World Journal of Gastroenterology

Submit a Manuscript: https://www.f6publishing.com

World J Gastroenterol 2019 October 14; 25(38): 5862-5882

DOI: 10.3748/wjg.v25.i38.5862

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

ORIGINAL ARTICLE

Observational Study

Quality of life, work productivity impairment and healthcare resources in inflammatory bowel diseases in Brazil

Rogerio S Parra, Julio MF Chebli, Heda MBS Amarante, Cristina Flores, Jose ML Parente, Odery Ramos, Milene Fernandes, Jose JR Rocha, Marley R Feitosa, Omar Feres, Antonio S Scotton, Rodrigo B Nones, Murilo M Lima, Cyrla Zaltman, Carolina D Goncalves, Isabella M Guimaraes, Genoile O Santana, Ligia Y Sassaki, Rogerio S Hossne, Mauro Bafutto, Roberto LK Junior, Mikaell AG Faria, Sender J Miszputen, Tarcia NF Gomes, Wilson R Catapani, Anderson A Faria, Stella CS Souza, Rosana F Caratin, Juliana T Senra, Maria LA Ferrari

ORCID number: Rogério Serafim Parra (0000-0002-5566-9284); Júlio Maria Chebli (0000-0003-1527-0663); Heda MBS Amarante (0000-0001-7449-1138); Cristina Flores (0000-0003-1623-4525); José Miguel Luz Parente (0000-0003-4563-2784); Odery Ramos (0000-0002-9730-6860); Milene Fernandes (0000-0002-6603-5092); Jose JR da Rocha (0000-0001-7118-0545); Marley R Feitosa (0000-0002-4440-2023); Omar Feres (0000-0003-3593-0526); António S Scotton (0000-0001-9247-0904); Rodrigo Bremer Nones (0000-0002-6256-2629); Murilo Moura Lima (0000-0002-0101-3781); Cyrla Zaltman (0000-0002-5236-6501); Carolina D Gonçalves (0000-0003-3663-4390); Isabella Miranda Guimaraes (0000-0003-3401-6580); Genoile Oliveira Santana (0000-0001-5936-9791); Ligia Yukie Sassaki (0000-0002-7319-8906); Rogerio Saad-Hossne (0000-0002-8166-0304); Mauro Bafutto (0000-0001-5585-3957); Roberto Luiz Kaiser Junior (0000-0003-1952-1255); Mikaell Alexandre Gouvea Faria (0000-0003-4121-0306); Sender J Miszputen (0000-0003-4487-5004); Tarcia NF Gomes (0000-0003-2897-0327); Wilson R Catapani (0000-0002-0412-2182); Anderson A Faria (0000-0002-7962-7396); Stella

Rogerio S Parra, Jose JR Rocha, Marley R Feitosa, Omar Feres, Department of Surgery and Anatomy, Ribeirao Preto Medical School, University of Sao Paulo, Ribeirao Preto, SP 14049-900, Brazil

Julio MF Chebli, Inflammatory Bowel Disease Center, Federal University of Juiz de Fora, Juiz de Fora, MG 36036-247, Brazil

Heda MBS Amarante, Hospital de Clinicas da Universidade Federal do Parana, Curitiba, PR 80060-900, Brazil

Cristina Flores, Hospital de Clinicas de Porto Alegre, Porto Alegre – RS 90035-007, Brazil

Jose ML Parente, Universidade Federal do Piaui, Teresina, PI 64073-500, Brazil

Odery Ramos, Hospital de Clínicas da Universidade Federal do Parana, Curitiba, PR 80060-900, Brazil

Milene Fernandes, CTI Clinical Trial & Consulting Services, Lisbon 1070-274, Portugal

Antonio S Scotton, CMIP Centro Mineiro de Pesquisa, Juiz de Fora, MG 36010-570, Brazil

Rodrigo B Nones, Hospital Nossa Senhora das Gracas, Curitiba, PR 80810-040, Brazil

Murilo M Lima, Hospital Universitario da Universidade Federal do Piaui, Teresina, PI 64049-550, Brazil

Cyrla Zaltman, Carolina D Gonçalves, Isabella M Guimaraes, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ 21941-913, Brazil

Genoile O Santana, Universidade do Estado da Bahia, - Salvador, BA 41150-000, Brazil

Ligia Y Sassaki, Rogerio S Hossne, Department of Internal Medicine, Botucatu Medical School at Sao Paulo State University (UNESP), Botucatu, SP 18618-687, Brazil

Mauro Bafutto, Instituto Goiano de Gastroenterologia e Endoscopia Digestiva Ltda, Goiania, GO 74535-170, Brazil

Roberto LK Junior, Mikaell AG Faria, Kaiser Clinica, Sao Jose do Rio Preto, SP 15015-110, Brazil

Cristina S Souza (0000-0002-1957-3111); Rosana Fusaro Caratin (0000-0003-0922-8530); Juliana Senra (0000-0001-6787-806X); Maria de Lourdes Abreu Ferrari (0000-0002-2122-5538).

Author contributions: Parra RS, Chebli J, Amarante HMBS, Flores C, Parente JML, Ramos O, Fernandes M, Scotton AS, Zaltman C, Santana GO, Sassaki LY, Bafutto M, Junior RLK, Miszputen SJ, Catapani WR and Ferrari ML provided substantial contributions to the concept and design of the study; Parra RS, Chebli J, Amarante HMBS, Flores C, Parente JML, Ramos O, Scotton AS, Zaltman C, Santana GO, Sassaki LY, Bafutto M, Junior RLK, Miszputen SJ, Catapani WR and Ferrari ML contributed for the acquisition of data; All authors contributed to the analysis and interpretation of data, revision of the manuscript for important intellectual content, granted final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Supported by Takeda Pharmaceuticals Brazil.

Institutional review board statement: The study protocol was reviewed and approved by the Ethics Committees of the participant centers.

Informed consent statement: All study participants provided written informed consent prior to study enrollment.

Conflict-of-interest statement: Parra RS has received fees for serving as a speaker and/or an advisory board member for AbbVie, Ferring Pharmaceuticals, Janssen, UCB Pharma and Takeda. Saad-Hossne R has received fees for serving as a speaker for AbbVie, Janssen, Pfizer and Takeda. Miszputen S has received fees for serving as a speaker and/or a consultant for Farmoquimica, Janssen and Marjan. He has received research funding from Ache, Roche and Takeda. Fernandes M is an employee of Eurotrials, now part of CTI, a CRO that provides services for pharmaceutical laboratories. Catapani WR has received fees for serving as a speaker and/or an advisory board member for Janssen and Takeda. Sassaki LY has received fees for

Sender J Miszputen, Escola Paulista de Medicina, Sao Paulo, SP 04023-900, Brazil

Tarcia NF Gomes, UNIFESP, Disciplina de Gastroenterologia, Sao Paulo, SP 04040-002, Brazil

Wilson R Catapani, Faculdade de Medicina do ABC, Santo Andre, SP 09060-870, Brazil

Anderson A Faria, Stella CS Souza, Maria LA Ferrari, Faculdade de Medicina UFMG, Belo Horizonte, MG, 30130-100, Brazil

Rosana F Caratin, Juliana T Senra, Takeda Pharmaceuticals Brazil, Sao Paulo, SP 04709-011, Brazil

Corresponding author: Rogerio Serafim Parra, MD, PhD, Assistant Professor, Department of Surgery and Anatomy, Ribeirao Preto Medical School, University of Sao Paulo, Ribeirao Preto, SP 14049-900, Brazil. rsparra@hcrp.usp.br
Telephone: +55-16-36022509

Abstract

BACKGROUND

Inflammatory bowel diseases (IBD) have been associated with a low quality of life (QoL) and a negative impact on work productivity compared to the general population. Information about disease control, patient-reported outcomes (PROs), treatment patterns and use of healthcare resources is relevant to optimizing IBD management.

AIM

To describe QoL and work productivity and activity impairment (WPAI), treatment patterns and use of healthcare resources among IBD patients in Brazil.

METHODS

A multicenter cross-sectional study included adult outpatients who were previously diagnosed with moderate to severe Crohn's disease (CD) or ulcerative colitis (UC). At enrolment, active CD and UC were defined as having a Harvey Bradshaw Index ≥ 8 or a CD Activity Index ≥ 220 or calprotectin > 200 μg/g or previous colonoscopy results suggestive of inadequate control (per investigator criteria) and a 9-point partial Mayo score ≥ 5, respectively. The PRO assessment included the QoL questionnaires SF-36 and EQ-5D-5L, the Inflammatory Bowel Disease Questionnaire (IBDQ), and the WPAI questionnaire. Information about healthcare resources and treatment during the previous 3 years was collected from medical records. Chi-square, Fisher's exact and Student's *t*-/Mann-Whitney *U* tests were used to compare PROs, treatment patterns and the use of healthcare resources by disease activity ($\alpha = 0.05$).

RESULTS

Of the 407 patients in this study (CD/UC: 64.9%/35.1%, mean age 42.9/45.9 years, 54.2%/56.6% female, 38.3%/37.1% employed), 44.7%/25.2% presented moderate-to-severe CD/UC activity, respectively, at baseline. Expressed in median values for CD/UC, respectively, the SF-36 physical component was 46.6/44.7 and the mental component was 45.2/44.2, the EQ-visual analog scale score was 80.0/70.0, and the IBDQ overall score was 164.0/165.0. Moderate to severe activity, female gender, being unemployed, a lower educational level and lower income were associated with lower QoL ($P < 0.05$). Median work productivity impairment was 20% and 5% for CD and UC patients, respectively, and activity impairment was 30%, the latter being higher among patients with moderate to severe disease activity compared to patients with mild or no disease activity (75.0% *vs* 10.0%, $P < 0.001$). For CD/UC patients, respectively, 25.4%/2.8% had at least one surgery, 38.3%/19.6% were hospitalized, and 70.7%/77.6% changed IBD treatment at least once during the last 3 years. The most common treatments at baseline were biologics (75.3%) and immunosuppressants (70.9%) for CD patients and 5-ASA compounds (77.5%) for UC patients.

CONCLUSION

Moderate to severe IBD activity, especially among CD patients, is associated with a substantial impact on QoL, work productivity impairment and an increased

serving as a speaker for AbbVie and Takeda. Gomes TNF has received research funding from *Coordenacao de Aperfeicoamento de Pessoal de Nivel Superior* (CAPES) and Takeda. She has received fees for serving as a speaker for Janssen. Chebli JMF has received fees for serving as a speaker for AbbVie, Janssen, UCB Pharma and Takeda. Senra JT and Caratin RF are employees of Takeda Pharmaceuticals Brazil. Nones RB has received fees for serving as a speaker for AbbVie, Ferring Pharmaceuticals, Janssen, Nestle, Novartis, Pfizer, UCB Pharma and Takeda. Parente JML has received fees for serving as a speaker for Takeda. Ferrari MLA has received fees for serving as a speaker and/or advisory board member for AbbVie, Ferring Pharmaceuticals, Janssen, UCB Pharma, and Takeda. Santana GO has received fees for serving as a speaker for Takeda, AbbVie, Janssen, and UCB Pharma. She has received research funding from Celgene and Roche. She has received fees for serving as an advisory board member for Janssen. Rocha JJR has received fees for serving as a speaker for Nestle. Feitosa MR has received fees for serving as a speaker for AbbVie and Janssen. Scotton AS has received fees for serving as a speaker for Janssen, Novartis, AbbVie, MSD, and EMS. He has received research funding from Janssen, Novartis, AbbVie, Roche, Pfizer, Bristol, Lilly, Novo Nordisk, Anthera, AstraZeneca, GSK, UCB, Sanofi, Takeda, Parexel, IQVIA, PPD, PRA, ICON, INP Research, Covance, and In Trials. Flores C has received fees for serving as a speaker for Janssen, Takeda, and AbbVie. She has received fees for serving as an advisory board member for Janssen. Zaltman C has received fees for serving as a speaker for UCB, Janssen, Takeda, and AbbVie. She has received research funding from AbbVie, Takeda, and Janssen. Bafutto M has received fees for serving as a speaker for Takeda, AbbVie, Janssen, UCB and Farmoquimica. He has received fees for serving as an advisory board member for AbbVie and Janssen. No conflict-of-interest: Omar Feres, Murilo Moura Lima, Roberto Luiz Kaiser Junior, Carolina Dias Gonçalves, Stella Cristina Silva de Souza, Anderson Antonio de Faria, Isabella de Miranda Guimaraes, Heda Maria Barska dos Santos Amarante, Mikaell Alexandre Gouvea Faria, Odery Ramos Junior.

Data sharing statement: No additional data are available.

number of IBD surgeries and hospitalizations in Brazil.

Key words: Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Quality of life; Healthcare resources

Core tip: In a large multicenter sample of patients with ulcerative colitis or Crohn's disease (CD), disease activity, female gender, unemployment, and lower education and income were associated with a poorer quality of life. Approximately one-third of patients had some work and activity impairment, the latter increasing with disease activity. CD patients used more health resources, with 25.4% having at least one surgery and 38.3% being hospitalized in the previous 3 years. Inflammatory bowel disease prevalence is increasing, and health services should be prepared to provide an adequate response, including optimal therapies, to manage the care of such patients.

Citation: Parra RS, Chebli JMF, Amarante HMBS, Flores C, Parente JML, Ramos O, Fernandes M, Rocha JJR, Feitosa MR, Feres O, Scotton AS, Nones RB, Lima MM, Zaltman C, Goncalves CD, Guimaraes IM, Santana GO, Sassaki LY, Hossne RS, Bafutto M, Junior RLK, Faria MAG, Miszputen SJ, Gomes TNF, Catapani WR, Faria AA, Souza SCS, Caratin RF, Senra JT, Ferrari MLA. Quality of life, work productivity impairment and healthcare resources in inflammatory bowel diseases in Brazil. *World J Gastroenterol* 2019; 25(38): 5862-5882
URL: https://www.wjgnet.com/1007-9327/full/v25/i38/5862.htm
DOI: https://dx.doi.org/10.3748/wjg.v25.i38.5862

INTRODUCTION

Crohn's disease (CD) and ulcerative colitis (UC) are chronic inflammatory bowel diseases (IBD) with periods of remission and relapse[1,2]. The incidence and prevalence of IBD have been increasing around the world, particularly in developing countries[3-7]. Furthermore, the impact on patients' quality of life (QoL) can be relevant when considering the onset at usually younger ages and the severity of IBD signs and symptoms, such as abdominal pain, rectal bleeding, diarrhea, and fatigue[1,8,9].

QoL refers to a person's physical functioning, social and emotional well-being, ability to work and freedom from disease symptoms, and has been reported to be significantly lower in IBD patients compared to the general population[10]. In 2007, a European survey observed that 75.6% of IBD patients reported having symptoms that interfered with their ability to enjoy leisure activities, and almost 70% stated that their symptoms negatively affected work performance[11]. Patients with an active disease usually have poor QoL[2,12], but other studies[13,14] have observed that stress level, anxiety or depression, female gender, and fatigue can also contribute to poor QoL in IBD patients. Several studies[12,15,16] have also shown that IBD impacts work productivity.

Knowing the distribution of IBD features such as disease control, patient-reported outcomes (PRO) and treatment patterns is of paramount relevance when optimizing IBD management and improving QoL[17,18]. Data from Latin American countries are needed, although the few studies available seem to indicate that the IBD burden is relevant[19]. In Brazil, epidemiological information about IBD is also scarce[6,9,12,20,21]. The Real-world Data of Moderate to Severe Inflammatory Bowel Disease in Brazil (RISE BR) study was a noninterventional study designed to evaluate disease control and treatment patterns and to compare the burden of disease and QoL in patients with moderate to severe IBD activity *vs* those with mild or no activity. In this work, we describe QoL and work and activity impairment experienced by IBD patients enrolled in the RISE BR study. In addition, we characterize treatment patterns and the use of healthcare resources in this setting.

STROBE statement: The authors have read the STROBE Statement-checklist of items, and the manuscript was prepared and revised according to the STROBE Statement-checklist of items.

Manuscript source: Unsolicited manuscript

Received: June 12, 2019
Peer-review started: June 12, 2019
First decision: July 22, 2019
Revised: August 30, 2019
Accepted: September 13, 2019
Article in press: September 13, 2019
Published online: October 14, 2019

P-Reviewer: Can G, Filik L, Yang MS, Zhang L
S-Editor: Gong ZM
L-Editor: A
E-Editor: Zhang YL

MATERIALS AND METHODS

Study design and participants

The RISE BR study was a multicenter, noninterventional study with a cross-sectional evaluation (baseline) and a 3-year retrospective data collection. In the study reported here, we recorded PROs at baseline and assessed the use of IBDs treatment and healthcare resources in the previous 3 years (*i.e.*, baseline-3 years). The study protocol was reviewed and approved by the Ethics Committees of the participant centers. All study participants provided written informed consent prior to study enrollment (ClinicalTrials.gov Identifier: NCT02822235).

Patients were enrolled consecutively from October 2016 to February 2017, when attending scheduled clinical appointments at one of the 14 reference IBD hospitals distributed across Brazilian geographical regions. Eligible patients were ≥ 18 years old, with a diagnosis, by a gastroenterologist, of moderate-to-severe CD or UC for at least 6 mo. Patients with indeterminate/unclassified colitis, who were hospitalized at baseline or who had participated in an experimental study within the 3 years prior to baseline were excluded.

Study variables

Sociodemographic data (age, gender, educational level and professional status), smoking habits, family history of IBD and extraintestinal manifestations were collected from medical records. Other variables included time since IBD diagnosis, location and severity/behavior of UC and CD (Montreal classification) and steroid behavior (dependent or refractory).

CD activity at baseline was evaluated with the Harvey Bradshaw Index (HBI)[22] and/or the Crohn's Disease Activity Index (CDAI)[23], according to local clinical practice. Moderately to severely active CD at baseline was considered when patients had an HBI ≥ 8 or a CDAI ≥ 220 or fecal calprotectin > 200 μg/g or previous colonoscopy results suggestive of inadequate control (as per investigator criteria)[22,24,25]. UC activity at baseline was assessed with the 9-point partial Mayo (pMayo) score[26] (moderate-to-severe activity: pMayo ≥ 5), according to local clinical practice[2,26].

QoL was assessed with three self-administered scales validated for the Brazilian population: The 36-item Short-Form Health Survey (SF-36)[27], the 5-dimensional EuroQoL measure (EQ-5D-5L)[28], and the Inflammatory Bowel Disease Questionnaire (IBDQ)[29]. The SF-36 evaluates eight health dimensions: Physical functioning, physical role functioning, bodily pain, general health perceptions, vitality, social role functioning, emotional role functioning, and mental health. Two summary scores (Physical Component Score and Mental Component Score) are obtained through a standardization of each dimension score and computation of aggregate scores. The component summary ranges from 0 to 100, with higher scores reflecting more a favorable health status[30-32]. The EQ-5D-5L considers five attributes (mobility, self-care, usual activity, pain/discomfort, anxiety/depression) scored with five possible levels (1-no problems, 2-slight problems, 3-moderate problems, 4-severe problems, 5-extreme problems) and a visual analog scale (VAS) where "100" indicates the best health imagined and a "0" represents the worst health imagined[2,15]. The IBDQ score comprises four domains: Bowel function, Emotional status, Systematic symptoms, and Social function[29,33]. Each IBDQ domain scores from 1 (poorest QoL) to 7 (best QoL), and the overall IBDQ score ranges from 32 to 224.

In addition, the impact of IBD on work productivity and daily activities was assessed with the Brazilian version of the Work Productivity and Activity Impairment (WPAI) questionnaire[34]. The WPAI topics are as follows: (1) If the patient was currently employed; (2) How many hours were missed due to the disease; (3) How many hours were missed for other reasons, (4) How many hours were worked; (5) To what degree did the disease affect productivity while working; and (6) To what degree did the disease affect regular activities. Based on the WPAI questionnaire, total work productivity impairment due to IBD (TWPI) was defined as the subjects' total percentage of impaired work time that resulted from both absenteeism (work time missed due to IBD) and presenteeism (impairment while working due to IBD)[16]. Total activity impairment (TAI) due to IBD was also estimated.

Utilization of healthcare resources during the previous 3 years was retrieved from medical records regarding imaging and laboratory testing, surgeries, hospitalizations, and consultations with gastroenterologists or other medical specialists. The type and duration of IBD treatment ongoing at baseline and received during the retrospective 3-year period was also collected.

Statistical analysis

The sample size was estimated for the primary objective of the RISE BR study to

estimate the prevalence of IBD activity. Hence, a sample size of 400 IBD patients was defined to allow estimates of disease activity at baseline with a 95% confidence interval (CI) and a margin of error less than 5%.

All analyses were presented by IBD type (UC or CD). Descriptive statistics were used to analyze sociodemographic, anthropometric and clinical variables. To compare QoL and WPAI according to disease activity at baseline (moderate to severe *vs*. mild or no activity), demographic characteristics and the presence of extraintestinal manifestations, the Chi-square or Fisher's exact tests were used for qualitative variables (*i.e.*, domain items) and the t-test for independent samples, the ANOVA test, the Kruskal-Wallis test or the Mann-Whitney *U* test were used for quantitative variables (*i.e.*, SF-36 domain scores or component summary scores, EQ-5D VAS, IBDQ domain scores or total score, and WPAI scores). The correlation of IBDQ scores and EQ-5D dimensions/VAS with SF-36 domain scores was determined using Spearman's correlation coefficient. There was no imputation of missing data in the study. Statistical tests were two-tailed, and significance was set at 5%. Statistical analysis was performed using SAS® (version 9.4, SAS Institute Inc., Cary).

RESULTS

Study participants and IBD characteristics

Of the 421 screened patients, 407 (96.7%) fulfilled the eligibility criteria and were included, 264 (64.9%) presented with CD and 143 (35.1%) had UC. The mean age (± standard-deviation, sd) was 42.9 ± 13.0 and 45.9 ± 13.8 years for CD and UC patients, respectively (Table 1). Most patients were female (54.2% CD and 56.6% UC patients), and over one-third were employed. The median time since the first diagnosis of CD and UC was 11.4 [range: 0.5-45.0] and 10.4 [range: 0.5-31.0] years, respectively. At baseline, CD patients had a median HBI of 2.0 [range: 0.0-37.0], a median CDAI of 137.0 [range: 25.0-495.0], and 44.7% (95%CI: 38.7-50.7%) presented moderate to severe activity. When considering UC patients, the median pMayo score was 1.0 [range: 0.0-9.0], and 25.2% (95%CI: 18.1-32.3%) presented moderate to severe activity.

QoL evaluation by IBD type and disease activity

Regarding the SF-36 results (Table 2), the median scores of the physical and mental components were 46.6 [range: 20.6-68.6] and 45.2 [range: 5.8-67.2] for CD patients and 44.7 [range: 23.4-63.8] and 44.2 [range: 7.9-65.0] for UC patients, respectively. CD patients with moderate to severe activity had significantly lower scores in all SF-36 domains except for the vitality domain and had a lower physical component score (median: 44.0 *vs* 48.6, $P < 0.001$) and mental component score (median: 42.3 *vs*. 48.4, $P = 0.022$) compared to CD patients with mild or no activity. For UC patients, those with moderate to severe activity also presented lower SF-36 scores in all domains, and both the physical component score (median: 40.5 *vs* 46.2, $P = 0.007$) and mental component score (median: 35.0 *vs* 46.6, $P < 0.001$) were lower than those of UC patients with mild or no activity.

The median [range] EQ-VAS scores for CD and UC patients were 80.0 [5.0-100.0] and 70.0 [0.0-100.0], respectively (Table 2). The majority of CD and UC patients had pain/discomfort (66.9% and 78.7%, respectively), anxiety/depression (63.9% and 63.8%), and problems with conducting their usual activities (52.5% and 53.2%). CD patients with moderate to severe activity had lower EQ-VAS scores (median: 70.0 *vs* 80.0, $P = 0.003$), and more patients reported problems of pain/discomfort ($P = 0.036$) and anxiety/depression ($P = 0.039$) compared to CD patients with mild or no activity. UC patients with moderate to severe activity had lower EQ-VAS scores (median: 50.0 *vs* 80.0, $P < 0.001$), and more patients reported problems in usual activities ($P = 0.009$) and pain/discomfort ($P = 0.012$) compared to UC patients with mild or no activity.

In both IBD types, EQ-VAS scores, as well as the EQ-5D dimensions, were statistically correlated with all SF-36 domains and component summary measures, except for the self-care and mental health dimensions in UC patients (Figure 1). Related dimensions presented larger coefficients, such as physical functioning in SF-36 and mobility in EQ-5D (CD: $r_s = -0.60$ and UC: $r_s = -0.69$) or body pain in SF-36 and pain/discomfort in EQ-5D (CD: $r_s = -0.64$ and UC: $r_s = -0.66$).

The median overall scores of the IBDQ for CD and UC patients were 164.0 and 165.0, respectively (Table 2). The lowest score was obtained for the systemic symptoms' domain (median: 4.8 for both CD and UC patients), and the highest score was observed for the bowel symptoms domain (median: 5.7/5.4 for CD/UC patients, respectively). In both IBD types, patients with moderate to severe activity at baseline presented statistically lower median scores in all IBDQ domains and overall score compared to patients with mild or no activity (CD: 153.5 *vs* 178.0, $P < 0.001$ and UC:

Table 1 Sociodemographic characteristics and clinical features of included patients

	CD patients (*n* = 264)	UC patients (*n* = 143)
Age (yr), mean ± SD	42.9 ± 13.0	45.9 ± 13.8
Female	143 (54.2)	81 (56.6)
Educational level		
Primary school	55 (26.6)	38 (38.8)
Secondary school	83 (40.1)	37 (37.7)
Higher education	69 (33.3)	23 (23.5)
Missing	57	45
Professional situation		
Employed	101 (44.3)	53 (42.7)
Unemployed	61 (26.8)	33 (26.6)
Student	10 (4.4)	5 (4.0)
Retired	30 (13.2)	15 (12.1)
Other	26 (11.4)	18 (14.5)
Missing	36	19
Current smokers[1]	24 (9.9)	3 (2.3)
Missing	22	11
Time since IBD diagnosis (yr), median [range]	10.0 [0.5-45.0]	10.0 [0.5-31.0]
Time since moderate-to-severe diagnosis (yr), median [range]	6.0 [0.5-30.0]	5.0 [0.5-25.0]
Steroid response[2]		
Steroid-dependent	31 (14.8)	23 (19.3)
Steroid-refractory	16 (7.7)	11 (9.2)
Not applicable (no previous use)	87 (41.6)	36 (30.3)
Unknown	75 (35.9)	49 (41.2)
Missing	55	24
Any extraintestinal manifestations	54 (37.8)	30 (38.0)
Family IBD history	33 (12.5)	15 (10.5)
Moderately to severely active disease at baseline[3]	118 (44.7)	36 (25.2)
UC location [*Montreal classification*]		
E1- distal UC	--	43 (30.1)
E2- left-sided	--	26 (18.2)
E3- pancolitis	--	74 (51.7)
UC severity [Montreal classification]		
S0- asymptomatic	--	57 (39.9)
S1- mild UC	--	32 (22.4)
S2- moderate UC	--	40 (28.0)
S3- severe UC	--	14 (9.8)
CD location [Montreal classification]		
L1- ileal	67 (25.4)	--
L2- colonic	42 (15.9)	--
L3- ileocolonic	150 (56.8)	--
L4- upper GI tract disease	17 (6.4)	--
CD behavior [Montreal classification]		
B1- Nonstricturing/nonpenetrating	58 (22.0)	--
B2- Stricturing	110 (41.7)	--
B3- Penetrating	91 (34.5)	--
Perianal disease	105 (39.8)	--
Ileal surface involved ≥ 1 m [*n* = 201]	38 (18.9)	--

Data are shown as *n* (%), except where otherwise mentioned.
[1]Patients were smoking at baseline and has smoked 100 cigarettes in his/her lifetime.
[2]Steroid-dependent disease: patients who either (1) Were unable to reduce steroids below the equivalent of prednisolone 10 mg/d within 3 mo of starting steroids, without recurrent disease, or (2) Had a relapse within 3 mo of stopping glucocorticoids. Steroid-refractory disease: active disease despite prednisolone up to 0.75 mg/kg/d over 4 wk.
[3]Moderate-to-severe activity at baseline was defined as pMayo ≥ 5 (UC) and having HBI ≥ 8 or CDAI ≥ 220 (CD). IBD: Inflammatory bowel disease; UC:

Ulcerative colitis; CD: Crohn's disease.

106.0 *vs* 178.5, $P < 0.001$). The IBDQ dimensions and overall score presented a significantly strong correlation with all SF-36 domains and component summary measures (Figure 1). The correlation coefficient of mental health in SF-36 and emotional health in IBDQ was higher than 0.8 (CD: $r_s = 0.81$ and UC: $r_s = 0.84$).

QoL vs. demographic and clinical characteristics

The SF-36 mental component score was statistically higher among CD/UC male and employed subjects, CD patients aged ≥ 60 years and UC patients with higher income (Table 3). The SF-36 physical component score was statistically higher among CD/UC male, employed subjects and those with higher income, and UC patients with higher education. For both IBD types, the EQ-VAS score was statistically higher among men. The EQ-VAS score was significantly different according to the professional situation of CD patients, with employed patients presenting higher scores. The IBDQ overall score was statistically higher in CD patients who were ≥ 60 years, male, and students. Considering UC patients, higher IBDQ scores were observed in males, employed individuals and those with a higher income.

Work productivity impairment due to IBD

Considering employed patients (CD: $n = 111$, 42.0%; UC: $n = 58$, 40.8%), the median TWPI was 20.0% (CD) and 5.0% (UC) (Table 2). The median TAI was 30.0% for both CD and UC patients. CD patients with moderate to severe disease activity presented higher absenteeism (median: 4.7% *vs* 0.0%, $P = 0.009$) and TAI (median: 50.0% *vs* 20.0%, $P < 0.001$) than those with mild or no disease activity. Moderately to severely active UC patients had higher TAI (75.0% *vs* 10.0%, $P < 0.001$).

Women presented higher activity impairment due to CD than men ($P = 0.014$). Activity impairment due to CD was significantly different by age group (p=0.007) and professional situation ($P < 0.001$) (Table 4). Higher TAI due to UC was observed in women when compared to men ($P = 0.043$). TAI due to UC presented statistically significant differences by professional situation ($P = 0.001$) and by income level ($P = 0.032$) (Table 4).

Healthcare utilization

A total of 108 surgeries were performed in 67 (25.4%) CD patients over the 3-year retrospective period. The median number of surgeries per CD patient was 1.0, and most (20.4%) were anal procedures (fistulectomy) (Table 5). Seven surgeries were performed in 4 (2.8%) UC patients (median 2.0), namely, 2 (28.6%) total colectomies and 2 (28.6%) enterostomy closures, among other interventions ($n = 3$, 42.9%). No statistically significant differences were observed when comparing patients by disease activity.

Regarding IBD hospitalizations, 101 (38.3%) CD patients had a total of 168 hospitalizations (median frequency: 1.0; median duration: 6 d), and 28 (19.6%) UC patients had 43 hospitalizations (median: 1.0; mean duration: 4 days). CD patients with moderate to severe disease activity at baseline had more hospitalizations (median: 2.0 *vs* 1.0 hospitalizations/patient, $P = 0.031$) than those with mild or no disease activity; no statistically significant differences were observed for UC patients by disease activity.

CD and UC patients attended 3192 (median 11.0) and 1541 (median 10.0) medical appointments, respectively. More than 90% of consultations were with IBD specialists for both IBD types. The assessment of disease activity through common scores, such as CDAI and HBI for CD patients and Partial Mayo Score for UC patients, was not performed in most medical appointments. When comparing by disease activity, no statistically significant differences were observed regarding the number or type of consultations for both IBD types. Changes in treatment occurred in 16.4% and 22.9% of CD and UC consultations, respectively, and CD patients with moderate to severe activity had a higher proportion of medical appointments with treatment changes (18.3% *vs* 14.7%, $P = 0.005$) than those with mild or low disease activity.

A total of 5674 imaging/laboratory tests were performed by 260 CD patients (median 19.0) and 2509 by 141 UC patients (median 15.0). Hemograms were the most frequent test, followed by quantification of C-reactive protein. Colonoscopies accounted for 6.1% (CD) and 9.1% (UC) of the total tests. No statistically significant differences were observed in IBD activity at baseline.

Most surgeries (CD/UC: 44.4%/71.5%) and hospitalizations (CD/UC: 47.6%/69.8%) occurred among IBD patients < 5 years since the first diagnosis of moderate to severe disease compared to patients diagnosed 5 to 10 years or 10 or more years prior (Figure 2). In addition, UC patients diagnosed for less than 5 years

Table 2 Quality of life according to type of inflammatory bowel disease and disease activity

	CD				UC			
	Total	Moderate to severe activity	No or mild activity	*P* value	Total	Moderate to severe activity	No or mild activity	*P* value
n	263	118	145		143	36	107	
Missing value[1]	1	0	1		0	0	0	
SF-36 scores								
Physical component	46.6 [20.6-68.6]	44.0 [20.6-62.3]	48.6 [27.1-68.6]	< 0.001	44.7 [23.4-63.8]	40.5 [23.4-58.8]	46.2 [23.9-63.8]	0.007
Physical functioning	75.0 [10.0-100.0]	70.0 [10.0-100.0]	85.0 [15.0-100.0]	< 0.001	70.0 [0.0-100.0]	55.0 [0.0-100.0]	77.5 [0.0-100.0]	0.043
Physical role	68.8 [0.0-100.0]	50.0 [0.0-100.0]	75.0 [0.0-100.0]	< 0.001	59.4 [0.0-100.0]	40.6 [0.0-100.0]	75.0 [0.0-100.0]	< 0.001
Body pain	52.0 [0.0-100.0]	51.0 [0.0-100.0]	62.0 [10.0-100.0]	< 0.001	51.0 [0.0-100.0]	31.0 [0.0-100.0]	60.5 [0.0-100.0]	0.001
General health	52.0 [0.0-100.0]	46.0 [0.0-100.0]	57.0 [10.0-100.0]	< 0.001	51.0 [5.0-100.0]	31.0 [5.0-100.0]	55.0 [5.0-100.0]	< 0.001
Mental component	45.2 [5.8-67.2]	42.3 [14.0-63.6]	48.4 [5.8-67.2]	0.022	44.2 [7.9-65.0]	35.0 [7.9-64.1]	46.6 [7.9-65.0]	< 0.001
Vitality	56.3 [0.0-100.0]	50.0 [6.3-100.0]	56.3 [0.0-100.0]	0.074	50.0 [0.0-100.0]	37.5 [0.0-93.8]	56.3 [0.0-100.0]	0.002
Social role functioning	62.5 [0.0-100.0]	50.0 [0.0-100.0]	75.0 [0.0-100.0]	0.002	62.5 [0.0-100.0]	50.0 [0.0-100.0]	62.5 [0.0-100.0]	0.002
Emotional role	75.0 [0.0-100.0]	66.7 [0.0-100.0]	79.2 [0.0-100.0]	0.012	75.0 [0.0-100.0]	45.8 [0.0-100.0]	75.0 [0.0-100.0]	0.002
Mental health	65.0 [0.0-100.0]	55.0 [0.0-100.0]	72.5 [0.0-100.0]	0.008	60.0 [0.0-100.0]	45.0 [5.0-100.0]	70.0 [0.0-100.0]	< 0.001
EQ-VAS (cm)	80.0 [5.0-100.0]	70.0 [5.0-100.0]	80.0 [15.0-100.0]	0.003	70.0 [0.0-100.0]	50.0 [0.0-100.0]	80.0 [0.0-100.0]	< 0.001
EQ-5D [no problems], *n* (%)								
Mobility	193 (73.4)	80 (67.8)	113 (77.9)	0.080[2]	85 (59.9)	17 (47.2)	68 (64.2)	0.073[2]
Self-care	225 (85.6)	95 (80.5)	130 (89.7)	0.052[2]	120 (84.5)	29 (80.6)	91 (85.8)	0.448[2]
Usual activities	125 (47.5)	47 (39.8)	78 (53.8)	0.158[2]	66 (46.8)	10 (27.8)	56 (53.3)	0.009[2]
Pain/discomfort	87 (33.1)	31 (26.3)	56 (38.6)	0.036[2]	30 (21.3)	3 (8.3)	27 (25.7)	0.012[2]
Anxiety/depression	95 (36.1)	31 (26.3)	64 (44.1)	0.039[2]	51 (36.2)	9 (25.0)	42 (40.0)	0.114[2]
IBDQ score	164.0 [50.0-224.0]	153.5 [50.0-222.0]	178.0 [57.0-224.0]	< 0.001	165.0 [47.0-224.0]	106.0 [48.0-217.0]	178.5 [47.0-224.0]	< 0.001
Bowel symptoms	5.7 [1.4-7.0]	5.3 [1.4-7.0]	6.0 [1.8-7.0]	< 0.001	5.4 [1.3-7.0]	3.7 [1.3-7.0]	6.1 [1.5-7.0]	< 0.001
Emotional health	4.8 [1.2-7.0]	4.4 [1.2-6.9]	5.3 [1.5-7.0]	0.001	4.9 [1.0-7.0]	2.9 [1.2-6.6]	5.3 [1.0-7.0]	< 0.001
Systemic symptoms	4.8 [1.0-7.0]	4.4 [1.2-7.0]	5.0 [1.0-7.0]	< 0.001	4.8 [1.0-7.0]	3.2 [1.0-7.0]	5.2 [1.0-7.0]	< 0.001
Social function	5.4 [1.2-7.0]	5.0 [1.2-7.0]	5.8 [1.4-7.0]	< 0.001	5.4 [1.2-7.0]	3.8 [1.2-7.0]	6.0 [1.2-7.0]	< 0.001
WPAI scores								
% TWPI	20.0 [0.0-100.0]	30.0 [0.0-100.0]	19.7 [0.0-100.0]	0.053	5.0 [0.0-100.0]	34.8 [0.0-100.0]	0.0 [0.0-100.0]	0.082
% work time missed	0.0 [0.0-100.0]	4.7 [0.0-100.0]	0.0 [0.0-64.0]	0.009	0.0 [0.0-100.0]	5.9 [0.0-100.0]	0.0 [0.0-100.0]	0.287
% impairment while working	10.0 [0.0-100.0]	10.0 [0.0-80.0]	10.0 [0.0-100.0]	0.336	0.0 [0.0-80.0]	20.0 [0.0-80.0]	0.0 [0.0-80.0]	0.08
% TAI	30.0 [0.0-100.0]	50.0 [0.0-100.0]	20.0 [0.0-100.0]	< 0.001	30.0 [0.0-100.0]	75.0 [0.0-100.0]	10.0 [0.0-100.0]	< 0.001

[1]The missing data is due to a patient who has not completed SF-36 at Day 1. All p-values from Mann-Whitney *U* test, except
[2]Chi-square test. Data are shown as median [range], except otherwise mentioned. CD: Crohn's disease; UC: Ulcerative colitis. SF-36: Short-form 36; EQ-5D: Euro quality of life – 5 dimensions; EQ-VAS: EQ-5D visual analog scale. IBDQ: Inflammatory bowel disease questionnaire. WPAI: Work Productivity and Activity Impairment Questionnaire. TWPI: Total work productivity impairment; TAI: Total activity impairment.

had the most medical appointments (45.0%), with 25.1% occurring in patients diagnosed between 6 months and 3 years prior. Medical appointments with treatment changes occurred most frequently (CD/UC: 38.5%/46.7%) among patients diagnosed for less than 5 years, as did imaging/laboratory tests (CD/UC: 44.5%/36.5%),

	EQ-5D						IBDQ				
	Mobility	Self-care	Usual activities	Pain / discomfort	Anxiety / depression	EQ-VAS	Bowel systems	Emotional health	Systematic systems	Social function	IBDQ score
Crohn's disease											
Physical functioning	-0.6	-0.4	-0.6	-0.54	-0.42	0.57	0.51	0.56	0.66	0.64	0.63
Physical role	-0.47	-0.29	-0.68	-0.54	-0.44	0.57	0.63	0.63	0.72	0.74	0.73
Body pain	-0.49	-0.32	-0.54	-0.64	-0.44	0.54	0.59	0.57	0.63	0.56	0.64
General health	-0.35	-0.28	-0.56	-0.58	-0.51	0.63	0.59	0.65	0.67	0.6	0.68
Vitality	-0.32	-0.24	-0.5	-0.54	-0.61	0.57	0.56	0.73	0.74	0.6	0.73
Social functioning	-0.4	-0.3	-0.6	-0.56	-0.57	0.51	0.62	0.73	0.72	0.65	0.74
Emotional role	-0.41	-0.24	-0.54	-0.5	-0.6	0.53	0.55	0.69	0.66	0.59	0.7
Mental health	-0.35	-0.27	-0.49	-0.58	-0.72	0.53	0.54	0.81	0.69	0.56	0.74
SF-36 summary											
Mental component score	-0.31	-0.23	-0.48	-0.55	-0.71	0.52	0.56	0.81	0.71	0.57	0.75
Physical component score	-0.55	-0.38	-0.66	-0.6	-0.34	0.61	0.61	0.53	0.68	0.69	0.66
Ulcerative colitis											
Physical functioning	-0.69	-0.38	-0.64	-0.63	-0.4	0.48	0.62	0.57	0.65	0.68	0.65
Role physical	-0.53	-0.28	-0.75	-0.62	-0.4	0.65	0.72	0.66	0.75	0.78	0.75
Body pain	-0.58	-0.36	-0.57	-0.66	-0.54	0.47	0.62	0.58	0.6	0.62	0.64
General health	-0.47	-0.26	-0.56	-0.52	-0.45	0.62	0.62	0.69	0.58	0.6	0.68
Vitality	-0.52	-0.25	-0.51	-0.59	-0.61	0.6	0.65	0.72	0.73	0.62	0.73
Social functioning	-0.45	-0.24	-0.58	-0.56	-0.51	0.54	0.64	0.71	0.67	0.69	0.72
Role-emotional	-0.43	-0.24	-0.54	-0.58	-0.58	0.51	0.64	0.71	0.64	0.66	0.71
Mental Health	-0.41	-0.16	-0.45	-0.53	-0.72	0.56	0.66	0.84	0.66	0.64	0.77
SF-36 summary											
Mental component score	-0.37	-0.16	-0.46	-0.53	-0.69	0.54	0.66	0.82	0.67	0.65	0.77
Physical component score	-0.67	-0.4	-0.73	-0.65	-0.34	0.57	0.67	0.56	0.67	0.72	0.68

Spearman's correlation coeficient:

0.10-0.29	Very low
0.30-0.49	Low
0.50-0.69	Moderate
⩾0.70	High

Figure 1 Spearman's correlation coefficients between domains and summary measures of the different quality of life measures. SF-36: Short-form 36; EQ-5D: Euro quality of life – 5 dimensions; EQ-VAS: EQ-5D visual analog scale; IBDQ: Inflammatory bowel disease questionnaire.

compared to patients diagnosed 5 to 10 years or 10 or more years.

IBD treatment at baseline and changes over the previous 3 years

At baseline, the majority of CD (95.1%) and UC (90.2%) patients were on IBD treatment (Table 6). The median number of concurrent medicines at baseline, by patient, was 2.0 for both CD and UC patients. The most common treatments at baseline were biologics (75.3%) and immunosuppressants (70.9%) for CD patients and 5-ASA compounds (77.5%) for UC patients. Considering each IBD medicine (Figure 3), azathioprine was used by 65.7% CD patients, followed by infliximab (42.2%) and adalimumab (31.1%). Among UC patients, 5-ASA (72.9%), azathioprine (45.7%) and infliximab (24.0%) were the three most frequently used treatments.

Most CD patients with moderate to severe disease activity were receiving an immunosuppressant (72.1%) and/or biologic (71.2%). Among CD patients with mild or no disease activity, most were receiving a biologic (78.6%) and/or immunosuppressant (70.0%) as well. With regard to UC patients, the majority were receiving at least one 5-ASA compound (84.4% *vs* 75.3%, in moderate to severe *vs*. mild or no disease activity, respectively) (Table 6).

The majority of CD (70.7%) and UC (77.6%) patients changed treatment at least once during the previous 3 years, including changes in antibiotics and corticosteroids. CD patients had fewer treatment changes than UC patients (median: 1.0 *vs* 2.0; P = 0.036), and changes were not statistically associated with disease activity in both IBD types. Most of the treatment changes were discontinuations (CD/UC: 43.5%/38.1%). When considering only biologics, immunosuppressants and 5-ASA compounds, most dose changes and discontinuations occurred in immunosuppressants (50.7% and 39.8%) for CD patients and 5-ASA compounds (69.5% and 64.1%) for UC patients. With regard to biologic therapy, dose changes were due to poor effectiveness

Table 3 Quality of Life scores by sociodemographic and clinical characteristics and by type of inflammatory bowel disease

	CD								UC							
	SF-36 mental component		SF-36 physical component		EQ-VAS		IBDQ score		SF-36 mental component		SF-36 physical component		EQ-VAS		IBDQ score	
	mean ± SD	*P* value	mean ± SD	*P* value	mean ± SD	*P* value	mean ± SD	*P* value	mean ± SD	*P* value	mean ± SD	*P* value	mean ± SD	*P* value	mean ± SD	*P* value
Age (years)		0.018		0.895		0.514		0.002		0.155[3]		0.263		0.534		0.847[3]
18-39	44.8 ± 13.0		43.1 ± 10.5		72.4 ± 20.3		158.9 ± 41.0		46.5 ± 10.0		46.0 ± 10.0		67.7 ± 22.2		151.6 ± 43.8	
40-59	41.9 ± 12.9		43.5 ± 14.3		73.4 ± 20.5		151.0 ± 43.4		43.1 ± 10.1		45.0 ± 9.8		65.5 ± 25.6		153.0 ± 54.8	
≥60	48.8 ± 9.4		42.0 ± 16.8		76.1 ± 19.8		178.7 ± 30.1		46.1 ± 9.7		48.2 ± 7.9		69.9 ± 30.5		157.2 ± 46.8	
Gender		< 0.001[1]		0.027[1]		0.004[1]		< 0.001[1]		0.004[1]		0.032[1]		0.042[1]		< 0.00[1]
Male	48.0 ± 11.3		45.9 ± 13.6		77.5 ± 18.0		169.5 ± 38.0		47.5 ± 9.7		47.3 ± 8.9		72.4 ± 22.0		169.7 ± 43.3	
Female	41.2 ± 12.9		41.0 ± 13.1		69.8 ± 21.4		149.9 ± 42.1		42.7 ± 9.9		44.8 ± 10.0		62.8 ± 26.8		140.7 ± 50.8	
Professional situation		0.002		0.030 [2]		0.003		< 0.001		< 0.001[2]		< 0.001		0.130		0.001
Employed	47.5 ± 11.5		47.6 ± 11.4		78.1 ± 19.4		168.1 ± 40.4		49.4 ± 8.9		49.2 ± 8.0		73.2± 23.2		175.7 ± 39.3	
Unemployed	40.0 ± 14.0		39.2 ± 13.5		67.6 ± 21.2		145.3 ± 40.6		41.2 ± 9.8		42.9 ± 9.3		64.9± 25.9		135.8 ± 51.5	
Student	43.0 ± 16.0		44.2 ± 11.2		75.5 ± 18.6		172.6 ± 42.8		42.0 ± 12.6		54.2 ± 9.8		61.6± 15.2		139.6 ± 35.3	
Retired	46.4 ± 8.2		39.3 ± 18.3		75.2 ± 15.8		165.2 ± 33.5		41.7 ± 10.7		45.4 ± 7.8		55.2± 31.4		135.7 ± 53.3	
Other	39.0 ± 14.0		40.3 ± 12.7		64.8 ± 23.4		135.5 ± 50.7		41.2 ± 8.9		39.8 ± 10.2		62.2± 24.3		138.4 ± 52.2	
Educational level		0.802		0.176 [2]		0.990		0.398 [2]		0.122 [2]		0.028[2]		0.510		0.185
Primary school	43.7 ± 11.4		43.7 ± 11.4		73.2 ± 20.8		156.3 ± 40.8		44.0 ± 9.3		44.0 ± 9.3		66.6 ± 27.9		143.0 ± 56.8	
Secondary school	43.0 ± 13.3		43.0 ± 13.3		73.1 ± 20.7		152.9 ± 44.9		45.3 ± 9.9		45.3 ± 9.9		66.4 ± 25.8		160.0 ± 47.6	
Higher education	44.1 ± 13.2		44.1 ± 13.2		72.8 ± 20.1		162.2 ± 39.1		48.4 ± 8.9		48.4 ± 8.9		76.0 ± 6.5		171.4 ± 42.3	
Income		0.112		0.007[2]		0.547		0.087[2]		< 0.001		0.095[2]		0.070[2]		0.002[2]
> 3x MW	46.2 ± 11.9		47.7 ± 9.2		74.6 ± 21.4		169.2 ± 39.6		52.3 ± 9.4		49.3 ± 8.0		75.3 ± 16.2		179.0 ± 39.7	
> 1x – 3x MW	43.6 ± 11.8		46.1 ± 14.0		73.9 ± 20.2		157.6 ± 40.2		44.1 ± 9.0		46.2 ± 9.1		69.8 ± 24.6		158.7 ± 49.3	
< 1x MW	40.4 ± 13.6		36.2 ± 13.3		70.9 ± 20.8		149.4 ± 43.9		39.2 ± 10.0		45.9 ± 9.8		58.8 ± 26.2		124.0 ± 50.7	

Any EIM	0.470[3]	0.924[3]	0.687[1]	0.750[1]	0.343[3]	0.242[3]	0.601[1]	0.701[1]
Yes	44.8 ± 13.0	42.0 ± 14.9	70.7 ± 19.6	158.0 ± 42.2	42.6 ± 8.6	44.4 ± 7.9	69.6 ± 19.0	149.6 ± 48.5
No	43.2 ± 11.9	42.3 ± 12.9	71.3 ± 22.0	161.0 ± 40.7	44.7 ± 10.4	46.2 ± 10.4	64.1 ± 27.8	152.2 ± 49.8

All *P*-values from Kruskal-Wallis test, except
[1]Mann-Whitney *U* test,
[2]ANOVA test, and
[3]*t*-test. EIM: Extraintestinal Manifestations; MW: Minimum wage.

according to physician criteria in 22 (41.5%) CD patients and poor effectiveness and serum level of the biologic drug in 3 (each) UC patients. Discontinuations of biologics were mainly due to adverse reactions (CD/UC: 29.2%/27.5%).

DISCUSSION

The RISE BR study is the first study with a real-world characterization of the burden of moderate to severe IBD in Brazil, both in the patient and payer perspectives. Overall, 407 (143 UC and 264 CD) patients diagnosed with moderate to severe disease were included, and at enrolment, 25% UC and 45% CD patients had moderately to severely active disease.

QoL was assessed with both generic and disease-specific questionnaires. Irrespective of IBD type, the SF-36 summary scores were low (*i.e*., scores less than 50, in a range from 1-100). Other Brazilian single-center studies have observed no low SF-36 scores[29] or that SF-36 was low regarding physical limitations and emotional aspects domains[35,36]. Our results may reflect that patients with a previous diagnosis of moderate to severe IBD, even though treated, still perceive their general health as poor and that IBD physically and emotionally impacts their life. These findings are supported by the EQ-5D results, with the most compromised dimensions being pain/discomfort and anxiety/depression and better results in the mobility and self-care dimensions. Not surprisingly, a correlation was observed between these two general questionnaires, especially when considering the EQ-VAS and the SF-36 summary scores and comparing between related dimensions (*e.g*., SF-36 physical functioning *vs*. EQ-5D mobility).

The IBDQ results are in line with those of the general QoL questionnaires, and a significant correlation was observed between SF-36 and IBDQ, as reported by other Brazilian studies[29,36]. Considering that the overall IBDQ score ranged between 32 and 224, the observed scores were slightly above the midpoint value, with poorer results for the emotional health and systemic symptoms domains, irrespective of IBD type. Pontes *et al*. observed a higher range of IBDQ overall scores (min-max: 114-222), probably due to the inclusion of mostly patients with no active IBD[29].

Notably, patients with moderate to severe active disease had lower QoL scores in SF-36 domains and summary measures, EQ-VAS and IBDQ dimensions and overall score versus those with mild or no disease activity. In fact, patients with moderate to severe disease activity had a median IBDQ greater than 170 and scored more than 16 points of difference when compared to patients with mild or no disease activity[37]. Other clinically significant differences were also observed in the SF-36 summary measures (more than 2 points of difference) and EQ-VAS scores (more than 8 points)[37,38]. This pattern has been described in several studies across different world regions[38,39]. For instance, one recent French survey reported that the risk of low QoL was significantly increased with greater disease activity[40]. A Polish study showed that CD patients in remission had lower QoL and work productivity impairment compared to patients with active disease[41]. The same trend was observed in one local single-site study conducted in Mato Grosso, Brazil[36]. Parra *et al*. also showed that during maintenance treatment with infliximab, adequate serum levels are associated with higher rates of clinical remission, mucosal healing and QoL[12]. In line with other studies[13,39,40,42,43], female gender, being unemployed, lower educational level and lower income were associated with poor QoL in almost all domains and summary measures of the different QoL scales. Pain and the intensity of other symptoms during relapses are disruptive of daily life and are particularly relevant for younger and more socially active patients. However, disease activity is not the only determinant of QoL, as other sociodemographic characteristics play a role in the way patients perceive their disease. To provide the best care to IBD patients, subgroups of patients at higher risk

Table 4 Work productivity and activity impairment scores by sociodemographic and clinical characteristics and by type of inflammatory bowel diseases

	CD								UC							
	% TWPI		% work time missed		% impairment while working		% TAI		% TWPI		% work time missed		% impairment while working		% TAI	
	mean ± SD	*P* value	mean ± SD	*P* value	mean ± SD	*P* value	mean ± SD	*P* value	mean ± SD	*P* value	mean ± SD	*P* value	mean ± SD	*P* value	mean ± SD	*P* value
Age (yr)		0.522		0.208		0.541		0.007		0.803		0.453		0.929		0.433
18-39	31.8 ± 32.4		13.8 ± 23.6		23.3 ± 26.4		36.3 ± 34.1		28.5 ± 34.6		13.7 ± 27.1		19.6 ± 28.0		44.3 ± 36.1	
40-59	35.2 ± 35.1		12.9 ± 25.8		27.4 ± 30.8		41.2 ± 34.2		23.7 ± 33.6		11.7 ± 29.3		15.9 ± 25.0		37.6 ± 37.5	
≥ 60	19.6 ± 25.8		4.2 ± 11.8		15.6 ± 21.3		21.2 ± 25.4		19.6 ± 29.4		3.6 ± 6.2		18.0 ± 26.8		37.4 ± 40.9	
Gender		0.186 [1]		0.914[1]		0.148 [1]		0.014[1]		0.465[1]		0.649[1]		0.092[1]		0.043[1]
Male	27.8 ± 30.5		13.0 ± 24.4		20.0 ± 23.4		30.4 ± 32.6		22.5 ± 32.0		13.4 ± 27.9		12.4 ± 21.9		31.8 ± 36.2	
Female	37.6 ± 35.5		12.2 ± 23.2		29.6 ± 32.0		40.3 ± 33.6		29.5 ± 35.1		9.3 ± 25.2		24.6 ± 29.8		45.9 ± 37.5	
Professional situation		0.198		0.753		0.078		< 0.001		-		-		-		0.001
Employed	30.1 ± 31.4		11.0 ± 20.5		23.0 ± 27.8		24.2 ± 30.6		23.4 ± 31.5		9.4 ± 23.8		17.7 ± 26.2		23.7 ± 30.7	
Unemployed	54.7 ± 18.0		5.4 ± 6.7		56.0 ± 16.7		49.8 ± 33.3		-		-		-		52.4 ± 39.1	
Student	-		-		-		23.0 ± 27.9		-		-		-		56.0 ± 24.1	
Retired	62.5 ± 17.7		25.0 ± 35.3		33.3 ± 28.9		32.3 ± 32.2		0.0		0.0		0.0		48.7 ± 43.4	
Other	45.0 ± 63.6		33.3 ± 47.1		35.0 ± 49.5		56.2 ± 29.1		-		-		-		51.1 ± 36.3	
Educational level		0.608		0.591		0.455		0.114		0.331		0.571		0.186		0.252
Primary school	37.4 ± 30.8		12.3 ± 15.6		28.6 ± 29.0		39.6 ± 34.9		15.7 ± 29.1		8.0 ± 17.7		8.0 ± 19.3		39.2 ± 40.8	
Secondary school	37.1 ± 33.4		9.0 ± 17.7		29.1 ± 30.5		43.6 ± 36.6		26.3 ± 32.5		10.1 ± 28.6		21.2 ± 26.0		42.2 ± 37.5	
Higher education	30.0 ± 33.6		16.0 ± 26.6		20.5 ± 25.6		29.1 ± 28.4		10.6 ± 19.4		1.1 ± 2.7		10.0 ± 18.3		25.7 ± 31.7	
Income		0.293		0.708		0.042		0.079		0.341		0.648		0.453		0.032
> 3x MW	33.0 ± 35.5		13.4 ± 25.6		25.8 ± 30.2		25.9 ± 30.8		23.0 ± 33.0		9.3 ± 27.5		22.0 ± 28.6		25.8 ± 36.7	
> 1x – 3x MW	28.0 ± 28.5		13.9 ± 23.8		16.8 ± 20.1		38.6 ± 34.2		27.6 ± 27.4		7.1 ± 16.4		16.7 ± 22.7		38.9 ± 36.8	
< 1x MW	60.0 ± 10.8		7.3 ± 8.9		50.0 ± 24.5		42.3 ± 35.1		0.0 ± 0.0		0.0 ± 0.0		0.0 ± 0.0		56.8 ± 35.8	
Any EIM		0.005[1]		0.004[1]		0.199 [1]		0.656[1]		0.345[1]		0.824[1]		0.214 [1]		0.896[1]
Yes	53.9 ± 33.4		23.3 ± 28.2		32.9 ± 31.8		37.2 ± 32.1		28.5 ± 31.2		1.8 ± 4.4		27.3 ± 31.0		37.0 ± 36.4	

No	23.5 ± 31.9	6.2 ± 15.4	21.0 ± 28.4	35.1 ± 33.8	19.0 ± 31.6	9.4 ± 26.6	13.7 ± 23.9	36.7 ± 38.4

All *P*-values from Kruskal-Wallis test, except
[1]Mann-Whitney *U* test. EIM: Extraintestinal manifestations; MW: Minimum wage; TWPI: Total work productivity impairment; TAI: Total activity impairment.

of poor QoL should be identified and offered additional coping strategies and social support.

IBD has a relevant impact on work productivity and daily activities. In our study, patients had approximately 30% impaired worktime, with approximately 12% absenteeism and 18%-24% presenteeism, and approximately 36%-40% TAI. Of note, unemployment frequency in IBD patients (23%) was higher than that of the general population of Brazil (12.6%), in 2017[44]. In addition, TAI was higher among IBD patients with moderate to severe disease activity but also among women, middle-aged patients (40-59 years old, CD only) and patients with lower income (UC only). Other studies have reported the same association, with a TAI of approximately 30%[15,40]. Froes *et al*. have described that IBD in Brazil leads to frequent and prolonged disability periods and contributes to early retirement, especially among CD patients[45]. A European survey conducted in 2010-2011 with 4670 IBD patients showed that, during previous year, only 25% had not been absent from work due to IBD and that 25% had been absent for more than 25 d[46].

To the best of our knowledge, this is the first study to report the use of healthcare resources for IBD patients in Brazil, even though studies from other countries have observed the high economic burden of these conditions[2,47-51]. Approximately one-quarter of CD patients had at least one surgery during the last 3 years. The proportion of UC patients with previous surgeries was considerably smaller (3%), but approximately 30% underwent a high-cost colectomy. Almost half of CD patients and approximately 35% of UC patients had at least one previous hospitalization, with a median duration of 6 and 4 days, respectively. Gibson *et al*. observed a higher frequency (43.5%) of hospitalization in UC patients in Australia, which may reflect differences in the access of hospital care[2]. On the other hand, the large majority of the medical appointments in our study were with IBD specialists, while in other countries, IBD follow-up is also performed by general practitioners[2,52-54]. Interestingly, CD patients with moderate to severe disease activity at baseline and those with less time since the first diagnosis of moderate to severe disease had more previous hospitalizations and medical appointments with treatment changes, which may reflect the difficulty of maintaining or achieving remission.

In our study, almost all patients had at least one imaging or laboratory test, with almost half having more than 20 tests in the previous 3 years. However, colonoscopy only accounted for approximately 6%-9% of the procedures, and other IBD-specific tests had an even smaller frequency. This finding, aligned with the rare use of clinical scores during medical appointments, make us speculate that other information (such as specific symptoms or patient-reported disease activity) may be more relevant for IBD specialists in Brazil when deciding about treatment[55].

Almost all IBD patients were on some form of treatment at baseline, mainly with immunosuppressants and biologics among CD patients and with 5-ASA compounds in UC patients. In fact, the treatment pattern at baseline is in line with other studies from Latin America[19]. International guidelines recommend the use of 5-ASA compounds (especially in proctitis and left-sided UC) and/or corticosteroids (preferred in CD patients) for the induction phase and, in more severe or refractory cases, azathioprine and biological agents, while salicylates, thiopurines and biologics are usually recommended for the maintenance period[56-58].

Some study limitations should be addressed. The retrospective data collection may bias the estimates of treatment changes and healthcare use due to missing data on patient's medical records. For instance, patients could have more than one IBD specialist, with medical appointments that are not registered, thus underestimating healthcare use. On the other hand, the cross-sectional evaluation does not enable us to conclude if patients with higher disease activity at baseline should have received a more effective treatment, especially when considering the relapsing and remission nature of IBD. We cannot exclude that the inclusion of patients with a previous diagnosis of moderate to severe disease, although deliberate, may have contributed to a higher rate of active disease at baseline, thus affecting the generalization of results to all IBD patients. Moreover, selection bias was minimized by the consecutive enrolment at scheduled clinical appointments, but patients with an active disease have a higher chance of having a medical appointment during the recruitment period. Finally, the smaller number of UC patients may have compromised the power of

Table 5 Utilization of healthcare resources during the retrospective 3-year period

	CD				UC			
	Total	Moderate to severe activity	No or mild activity	*P* value	Total	Moderate to severe activity	No or mild activity	*P* value
n	264	118	146		143	36	107	
IBD surgeries								
At least one IBD surgery	67 (25.4)	32 (27.1)	35 (24.0)	0.559 [1]	4 (2.8)	1 (2.8)	3 (2.8)	--
Surgeries, *n*	108	45	63		7	2	5	
Surgeries/pt, median [range]	1.0 [1-5]	1.0 [1-4]	2 [1-5]	0.074	2.0 [1-2]	2	2.0 [1-2]	--
More than one IBD surgery	28 (41.8)	10 (31.2)	18 (51.5)		3 (75.0)	1 (100.0)	2 (66.7)	
Type [frequency ≥ 5%]								
Partial colectomy	13 (12.0)	5 (11.1)	8 (12.7)		0 (0.0)	0 (0.0)	0 (0.0)	
Total colectomy	1 (0.9)	0 (0.0)	1 (1.6)		2 (28.6)	1 (50.0)	1 (20.0)	
Drainage of anorectal abscess	6 (5.6)	3 (6.7)	3 (4.8)		0 (0.0)	0 (0.0)	0 (0.0)	
Fistulectomy	22 (20.4)	9 (20.0)	13 (20.6)		0 (0.0)	0 (0.0)	0 (0.0)	
Enterostomy	13 (12.0)	6 (13.3)	7 (11.1)		0 (0.0)	0 (0.0)	0 (0.0)	
Enterostomy closure	5 (4.6)	5 (11.1)	0 (0.0)		2 (28.6)	0 (0.0)	2 (40.0)	
IBD hospitalizations								
At least one IBD hospitalization	101 (38.3)	51 (43.2)	50 (34.2)	0.136 [1]	28 (19.6)	11 (30.6)	17 (15.9)	0.055 [1]
Hospitalizations, *n*	168	93	75		43	18	25	
Hospitalizations/pt, median [range]	1.0 [1-5]	2.0 [1-4]	1.0 [1-5]	0.031	1.0 [1-5]	1.0 [1-5]	1.0 [1-3]	0.978
More than one hospitalization	47 (46.5)	29 (56.8)	18 (36.0)		10 (35.7)	4 (36.4)	6 (35.3)	
Duration (d), median [range]	6 [1-98]	5 [0-76]	4.5 [0-97]		4 [1-737]	2.5 [0-20]	5 [0-737]	
IBD medical appointments								
At least one IBD consultation	263 (99.6)	117 (99.2)	146 (100.0)		143 (100.0)	36 (100.0)	107 (100.0)	
Consultations, *n*	3192	1466	1726		1541	423	1118	
Consultations/pt, median [range]	11.0 [1-45]	12.0 [1-45]	11.0 [1-35]	0.801	10.0 [1-39]	9.5 [1-39]	10.0 [2-30]	0.896
More than 20 consultations	27 (10.3)	15 (12.8)	12 (8.2)		9 (6.3)	4 (11.1)	5 (4.7)	
Type								
IBD specialist	2989 (93.6)	1356 (92.4)	1633 (94.6)		1426 (92.5)	394 (93.1)	1032 (92.3)	
Emergency	43 (1.3)	25 (1.7)	18 (1.0)		34 (2.2)	20 (4.7)	14 (1.3)	
Other specialist	160 (5.0)	85 (5.8)	75 (4.3)		81 (5.3)	9 (2.1)	72 (6.4)	

Consultations with registered score								
HBI	11 (0.3)	1 (0.1)	10 (0.6)		--	--	--	
CDAI	103 (3.2)	54 (3.7)	49 (2.8)		--	--	--	
Other CD scores	30 (0.9)	21 (1.4)	9 (0.5)		--	--	--	
pMayo score	--	--	--		95 (6.2)	12 (2.8)	83 (7.4)	
Consultations with change of IBD treatment	522 (16.4)	269 (18.3)	253 (14.7)	0.005 [1]	353 (22.9)	86 (20.3)	267 (23.9)	0.139 [1]
IBD imaging and laboratory testing								
At least one IBD test	260 (98.5)	116 (98.3)	144 (98.6)	--	141 (98.6)	36 (100.0)	105 (98.1)	--
IBD tests, *n*	5674	2722	2952		2509	643	1866	
Tests/pt, median [range]	19.0 [1-143]	20.0 [1-143]	16.0 [1-94]	0.372	15.0 [1-82]	14.5 [2-82]	16 [1-75]	0.767
More than 20 tests	118 (45.4)	56 (48.3)	62 (43.1)		57 (40.4)	15 (41.7)	42 (40.0)	
Type [frequency ≥ 5%]								
Complete blood cell count	2317 (40.8)	1077 (39.6)	1240 (42.0)		973 (38.8)	250 (38.9)	723 (38.7)	
C-reactive protein	1773 (31.2)	837 (30.7)	936 (31.7)		748 (29.8)	214 (33.3)	534 (28.6)	
Serum albumin	647 (11.4)	346 (12.7)	301 (10.2)		356 (14.2)	59 (9.2)	297 (15.9)	
Colonoscopy	346 (6.1)	183 (6.7)	163 (5.5)		228 (9.1)	57 (8.9)	171 (9.2)	

All *P*-values from Mann-Whitney *U* test, except
[1]Chi-square test. Data are shown as *n* (%), except otherwise mentioned. CD: Crohn's disease; UC: Ulcerative colitis; IBD: Inflammatory bowel disease; pt: Patient.

statistical analysis by subgroup.

This was the first multicenter real-world study in Brazil that assessed several PROs, providing insight about the patient and payer perspectives that can contribute to optimizing IBD treatment. Based on clinical and patient-reported assessments, we conclude that moderate-to-severe disease activity, especially among CD patients, is associated with a substantial impact on QoL, work productivity impairment and consumption of healthcare resources (namely, IBD hospitalizations and surgeries) in Brazil. The large sample size selected from reference centers of the most populated regions of Brazil allows a good comprehension of IBD burden and management in the Brazilian context. However, the low use of clinical scores and laboratory examinations of recognized biomarkers (such as fecal calprotectin) should be addressed through specific medical education programs. The frequency of IBD is increasing, and health services should be prepared to provide an adequate response, including by addressing unmet medical needs regarding the access and use of more effective therapies, to help patients with IBD.

Table 6 Treatment for inflammatory bowel diseases at baseline and changes during the previous 3 years

	CD				UC			
	Total	Moderate to severe activity	No or mild activity	*P* value	Total	Moderate to severe activity	No or mild activity	*P* value
n	264	118	146		143	36	107	
IBD treatment at baseline								
Treated patients	251 (95.1)	111 (94.1)	140 (95.9)		129 (90.2)	32 (88.9)	97 (90.7)	
IBD medicines/pt, median [range][2]	2.0 [1-7]]	2.0 [1.6]	2.0 [1-7]		2.0 [1-6]	3 [1-6]	2 [1-5]	
Main IBD therapy[3]								
5-ASA compounds	39 (15.5)	20 (18.0)	19 (13.6)		100 (77.5)	27 (84.4)	73 (75.3)	
Biologic therapy	189 (75.3)	79 (71.2)	110 (78.6)		41 (31.8)	11 (34.4)	30 (30.9)	
Immunosuppressants	178 (70.9)	80 (72.1)	98 (70.0)		63 (48.8)	17 (53.1)	46 (47.4)	
Any corticosteroid	30 (12.0)	17 (15.3)	14 (10.0)		26 (20.2)	13 (40.6)	13 (13.4)	
Any antibiotic	14 (5.6)	11 (9.9)	3 (2.1)		7 (5.4)	5 (15.6)	2 (2.1)	
Changes to IBD treatment								
Treatment changes /pt, median [range][2]	1 [0-23]	1 [0-23]	1 [0-9]	0.526	2 [0-15]	1 [0-15]	2 [0-10]	0.226
At least one change on IBD treatment[2]	186 (70.7)	81 (69.2)	105 (71.9)	0.634[1]	111 (77.6)	24 (66.7)	87 (81.3)	0.068[1]
Type of change[2]								
Ongoing or beginning	437 (35.6)	190 (31.6)	247 (39.5)		265 (36.1)	75 (38.7)	190 (35.2)	
Dose change	256 (20.9)	128 (21.3)	128 (20.4)		189 (25.7)	39 (20.1)	150 (27.8)	
Discontinued	534 (43.5)	283 (47.1)	251 (40.1)		280 (38.1)	80 (41.2)	200 (37.0)	
Dose change by main IBD therapy	146	71	75		128	31	97	
5-ASA compounds	19 (13.0)	5 (7.0)	14 (18.7)		89 (69.5)	20 (64.5)	69 (71.1)	
Biologic therapy	53 (36.3)	27 (38.0)	26 (34.7)		12 (9.4)	5 (16.1)	7 (7.2)	
Immunosuppressants	74 (50.7)	39 (54.9)	35 (46.7)		27 (21.1)	6 (19.4)	21 (21.6)	
Discontinuation by main IBD therapy	226	123	103		128	36	92	
5-ASA compounds	64 (28.3)	33 (26.8)	31 (30.1)		82 (64.1)	20 (55.6)	62 (67.4)	
Biologic therapy	72 (31.9)	44 (35.8)	28 (27.2)		11 (8.6)	8 (22.2)	3 (3.3)	
Immunosuppressants	90 (39.8)	46 (37.4)	44 (42.7)		35 (27.3)	8 (22.2)	27 (29.3)	
Reason for dose change of biologics [frequency ≥ 5%][4]								

Adverse reaction	0 (0.0)	0 (0.0)	0 (0.0)	2 (16.7)	2 (40.0)	0 (0.0)
Patient decision/adherence	1 (1.9)	1 (3.7)	0 (0.0)	2 (16.7)	0 (0.0)	2 (28.6)
Poor effectiveness	22 (41.5)	12 (44.4)	10 (38.5)	3 (25.0)	1 (20.0)	2 (28.6)
Remission	5 (9.4)	2 (7.4)	3 (11.5)	0 (0.0)	0 (0.0)	0 (0.0)
Serum level of biologic drug	2 (3.8)	1 (3.7)	1 (3.8)	3 (25.0)	1 (20.0)	2 (28.6)
Reason for discontinuation of biologics [frequency ≥ 5%]						
Adverse reaction	21 (29.2)	13 (29.5)	8 (28.6)	3 (27.5)	2 (25.0)	1 (33.3)
Contraindication	6 (8.3)	5 (11.4)	1 (3.6)	1 (9.1)	0 (0.0)	1 (33.3)
Patient decision/adherence	5 (6.9)	4 (9.1)	1 (3.6)	2 (18.2)	1 (12.5)	1 (33.3)
Poor effectiveness	6 (8.3)	2 (4.5)	4 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)

All *P*-values from Mann-Whitney *U* test, except
[1]Chi-square test. Data are shown as *n* (%), except otherwise mentioned.
[2]Including antibiotics and corticosteroids.
[3]Patients with at least one of the main IBD drug classes, excluding antibiotics, corticosteroids and other medications.
[4]More than one possible reason for dose change. CD: Crohn's disease; UC: Ulcerative colitis; IBD: Inflammatory bowel disease; pt: Patient.

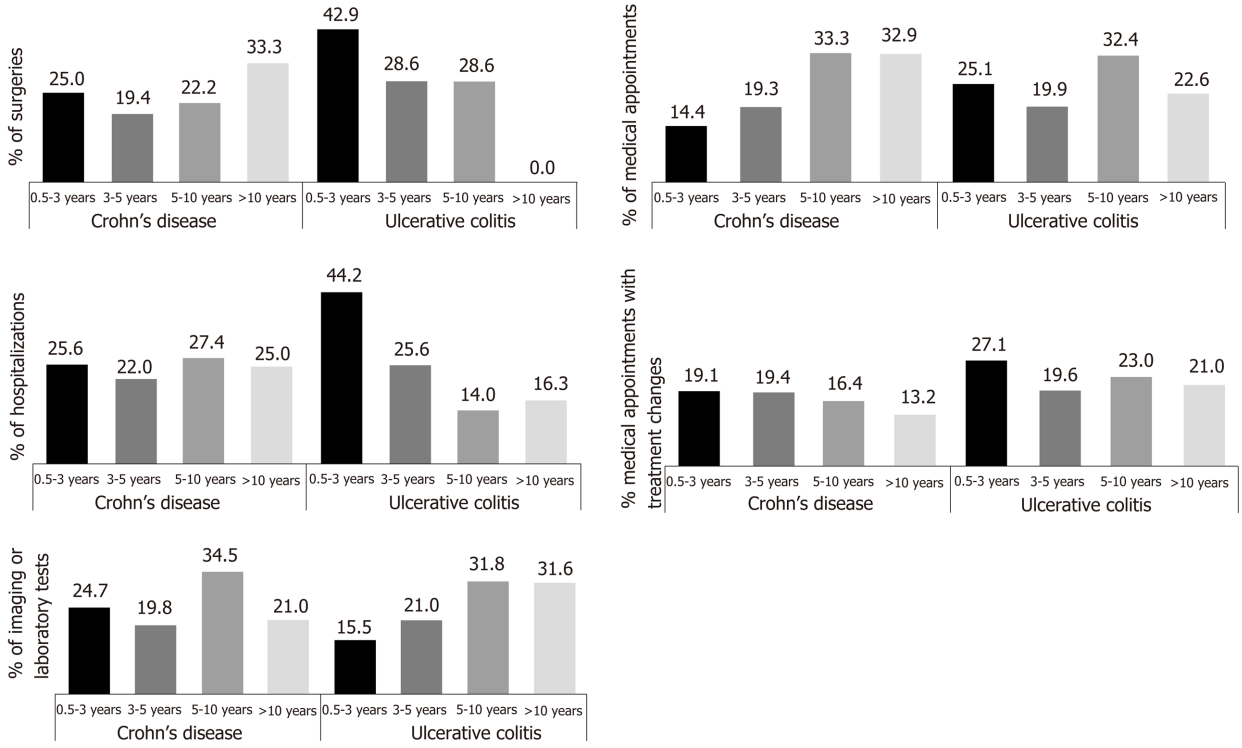

Figure 2 Healthcare resource utilization by time since the first diagnosis of moderate to severe inflammatory bowel diseases.

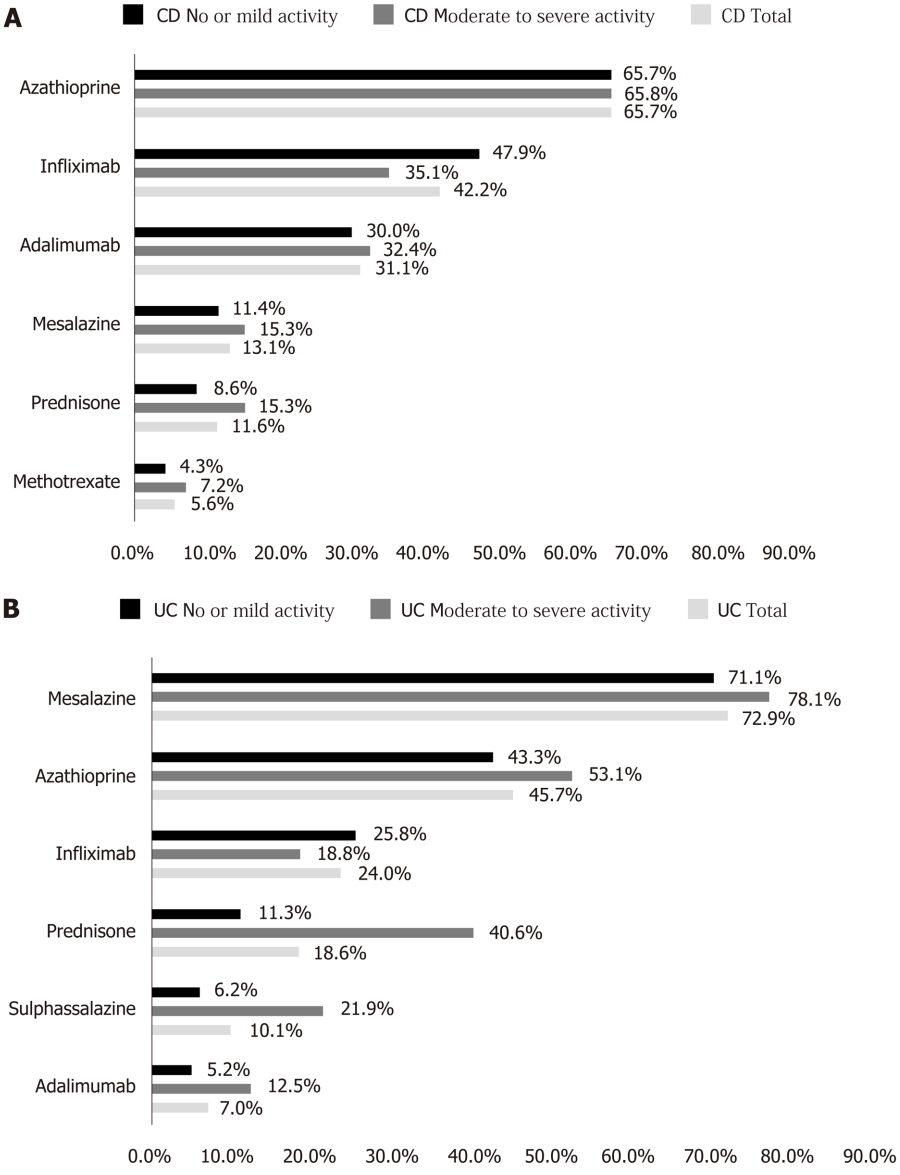

Figure 3 Most frequently used drugs for inflammatory bowel diseases (overall frequency ≥ 5%). A: Drugs used by patients with Crohn's disease (total and by disease activity); B: Drugs used by patients with ulcerative colitis (total and by disease activity). Note: % refers to patients using at least one medicine. CD: Crohn's disease; UC: Ulcerative colitis.

ARTICLE HIGHLIGHTS

Research background

Inflammatory bowel diseases (IBD) have been associated with a low quality of life (QoL) and a negative impact on work productivity compared to the general population, across several world regions.

Research motivation

Information about the impact of IBD on QoL and work productivity in Latin American countries is scarce and, in Brazil, emerges mostly from single-center studies. It is important to describe IBD control, patient-reported outcomes (PROs), treatment patterns and use of healthcare resources, so that clinicians and health services can optimize IBD management.

Research objectives

To describe QoL and work productivity and activity impairment (WPAI), treatment patterns and use of healthcare resources among IBD patients in Brazil. The association of disease activity with these outcomes was also evaluated.

Research methods

We conducted a multicenter cross-sectional study in several Brazilian IBD centers, with adult IBD outpatients, with clinical evaluation of disease activity at enrolment, chart review of the

previous 3-years for collection of treatment and healthcare use, and an extensive collection of PROs, namely: General measures of QoL such as short-form 36 and EQ-5D-5L questionnaires, the Inflammatory and Bowel Disease Questionnaire (IBDQ, a disease-specific QoL measure) and the WPAI questionnaire.

Research results

In a large sample (n = 407) of patients with ulcerative colitis (n = 143) or Crohn's disease (n = 264), almost half of CD patients (44.7%) and about a quarter of UC patients (25.2%) presented active disease at baseline. Irrespective of IBD type, QoL scores (SF-36, EQ-5D and IBDQ) were low. Disease activity, female gender, unemployment, and lower education and income were associated with a poorer QoL. IBD patients with active disease had a median IBDQ score 16 points higher (i.e., power QoL) than patients with mild or no disease activity, as well as in SF-36 summary measures (more than 2 points of difference) and EQ-VAS scores (more than 8 points). In our study, patients had approximately 30% impaired worktime, with approximately 12% absenteeism and 18%-24% presenteeism, and approximately 36%-40% total activity impairment. Patients with active IBD showed higher total activity impairment. With regard to use of healthcare resources, approximately one-quarter of CD patients had at least one surgery during the last 3 years. The proportion of UC patients with previous surgeries was considerably smaller (3%), but approximately 30% underwent a high-cost colectomy. Almost half of CD patients and approximately 35% of UC patients had at least one previous hospitalization. Almost all IBD patients were on some form of treatment at baseline, mainly with immunosuppressants and biologics among CD patients and with 5-ASA compounds in UC patients.

Research conclusions

Active IBD, especially among CD patients, is associated with a substantial impact on QoL, work productivity impairment and an increased number of IBD surgeries and hospitalizations in Brazil. This is particularly relevant due to the large proportion of IBD patients with active disease at enrolment and to the increase of IBD prevalence, suggesting the need to improve treatment but also the social support and follow-up of IBD patients in Brazil.

Research perspectives

Future research should address the evolution of PROs and its association with treatment changes and control of IBD activity, in a cohort of newly diagnosed patients in Brazil.

ACKNOWLEDGEMENTS

The authors would like to thank the study participants and site staff who collaborated in the study. In addition, the authors acknowledge Eurotrials Scientific Consultants, now a part of CTI Clinical Trial & Consulting Services, for study monitoring, statistical analysis and medical writing assistance.

REFERENCES

1 **Moreau J**, Mas E. Drug resistance in inflammatory bowel diseases. *Curr Opin Pharmacol* 2015; **25**: 56-61 [PMID: 26645664 DOI: 10.1016/j.coph.2015.11.003]
2 **Gibson PR**, Vaizey C, Black CM, Nicholls R, Weston AR, Bampton P, Sparrow M, Lawrance IC, Selby WS, Andrews JM, Walsh AJ, Hetzel DJ, Macrae FA, Moore GT, Weltman MD, Leong RW, Fan T. Relationship between disease severity and quality of life and assessment of health care utilization and cost for ulcerative colitis in Australia: a cross-sectional, observational study. *J Crohns Colitis* 2014; **8**: 598-606 [PMID: 24345767 DOI: 10.1016/j.crohns.2013.11.017]
3 **Loftus EV**. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. *Gastroenterology* 2004; **126**: 1504-1517 [PMID: 15168363 DOI: 10.1053/j.gastro.2004.01.063]
4 **Kaplan GG**. The global burden of IBD: from 2015 to 2025. *Nat Rev Gastroenterol Hepatol* 2015; **12**: 720-727 [PMID: 26323879 DOI: 10.1038/nrgastro.2015.150]
5 **Lakatos PL**. Recent trends in the epidemiology of inflammatory bowel diseases: up or down? *World J Gastroenterol* 2006; **12**: 6102-6108 [PMID: 17036379 DOI: 10.3748/wjg.v12.i38.6102]
6 **Lima Martins A**, Volpato RA, Zago-Gomes MDP. The prevalence and phenotype in Brazilian patients with inflammatory bowel disease. *BMC Gastroenterol* 2018; **18**: 87 [PMID: 29914399 DOI: 10.1186/s12876-018-0822-y]
7 **Ng SC**, Shi HY, Hamidi N, Underwood FE, Tang W, Benchimol EI, Panaccione R, Ghosh S, Wu JCY, Chan FKL, Sung JJY, Kaplan GG. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *Lancet* 2018; **390**: 2769-2778 [PMID: 29050646 DOI: 10.1016/S0140-6736(17)32448-0]
8 **Mowat C**, Cole A, Windsor A, Ahmad T, Arnott I, Driscoll R, Mitton S, Orchard T, Rutter M, Younge L, Lees C, Ho GT, Satsangi J, Bloom S; IBD Section of the British Society of Gastroenterology. Guidelines for the management of inflammatory bowel disease in adults. *Gut* 2011; **60**: 571-607 [PMID: 21464096 DOI: 10.1136/gut.2010.224154]
9 **Vilela EG**, Torres HO, Martins FP, Ferrari Mde L, Andrade MM, Cunha AS. Evaluation of inflammatory activity in Crohn's disease and ulcerative colitis. *World J Gastroenterol* 2012; **18**: 872-881 [PMID: 22408345 DOI: 10.3748/wjg.v18.i9.872]
10 **LeBlanc K**, Mosli MH, Parker CE, MacDonald JK. The impact of biological interventions for ulcerative colitis on health-related quality of life. *Cochrane Database Syst Rev* 2015; CD008655 [PMID: 26393522

DOI: 10.1002/14651858.CD008655.pub3]
11 **Ghosh S**, Mitchell R. Impact of inflammatory bowel disease on quality of life: Results of the European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) patient survey. *J Crohns Colitis* 2007; **1**: 10-20 [PMID: 21172179 DOI: 10.1016/j.crohns.2007.06.005]
12 **Parra RS**, Feitosa MR, Ribeiro LCH, Castro LA, Rocha JJR, Féres O. Infliximab Trough Levels and Quality of Life in Patients with Inflammatory Bowel Disease in Maintenance Therapy. *Gastroenterol Res Pract* 2018; **2018**: 1952086 [PMID: 29853857 DOI: 10.1155/2018/1952086]
13 **van der Have M**, van der Aalst KS, Kaptein AA, Leenders M, Siersema PD, Oldenburg B, Fidder HH. Determinants of health-related quality of life in Crohn's disease: a systematic review and meta-analysis. *J Crohns Colitis* 2014; **8**: 93-106 [PMID: 23746864 DOI: 10.1016/j.crohns.2013.04.007]
14 **Magalhães J**, Castro FD, Carvalho PB, Moreira MJ, Cotter J. Quality of life in patients with inflammatory bowel disease: importance of clinical, demographic and psychosocial factors. *Arq Gastroenterol* 2014; **51**: 192-197 [PMID: 25296078 DOI: 10.1590/S0004-28032014000300005]
15 **Van Assche G**, Peyrin-Biroulet L, Sturm A, Gisbert JP, Gaya DR, Bokemeyer B, Mantzaris GJ, Armuzzi A, Sebastian S, Lara N, Lynam M, Rojas-Farreras S, Fan T, Ding Q, Black CM, Kachroo S. Burden of disease and patient-reported outcomes in patients with moderate to severe ulcerative colitis in the last 12 months - Multicenter European cohort study. *Dig Liver Dis* 2016; **48**: 592-600 [PMID: 26935454 DOI: 10.1016/j.dld.2016.01.011]
16 **Reilly MC**, Gooch KL, Wong RL, Kupper H, van der Heijde D. Validity, reliability and responsiveness of the Work Productivity and Activity Impairment Questionnaire in ankylosing spondylitis. *Rheumatology (Oxford)* 2010; **49**: 812-819 [PMID: 20100797 DOI: 10.1016/j.clinthera.2008.02.016]
17 **Brazilian Study Group of Inflammatory Bowel Diseases**. Consensus guidelines for the management of inflammatory bowel disease. *Arq Gastroenterol* 2010; **47**: 313-325 [PMID: 21140096 DOI: 10.1590/S0004-28032010000300019]
18 **Williet N**, Sandborn WJ, Peyrin-Biroulet L. Patient-reported outcomes as primary end points in clinical trials of inflammatory bowel disease. *Clin Gastroenterol Hepatol* 2014; **12**: 1246-1256.e6 [PMID: 24534550 DOI: 10.1016/j.cgh.2014.02.016]
19 **Calderón M**, Minckas N, Nuñez S, Ciapponi A. Inflammatory Bowel Disease in Latin America: A Systematic Review. *Value Health Reg Issues* 2018; **17**: 126-134 [PMID: 29936359 DOI: 10.1016/j.vhri.2018.03.010]
20 **Victoria CR**, Sassak LY, Nunes HR. Incidence and prevalence rates of inflammatory bowel diseases, in midwestern of São Paulo State, Brazil. *Arq Gastroenterol* 2009; **46**: 20-25 [PMID: 19466305 DOI: 10.1590/S0004-28032009000100009]
21 **Parente JM**, Coy CS, Campelo V, Parente MP, Costa LA, da Silva RM, Stephan C, Zeitune JM. Inflammatory bowel disease in an underdeveloped region of Northeastern Brazil. *World J Gastroenterol* 2015; **21**: 1197-1206 [PMID: 25632193 DOI: 10.3748/wjg.v21.i4.1197]
22 **Harvey RF**, Bradshaw JM. A simple index of Crohn's-disease activity. *Lancet* 1980; **1**: 514 [PMID: 6102236 DOI: 10.1016/S0140-6736(80)92767-1]
23 **Winship DH**, Summers RW, Singleton JW, Best WR, Becktel JM, Lenk LF, Kern F. National Cooperative Crohn's Disease Study: study design and conduct of the study. *Gastroenterology* 1979; **77**: 829-842 [PMID: 38175 DOI: 10.1016/0016-5085(79)90383-4]
24 **Best WR**. Predicting the Crohn's disease activity index from the Harvey-Bradshaw Index. *Inflamm Bowel Dis* 2006; **12**: 304-310 [PMID: 16633052 DOI: 10.1097/01.MIB.0000215091.77492.2a]
25 **Lahiff C**, Safaie P, Awais A, Akbari M, Gashin L, Sheth S, Lembo A, Leffler D, Moss AC, Cheifetz AS. The Crohn's disease activity index (CDAI) is similarly elevated in patients with Crohn's disease and in patients with irritable bowel syndrome. *Aliment Pharmacol Ther* 2013; **37**: 786-794 [PMID: 23432394 DOI: 10.1111/apt.12262]
26 **Lewis JD**, Chuai S, Nessel L, Lichtenstein GR, Aberra FN, Ellenberg JH. Use of the noninvasive components of the Mayo score to assess clinical response in ulcerative colitis. *Inflamm Bowel Dis* 2008; **14**: 1660-1666 [PMID: 18623174 DOI: 10.1002/ibd.20520]
27 **Ciconelli RM**. Tradução para o português e validação do questionário genérico de avaliação de qualidade de vida "Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36)". Thesis, Escola Paulista de Medicina, Universidade Federal de São Paulo. São Paulo, 1997. Available from: http://repositorio.unifesp.br/handle/11600/15360
28 **Viegas Andrade M**, Noronha K, Kind P, Maia AC, Miranda de Menezes R, De Barros Reis C, Nepomuceno Souza M, Martins D, Gomes L, Nichele D, Calazans J, Mascarenhas T, Carvalho L, Lins C. Societal Preferences for EQ-5D Health States from a Brazilian Population Survey. *Value Health Reg Issues* 2013; **2**: 405-412 [PMID: 29702778 DOI: 10.1016/j.vhri.2013.01.009]
29 **Pontes RM**, Miszputen SJ, Ferreira-Filho OF, Miranda C, Ferraz MB. [Quality of life in patients with inflammatory bowel diseases: translation to Portuguese language and validation of the "Inflammatory Bowel Disease Questionnaire" (IBDQ)]. *Arq Gastroenterol* 2004; **41**: 137-143 [PMID: 15543390 DOI: 10.1590/S0004-28032004000200014]
30 **Ware JE**. SF-36 health survey update. *Spine (Phila Pa 1976)* 2000; **25**: 3130-3139 [PMID: 11124729 DOI: 10.1097/00007632-200012150-00008]
31 **Ware JE**, Kosinski M. Interpreting SF-36 summary health measures: a response. *Qual Life Res* 2001; **10**: 405-413; discussion 415-420 [PMID: 11763203 DOI: 10.1023/A:1012588218728]
32 **Knowles SR**, Keefer L, Wilding H, Hewitt C, Graff LA, Mikocka-Walus A. Quality of Life in Inflammatory Bowel Disease: A Systematic Review and Meta-analyses-Part II. *Inflamm Bowel Dis* 2018; **24**: 966-976 [PMID: 29688466 DOI: 10.1093/ibd/izy015]
33 **Guyatt G**, Mitchell A, Irvine EJ, Singer J, Williams N, Goodacre R, Tompkins C. A new measure of health status for clinical trials in inflammatory bowel disease. *Gastroenterology* 1989; **96**: 804-810 [PMID: 2644154 DOI: 10.1016/0016-5085(89)90905-0]
34 **Ciconelli RM**, Soárez PC, Kowalski CC, Ferraz MB. The Brazilian Portuguese version of the Work Productivity and Activity Impairment: General Health (WPAI-GH) Questionnaire. *Sao Paulo Med J* 2006; **124**: 325-332 [PMID: 17322953 DOI: 10.1590/S1516-31802006000600005]
35 **Calixto RP**, Flores C, Francesconi CF. Inflammatory Bowel Disease: Impact on Scores of Quality of Life, Depression and Anxiety in Patients Attending a Tertiary Care Center in Brazil. *Arq Gastroenterol* 2018; **55**: 202-207 [PMID: 30540078 DOI: 10.1590/s0004-2803.201800000-54]
36 **de Souza MMH**, Barbosa DA, Espinosa MM, Belasco AGS. Qualidade de vida de pacientes portadores de doença inflamatória intestinal. *Acta Paul Enferm* 2011; **24**: 479-484 [DOI: 10.1590/S0103-21002011000400006]

37 **Vogelaar L**, Spijker AV, van der Woude CJ. The impact of biologics on health-related quality of life in patients with inflammatory bowel disease. *Clin Exp Gastroenterol* 2009; **2**: 101-109 [PMID: 21694833 DOI: 10.2147/CEG.S4512]

38 **Coteur G**, Feagan B, Keininger DL, Kosinski M. Evaluation of the meaningfulness of health-related quality of life improvements as assessed by the SF-36 and the EQ-5D VAS in patients with active Crohn's disease. *Aliment Pharmacol Ther* 2009; **29**: 1032-1041 [PMID: 19222413 DOI: 10.1111/j.1365-2036.2009.03966.x]

39 **Høivik ML**, Bernklev T, Solberg IC, Cvancarova M, Lygren I, Jahnsen J, Moum B; IBSEN Study Group. Patients with Crohn's disease experience reduced general health and vitality in the chronic stage: ten-year results from the IBSEN study. *J Crohns Colitis* 2012; **6**: 441-453 [PMID: 22398064 DOI: 10.1016/j.crohns.2011.10.001]

40 **Williet N**, Sarter H, Gower-Rousseau C, Adrianjafy C, Olympie A, Buisson A, Beaugerie L, Peyrin-Biroulet L. Patient-reported Outcomes in a French Nationwide Survey of Inflammatory Bowel Disease Patients. *J Crohns Colitis* 2017; **11**: 165-174 [PMID: 27516406 DOI: 10.1093/ecco-jcc/jjw145]

41 **Holko P**, Kawalec P, Mossakowska M, Pilc A. Health-Related Quality of Life Impairment and Indirect Cost of Crohn's Disease: A Self-Report Study in Poland. *PLoS One* 2016; **11**: e0168586 [PMID: 27992531 DOI: 10.1371/journal.pone.0168586]

42 **Huppertz-Hauss G**, Lie Høivik M, Jelsness-Jørgensen LP, Henriksen M, Høie O, Jahnsen J, Hoff G, Moum B, Bernklev T. Health-related Quality of Life in Patients with Inflammatory Bowel Disease 20 Years After Diagnosis: Results from the IBSEN Study. *Inflamm Bowel Dis* 2016; **22**: 1679-1687 [PMID: 27206016 DOI: 10.1097/MIB.0000000000000806]

43 **Slonim-Nevo V**, Sarid O, Friger M, Schwartz D, Chernin E, Shahar I, Sergienko R, Vardi H, Rosenthal A, Mushkalo A, Dizengof V, Ben-Yakov G, Abu-Freha N, Munteanu D, Gaspar N, Eidelman L, Segal A, Fich A, Greenberg D, Odes S; Israeli IBD Research Nucleus (IIRN). Effect of psychosocial stressors on patients with Crohn's disease: threatening life experiences and family relations. *Eur J Gastroenterol Hepatol* 2016; **28**: 1073-1081 [PMID: 27203602 DOI: 10.1097/MEG.0000000000000666]

44 **OECD**. Employment Outlook 2017: How does Brazil compare? *OECD Publishing* 2017 [DOI: 10.1787/empl_outlook-2017-en]

45 **de S B Fróes R**, Carvalho ATP, de V Carneiro AJ, de Barros Moreira AMH, Moreira JPL, Luiz RR, de Souza HS. The socio-economic impact of work disability due to inflammatory bowel disease in Brazil. *Eur J Health Econ* 2018; **19**: 463-470 [PMID: 28523493 DOI: 10.1007/s10198-017-0896-4]

46 **Lönnfors S**, Vermeire S, Greco M, Hommes D, Bell C, Avedano L. IBD and health-related quality of life -- discovering the true impact. *J Crohns Colitis* 2014; **8**: 1281-1286 [PMID: 24662394 DOI: 10.1016/j.crohns.2014.03.005]

47 **Bernstein CN**, Longobardi T, Finlayson G, Blanchard JF. Direct medical cost of managing IBD patients: a Canadian population-based study. *Inflamm Bowel Dis* 2012; **18**: 1498-1508 [PMID: 22109958 DOI: 10.1002/ibd.21878]

48 **Bähler C**, Vavricka SR, Schoepfer AM, Brüngger B, Reich O. Trends in prevalence, mortality, health care utilization and health care costs of Swiss IBD patients: a claims data based study of the years 2010, 2012 and 2014. *BMC Gastroenterol* 2017; **17**: 138 [PMID: 29197335 DOI: 10.1186/s12876-017-0681-y]

49 **Gunnarsson C**, Chen J, Rizzo JA, Ladapo JA, Lofland JH. Direct health care insurer and out-of-pocket expenditures of inflammatory bowel disease: evidence from a US national survey. *Dig Dis Sci* 2012; **57**: 3080-3091 [PMID: 22790905 DOI: 10.1007/s10620-012-2289-y]

50 **Niewiadomski O**, Studd C, Hair C, Wilson J, McNeill J, Knight R, Prewett E, Dabkowski P, Dowling D, Alexander S, Allen B, Tacey M, Connell W, Desmond P, Bell S. Health Care Cost Analysis in a Population-based Inception Cohort of Inflammatory Bowel Disease Patients in the First Year of Diagnosis. *J Crohns Colitis* 2015; **9**: 988-996 [PMID: 26129692 DOI: 10.1093/ecco-jcc/jjv117]

51 **van der Valk ME**, Mangen MJ, Leenders M, Dijkstra G, van Bodegraven AA, Fidder HH, de Jong DJ, Pierik M, van der Woude CJ, Romberg-Camps MJ, Clemens CH, Jansen JM, Mahmmod N, van de Meeberg PC, van der Meulen-de Jong AE, Ponsioen CY, Bolwerk CJ, Vermeijden JR, Siersema PD, van Oijen MG, Oldenburg B; COIN study group and the Dutch Initiative on Crohn and Colitis. Healthcare costs of inflammatory bowel disease have shifted from hospitalisation and surgery towards anti-TNFα therapy: results from the COIN study. *Gut* 2014; **63**: 72-79 [PMID: 23135759 DOI: 10.1136/gutjnl-2012-303376]

52 **Bennett AL**, Munkholm P, Andrews JM. Tools for primary care management of inflammatory bowel disease: do they exist? *World J Gastroenterol* 2015; **21**: 4457-4465 [PMID: 25914455 DOI: 10.3748/wjg.v21.i15.4457]

53 **Rubin GP**, Hungin AP, Kelly PJ, Ling J. Inflammatory bowel disease: epidemiology and management in an English general practice population. *Aliment Pharmacol Ther* 2000; **14**: 1553-1559 [PMID: 11121902 DOI: 10.1046/j.1365-2036.2000.00886.x]

54 **Hilsden RJ**, Verhoef MJ, Best A, Pocobelli G. A national survey on the patterns of treatment of inflammatory bowel disease in Canada. *BMC Gastroenterol* 2003; **3**: 10 [PMID: 12791168 DOI: 10.1186/1471-230X-3-10]

55 **Derwa Y**, Williams CJM, Sood R, Mumtaz S, Bholah MH, Selinger CP, Hamlin PJ, Ford AC, Gracie DJ. Factors affecting clinical decision-making in inflammatory bowel disease and the role of point-of-care calprotectin. *Therap Adv Gastroenterol* 2018; **11**: 1756283X17744739 [PMID: 29383026 DOI: 10.1177/1756283X17744739]

56 **Teixeira FV**, Hossne RS, Kotze PG, Denadai R, Miszputen SJ. Biological therapy in the treatment of moderate-to-severe ulcerative colitis patients: can colectomy be prevented? *J Coloproctol (Rio de Janeiro)* 2011; **31**: 325-329 [DOI: 10.1590/S2237-93632011000400002]

57 **Alencar SSS de**, Corrêa R da S, Bezerra C de F, Menezes ESC de, Nascimento AL do, Costa DAA da, Alencar MJC. The surgical treatment of patients with ulcerative colitis from an university hospital at Natal, Brazil. *J Coloproctol (Rio de Janeiro)* 2012; **32**: 265-270 [DOI: 10.1590/S2237-93632012000300010]

58 **Kornbluth A**, Sachar DB; Practice Parameters Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology, Practice Parameters Committee. *Am J Gastroenterol* 2010; **105**: 501-23; quiz 524 [PMID: 20068560 DOI: 10.1038/ajg.2009.727]

Published By Baishideng Publishing Group Inc
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-2238242
E-mail: bpgoffice@wjgnet.com
Help Desk:http://www.f6publishing.com/helpdesk
http://www.wjgnet.com