



ORIGINAL ARTICLE

Assessment of the length of sick leave in patients with inflammatory bowel disease



Sara Nieves Ramos-Cozar^a, Rafael Martín-Masot^{b,c,*}, Begoña Rodríguez-Gallego^a, Leticia Rubio^{c,d}, Juan Luis Cabanillas-Moruno^e, Víctor Manuel Navas-López^{b,c}

^a Unidad Médica del Equipo de Valoración de Incapacidades (UMEVI) del Instituto Nacional de la Seguridad Social (INSS) de Málaga, Málaga, Spain

^b Hospital Regional Universitario de Málaga, Málaga, Spain

^c Instituto de Investigación Biomédica de Málaga, IBIMA, Málaga, Spain

^d Departamento de Anatomía Humana, Medicina Legal e Historia de la Ciencia, Facultad de Medicina, Universidad de Málaga, Málaga, Spain

^e Salud Pública y Consumo, Consejería de Políticas Sociales y Salud Pública, Ciudad Autónoma de Melilla, Málaga, Spain

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Abstract

Introduction: Inflammatory bowel disease (IBD) is a chronic disorder that can lead to periods of work-related temporary disability (TD), which may result in the need for permanent disability. The objective was to assess the impact of IBD on patients' temporary disability by analyzing periods, duration, and causes. It also investigates risk factors influencing the severity, frequency, and duration of flare-ups and associated complications in IBD patients.

Method: The study includes patients aged 18–65, with at least 1 day of TD in 2019 (Pre-COVID), referred or not by UMEVI, due to reasons related to IBD.

Results: A total of 172 patients were included, and in all cases, TD was associated with IBD. TD was higher in patients over 30 years old, with anxious depressive disorder, who required hospitalization and did not receive prednisone treatment ($p < 0.05$). TD duration was longer in patients belonging to the Special Regime for Self-Employed Workers (RETA): 67 days (IQR: 22–160) versus the General Regime (RG): 33 days (IQR: 8–110), with no statistically significant difference ($p = 0.120$). The mean cost (€) per worker in this series was €745.5 (IQR: 231–2608.2).

Conclusions: IBD has a significant impact on patients' temporary work disability. The duration of TD was longer in patients older than 30 years, with anxious-depressive disorder, who required hospital admission and did not receive steroid treatment.

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* Corresponding author.

E-mail address: rafammgr@gmail.com (R. Martín-Masot).

PALABRAS CLAVE

Enfermedad
inflamatoria
intestinal;
Incapacidad
temporal;
Incapacidad
permanente;
Baja laboral

Evaluación de la duración de la baja laboral en pacientes con enfermedad inflamatoria intestinal

Resumen

Fundamentos: La enfermedad inflamatoria intestinal es un trastorno crónico que puede dar lugar a períodos de incapacidad temporal en el trabajo, que va a depender de diversos factores, pudiendo considerarse necesaria la incapacidad permanente. El objetivo fue evaluar el impacto de la enfermedad inflamatoria intestinal en la incapacidad temporal de los pacientes, analizando períodos, duración y causas e investigar factores de riesgo que influyen en la gravedad, frecuencia y duración de los brotes y complicaciones asociadas en pacientes con EII.

Métodos: Estudio observacional que incluye pacientes de 18 a 65 años, con al menos 1 día de incapacidad temporal en 2019 (Pre-COVID), citados o no por UMEVI, por motivos relacionados con EII.

Resultados: 172 pacientes, en todos los casos la incapacidad temporal estaba en relación con la enfermedad inflamatoria intestinal. La incapacidad temporal fue mayor en pacientes mayores de 30 años, con trastorno ansioso depresivo, que requirieron hospitalización y no recibieron tratamiento con prednisona ($p < 0,05$). La duración de la incapacidad temporal fue superior en aquellos pacientes pertenecientes al RETA: 67 días (RIQ 22–160) vs RG: 33 días (RIQ 8–110), $p = 0,120$. El gasto medio (€) por trabajador de esta serie fue de 745,5 € (RIQ 231–2608,2).

Conclusiones: La EII es una enfermedad crónica grave con un alto impacto en la incapacidad temporal de los pacientes. La duración de la IT fue superior en los pacientes mayores de 30 años, con trastorno ansioso-depresivo, que requirieron ingreso hospitalario y no recibieron tratamiento con esteroides.

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Introduction

Inflammatory bowel disease (IBD) is a complex disorder involving chronic inflammation of the gastrointestinal tract. Crohn's disease (CD) and ulcerative colitis (UC) both come under the umbrella of IBD. CD and UC are characterised by periods of stability or remission and phases of exacerbation or flare-ups. During flare-ups, patients develop symptoms, with the most significant being diarrhoea, abdominal pain, fever and general malaise in CD and diarrhoea and rectal bleeding in UC.¹ The incidence of IBD is estimated at 16 cases/100,000 population/year² and the prevalence, 0.39% (CI 95%, 0.02–0.76).³ Despite having a lower prevalence compared to other more common diseases in Spain, such as cancer or diabetes, IBD represents a major challenge due to its significant social, psychological and economic impact on patients, the healthcare system and society as a whole. These disorders involve high associated costs that affect many different aspects.⁴

From a social perspective, patients suffering from IBD may face limitations in their quality of life and the need to adapt their daily routine to manage symptoms and treatments. It is estimated that 75% of patients have felt depressed at some point during the course of their illness.⁵

In economic terms, medical care and treatment of IBD entail significant costs for the healthcare system. These costs can include frequent doctor visits, hospital admissions, specialised medications and biologic therapies, as well as surgical interventions in more severe cases. Absences from work and reduced productivity due to illness also have an

impact on the economy at both individual and collective levels. Direct costs (which include the use of healthcare resources for diagnosis and treatment and non-healthcare expenses caused by the disease) per patient per year are estimated at €5,614 (€4,910 UC vs €6,590 CD), mainly stemming from drug treatments. Indirect costs (consisting of the productivity lost due to the loss or reduction of capacity of individuals due to illness) are estimated at €4,876 per patient/year.⁶

Although the employment rate of people with IBD is identical to that of the general population (58.55% according to the Instituto Nacional de Estadística (INE) [Spanish National Institute of Statistics], quarter 1/2023),⁷ patients with IBD encounter significant challenges in leading a normal working life.⁸ In a study carried out here in Spain, it is estimated that more than 40% of people with CD or UC who are actively employed have been absent from work at some point in the last three months due to their illness.⁹ Work absenteeism is higher in patients with IBD compared to the general population, due to the permanent feeling of tiredness and fatigue, the frequency of visits to the doctor, acute abdominal pain and/or admissions to hospital. However, despite the fact that these are justified reasons, one in five patients reports having received complaints from their superiors related to the disease. Furthermore, 10% of patients willing to have a full-time job find themselves involuntarily employed part-time due to having IBD. It is estimated that an IBD patient loses an average of 10.7 days of work due to the disease. These temporary absences from work represent an annual cost of €41.4 M. The annual cost of sick leave amounts to €382 M.⁴

The economic and social burden of IBD highlights the need for comprehensive care and a multidisciplinary approach for management of the disease. It is essential to develop strategies to achieve early diagnosis, optimise treatments and provide psychological support, to reduce the negative impact of these diseases on the lives of those affected and on the sustainability of the healthcare system. There is very little in the literature on the factors involved in the occurrence and duration of periods of temporary disability (TD) in this group of patients.

Based on the above, the objectives of this study are as follows:

- 1 To assess the impact of IBD on patients' TD, analysing the periods of sick leave required, their duration and the causes that generated them, in order to study the effect on absence from work related to this disease.
- 2 To investigate the risk factors that can lead to TD in patients with IBD, and how they influence the severity, frequency and duration of flare-ups and associated complications.

Material and method

Descriptive, observational, cross-sectional study that included all patients between the ages of 18 and 65 who were on sick leave for at least one day in 2019 (Pre-COVID), whether or not they were called in during that sick leave period by the provincial Unidad Médica del Equipo de Valoración de Incapacidades (UMEVI) [Disability Assessment Team Medical Unit]. Only those patients whose reason for TD was related to IBD are considered. STD is understood as the situation in which workers are temporarily unable to work due to common or occupational illness or accident, whether or not it is work-related, while receiving Social Security medical assistance. Periods of observation due to occupational illness in which the patient is on leave from work will also be considered as situations determining TD. The rating deferment is the extension of the TD situation for a period longer than the initial 18 months maximum duration of the same. A permanent disability (PD) application process may be initiated at the request of the interested party or the pertinent official body.

For these purposes, we made a request to the General Secretariat of the Instituto Nacional de la Seguridad Social (INSS) [Spanish National Social Security Institute] (INSS) for the provision of data on all workers who, being on TD for any period of time in 2019, had any of the selected diagnostic codes. All diagnoses that encompass IBD were indicated; the International Classification of Diseases (ICD) diagnostic codes used were 555 (555, 555.0, 555.1, 555.2, 555.9) and 556 (556, 556.0, 556.1, 556.2, 556.3, 556.4, 556.5, 556.6, 556.8 and 556.9) from ICD-9, and codes K50 and K51 from ICD-10.

Special attention was paid to how this period of TD was resolved; whether it ended with certification of being fit to work with reinstatement in their job activity/position, or whether after their sick leave they needed some degree of

PD, either due to physical limitations or IBD-related sequelae.

In general, a total of 112 items were analysed for each of these patients, where we collected identifying data (gender and date of birth), profession, postcode, relevant previous medical history, previous periods of sick leave, duration of TD, whether they were admitted to hospital during the TD period, treatments related to IBD received both during the TD period assessed and those administered previously (type of treatment, adherence to it, application periods, side effects, failure of the same), type of IBD (UC or CD), whether they have required any type of surgery, outcome after the TD period (fir for work or PD), assessments carried out in the Inspection by the Disability Assessment Team Medical Unit (UMEVI), assessment of the patient's medical records with regard to their limitations when PD is proposed, Spanish national insurance scheme contributions in the case of PD, and result of any follow-up carried out of said disabilities. To calculate daily expenditure on TD, we took the figures from a previous study in which TD was mapped in Spain.¹⁰

The study data were collected and managed using the Research Electronic Data Capture (REDCap) electronic data capture tools hosted by the Sociedad Española de Gastroenterología, Hepatología y Nutrición Pediátrica (SEGHN) [Spanish Society of Paediatric Gastroenterology, Hepatology and Nutrition].

Technical support was provided by the Asociación Española de Gastroenterología (AEG) [Spanish Association of Gastroenterology]-REDCap Support Unit, shared with the AEG. *Research Electronic Data Capture* REDCap is a secure software platform designed to support data capture for research studies by providing: (1) an intuitive interface for capturing validated data; (2) audit trails to track data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for data integration and interoperability with external sources.

Statistical analysis

Variables with normal distribution are expressed as mean $\pm$ standard deviation (SD) and those without, as median and interquartile range (IQR). Normality of distribution was verified by the Kolmogorov-Smirnov test. The χ^2 test was used to compare proportions. Student's *t* test was used to compare variables with normal distribution and the Mann-Whitney *U* test for those without normal distribution. Predictive models were built using univariate and multivariate logistic regression tests. For the construction of the multivariate model, we included variables which showed statistically significant differences or a trend ($p < 0.15$) in the univariate analysis, together with the variables which, based on theoretical or empirical knowledge, were considered related to the dependent variable. We measured the magnitude of the association between the predictive variables of the model and the dependent variable with the odds ratio (OR) and its corresponding 95% confidence interval (CI). A *p*-value of <0.05 was considered statistically significant.

Results

We included 172 patients, 99 (57.6%) female, with a median age of 41.7 (31.9–48.1). Of the 172 patients, 86 (50%) had CD and 86 (50%) UC. The baseline characteristics of the patients are detailed in Table 1. The distribution of the professions of the population studied is shown in Table 2.

Previous temporary disability

A total of 328 TD episodes were recorded prior to the current one in 2019 for the 172 patients included in the analysis. Most patients (68.6%) had one (142, 43.3%) or two episodes (83, 25.3%) of TD. Of these, three corresponded to extended TD (ETD) and 325 to TD. Of the 328 previous TD cases, 186 (56.7%) were related to IBD (flare-up or surgery) and 142 (43.3%) were not. The TD periods were longer in those related to IBD, 20 days (IQR 5–50) vs seven days (IQR 2–20), $p < 0.0001$, with no differences between UC and CD. The median duration for both causes was 12 days (IQR 3–39). Analysing the median number of TD episodes in each of the groups, the series studied had 1.5 episodes (IQR 1–2) not related to their underlying disease vs two episodes (IQR 1–4) which were related, $p < 0.0001$. The reasons for previous TD not related to IBD are shown in Fig. 1.

Present temporary disability

In 2019 in the province being studied, 194,506 TD episodes were initiated (182,128 under the general regime and 12,378 under the special regime for self-employed workers).¹⁴ Of the 172 patients, 146 (84.8%) belonged to the general regime of the Spanish Social Security system (0.08% of all processes initiated in 2019) and 26 (15.2%) to the special regime for self-employed workers (0.2% of all TD processes initiated in 2019). In all cases, the event that caused the sick leave was common illness. The type of organisation handling the TD was the Mutual Benefit Society in 121 cases (70.4%) and the Instituto Nacional de la Seguridad Social (INSS) [Spanish National Institute of Social Security] in 51 (29.6%). Regarding the type of TD, 159 were TD (91.9%), 9 (5.2%) ETD, and 5 (2.9%) were rating deferments. In 38 of the 172 cases (22.1%) the patients had been assessed by the UMEVI.

Regarding the relationship of the TD with their underlying disease, in all cases the TD was related to IBD (for example, flare-up, asthenia, need for surgical treatment or active perianal disease). The median duration of TD was 35.5 days (IQR 11–124.2); 36 days (IQR 8–135.5) for patients with CD vs 33 days (IQR 11.7–120.7) for those with UC, $p = 0.771$. In eight patients, this period of TD coincided with the onset of the disease, requiring hospital admission in four cases, with an average stay of 17.5 ± 1 days. The duration of TD was longer, although not significantly, in patients belonging to the special regime for self-employed workers: 67 days (IQR 22–160) vs general regime: 33 days (IQR 8–110), $p = 0.120$. The average expenditure (€) per worker in the period of TD of this series was €745.5 (IQR 231–2,608.2).

In addition to the treatments listed in Table 3, 15 patients (9.1%) were treated with anxiolytics or antidepressants for anxiety-depressive disorder and 12 (7.3%) patients were taking painkillers to control the pain caused by IBD. Treatment adherence is only recorded for 43 (25%) of the 172 patients; 33 cases were good and 10 cases were bad.

Of the 172 patients, 47 patients (27.3%) required at least one admission in 2019 (26 patients with CD vs 21 patients with UC), 9 patients (5.2%) were admitted twice (three with UC and six with CD) and one patient was admitted three times (CD). The reason for the admission, as well as its duration and the difference between the two conditions are shown in Table 4.

Table 5 lists the factors related to a longer duration of the TD episode.

Patients evaluated at the Disability Assessment Team Medical Unit. Proposals for permanent Disability

A total of 37 patients out of 172 (21.5%) were assessed at the Disability Assessment Team Medical Unit (UMEVI). The median duration of sick leave in those assessed at the UMEVI was 329 days (IQR 126.5–525.0) vs 21 days (IQR 7.0–53.0) in those who were not assessed, $p < 0.0001$. The age of those who were assessed by the UMEVI was 44.8 (IQR 40.1–54.8) vs 40.3 (31.4–46.9) in those not assessed, $p = 0.010$, with a respective time since diagnosis of 7.2 years (IQR 1.32–14.6) vs 6.71 years (IQR 3.2–14.0), $p = 0.964$.

In 2019, 4,838 PD application processes were decided on; of the 1,989 (41%) which were approved, 29 (1.5%) were partial PD, 57 (2.9%) serious disability, 753 (37.9%) absolute PD (APD) and 1,150 (57.8%) total PD (TPD).

Of the 37 patients assessed at the UMEVI during their TD, 13 (35.1%) were proposed for PD by the pertinent official body and seven patients applied for it on their own behalf after 553 days (IQR 543–672) of sick leave. PD was denied to 4/13 proposed patients, seven were granted TPD and two were granted APD. Of the seven applications for PD at the request of the patients themselves, one patient was in TD and was accepted as an ETD. The other six cases were not in a situation of TD, and all were denied. All PD were subject to review within 12 months (IQR 11–19). The median national insurance contribution period was 14.7 years (IQR 6.1–23.2). The duration of the sick leave prior to receiving the PD benefit was 544 days (IQR 538–584).

The Clasificación Nacional de Ocupaciones (CNO) [Spanish National Classification of Occupations] categories for the professions of the patients who were accepted as having PD were: nine (four patients); five (three patients); seven (two patients); and eight (one patient). The duration of the sick leave in days before the PD proposal was related to the acceptance of the proposal [OR: 1.006 (95% CI, 1.00–1.011), $p = 0.034$].

Table 6 describes in detail the related aspects for the patients who were accepted as having PD.

Table 1 Clinical characteristics of the patients on TD.

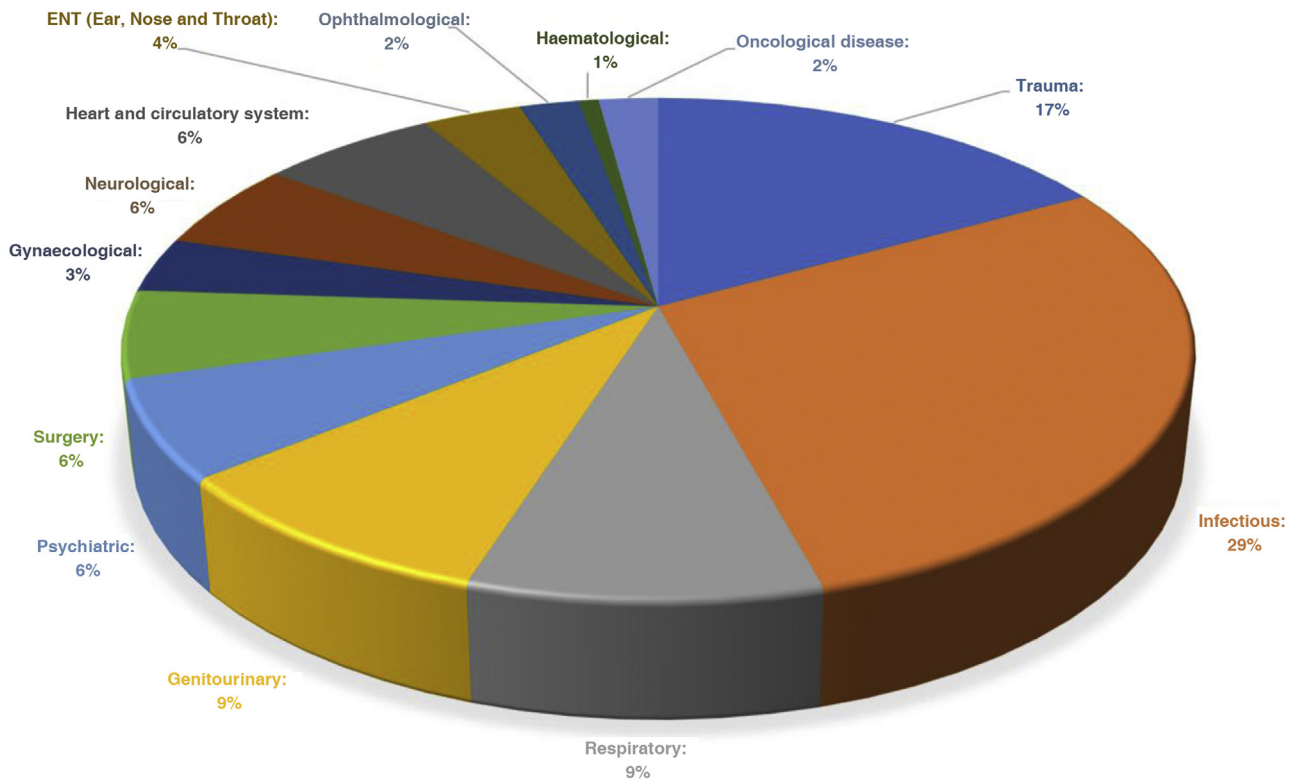
Variable	Total	CD	UC	p
<i>N</i> (%)	172	86 (50)	86 (50)	
Female, <i>n</i> (%)	99 (57.6)	46 (53.5)	53 (61.6)	0.280
Age (years) at diagnosis, median (IQR)	30 (23.5–40.5)	27.2 (22.0–36.4)	33.7 (25.5–43.7)	0.004
Time (years) from diagnosis to 2019	6.8 (3.0–14.2)	8.7 (3.5–14.4)	6.0 (3.0–14.0)	0.553
Current age (years) (2019)	41.7 (31.9–48.1)	39.8 (30.9–46.3)	43.4 (34.0–52.9)	0.034
Montreal classification at diagnosis, <i>n</i> (%) ^{11,12}				
E1 (proctitis)			27 (15.7)	
E2 (left-sided colitis)			28 (16.3)	
E3 (pancolitis)			31 (18.0)	
<i>A</i> (age)				
A1 (<17 years)		6 (7)		
A2 (17 to <40 years)		64 (74.4)		
A3 (≥40 years)		16 (18.6)		
<i>L</i> (location)				
L1 (terminal ileum)		24 (27.9)		
L2 (colon)		6 (7)		
L3 (ileocolonic)		47 (54.7)		
L4 (upper gastrointestinal tract)		9 (10.5)		
<i>B</i> (Behaviour)				
B1 (inflammatory)		46 (53.5)		
B2 (stricturing)		24 (27.9)		
B3 (penetrating)		16 (18.6)		
<i>p</i> (perianal disease)		21 (24.4)		
Prior medical treatments				
Oral mesalazine	136 (79.1)	55 (64)	81 (94.2)	<0.0001
Rectal mesalazine	70 (40.7)	7 (8.1)	63 (73.3)	<0.0001
Oral budesonide	50 (29.1)	46 (53.5)	4 (4.7)	<0.0001
Rectal budesonide	16 (9.3)	1 (1.2)	15 (17.4)	0.001
Prednisone/Methylprednisolone	94 (54.7)	50 (58.1)	44 (51.2)	0.462
Beclomethasone dipropionate	45 (26.2)	8 (9.3)	37 (43)	<0.0001
Azathioprine	86 (50)	54 (62.8)	32 (37.2)	0.01
Mercaptopurine	14 (8.1)	11 (12.8)	3 (3.5)	0.05
Methotrexate	7 (4.1)	7 (8.1)	0 (0)	0.016
Tacrolimus	3 (1.7)	0 (0)	3 (3.5)	0.121
Ciclosporin	1 (0.6)	0 (0)	5 (5.8)	0.497
Apheresis	6 (3.5)	1 (1.2)	5 (5.8)	0.102
Infliximab	50 (29.1)	32 (37.2)	18 (20.9)	0.012
Adalimumab	37 (21.5)	29 (33.7)	8 (9.3)	<0.0001
Golimumab	0 (0)	0 (0)	0 (0)	N/A
Vedolizumab	11 (6.4)	5 (5.8)	6 (7.0)	0.508
Ustekinumab	20 (11.6)	17 (19.8)	3 (3.5)	0.001
Tofacitinib	4 (2.3)	0 (0)	4 (4.7)	0.059
Corticosteroid-dependent patients	30 (17.4)	16 (18.6)	14 (16.3)	0.420
Corticosteroid-resistant patients	4 (2.3)	2 (2.3)	2 (2.3)	0.690
Biological drugs used				
IFX → ADA	9 (5.2)	7 (8.1)	2 (2.3)	
IFX → ADA → UST	6 (3.4)	6 (6.9)	0 (0)	
IFX → UST	5 (2.9)	5 (5.8)	0 (0)	
IFX → ADA → VDZ → UST	3 (1.7)	3 (3.4)	0 (0)	0.004
IFX → VDZ	3 (1.7)	0 (0)	3 (3.4)	
IFX → ADA → VDZ → UST → TOFA	2 (1.1)	0 (0)	2 (2.2)	
VDZ → UST	1 (0.6)	1 (1.2)	0 (0)	
ADA → UST	1 (0.6)	0 (0)	1 (1.2)	
ADA → VDZ → UST	1 (0.6)	1 (1.2)	0 (0)	
IFX → TOFA	1 (0.6)	0 (0)	1 (1.2)	
IFX → VDZ → TOFA	1 (0.6)	0 (0)	1 (1.2)	
Total	33 (19.1)	23 (24.7)	10 (11.6)	

IFX: infliximab; ADA: adalimumab; UST: ustekinumab; VDZ: vedolizumab; TOFA: tofacitinib; N/A: not applicable.

Table 2 Spanish National Classification of Occupations in the patient sample, n (%)¹³.

CNO code	Description	Total	CD	UC	p
1	Directors and managers.	9	4 (4.7)	5 (5.8)	0.741
2	Scientific technologists and professionals and intellectuals.	24	8 (9.3)	16 (18.6)	
3	Technicians; associate professionals.	22	14 (16.3)	8 (9.3)	
4	Accounting, administrative and other clerical workers.	24	11 (12.8)	13 (15.1)	
5	Service (restaurants and food, personal services, protection) and sales workers.	53	31 (36.0)	22 (25.6)	
6	Skilled agricultural, livestock farming, forestry and fishery workers	2	0 (0)	2 (2.3)	
7	Craft workers and related trades workers in manufacturing and construction industries (except plant and machinery operators).	10	5 (5.8)	5 (5.8)	
8	Plant and machine operators, and assemblers	6	2 (2.3)	4 (4.7)	
9	Elementary occupations.	22	11 (12.8)	11 (12.8)	

CNO: Clasificación Nacional de Ocupaciones [Spanish National Classification of Occupations].

**Figure 1** Distribution of causes of previous TD not related to IBD.

Discussion

IBD is a serious chronic condition which affects a significant number of people worldwide. Due to the debilitating nature of this disease, a significantly higher prevalence of work disability has been observed in patients with IBD com-

pared to the general population.¹⁵ Recurrent symptoms, unpredictable exacerbations, and the need for ongoing medical treatments can result in functional limitations that significantly interfere with patients' ability to maintain sustained work activity. The complexity of IBD and its impact on patients' working lives highlight the importance of an

Table 3 Current medical treatments (n = 172).

n (%)	Totals (n = 172)	CD (n = 86)	UC (n = 86)	p
Oral mesalazine	106 (61.6)	32 (37.2)	74 (86.0)	<0.0001
Rectal mesalazine	60 (34.9)	6 (7.0)	54 (62.8)	<0.0001
Oral budesonide	30 (17.4)	29 (33.7)	1 (1.2)	<0.0001
Rectal budesonide	10 (5.8)	0 (0)	10 (11.6)	0.001
Prednisone/methylprednisolone	67 (39.0)	32 (37.2)	35 (40.7)	0.361
Beclomethasone dipropionate	25 (14.5)	5 (5.8)	20 (23.3)	0.001
Azathioprine	51 (29.7)	31 (36.0)	20 (23.3)	0.035
Mercaptopurine	6 (3.5)	5 (5.8)	1 (1.2)	0.097
Methotrexate	3 (1.7)	3 (3.5)	0 (0)	0.116
Tacrolimus	3 (1.7)	0 (0)	3 (3.5)	0.130
Ciclosporin	1 (0.6)	0 (0)	1 (1.2)	0.509
Apheresis	3 (1.7)	0 (0)	3 (3.5)	0.130
Infliximab	30 (17.4)	19 (22.1)	11 (12.8)	0.068
Adalimumab	17 (9.9)	12 (14.0)	5 (5.8)	0.052
Golimumab	0 (0)	0 (0)	0 (0)	N/A
Vedolizumab	6 (3.5)	3 (3.5)	3 (3.5)	0.629
Ustekinumab	9 (5.2)	7 (8.1)	2 (2.3)	0.070
Tofacitinib	3 (1.7)	0 (0)	3 (3.5)	0.135
Biologics (IFX, ADA, VDZ or UST)	54 (31.4)	35 (40.7)	19 (22.1)	0.004
Dual therapy	8 (4.7)	5 (5.9)	3 (3.5)	0.588
IFX + UST	4 (2.3)	4 (4.7)	0 (0)	
IFX + VDZ	1 (0.6)	0 (0)	1 (1.2)	
IFX + TOFA	1 (0.6)	0 (0)	1 (1.2)	0.291
VDZ + UST	1 (0.6)	1 (1.2)	0 (0)	
UST + TOFA	1 (0.6)	0 (0)	1 (1.2)	

Dual therapy: 2 biologics or 1 biologic + JAK inhibitor. IFX: infliximab.

ADA: adalimumab; VDZ: vedolizumab; UST: ustekinumab; TOFA: tofacitinib.

Table 4 Reasons for and duration of patient admissions during this period of TD.

Reason for admission	All	CD	UC
Onset of the disease	4	3	1
Moderate/severe flare-up ^a	40	20	20
Surgical resection ^b	11	7	4
Abscess drainage	2	2	0
Appendectomy	1	1	0
CMV infection	6	0	6
Lysis of adhesions	1	0	1
Seton placement/fistulotomy/fistulectomy	2	2	0
Febrile neutropenia	1	1	0
Stay in days [median (IQR)]	8 (6–14)	8 (4–13) ^c	11.5 (8–20) ^c

^a Pseudo-obstructive conditions are included.^b In two cases, one UC and one CD, surgical resection was performed due to confirmed suspicion of adenocarcinoma.^c p = 0.029.**Table 5** Factors related to TD duration > P75 (125 days).

Variable	UnivariateOR (95% CI)	p	MultivariateOR (95% CI)	p
Admission during the period of TD	3.3 (1.5–7.3)	0.003	2.7 (1.1–6.7)	0.023
No use of prednisone	2.9 (1.3–6.4)	0.007	2.9 (1.2–7.2)	0.023
Anxiety-depressive disorder	3.7 (1.2–10.8)	0.016	3.5 (1.1–10.9)	0.028
Age over 30	4.1 (0.9–18.5)	0.059	5.0 (1.0–23.8)	0.042

Hosmer-Lemeshow test: p = 0.506; Cox-Snell R²: 0.141. Nagelkerke R²: 0.224; sensitivity: 100 (51–100); specificity 83 (76–88); PPV: 18 (7–36); NPV: 100 (96–100). Note: This table only shows the results of the univariate analysis of the variables that were ultimately included in the multivariate analysis. The model presented here is significant; it explains between 0.141 and 0.224 of the dependent variable and correctly classifies 83.8% of the cases.

Table 6 Description of cases accepted as permanent disability.

CNO code	Previous TD (duration days) ^a	Gender	Type of IBD	Start of PD	Clinical situation at the time of PD	Treatment used	Days in TD when proposed for PD	Age (years) when proposed for PD	Time from disease onset to start of PD (years)	Type of PD	Review (months)	NI contrib. (years)
5,941	3 (789)	Male	UC	TPD exhausted	Total colectomy due to lack of symptom control. Ileostomy	5-ASA, STER, AZA, IFX, ADA, VDZ, UST, TOFA	530	42.9	15.6	APD	18	24.6
5,120	0 (0)	Male	UC	Proposal after extension	Colectomy for refractory UC. Colon adenocarcinoma IV (liver METS). Ileostomy.	RB, STER, LCA, IFX, ADA	548	32.9	15.1	APD	6	1.6
9,229	0 (0)	Female	CD	Rating deferment exhausted	Primary biliary cirrhosis. Major depressive disorder.	OB	725	44.8	26.1	TPD	24	9.5
7,899	2 (19)	Male	CD	Rating deferment exhausted	Uncontrolled disease, stricturing pattern	5-ASA, STER, AZA, IFX, ADA	694	46.8	18.2	TPD	12	22.5
9,228	0 (0)	Male	CD	TPD exhausted	Ileostomy, Colostomy. Peristomal fistula.	5-ASA, STER, IFX, ADA, UST	545	34.3	15.9	TPD	12	3.6
7,834	0 (0)	Female	UC	TPD exhausted	Uncontrolled disease, pending initiation of treatment with biologics	5-ASA, STER, RB, 6-MP,	540	41.8	12.1	TPD	12	3.1
9,441	0 (0)	Female	UC	TPD exhausted	Uncontrolled disease. Waiting for response to ADA	5-ASA, STER, AZA, LCA, ADA	545	55.4	11.6	TPD	9	18.5
8,411	2 (296)	Male	UC	TPD exhausted	Uncontrolled disease. Waiting for response to ADA	5-ASA, STER, BDP, AZA, ADA	535	46.1	7.4	TPD	12	22.8
9,310	0 (0)	Female	UC	TPD exhausted	Colectomy due to lack of response to treatment	5-ASA, AZA, FK, IFX, VDZ, TOFA	541	49.5	2.3	TPD	24	11
5,300	0 (0)	Male	CD	TPD exhausted	Uncontrolled disease.	5-ASA, OB, STER, AZA	544	40.9	2.16	TPD	18	7.1

CNO: *Clasificación Nacional de Ocupaciones* [Spanish National Classification of Occupations]; CNO-5: service (restaurants and food, personal services, protection) and sales workers; CNO-7: craft and related trades workers in manufacturing and construction (except plant and machinery operators); CNO-8: plant and machine operators, and assemblers; CNO-9: elementary occupations. TD: temporary disability; MET: metastasis; UC: ulcerative colitis; CD: Crohn's disease; IBD: inflammatory bowel disease; APD: absolute permanent disability; TPD: total permanent disability; ETD: extended temporary disability; 5-ASA: 5-aminosalicylic acid; STER: oral and/or intravenous steroids; AZA: azathioprine; IFX: infliximab; ADA: adalimumab; VDZ: vedolizumab; UST: ustekinumab; TOFA: tofacitinib; RB: rectal budesonide; LCA: leucapheresis; OB: oral budesonide; 6-MP: mercaptopurine; BDP: beclomethasone dipropionate; FK: tacrolimus; NI contrib.: Spanish National Insurance contributions.

^a Related to IBD.

early and thorough assessment of the risk factors associated with work disability, with the aim of implementing appropriate strategies to mitigate the effects and promote a better quality of life for people suffering this chronic disease.

In 2019 in Spain, 12,378 TD episodes began in the special regime for self-employed workers and 182,128 in the general regime. In our series, the percentage of patients with IBD in the special regime for self-employed workers was higher than the national average. This may be due to the disabling nature of the disease, leading to the need for TD regardless of the contributory regime.¹⁴ It is important to consider this aspect when evaluating the distribution of resources and the implementation of policies that support workers affected by IBD. The duration of the TD periods in both the special regime for self-employed workers and the general regime was lower in our series compared to the provincial, regional and national averages.¹⁴ These data are similar to those analysed by Moreira.¹⁶ This indicates that, despite the complexity of IBD, patients achieved a faster recovery compared to other TD processes.

In our series, 60% of patients had a record of previous periods of TD associated with IBD, either due to a flare-up or the need for surgical treatment. All TD episodes in our study period were IBD-related; 40% of patients received treatment with systemic corticosteroids and 32% biologic therapy. Approximately half of these TD episodes required hospital admission, and 25% of the admissions were due to disease flare-ups. These data suggest the need to re-evaluate and optimise treatment regimens, as well as intensify patient monitoring.

In our series, the profile of cases that experienced a longer TD process was of patients aged over 30, with depressive anxiety disorder, who required admission to hospital and did not receive treatment with prednisone. These findings highlight the importance of early detection and appropriate management of mental health conditions in patients with IBD, since anxiety and depression have a significant impact on the progression of the disease and the duration of TD.¹⁷ Depression and anxiety are common comorbidities in IBD, with a two-way relationship. Mechanisms involve proinflammatory cytokines, vagal nerve signalling, gut dysbiosis and brain changes. Antidepressants and behavioural therapies may be effective in treating both conditions and relieving IBD symptoms.¹⁸ The need for hospitalisation may also indicate more severe cases of IBD which require more intensive medical care or even surgery and close monitoring to ensure proper recovery. Also, the lack of treatment with prednisone could suggest the need to seek other more effective long-term therapeutic options for these patients, including the consideration of biologic therapies or small molecules, which have shown promising results in the control of IBD. However, the onset of action of these therapeutic modalities is relatively longer than that of steroids.¹⁹ It is essential to address these risk factors in order to avoid longer TD and to design comprehensive management strategies that promote a prompt recovery and improve the quality of life of patients affected by IBD. Moreover, further research is required to fully understand the interaction between IBD, anxiety-depressive disorders and treatment response, in order to help develop more per-

sonalised and effective approaches to the care of these patients.

In terms of costs, IBD imposes a significant burden on the healthcare system.^{20–22} Holko et al.²³ assessed the cost of absenteeism and presenteeism at work, and of informal care, which was measured by the time spent looking after patients by family and friends. The average annual costs of absenteeism, presenteeism and informal care respectively varied from €1,253 (Bulgaria) to €7,915 (Spain), from €2,149 (Bulgaria) to €14,524 (Belgium), and from €1,729 (Poland) to €12,063 (Italy). Compared to patients with active disease, in those with IBD in remission, indirect costs were 54% lower for presenteeism ($p < 0.001$) and 75% lower for absenteeism and informal care ($p < 0.001$). In our series, the average expenditure per worker during the TD period was €745.5 (IQR 231–2,608.2), corresponding to 0.82 (IQR 0.25–2.89) times the interprofessional minimum wage for 2019. It is essential to take into account the average daily expenditure associated with the disease to understand the magnitude of this economic impact. Careful cost assessment and efficient resource management are required to ensure adequate care for IBD patients while minimising costs to the healthcare system.

The importance of psychological care for patients with IBD is also evident in our results. A high percentage of patients with mental health problems highlights the need for psychological care as an integral part of disease management.^{24–26} Multidisciplinary teams that include mental health experts play a crucial role in the emotional support and psychological well-being of IBD patients, and can at the same time contribute to a faster recovery and a better quality of life.

In addition to addressing the duration of TD, it is important to consider the impact of IBD on patients' quality of life. Multiple studies have shown an association between chronic disease and decreased quality of life. Therefore, comprehensive care that addresses both the medical and the psychological and social aspects of IBD is required to improve patients' quality of life and promote their long-term well-being.²⁷

In 2019, 0.2% of APD and 0.6% of TPD in the province corresponded to patients with IBD. Regarding these PD processes, in our series, five cases were due to a post-surgical situation (colectomy or colostomy). These PD were reviewed at a mean of six to 18 months based on data suggesting or predicting possible improvement in the PD situation after surgery.⁸ In a series of 214 patients with IBD, 12 (4.1%) received PD benefits; this rate was higher than that of the general working population of the province, OR 2.07 (95% CI: 1.16–3.72; $p = 0.014$).²⁸ In our series we did not find factors related to PD. In their systematic review, Leso et al.²⁹ suggest several factors for predicting work disability, although with heterogeneous results. Having CD was noted as a significantly better predictor of PD compared to UC, perhaps related to the more severe course of the disease. IBD activity and severity, also indicated by the need for surgical treatment and comorbidities, were associated with a significantly increased risk of PD, although the exact role of other variables such as specific symptoms (faecal incontinence) or disease pattern remains to be clarified. Among demographic factors, a certain predisposition in females has been suggested.

Finally, it is worth mentioning the advent of biological treatments and small molecules as disease course modifiers.³⁰ These advances have been shown to reduce the need for surgery and could have a positive impact by simultaneously reducing the time required for long-term sick leave. However, further research is required to fully evaluate its effectiveness and determine its contribution to shorter TD duration in patients with IBD.

The limitations of the present study are its retrospective nature and a possible selection bias due to the coding (ICD-9 or ICD-10) of the disease that led to the TD. However, one of its strengths is that, this is the first study conducted here in Spain to analyse in detail the timing and causes of TD in patients with IBD.

Conclusions

IBD is a serious chronic disease with a high impact on patients' TD. Ongoing assessment and monitoring by multidisciplinary teams including mental health experts is needed. It is essential to identify the risk factors associated with the duration of TD (age over 30 years, anxiety-depressive disorder and hospital admission) and work on mitigating them. The implementation of new treatments and appropriate support for patients can help reduce the duration of TD. In addition, there is a need to assess the costs associated with IBD and develop effective strategies to optimise patient care and healthcare system resources.

Author contributions

Conceptualisation, SNR-C., RM-M., and VMN-L.; methodology, VMN-L. and RM-M.; validation, SNR-C., RM-M. and VMN-L.; formal analysis, VMN-L.; investigation, SNR-C., MBR-G. and LR; data curation, SNR-C. and VMN-L.; original draft preparation, SNR-C., VMN-L. and JL.C.-M.; writing, review, and editing, SNR-C., MBR-G., LR, JL.C.-M., RM-M. and VMN-L.; project administration, VMN-L.

Conflicts of interest

The authors declare that they have no conflicts of interest in relation to this study.

References

- Vant M. Environmental factors in the epidemiology of inflammatory bowel disease. In: Baumgart D, editor. *Crohn's Disease and Ulcerative Colitis: From Epidemiology and Immunobiology to a Rational Diagnostic and Therapeutic Approach*. Springer; 2012. p. 17–38.
- Chaparro M, Garre A, Núñez Ortiz A, Diz-Lois Palomares M, Rodríguez C, Riestra S, et al. Incidence, clinical characteristics and management of inflammatory bowel disease in Spain: large-scale epidemiological study. *J Clin Med*. 2021; 10(13):2885.
- Puig L, Ruiz de Morales JG, Dauden E, Andreu JL, Cervera R, Adán A, et al. [Prevalence of ten Immune-mediated inflammatory diseases (IMID) in Spain]. *Rev Esp Salud Publica*. 2019;93:e201903013.
- Ernest & Young. In: *Enfermedad Inflamatoria Intestinal: situación actual y retos asistenciales*; 2016.
- Guardiola J, Marín L, P Gisbert J, Gomollón F, Cohen J, Conde C. Mejora de la atención al paciente con enfermedad inflamatoria intestinal: Proyecto KOAN. *Rev Esp Econ Salud*. 2019;14(4):806–21.
- Fernández García A, Gálvez González AM, Villar Valdés R. Fundamentos de los estudios de costo de la enfermedad: valoración actual del costo del glaucoma. *Rev Cuba Med Gen Integral*. 2010;26.
- Netjes JE, Rijken M. Labor participation among patients with inflammatory bowel disease. *Inflamm Bowel Dis*. 2013;19(1):81–91.
- Büsch K, Da Silva SA, Holton M, Rabacow FM, Khalili H, Ludvigsson JF. Sick leave and disability pension in inflammatory bowel disease: A systematic review. *J Crohns Colitis*. 2014;8(11):1362–77.
- Incapacidad temporal y enfermedad inflamatoria [Internet]. 2015. Available from: <https://www.in-pacient.es/noticia/incapacidad-laboral-y-enfermedad-inflamatoriaintestinal/>.
- Alba Jurado M. Mapa de la incapacidad temporal en España. Málaga: Análisis de los factores implicados. Tesis doctoral; 2021.
- Silverberg MS, Satsangi J, Ahmad T, Arnott IDR, Bernstein CN, Brant SR, et al. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. *Can J Gastroenterol J Can Gastroenterol*. 2005;19 Suppl A:5A–36A.
- Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377–81.
- Real Decreto 1591/2010, de 26 de noviembre, por el que se aprueba la Clasificación Nacional de Ocupaciones 2011. [Internet]. Dec 17, 2010 p. 104040–104060. Available from: https://www.boe.es/diario_boe/txt.php?id=BOE-A-2010-19389.
- Informe 2019. Seguridad social. Contingencias comunes. Régimen general. R.E. Autónomos. [Internet]. 2020. Available from: <https://www.seg-social.es/wps/portal/wss/internet/EstadisticasPresupuestosEstudios/Estadisticas/EST45/EST46/66ba032d-8ed4-484a-a1f6-9a6cfd12c6e6>.
- Spekhorst LM, Oldenburg B, van Bodegraven AA, de Jong DJ, Imhann F, van der Meulen-de Jong AE, et al. Prevalence of- and risk factors for work disability in Dutch patients with inflammatory bowel disease. *World J Gastroenterol*. 2017;23(46):8182–92.
- Moreira Alonso MC. Available from: <http://hdl.handle.net/2445/7081>, 2009.
- Bisgaard TH, Poulsen G, Allin KH, Keefer L, Ananthakrishnan AN, Jess T. Longitudinal trajectories of anxiety, depression, and bipolar disorder in inflammatory bowel disease: a population-based cohort study. *EClinicalMedicine*. 2023;59: 101986.
- Bisgaard TH, Allin KH, Keefer L, Ananthakrishnan AN, Jess T. Depression and anxiety in inflammatory bowel disease: epidemiology, mechanisms and treatment. *Nat Rev Gastroenterol Hepatol*. 2022;19(11):717–26.
- Vasudevan A, Gibson PR, van Langenberg DR. Time to clinical response and remission for therapeutics in inflammatory bowel diseases: What should the clinician expect, what should patients be told? *World J Gastroenterol*. 2017;23(35): 6385–402.
- Khalili H, Everhov ÅH, Halfvarson J, Ludvigsson JF, Askling J, Myrelid P, et al. Healthcare use, work loss and total costs in incident and prevalent Crohn's disease and ulcerative colitis:

- results from a nationwide study in Sweden. *Aliment Pharmacol Ther.* 2020;52(4):655–68.
21. Mandel MD, Bálint A, Lovász BD, Gulácsi L, Strbák B, Golovics PA, et al. Work disability and productivity loss in patients with inflammatory bowel diseases in Hungary in the era of biologics. *Eur J Health Econ HEPAC Health Econ Prev Care.* 2014;15 Suppl 1:S121–128.
 22. Walter E, Hausberger SC, Groß E, Siebert U. Health-related quality of life, work productivity and costs related to patients with inflammatory bowel disease in Austria. *J Med Econ.* 2020;23(10):1061–71.
 23. Holko P, Kawalec P, Sajak-Szczerba M, Avedano L, Mossakowska M. Indirect costs of inflammatory bowel diseases: a comparison of patient-reported outcomes across 12 European countries. *Inflamm Bowel Dis.* 2023;29(5):752–62.
 24. Neuendorf R, Harding A, Stello N, Hanes D, Wahbeh H. Depression and anxiety in patients with Inflammatory Bowel Disease: a systematic review. *J Psychosom Res.* 2016;87:70–80.
 25. De Boer AGEM, Bennebroek Evertsz' F, Stokkers PC, Bockting CL, Sanderman R, Hommes DW, et al. Employment status, difficulties at work and quality of life in inflammatory bowel disease patients. *Eur J Gastroenterol Hepatol.* 2016;28(10):1130–6.
 26. Argollo M, Gilardi D, Peyrin-Biroulet C, Chabot JF, Peyrin-Biroulet L, Danese S. Comorbidities in inflammatory bowel disease: a call for action. *Lancet Gastroenterol Hepatol.* 2019;4(8):643–54.
 27. Christiansen LK, Lo B, Bendtsen F, Vind I, Vester-Andersen MK, Burisch J. Health-related quality of life in inflammatory bowel disease in a Danish population-based inception cohort. *United Eur Gastroenterol J.* 2019;7(7):942–54.
 28. Ramos A, Calvet X, Sicilia B, Vergara M, Figuerola A, Motos J, et al. IBD-related work disability in the community: prevalence, severity and predictive factors. A cross-sectional study. *United Eur Gastroenterol J.* 2015;3(4):335–42.
 29. Leso V, Gervetti P, Macrini MC, Russo F, Iavicoli I. Inflammatory bowel diseases and work disability: a systematic review of predictive factors. *Eur Rev Med Pharmacol Sci.* 2021;25(1):165–81.
 30. Martín-Masot R, Ortiz Pérez P, Torcuato Rubio E, Blasco Alonso J, Herrador López M, Gallego Fernández C, et al. The new molecules are changing the course of pediatric chronically active ulcerative colitis: a series of pediatric cases. *JPGN Rep.* 2021;2(3):e100.