

ORIGINAL RESEARCH

Epidemiology and hospital resources use in the treatment of ulcerative colitis at gastroenterology units in Spain (EPICURE study)

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Abstract

Background and aim: Nationwide epidemiological data on ulcerative colitis (UC) in Spain are lacking. The primary objective was to assess the epidemiology of UC at hospital gastroenterology units and the use of hospital resources (characteristics and facilities) for the management of UC in Spain.

Methods: A retrospective, multicenter, epidemiological, cross-sectional study (EPICURE study) analyzed data from hospital registries and records from UC patients admitted and treated in 2011 at a representative selection of Spanish sites. The prevalence of UC in gastroenterology units was calculated as the total UC patients divided by the total inhabitants covered by those sites. Incidence was defined as the number of new UC cases during 2011 divided by the total inhabitants covered by those sites.

Results: In 2011, a total of 42,000 patients were attended for UC in gastroenterology units in Spain with a prevalence rate of 88.7 UC cases (95% CI: 69.6–106.0) per 100,000 inhabitants. The incidence rate was of 5.7 cases (95% CI: 1.2–10.8)/100,000 inhabitants. Six percent of patients being attended for UC

were hospitalized in the 58 units analyzed in 2011. There were 1075 hospitalizations related to UC in total (approximately 14 per gastroenterology unit; median hospital stay length: 8 days). Six out of 1000 UC patients underwent colectomy in 2011. Near one third (32.7%) were emergency colectomies. Most hospitals had specific IBD units (87.9%) and colorectal surgeons (93.1%).

Conclusions: Our study provides the first national data on the prevalence and incidence of UC in gastroenterology units in Spain. Hospitalization and surgical burden associated with UC was low.

Keywords: colitis, incidence, patient care, prevalence, Spain, ulcerative epidemiology.

Citation

Marín-Jiménez I, Saro C, Díaz V, Barreiro-de Acosta M, Gómez-García M, Casbas AG, on behalf of the working group of EPICURE study. Epidemiology and hospital resources use in the treatment of ulcerative colitis at gastroenterology units in Spain (EPICURE study). *Drugs in Context* 2018; 7: 212505. DOI: [10.7573/dic.212505](https://doi.org/10.7573/dic.212505)

Introduction

Inflammatory bowel diseases (IBD) are caused by the interaction of genetic and environmental factors, such as intestinal microbiota and mucosal immune regulation [1–3]. The frequency rates of inflammatory bowel diseases have constantly changed worldwide [4–6]. The causes leading to the continuous and rapid changes in IBD incidence are still unknown. However, there is evidence to support the possible role of environmental factors such as dietary habits, lifestyle and other factors associated with industrial development [7]. In fact, epidemiological data in the last decade showed a 3:1

north–south [6] gradient. Moreover, recently, a 2:1 west–east [4] gradient has been noted, which suggests that the risk of IBD is linked to the developmental status of the geographic region/country.

Ulcerative colitis (UC) is a chronic IBD that affects the large bowel (rectum and colon), which is clinically characterized by an increased frequency of bowel movements and bloody diarrhea. UC requires a long-term chronic management based on different therapies such as mesalamine, steroids, thiopurines, and biologic drugs (antagonists to tumor necrosis factor and integrins), with significant health-care

resource consumption. Several studies have evaluated the epidemiological aspects of the disease in Spain. The majority of these studies were retrospective and included hospital case reports, studies from regional areas, and population studies [8–29]. Particularly, four Spanish cities (Sabadell, Vigo, Mallorca and Motril) were studied within a European prospective study with an observational period of 2 years (1991–1993) and using a standard protocol for the definition and detection of cases. From their findings, it can be concluded that the global incidence rate of UC in the four of the Spanish areas studied (8.0 per 100.000) was statistically significant [11]. The prevalence of UC is estimated to be nearly 10–14-fold higher than the incidence of UC [30]. Thus, the available data of prevalence of UC in Spain, indirectly calculated from incidence data, show a range from 118 to 566 cases per 100,000 inhabitants [15].

Nevertheless, the global prevalence and epidemiological data of UC patients in Spain are out of date and show considerably lower rates than those reported by recent studies in Europe and some areas of Spain [10]. Moreover, other factors such as differences in study design (population vs hospital or prospective vs retrospective), methodology used for the detection of cases, and criteria for case definition might have influenced the rates observed so far. A nationwide study on the epidemiological features of UC in Spain, based on standardized data collected from a heterogeneous sample of patients and health-care sites, provides us the first step to understand the real medical importance of UC.

In addition, UC patients require adequate health-care facilities (medical visits, hospitalization, examinations, surgical procedures, medication expenses, diagnostic tests) and access to specialized staff (physicians, nurses and other health-care staff), which are poorly studied in our country [31].

The purpose of this retrospective, multicenter, epidemiological, cross-sectional study (EPICURE study) was to estimate the prevalence and incidence of UC, diagnosed according to the European Crohn's and Colitis Organization (ECCO) guidelines [32], at hospital gastroenterology (GE) units in Spain (primary objective) and to assess the use of hospital resources (characteristics and facilities) for the management of patients with UC in Spain (secondary objective). This study will provide an updated overview of the prevalence of UC in Spain (nationwide, not only from local regions) and its clinical management. Obtaining approximate incidence and prevalence values is crucial at all health-care levels. It is useful for governments to calculate costs and resources, and, also, necessary to perform comparisons between countries.

Methods

Study design and data source

This was a retrospective multicenter, epidemiological, cross-sectional study, in patients cared for UC at the Spanish National Health Care system SNS (*Sistema Nacional de Salud*). The cohort

of patients to be studied was adult patients with confirmed UC diagnosis according to ECCO guidelines [32], at any stage or extent of disease, and in active follow-up during the last year (2011) in a GE unit at selected sites within the Spanish SNS. The SNS provides health-care free of charge to the Spanish population and is uniformly organized along the country (with experienced gastroenterologists who use commonly accepted diagnostic procedures and criteria). Reference and community hospitals with similar characteristics in each region were selected to participate in the study. To participate in the study the health-care site was required to have a database in order to collect the data. The study was not registered in a clinical trial database owing to its epidemiological nature.

The primary objective of the study was to estimate the prevalence and incidence of UC diagnosed at GE units in Spain. To fulfill the primary objective, data on the number of UC/IBD patients in active follow-up during 2011 and cared for UC/IBD at the participating GE units were collected. The total number of patients cared for UC at the health-care site in 2011 was also collected. The data on the use of hospital resources (characteristics and facilities) for the management of patients with UC in Spain were provided by the health-care site and analyzed as a secondary objective of the study. For this end, each study site collected data on specific units for IBD, availability for medication administration, magnetic resonance imaging (MRI) services, availability of endoscopy and surgery services specific for IBD/UC, number of UC patients cared for per year, number of new diagnoses per year, and type and number of surgical procedures performed on these patients.

Statistical methods

The prevalence of UC in the GE units of the study sites was calculated as the total number of patients cared for UC at the GE units divided by the total inhabitants covered by those sites. Incidence was defined as the number of new cases actively cared for UC divided by the total number of inhabitants covered by those sites during 2011. The data on the Spanish population on 2011 published by the INE (National Statistics Institute in Spain) were used to calculate the total of patients that were cared for UC in GE units in Spain. Among gastrointestinal diseases likely to present with symptoms similar to UC are those entities also considered IBD, that is, Crohn's disease and indeterminate colitis. Assuming an estimated prevalence of IBD in Spain of 180,000 cases and distributed them as follows: 54% UC, 40% Crohn's disease and 6% indeterminate colitis; a total of 807 assessable patients with IBD were required to exhibit an error (accuracy) of 3.5% within the 95% CI and 80% of power. Moreover, considering an information loss rate of 20%, it was necessary to include a minimum of 968 patients with IBD. This sample would provide an expected group of 523 patients with UC for the secondary objectives of the study. A foreseen number of 60 GE units in Spanish hospitals were expected to be contacted to achieve the total of assessable patients with UC to be analyzed for

Table 1. Study population.

	Number of sites	Missing	Mean (SD)	Median [Q1, Q3]	Min; Max
Population cared for at the site in 2011 [†]	58		368.8 (507.8)	274.6 [200.0, 376.0]	70.0; 4000
Number of IBD patients in follow-up at the GE unit	57	1	690.0 (402.4)	600.0 [400.0, 951.0]	70.0; 2000
Number of UC patients in follow-up at the GE unit	58		327.0 (193.1)	286.5 [200.0, 406.0]	33.0; 900

[†]Data expressed as thousand patients.

GE, gastroenterology; IBD, intestinal bowel disease; Max, maximum; Min, minimum; Q1, Quarter 1; Q3, Quarter 3; SD, standard deviation; UC, ulcerative colitis.

the secondary objectives in the second part of the study. We first identified all candidate hospitals from urban (reference hospitals) and rural areas. Those hospitals with GE units with no available database of IBD patients were subsequently excluded to participate in the study. To ensure the sample homogeneity throughout the Spanish territory, a stratification of hospitals was undertaken by grouping them into geographic areas with more than 2,100,000 inhabitants. Thus, each participating center included a total of 10 cases of UC.

Statistical analysis was mainly descriptive. The categorical variables were summarized and presented as absolute and relative frequencies. The continuous variables were summarized by mean, standard deviation, median, first and third quartiles, and minimum and maximum values. Whenever possible, 95% bilateral CIs were provided.

The study was performed after approval by the Independent Ethics Committee of each participating site and in accordance with the Declaration of Helsinki, the Good Clinical Practices, and local ethical and legal requirements.

Results

Characteristics of health-care sites

From October 2012 until May 2013, a total of 58 GE units accepted to participate in this cross-sectional study. Most (96.6%) of the sites analyzed were located in areas with more than 100,000 inhabitants.

The sites analyzed cared for a median reference population of 274,640 inhabitants in 2011. A median of 600 (interquartile range [IQR]: 400–951) patients were cared for IBD, and a median of 286 (IQR: 200–406) patients were cared for UC at the study sites (Table 1).

Most hospitals had specific IBD units (87.9%) or colorectal surgery services (93.1%). Moreover, all had an outpatient clinic for the follow-up and treatment of patients with IBD. Most sites (93.1%) included in the analysis had an MRI, endoscopy or ultrasound service. These services were specific for IBD patients

Table 2. Characteristics of sites.

Study sites (n=58)	n (%)	Total	Mean
Specific IBD units	51 (87.9)		
Specific surgery services for coloproctology	54 (93.1)		
<i>MRI services</i>			
General	54 (93.1)		
Specific [†]	39 (67.2)		
<i>Endoscopy services</i>			
General	54 (93.1)		
Specific [†]	44 (75.9)		
<i>Ultrasound services</i>			
General	54 (93.1)		
Specific [†]	35 (60.3)		
Outpatient clinic	58 (100.0)		
Nurses		58	1.0
Physician specialists		160	2.8

[†]Specific for IBD/UC patients.

IBD, intestinal bowel disease; MRI, magnetic resonance imaging; UC, ulcerative colitis.

in 67.2% (n=39), 75.9% (n=44) and 60.3% (n=35) of the sites, respectively (Table 2). Regarding the health-care professionals, the sites had a mean of one nurse and three physicians specialized in treating UC patients at the IBD units (Table 2).

Prevalence and incidence of UC in 2011

During 2011, 18,967 patients were cared for UC in the GE units of the hospitals participating in the study: with these data, it is estimated that 41,840 patients (95% CI: 41,433–42,236) were cared for UC in GE units in Spain during that period, which corresponds to a prevalence rate of 88.7 UC cases (95% CI: 69.6–106.0) per 100,000 inhabitants. A median of 17

Table 3. Use of hospital resources owing to UC in 2011.

Year 2011	Number of sites	Mean (SD)	Median [Q1, Q3]	Min; Max
Number of hospitalizations owing to UC	58	18.5 (13.5)	14.5 [8.0, 26.0]	3.0; 65.0
Length of hospital stay (days)	58	8.9 (2.7)	8.0 [7.0, 10.0]	4.0; 16.0
Number of patients receiving a colectomy owing to UC (only sites with any colectomy)	39	3.1 (2.0)	3.0 [2.0, 4.0]	1.0; 12.0
Percentage of emergency colectomies (only sites with any colectomy)	39	32.7 (35.1)	25.0 [0.0, 50.0]	0.0; 100.0
Percentage of programmed colectomies (only sites with any colectomy)	39	65.6 (36.2)	70.5 [50.0, 100.0]	0.0; 100.0
Median length of stay at hospital for colectomies (only sites with any colectomy)	39	14.6 (8.0)	13.0 [8.0, 17.0]	5.0; 45.0

Max, maximum; Min, minimum; Q1, Quarter 1; Q3, Quarter 3; SD, standard deviation; UC, ulcerative colitis.

(IQR: 14.0, 27.0) *de novo* cases of UC were diagnosed per site in 2011. Hence, the incidence rate for UC was 5.7 cases (95% CI: 1.2–10.8) per 100,000 inhabitants/year.

Use of hospital resources for UC in 2011

Six percent of patients with UC diagnosis were hospitalized in any of the 58 units analyzed in Spain in 2011. There were a total of 1075 hospitalizations owing to UC in 2011, and the median length of hospital stay was 8 days (IQR: 7.0, 26.0) (Table 3).

At least one colectomy was performed during 2011 in 67.2% (n=39) of the sites analyzed. No colectomies were performed in the GE units where a surgical specialized unit was not available. In general, a median of 3 patients per site underwent colectomy owing to UC during 2011 in the 39 hospital sites that performed colectomies. Nearly 0.6% of patients received colectomy owing to UC in 2011. It is estimated that approximately 263 (95% CI: 230–294) colectomies owing to UC were performed at public hospitals in Spain in 2011. Nearly a third (32.7%) of the colectomies performed in the study sites were emergency colectomies. The median length of stay at hospital for colectomy owing to UC was 13 days (IQR: 8.0; 17.0) (Table 3).

Discussion

To date, there have been several attempts to determine the incidence and prevalence of UC in Spain circumscribed to some local regions of Spain, but a national study was lacking. The present study provides the first national and most current data on the prevalence and incidence of UC in GE units in Spain, important for making comparisons between other national studies.

Data from a heterogeneous patient population representative of every region of Spain were collected in a consistent manner. The GE units, as part of the SNS in Spain, are uniformly

organized along the country and follow standardized protocols for the definition and detection of cases. In addition, health care is provided free of charge enabling homogeneity and comparability between regions.

The prevalence rate of 88.7 UC cases (95% CI: 69.6–106.0) per 100,000 inhabitants/year observed in our national study is lower than the range from 118 to 566 cases per 100,000 inhabitants, indirectly calculated from incidence ranges by region in Spain by Lopez Serrano [15]. The incidence rate for UC during 2011 of 5.7 cases (95% CI: 1.2–10.8) per 100,000 inhabitants that we have observed in Spain is quite similar to that reported by Brullet et al. in four Spanish areas (overall adjusted incidence rate: 8.0 per 100,000; 95% CI: 6.3–9.7) [11] but lower than the majority of the population prospective studies reported in Spain [33], which were primarily in the northern areas of Spain (Asturias, Pamplona, Sabadell). However, UC incidence was particularly underestimated in some Autonomous Communities in our study owing to poor representation of large hospitals; this fact has probably influenced the low rate observed compared with prior studies. However, the results of a recent retrospective study of the epidemiology and temporal trends of IBD in Castilla-La Mancha Autonomous Community (Spain) by Lucendo and colleagues suggest an interesting alternative to consider. The authors found a decreasing trend in the incidence of UC in parallel to an increasing trend in the incidence and prevalence for Crohn's disease within the last 10 years [29]. We do not know whether this trend change could also be observed at a national level as the epidemiology of Crohn's disease was not the object of our study. As the authors suggest, the existence of a progressive reduction in UC incident cases in Spain and its relationship with the epidemiology of Crohn's disease should be addressed in future prospective studies.

Despite these limitations, the present nationwide study facilitates an epidemiological comparison with other European countries. Moreover, in this comparison, Spain might be

considered as a key factor for understanding UC disease. The UC incidence of 5.7 cases per 100,000 habitants observed in our study is within the range of European UC incidence rates collected in a review of studies published from 1996 to 2012 by Ng et al. [7], and, particularly, within that characteristic of South Europe (3.9–8.6 per 100,000 inhabitants) in the European Collaborative study (EC-IBD) in 1996 [6]. Noteworthy, the incidence of UC in Spain in our study seems to be closer to the median crude annual incidence rate observed recently in the Eastern (4.1/100,000 inhabitants) European medical centers compared to that of the Western (10.8/100,000 inhabitants) European centers included in the European Crohn's and Colitis Organization-Epidemiological Committee (ECCO-EpiCom) study [4]. The ECCO-EpiCom cohort study is a prospective, population-based, inception cohort of 1367 IBD patients diagnosed in 2010 from 31 European centers that were followed during 1 year. Results from a second inception cohort of patients diagnosed in 2011 from participating centers confirmed the incidence reported in the 2010 ECCO-EpiCom [34].

A variety of hypotheses have tried to explain the north–south geographic distribution of UC. The variable genetic susceptibility or predisposition to the development of UC of the different populations is important but cannot explain most cases observed. Environmental factors related with industrialization seem to play an important role in the pathogenesis of these diseases. Barreiro De Acosta observed that second-generation immigrants from low-incidence countries who emigrated to westernized countries have a higher risk for developing IBD, especially UC [35]. Climatic, dietary, economic and other factors might have contributed to differences found in Europe [6], but not those observed in the United States [36] where there is a genetically diverse population with dietary and economic conditions quite similar along the country. Schultz and Butt suggest that it is a more global phenomenon related to latitude of residence and the sunlight exposure and production of vitamin D associated with it [36]. Other environmental and lifestyle factors that might influence in gut flora, such as hygiene habits [37] or influence of summer temperature [38] have been proposed. A suitable explanation for the eastern–western gradient recently observed in Europe is essential. Spain can be considered a western country as regards to industrialization experienced during the last two decades. However, the incidence rates are similar to those of the eastern countries. Thus, a detailed analysis of factors (whether climatic, dietary or industrialized)

affecting UC in Spain can be a key factor for the understanding of UC disease.

In the present study, the use of hospital resources, that is, hospitalization and surgical burden, associated with UC was low. During the previous year, approximately 0.6% of UC patients had received a colectomy and a 6% of UC patients had been hospitalized. These rates obtained resemble that of the eastern European countries (1% patients with surgery and 8% hospitalized) included in the 2010 EpiCom study [39] and are far from those reported for western Europe (4% with surgery and 14% patients hospitalized). Possibly, this is a consequence of the low incidence rates compared to the western European countries but other factors could have contributed. Economic factors have little to add as most hospitals included had specific IBD units (87.9%) and colorectal surgeons (93.1%). Moreover, health-care services are provided free of charge. The adequate management of UC patients (by following international guidelines) and the efficient use of health resources by health-care personnel might have contributed. A more detailed analysis of the use of health-care facilities (medical visits, hospitalization, examinations, surgical procedures, medication expenses, diagnostic tests) in a representative subset of UC patients will be provided in a further communication.

The strength of this study is the relatively large number of cases sampled from public Hospital areas, where access to healthcare facilities and economic conditions are relatively equal. A retrospective 12-month chart review was performed in patients for evaluating a long-term period under similar conditions and with the same criteria for diagnosis and for the definition of the date of disease debut. On the other hand, few hospitals without an IBD unit were included as they typically did not have a database necessary for the data collection. This lack of uniformity in the selection criteria for the health-care sites included in every autonomous community/region constitutes the primary limitation of the study. An additional study including hospital areas of less than 100,000 inhabitants uniformly selected might complement the present study.

In conclusion, our study provides the first national data on the prevalence and incidence of UC in GE units in Spain. Rates of UC incidence for Spain are lower than the ones previously reported in other studies and resemble those of the eastern European countries. Hospitalization and surgical burden associated with UC was low compared to other western industrialized countries. Contribution of other factors other than industrialization should be studied.

Contributions: IM-J, CSG, MBD, MGG and AG carried out the study, and participated in its design and coordination and helped to draft the manuscript. VG participated in the design of the study and data analyses and drafted the manuscript. All authors read and approved the final manuscript. Other institutions and principal investigators who participated in the study are as follows: Victor Amo (H Carlos Haya, Málaga), Álvaro Hernández Martínez (H Torrecárdenas, Almería), Raquel Camargo Camero (H Virgen de la Victoria, Málaga), Juan Jesús Puente Gutiérrez (H Alto Guadalquivir, Jaén), Ana M^o Trapero (H de Jaén, Jaén), Rebeca Ruiz Morales (H de Cabra, Córdoba), María Dolores Retamero Orta (H Comarcal de la Axarquía, Málaga), María Rojas (H de Valme, Sevilla), Beatriz Benítez Rodríguez (H Juan Ramón Jiménez, Huelva), Alfredo Abraldes Bechiarelli (H Puerta del Mar, Cádiz), Sonia Gallego Montañés (H Miguel Servet, Zaragoza), Sabino Riestra Menéndez (H Central de

Asturias, Oviedo), Daniel Ceballos Santos (H Dr Negrín, Gran Canaria), Samir Amine Salha (H Dr José Molina Orosa, La Palma), Montserrat Rivero (H de Valdecilla, Santander), Óscar Roncero García Escribano (H de Alcázar de San Juan, Ciudad Real), Jesús Barrio Andrés (H Río Hortega, Valladolid), Fernando Muñoz (H de León, León), Beatriz Sicilia Aladrén (Complejo Asistencial Universitario de Burgos, Burgos), Eduard Cabré (Hospital Germans Trias i Pujol, Barcelona), Jose Miguel Boudet (H Arnau de Vilanova de Lleida), David Busquets Casals (H Josep Trueta de Girona), David Monfort Miquel (Consortio Sanitario de Terrassa, Barcelona), Mercedes Navarro Llavat (H Sant Joan Despi Moisés Broggi, Barcelona), Xavier Calvet (H Parc Taulí, Barcelona), Sandra Torra Alsina (Parc Sanitari Sant Joan de Deu, Barcelona), M^a del Mar Alcalde Rubio (H Infanta Cristina, Badajoz), María Dolores Hernández Durán (H Virgen del Puerto; Cáceres), Ana Echarri Piudo (H Arquitecto Marcide; A Coruña), Luisa de Castro Parga (H Meixoeiro, Vigo), Rocío Ferreiro (Hospital Clínico Universitario de Santiago de Compostela), Carlos Taxonera Samsó (H Clínico San Carlos, Madrid), Javier Pérez Gisbert (H La Princesa, Madrid), Elena Garrido Gómez (H Ramón y Cajal, Madrid), Isabel Vera Mendoza (H Puerta de Hierro, Madrid), Ángeles Masedo González (H 12 de Octubre, Madrid), M^a Dolores Martín Arranz (H La Paz, Madrid), Luis Menchen Viso (H Gregorio Marañón, Madrid), Daniel Martín Rodríguez (H Infanta Cristina, Madrid), Ramón Pajares Villarroya (H Infanta Sofía, Madrid), Emilio Torrella Cortés (H Morales Meseguer, Murcia), Teresa Martínez Giménez (H Rafael Méndez, Murcia), Patricia Romero Cara (H Santa Lucía, Murcia), Cristina Rodríguez Gutiérrez (H de Navarra, Pamplona), Carmen Muñoz Villafranca (H de Basurto, Vizcaya), Carmen Molina Álvarez (H Santiago Apóstol, Miranda de Ebro, Burgos), Silvia Estrada Oncins (H Txangorritxu, Guipuzcoa), Sam Khorrami Minaei (H Son Espases, Palma de Mallorca), José M^a Paredes Arquiola (H Dr Peset, Valencia), Maríam Aguas Peris (H La Fe, Valencia), Joaquín Hinojosa del Val (H de Manises, Valencia), Xavier Cortés (H de Sagunto, Valencia).

Disclosure and potential conflicts of interest: The design, study conduct and financial support for the clinical trial was provided by AbbVie. AbbVie participated in the interpretation of data, review and approval of the manuscript. Dr IM-J has served as a speaker, a consultant and advisory member for or has received research funding from MSD, Abbvie, Takeda, Janssen-Cilag, Ferring, Faes Farma, Shire Pharmaceuticals, Dr Falk Pharma, Chiesi, Gebro Pharma, Otsuka Pharmaceutical and Tillots. Dr CSG has served as a consultant for AbbVie, MSD, Ferring and Tillots, and has received research funding from AbbVie, and speaker fees from AbbVie, MSD, Ferring and Tillots. VD is an employee of AbbVie. Dr MBD has served as a speaker, a consultant and advisory member for, and has received research funding from MSD, Takeda, Khern, Abbvie, Hospira, Ferring, Falk, Faes Farma, Shire Pharmaceuticals and Chiesi. Dr MGG has served as a consultant for AbbVie and Centocor Ortho-Biotech, and speaker fees from Centocor Ortho-Biotech. Dr AG has served as a consultant for AbbVie, MSD, Hospira and has received research funding from AbbVie and MSD and speaker fees from Abbvie, MSD, Hospira, Ferring and Shire. The International Committee of Medical Journal Editors (ICMJE) Potential Conflicts of Interests form for the authors are available for download at: <http://www.drugsincontext.com/wp-content/uploads/2018/02/dic.212505-COI.pdf>

Acknowledgements: Editorial assistance was provided by Content Ed Net (Madrid, Spain).

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Article URL: <http://www.drugsincontext.com/epidemiology-and-hospital-resources-use-in-the-treatment-of-ulcerative-colitis-at-gastroenterology-units-in-spain-epicure-study>

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Provenance: submitted; externally peer reviewed.

Submitted: 30 June 2017; **Peer review comments to author:** 20 July 2017; **Revised manuscript received:** 29 January 2018; **Accepted:** 3 February 2018; **Publication date:** 6 March 2018.

Drugs in Context is published by BioExcel Publishing Ltd. Registered office: Plaza Building, Lee High Road, London, England, SE13 5PT. BioExcel Publishing Limited is registered in England Number 10038393. VAT GB 252772009.

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