An average patient with CD is estimated to cost 9.091 euros to the SHS per year. In particular, an average patient with severe, moderate, or mild CD costs 18.223 euros, 11.036 euros, and 3.145 euros per year, respectively.

The main drivers of the overall cost were, in order of importance, the cost associated with pharmacologic treatments (30 per cent), inpatient visits (25 per cent), surgeries (20 per cent), medical visits and tests for follow-up (13 per cent), monitoring treatments (9 per cent), and managing adverse events (3 per cent; Table 3). Biologic agents accounted for 91 per cent of the cost of pharmacologic treatments.

It was estimated that treatment of flare-ups in patients with UC cost 46.316.670 euros per year and represented 20 per cent of the overall cost of UC. For patients with CD, treatment of flare-ups cost 30.195.975 euros, 10 per cent of the total cost of the disease.

**Results from the societal point of view**

Overall, 706.974.164 euros is spent by society each year on IBD, 306.669.407 euros for UC and 400.304.757 euros for CD. The loss of productivity is estimated to be 38.131.469 euros for patients with UC and 26.019.637 euros for patients with CD, 12 per cent and 6 per cent of the overall expenditure for these patients, respectively.

**TABLE 3**

DIRECT ANNUAL COSTS ASSOCIATED WITH CD FROM THE POINT OF VIEW OF THE SHS

Type of cost	Total cost of CD	Severe CD	Moderate CD	Mild CD
<b>Cost per average patient per year</b>				
Sum	9.091€	18.223€	11.036€	3.145€
Pharmacologic treatment	2.694€	6.113€	3.551€	656€
Treatment monitorization	783€	1.468€	1.033€	294€
Management of adverse events	305€	547€	437€	87€
Medical visits and tests	1.204€	1.917€	1.445€	715€
Hospitalizations	2.312€	4.092€	2.621€	1.393€
Surgery	1.792€	4.086€	1.950€	0€
<b>Total patient population cost per year</b>				
Sum	370.404.727€	105.221.858€	196.428.928€	54.014.235€
Pharmacologic treatment	109.757.493€	35.296.237€	63.202.508€	11.258.748€
Treatment monitorization	31.909.823€	8.475.654€	18.380.015€	5.054.154€
Management of adverse events	12.427.909€	3.159.168€	7.774.547€	1.494.194€
Medical visits and tests	49.063.829€	11.070.335€	25.714.927€	12.278.567€
Hospitalizations	94.211.390€	23.625.905€	46.656.912€	23.928.573€
Surgery	73.034.284€	23.594.557€	34.700.020€	0€

CD: Crohn's disease.



The mean cost per patient per year due to loss of productivity was 744 euros and 639 euros for UC and CD, respectively. The overall average cost of a patient with UC from the societal perspective is 5.986 euros per year, while the average cost associated to a patient with CD is 9.825 euros per year. The cost per patient and overall cost of UC and CD by type of cost are shown in Table 4 and Table 5.

#### Analysis of comorbidities

If the costs of associated comorbidities were taken into account to calculate the overall burden of IBD, the estimated annual cost of UC and CD would be increased by 104.911.238 euros and 94.059.448 euros, respectively.

#### DISCUSSION

The results of the study indicate that patients with IBD cost annually 629.600.000 euros to the SHS, representing 1 per cent of the overall public sanitary expense in Spain in 2013<sup>20</sup>. Approximately 59 per cent of the burden of IBD can be attributed to treatment of patients with CD; the remainder corresponds to patients with UC. Furthermore, when the societal point of view is considered, the cost of IBD increases up to 706.900.000 euros, 77.000.000 euros more than the cost estimated from the SHS perspective. This difference can be attributed to the indirect costs of the illness (83 per cent) and the copayment borne by patients. The copayment system<sup>13</sup> was introduced in Spain in 2012 as a consumption dissuasive measure and affects only retail drugs.

Pharmacologic treatments are the major contributor to the overall cost of both UC and CD. In the present study, biologic agents appear to be the main drivers of overall pharmacologic costs, mainly in patients with CD. This is in concordance with current clinical practice. Many patients receive pharmacologic treatments to control disease, and during the past decade, biologic agents have had a considerable impact in the treatment of UC and CD<sup>21</sup>. Although the cost of biologics is higher than the cost of other therapies, these agents have been successful in inducing and elongating periods of remission<sup>3</sup>. A recent Spanish study

found that the introduction of biologic agents in the management of patients with CD significantly reduced costs attributed to doctor visits, emergency visits, blood tests, diagnostic examinations, and non-biologic drug treatments<sup>22</sup>. Our results indicate that the cost of hospitalizations decreased compared with the results observed in studies conducted before the introduction of biologic agents<sup>11, 23, 24</sup>. This might be explained by the improved disease control with the introduction of biologic agents. In addition, as expected with chronic diseases, the cost of patient follow-up in UC and CD is also important; this is reflected in the study, as medical visits and tests represent 21 per cent and 13 per cent of the total cost in UC and CD, respectively.

Looking at the cost per patient analysis, from the point of view of the SHS, an average patient with CD costs 4.033 euros more each year than an average patient with UC. This additional cost is attributable to hospitalizations, surgeries, and drug use in the treatment of patients with CD. The study showed that the cost related to hospitalizations is higher in patients with CD than in UC, reflecting the fact that patients with CD, both in remission or with disease flare-up, require more hospitalizations and surgical interventions than patients with UC. The difference in the pharmacologic cost between CD and UC is mainly attributable to the higher prescription of biologic agents in CD. As expected, there is a relationship between the severity of the disease and the increase in health resource consumption.

Concerning the societal perspective, it was observed that the annual cost per patient attributable to loss of productivity was higher in patients with UC (744 euros) than CD (639 euros). This might be explained by the duration of flare-ups and clinical characteristics. Thus, absenteeism is more relevant in patients with a diagnosis of UC than in those with CD.

Furthermore, if comorbidities are taken into account when assessing the burden of UC and CD, apart from worsening disease, the overall cost of each illness would increase by 105.000.000 euros and 94.000.000 euros, respectively.

TABLE 4

ANNUAL COST OF UC BY TYPE OF COST AND FROM SOCIETAL POINT OF VIEW

Type of cost	Total cost of UC	Severe UC	Moderate UC	Mild UC
<b>Cost per average patient per year</b>				
<b>Sum</b>	<b>5.986€</b>	<b>10.680€</b>	<b>7.278€</b>	<b>3.738€</b>
<b>Total direct costs</b>	<b>5.242€</b>	<b>9.528€</b>	<b>6.652€</b>	<b>2.965€</b>
Pharmacologic treatment	2.076€	3.001€	2.956€	1.045€
Treatment monitorization	613€	1,110€	742€	387€
Management of adverse events	194€	417€	276€	69€
Medical visits and tests	1.042€	1.675€	1.220€	740€
Hospitalizations	740€	890€	724€	724€
Surgery	578€	2.436€	735€	0€
<b>Total cost due to loss of productivity</b>	<b>744€</b>	<b>1.152€</b>	<b>626€</b>	<b>773€</b>
Borne by the company	344€	551€	338€	307€
Borne by the Ministry of Employment and Social Security	400€	601€	288€	466€
<b>Total patient population cost per year</b>				
<b>Sum</b>	<b>306.669.407€</b>	<b>52.457.428€</b>	<b>164.574.018€</b>	<b>88.618.161€</b>
<b>Total direct costs</b>	<b>268.537.937€</b>	<b>46.800.707€</b>	<b>150.416.941€</b>	<b>70.300.490€</b>
Pharmacologic treatment	106.348.059€	14.738.735€	66.835.640€	24.773.684€
Treatment monitorization	31.402.408€	5.452.363€	16.771.417€	9.178.629€
Management of adverse events	9.930.027€	2.046.621€	6.238.354€	1.645.052€
Medical visits and tests	53.361.647€	8.227.293€	27.587.927€	17.546.427€
Hospitalizations	37.891.934€	4.372.164€	16.363.071€	17.156.698€
Surgery	29.603.861€	11.963.529€	16.620.532€	0€
<b>Total cost due to loss of productivity</b>	<b>38.131.469€</b>	<b>5.656.721€</b>	<b>14.157.077€</b>	<b>18.317.671€</b>
Borne by the company	17.631.822€	2.705.559€	7.644.482€	7.281.781€
Borne by the Ministry of Employment and Social Security	20.499.647€	2.951.162€	6.512.596€	11.035.889€

UC: Ulcerative colitis.

**TABLE 5**

ANNUAL COST OF CD BY TYPE OF COST AND FROM SOCIETAL POINT OF VIEW

Type of cost	Total cost of CD	Severe CD	Moderate CD	Mild CD
<b>Cost per average patient per year</b>				
<b>Sum</b>	<b>9.825€</b>	<b>19.144€</b>	<b>11.679€</b>	<b>3.910€</b>
<b>Total direct costs</b>	<b>9.186€</b>	<b>18.293€</b>	<b>11.130€</b>	<b>3.251€</b>
Pharmacologic treatment	2.789€	6.182€	3.645€	761€
Treatment monitorization	783€	1.468€	1.033€	294€
Management of adverse events	305€	547€	437€	87€
Medical visits and tests	1.204€	1.917€	1.445€	715€
Hospitalizations	2.312€	4.092€	2.621€	1.393€
Surgery	1.792€	4.086€	1.950€	0€
<b>Total cost due to loss of productivity</b>	<b>639€</b>	<b>852€</b>	<b>549€</b>	<b>660€</b>
Borne by the company	347€	513€	358€	280€
Borne by the Ministry of Employment and Social Security	292€	339€	191€	380€
<b>Total patient population cost per year</b>				
<b>Sum</b>	<b>400.304.757€</b>	<b>110.540.235€</b>	<b>207.872.889€</b>	<b>67.151.926€</b>
<b>Total direct costs</b>	<b>374.285.120€</b>	<b>105.622.142€</b>	<b>198.099.157€</b>	<b>55.824.114€</b>
Pharmacologic treatment	113.637.886€	35.696.521€	64.872.737€	13.068.627€
Treatment monitorization	31.909.823€	8.475.654€	18.380.015€	5.054.154€
Management of adverse events	12.427.909€	3.159.168€	7.774.547€	1.494.194€
Medical visits and tests	49.063.829€	11.070.335€	25.714.927€	12.278.567€
Hospitalizations	94.211.390€	23.625.905€	46.656.912€	23.928.573€
Surgery	73.034.284€	23.594.557€	34.700.020€	0€
<b>Total cost due to loss of productivity</b>	<b>26.019.637€</b>	<b>4.918.093€</b>	<b>9.773.732€</b>	<b>11.327.812€</b>
Borne by the company	14.137.065€	2.962.221€	6.366.604€	4.808.240€
Borne by the Ministry of Employment and Social Security	11.882.573€	1.955.872€	3.407.128€	6.519.572€

CD: Crohn's disease.

As is often the case, there are some limitations to the present analysis. The costs of comorbidities were obtained from different studies; consequently, there are different methodologies and types of costs considered among the studies. Moreover, given the difficulty in distinguishing between the cost of the treatment and the cost of the comorbidity, there is a risk of overestimation of costs.

There are other studies that have calculated the cost of subpopulations of patients with UC or CD in Spain. A study that evaluated the cost of an average patient with a moderate to severe UC flare-up<sup>9</sup> reported that the annual cost per patient was 6.959 euros in 2004 (8.622 euros if updated to 2013 euros according to the Spanish CPI); in our study, a patient with a flare-up would cost 9.577 euros, almost 1.000 euros more. This divergence could be attributed to the difference in the prescriptions trend over the past decade, mainly due to the inclusion of the biologic agents in the management of patients with UC. Two CD studies were also identified<sup>10, 11</sup>; both included only patients in a hospital setting, and the study conducted in 2003 was performed before the introduction of biologic agents. Consequently, our results in terms of cost per patient per year are similar to Casellas et al. (7.722 euros in 2007 [8.803 euros when updated to 2013 euros]) and disparate from the results obtained by Juan et al. (2.104 euros in 1997 [3.011 euros when updated to 2013 euros]). Furthermore, Juan et al found that the items with a higher contribution to the overall cost were hospitalizations (52 per cent); in the present study, hospitalizations accounted for 25 per cent of the overall cost (45 per cent if surgeries are considered). These data suggest that the increased prescription of biologic drugs may provide better disease control, which in turn may reduce the number of hospitalizations and surgeries, resulting in improvements in quality of life.

The indirect cost estimated by Juan et al (2.218 euros in 1997 [3.174 euros when updated to 2013 euros]) was higher than in our study (639 euros), likely because that study included more types of indirect costs, such as the inclusion of transportation costs to the hospital or the cost of extra home care.

There are some limitations to this study that are mainly attributable to the methodology used to obtain some of the model inputs, as the utilization of health resources is based on the opinion of 4 gastroenterologists (with the exception of the management of severe adverse events). Nevertheless, no appropriate data in the literature were identified to populate the model. In the societal perspective, the estimation of loss of productivity was based on the time spent in a flare-up (absenteeism) and the work hours lost to attend a medical visit (presenteeism). As this data was also obtained from the opinion of the clinical experts, it should be interpreted with caution.

All in all, this study highlights the burden of IBD for the SHS and for society as a whole. Although the prevalence of CD is lower than the prevalence of UC, the cost of CD is higher because of the increase in hospitalizations and surgeries. Further studies are needed to better capture the indirect costs associated to IBD.

**Funding:**

This work was supported by AbbVie. IMS Health received funding from AbbVie for the development of the model.

**Competing interests:**

Lucía Márquez has received consulting fees from AbbVie and speaker fees from MSD. Laura Ramos and Xavi Cortes don't have conflict of interest. Luis Fernandez-Salazar has been granted by AbbVie and has received travel accommodation for meetings by Ferring, MSD and Pfizer. Cristina is a salaried employee of AbbVie Spain. Laura Planellas and David Gasche are salaried employees of IMS Health.



# REFERENCIAS

1. Saro Gismera C, Riestra Menéndez S, Milla Crespo A, Sánchez Fernández R, Lacort Fernández M, Argüelles Fernández G et al. Incidence and prevalence of inflammatory bowel disease. Asturian study in 5 areas (EIICEA). Spain. *An Med Interna*. 2003; 20(1): 3-9.
2. I. Cueto Torreblanca, M. Gutierrez Bedmar, R. Camargo Camero, J.V. Martos Vandusen1\*, R.J. Andrade Bellido, G. Alcaín Martínez. Incidence study and follow-up of a cohort of patients with inflammatory bowel disease (IBD) in Málaga (Spain). Poster P613, presented at the European Crohn's and Colitis Organisation Congress. 2014.
3. Saro Gismera C, Riestra Menéndez S, Sánchez Fernández R, Milla Crespo A, Lacort Fernández M, Argüelles Fernández G et al. Epidemiology in inflammatory bowel disease in five areas of Asturias. Spain. *An Med Interna*. 2003 May;20(5):232-8.
4. Medina Benítez E, Fuentes Lugo D, Suárez Cortina L, Prieto Bozano G. . Enfermedad inflamatoria intestinal. In: *Protocolos diagnóstico-terapéuticos de Gastroenterología, Hepatología y Nutrición Pediátrica*, Eds. Sociedad española de gastroenterología, hepatología y nutrición pediátrica (EGHNP) y Asociación Española de Pediatría (AEP). 2010: 151-160.
5. Bernstein CN, Papineau N, Zajackowski J, Rawsthorne P, Okrusko G, Blanchard JF. Direct hospital costs for patients with inflammatory bowel disease in a Canadian tertiary care university hospital. *Am J Gastroenterol* 2000; 95: 677-683.
6. Bodger K. Cost of illness of Crohn's disease. *Pharmacoeconomics* 2002; 20: 639-652.
7. López Blanco B, Moreno-Jiménez B, Devesa Múgica JM, Rodríguez Muñoz A. Relationship between socio-demographic and clinical variables, and health-related quality of life in patients with inflammatory bowel disease. *Rev Esp Enferm Dig* 2005; 97: 887-898.
8. Honeycutt A, Hoerger T, Hardee A, Brown A, Smith K. Assessment of the state of the art for measuring burden of illness. 2011. <https://aspe.hhs.gov/sites/default/files/pdf/76381/index.pdf>. Accessed February 11, 2014.
9. Panés J, Guilera M, Ginard D, Hinojosa J, González-Carro P, González-Lara V et al. Treatment cost of ulcerative colitis. Is apheresis with Adacolumn® cost-effective? *Dig Liver Dis* 2007; 39: 617-625.
10. Casellas F, Panés J, García-Sánchez V, D. Ginard, F. Gomollón, J. Hinojosa et al. Costes médicos directos de la enfermedad de Crohn en España. *Pharmacoeconomics* 2010; 7: 38-46.
11. Juan J, Estiarte R, Colomé E, Artés M, Jiménez FJ, Alonso J. . Burden of illness of Crohn's disease in Spain. *Dig Liver Dis* 2003; 35: 853-861.
12. Consejo General de Colegios Oficiales de Farmacéuticos. Bot Plus 2.0. <https://botplusweb.portal-farma.com/botplus.aspx>. Accessed July 22, 2014
13. Boletín Oficial del Estado. Real Decreto-ley 16/2012, de 20 de abril, de medidas urgentes para garantizar la sostenibilidad del Sistema Nacional de Salud y mejorar la calidad y seguridad de sus prestaciones. BOE núm 98 de 24/04/2012.
14. Oblikue Consulting. eSalud – Información económica del sector sanitario. 2014. <http://www.oblikue.com/bddcostes>. Accessed July 22, 2014.
15. Instituto Nacional de Estadística (INE). 2013a. Notas de prensa: Encuesta trimestral de Coste Laboral (ETCL). Tercer trimestre de 2013. [www.ine.es](http://www.ine.es). Accessed July 22, 2014
16. Instituto Nacional de Estadística (INE). Encuesta de Población Activa. Tasas de actividad, paro y empleo, por sexo y distintos grupos de edad, por comunidad autónoma. 2013b. ([www.ine.es](http://www.ine.es)). Accessed July 22, 2014
17. Lázaro P, Parody E, García-Vicuña R, Gabriele G, Jover JÁ, Sevilla J. Cost of temporary work disability due to musculoskeletal diseases in Spain. *Reumatol Clin*. 2014; 10(2): 109-112.
18. Rutter MD, Saunders BP, Wilkinson KH, Rumbles S, Schofield G, Kamm MA, et al.. Thirty-year analysis of a colonoscopic surveillance program for neoplasia in ulcerative colitis. *Gastroenterology*. 2006 Apr;130(4):1030-8.
19. Freeman HJ. Colorectal cancer risk in Crohn's disease. *World J Gastroenterol*. 2008 Mar 28;14(12):1810-1.
20. Ministerio de Sanidad, Servicios Sociales e Igualdad (MSSSI). Estadística de gasto sanitario público 2012: Principales resultados. 2014. <http://www.msssi.gob.es>. Accessed February 11, 2014.
21. Armuzzi A, Pugliese D, Nardone OM, Guidi L. Management of difficult-to-treat patients with ulcerative colitis: focus on adalimumab. IBD Unit, Complesso Integrato Columbus, Catholic University, Rome, Italy. *Drug Des Devel Ther* 2013; 7: 289-296.
22. Saro C, Ceballos D, Muñoz F, De la Coba C, Aguilar MD, Lázaro P. . Resources utilization and costs the year before and after starting treatment with adalimumab in Crohn's disease patients. *Inflamm Bowel Dis*. 2015; 21(7): 1631-1640.
23. Blomqvist P, Ekbohm A. Inflammatory bowel diseases: health care and costs in Sweden in 1994. *Scan J Gastroenterol* 1997; 32: 1134-1139.
24. Hay JW, Hay AR. Inflammatory bowel disease: Costs-of-illness. *J Clin Gastroenterol* 1992; 14: 309-317.