

# Quality of life and special issues in women with inflammatory bowel diseases

Gabriel Constantinescu<sup>1</sup>, Gina Gheorghe<sup>1\*</sup>, Ecaterina Rinja<sup>1</sup>, Oana Plotogea<sup>1</sup>, Vasile Sandru<sup>2</sup>, Andreea Butuc<sup>2</sup>, Camelia Cristina Diaconu<sup>3\*</sup>, Anca Macovei Oprescu<sup>4</sup>, Bogdan Popa<sup>5</sup>, Madalina Ilie<sup>1,2</sup>

<sup>1</sup>CAROL DAVILA UNIVERSITY OF MEDICINE AND PHARMACY, DEPARTMENT OF GASTROENTEROLOGY, CLINICAL EMERGENCY HOSPITAL OF BUCHAREST, BUCHAREST, ROMANIA

<sup>2</sup>CLINICAL EMERGENCY HOSPITAL OF BUCHAREST, DEPARTMENT OF GASTROENTEROLOGY, BUCHAREST, ROMANIA

<sup>3</sup>CAROL DAVILA UNIVERSITY OF MEDICINE AND PHARMACY, DEPARTMENT OF INTERNAL MEDICINE, CLINICAL EMERGENCY HOSPITAL OF BUCHAREST, BUCHAREST, ROMANIA

<sup>4</sup>CAROL DAVILA UNIVERSITY OF MEDICINE AND PHARMACY, DEPARTMENT OF GASTROENTEROLOGY, CLINICAL EMERGENCY HOSPITAL PROF. DR. AGRIPPA IONESCU, ROMANIA

<sup>5</sup>CAROL DAVILA UNIVERSITY OF MEDICINE AND PHARMACY, DEPARTMENT OF RADIOLOGY AND MEDICAL IMAGING, CLINICAL EMERGENCY HOSPITAL OF BUCHAREST, ROMANIA

## ABSTRACT



**Introduction.** The impact of inflammatory bowel diseases (IBD) on the quality of life (QoL) of patients is significant and it has important social and professional consequences. **Materials and methods.** We aimed to describe the patients' perspective regarding the impact of IBD on their overall QoL and to evaluate the differences between men and women. An observational cross-sectional study, that included 180 patients with IBD in clinical remission, was conducted. All the patients completed a number of 3 questionnaires in order to evaluate the general aspects of their QoL. A separate questionnaire was created regarding gender-specific issues in women with IBD encounter. Also, particular features such as the incidence of anemia and osteoporosis among IBD patients were documented. The data obtained were analyzed and compared between the two gender-classified groups. **Results.** According to the Short Inflammatory Bowel Disease Questionnaire (SIBDQ), patients had a general perception of a good QoL, but the impact was higher in women. Fatigue and tiredness were severely perceived almost to the same degree regardless of their gender, whereas anxiety and unemployment were more present in men. No significant differences in women with IBD during the active disease and during disease remission were found. **Conclusions.** The overall quality of life of IBD patients is affected in many aspects, leading to the deterioration of their social and professional lives, for both men and women, but some aspects remain gender-specific and require a personalized standard of care.

**Category:** Original Research Paper

**Received:** March 18, 2021

**Accepted:** April 29, 2021

**Published:** October 10, 2021

### Keywords:

inflammatory bowel disease, quality of life, quality improvement, gender, biological treatment

### \*Corresponding authors:

Gina Gheorghe, Camelia Cristina Diaconu,

Carol Davila University of Medicine and Pharmacy, Clinical Emergency Hospital of Bucharest, Calea Floreasca no. 8, Bucharest, Romania

E-mails:

[gheorghe\\_gina2000@yahoo.com](mailto:gheorghe_gina2000@yahoo.com); [drcameliadiaconu@gmail.com](mailto:drcameliadiaconu@gmail.com)

## Introduction

Inflammatory bowel diseases (IBD) have a great impact on the quality of life (QoL), in both men and women, and represent a substantial burden on the patient and the caregivers. The consequences can be observed in the increased rates of depression, anxiety, chronic fatigue and reduced workforce participation seen in patients with Crohn's disease or ulcerative colitis [1, 2].

The impact of IBD on the QoL is multifaceted, from direct physical distress because of symptoms, in addition to psychological impairment, financial burden and low work productivity [1]. People with IBD frequently require multidisciplinary care, including mental health care, that

can help in the development of adaptive coping mechanisms in order to reduce psychological distress.

Several studies have demonstrated that the QoL is impaired in these patients in comparison with the general population [3,4], but only a few evaluated the differences between men and women. As women are regarded as being more sensitive to social stigma of having a chronic disease and being prone to anxiety and depression [5], we tend to think that women with IBD should be more affected than men, but are they really so?

In order to answer this question, we aimed to make a comparison between women and men regarding the impact of IBD on their overall QoL. We tried to raise physicians' awareness on the gender-specific aspects women with IBD

may have and the impact on their self-esteem, resilience and overall coping mechanisms on the daily basis.

## Materials and Methods

We conducted an observational cross-sectional study, that included patients with IBD who attended our Gastroenterology and Interventional Endoscopy Department from January 2017 until January 2020.

Patients previously diagnosed with IBD, either ulcerative colitis or Crohn's disease, who achieved clinical remission under treatment with biologic agents, were included. Patients' consent for data registration and subsequent use in clinical research was obtained at the time of inclusion in the current study, after the approval of the local ethics committee was obtained. Each patient received a number of questionnaires regarding their perception on the overall QoL, using the Short Inflammatory Bowel Disease Questionnaire (SIBDQ) [6], the degree of chronic fatigue using the Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F) [7], the level of anxiety and depression caused by numerous hospital admissions (HADS) [8] and the impact of the disease on work productivity. Furthermore, a particular questionnaire was created for women with IBD specifically, concerning issues such as menstruation (age of menarche, variations of menstruation symptoms during remission and active disease) and the possibility of obtaining a full-term pregnancy with or without continuing the biologic treatment, the Special Issues of Women with IBD Questionnaire (SIWIBDQ) (Table 1).

Nevertheless, the incidence of osteoporosis and anemia among our patients was also documented from the data provided by the periodical biological examinations and bone density scans of each patient.

A total of 180 adult patients achieved sustained clinical and biochemical remission under biologic treatment. The data regarding the symptoms and patient-reported outcomes were gathered using the previously stated questionnaires, after a minimum of 6 months of persistent clinical remission. Clinical remission was defined as the absence of symptoms: resolution of diarrhea and bleeding, abdominal pain and weight loss. However, laboratory testing was performed for each patient in order to correlate clinical with biochemical remission. Laboratory tests included complete blood count, inflammatory markers (C-reactive protein), albumin level and fecal calprotectin levels. All patients included in this study had no leukocytosis on complete blood count tests and C-reactive protein and albumin levels were within normal range. Also, fecal calprotectin levels were normal.

The exclusion criteria for participation in this study were pre-existing diagnoses of depression or anxiety disorder and continuous or intermittent treatment with anti-depressant or anti-anxiety medications.

**Table 1.** Special issues of women with IBD Questionnaire (SIWIBDQ)

1. What was your menarche age?	Points
• 12-13 years	0
• < 12 years	1
• ≥ 14 years	2
2. How do you perceive menstruation symptoms during clinical remission of IBD versus active disease phase?	
• Menstruation symptoms are less severe	0
• Menstruation symptoms are the same	1
• Menstruation symptoms are more severe	2
3. Did you have any pregnancy since the biological treatment for IBD was initiated?	
• No	0
• Yes	1
4. If the answer to question 3 was yes, did you discontinue the biological treatment during pregnancy?	
• No	0
• Yes	1

Tick the box beside the reply that best describes your current situation. Please answer all the questions.

Scoring:

Total score: \_\_\_\_\_

Normal = 0-3; Abnormal (case) = 4-6.

From a total of 180 patients who met the inclusion criteria, 65 were women and 115 were men, with an average age of 37 years. Therefore, two groups were created based on the gender classification.

All patients included in this study completed the following questionnaires: (1) Short Inflammatory Bowel Disease Questionnaire (SIBDQ); (2) Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) and (3) Hospital Anxiety and Depression Scale (HADS). Women also completed the (4) Special issues of women with IBD Questionnaire (SIWIBDQ).

The SIBDQ is a disease-specific health-related quality of life (HRQoL) measuring tool, meant to evaluate four domains – bowel, emotion, social and daily activities, and general well-being. Its importance lies in the capacity to address key points in one's life, such as social life, psychological well-being, the degree of fatigue, the presence of depression and body image. The questionnaire contains 10 items, and each item has a 7-point scale from 1 to 7. The absolute SIBDQ score ranges from 10 to 70, with higher values suggesting a better QoL.

The Functional Assessment of Chronic Illness Therapy - fatigue (FACIT-fatigue) scale is an instrument designed

to assess fatigue and tiredness and their impact on daily activities and functioning in patients with chronic diseases. This score contains 13 items, each item being ranked from 0 to 4 points, with a total score of 52 points. The instrument includes aspects such as tiredness, weakness, lack of energy, listlessness and the impact of these feelings on daily activities (for example sleeping and social activities). A score under 30 points is representative for severe fatigue and the higher the score, the better the QoL of patients.

In assessing the QoL of patients included in this study, a questionnaire consisting of a 7-question anxiety assessment and 7-question depression assessment, the HADS score, was also used. The score for each item ranges from zero to three, with three indicating the highest anxiety or depression level. A total subscale score of more than 11 points out of 21 possible points suggests considerable symptoms of depression or anxiety, between 8 and 10 being borderline abnormal, and less than 7 being normal.

In order to fully understand the women-specific issues, we created the Special Issues of Women with IBD Questionnaire (SIWIBDQ), consisting of 4 questions regarding the menarche age, menstruation symptoms assessment during clinical remission in comparison with active disease phase and pregnancy (Table 1).

All the data obtained were analyzed and compared between the two gender-classified groups.

## Results

A total of 180 patients were included in this study. From these, 115 patients were men and 65 women, aged between 19-47 years, thus balancing the scale towards men, with a percentage of 63.89%. The majority of the patients had no other comorbidities (91.67%). Overall, median SIBDQ, FACIT-F, HADS-anxiety and HADS-depression for males were 53.52, 17.04, 5.21, and 4.56, respectively, and for women, 52.30, 18.53, 4.69, and 4.07. the demographic data including patients' clinical characteristics are shown in Table 2.

### *The SIBDQ score*

A very useful tool in measuring health-related QoL is the Short Inflammatory Bowel Disease Questionnaire (SIBDQ). When asked to fill in the SIBDQ questionnaire, women included in this study (36.11% from the total of patients) obtained total scores ranging from 38 and 67 points, with a median score of 52.30 points. Most of the patients were men (63.89%) and similar results were observed in this subgroup: their scores varied from 27 to 68 points and the median score was 53.52 points. High median scores were identified in both subgroups, which means that the patients had a general perception of good QoL, but the impact was higher in women who obtained lower scores than men.

### *The FACIT-F score*

The impact of the disease on the perception of fatigue was evaluated for the 115 male subjects in the study: the scores in this category of patients varied from 7 to 42, with a median score of 17.04 points. Women who completed this questionnaire and graded their symptoms obtained scores from 9 to 33 points, the median score among them being 18.53 points. Therefore, fatigue and tiredness were severely perceived by the two groups almost to the same degree.

### *The HADS score*

The HADS score can be divided into two subgroups HADS-anxiety and HADS-depression. The majority of the patients in our study were within the normal range, without significant differences between men and women for both the HADS-anxiety (78.26% vs. 76.92%) and HADS-depression (78.26% vs. 84.61%). In the borderline category, we encountered more women than men (15.38% vs. 4.34%) in the HADS-anxiety subgroup, whereas in the HADS-depression subgroup there were only men (17.40%). In the abnormal category there were only 5 patients for the HADS-anxiety and 3 patients for HADS-depression. But here, in comparison, the gender scale is inverted, as more men than women felt severe anxiety (17.4% men, 7.70% women) (Table 3) and more women than men felt severe depression (15.39% vs. 4.34%) (Table 4).

**Table 2.** Demographic and clinical characteristics of patients with IBD.

Variables	N = 36
<b>Median age, years</b>	42 (19-47)
Males, n (%)	115 (63.89%)
Females, n (%)	65 (36.11%)
<b>Other comorbidities, n (%)</b>	
Diabetes mellitus	5 (2.78%)
Arterial hypertension	10 (5.55%)
None	165 (91.67%)
<b>Unemployment</b>	
Males, n (%)	40 (22.23%)
Females, n (%)	25 (13.89%)
<b>Anemia</b>	
Present, n (%)	15 (8.33%)
Absent, n (%)	165 (91.67%)
<b>Osteoporosis</b>	
Males, n (%)	0 (0%)
Females, n (%)	(8.33%)
<b>Median SIBDQ</b>	
Males	53.52
Females	52.30
<b>Median FACIT-F</b>	
Males	17.04
Females	18.53
<b>Median HADS-anxiety</b>	
Males	5.21
Females	4.69
<b>Median HADS-depression</b>	
Males	4.56
Females	4.07
<b>Median SIWIBDQ</b>	1.85

**Table 3.** HADS - anxiety score.

	<b>Women percentage (number of cases)</b>	<b>Men percentage (number of cases)</b>
Normal	76.92% (50)	78.26% (90)
Borderline abnormal	15.38% (10)	4.34% (5)
Abnormal	7.70% (5)	17.4% (20)
Total	100% (65)	100% (115)

**Table 4.** HADS - depression score.

	<b>Women percentage (number of cases)</b>	<b>Men percentage (number of cases)</b>
Normal	84.61% (55)	78.26% (90)
Borderline abnormal	0% (0)	17.40% (20)
Abnormal	15.39% (10)	4.34% (5)
Total	100% (65)	100% (115)

**Table 5.** Menarche and the evaluation of dysmenorrhea during the active disease

<b>Age of menarche</b>	<b>Number of patients (percentage)</b>
11 years	15 (23.07%)
12 years	25 (38.48%)
13 years	15 (23.07%)
14 years	10 (15.38%)
<i>Dysmenorrhea during the active stage of the disease</i>	
More painful	5 (7.69%)
Equally painful	55 (84.62%)
Less painful	5 (7.69%)
<i>Pregnancy</i>	
No pregnancies	50 (77%)
At least one pregnancy	15 (33%)
Continued biological treatment during pregnancy	10 (66.60%)
Discontinued biological treatment during pregnancy	5 (33.40%)

*The impact on work activity and daily activities*

Regarding the employment status and work productivity of IBD patients, we observed that more than one third was unemployed, i.e., more men than women (22.23% vs. 13.89%). Regarding the work productivity and the number of hours missed from work due to bowel

problems, the majority (56%) of the patients, all women, did not miss one single hour from work. Only men (8%) had missed a few hours from work because of bowel problems and general malaise.

*Special issues of women with IBD and the safety of biologic agents during pregnancy*

Regarding the specific issues of women with IBD such as menstruation, the mean age of menarche was between 12 and 13 years (61.55%), the same as the one for the general population [9]. Moreover, we did not find significant differences in women with IBD between dysmenorrhea during the active disease and during disease remission, as 84.62% (55 patients) experienced equally painful periods (Table 5).

Although 77% of the women did not have any pregnancy prior to the diagnosis, 23% were able to deliver a full-term baby without complications, out of which 66.60% continued the biologic treatment during pregnancy and only 33.40% discontinued it.

*Anemia and osteoporosis among IBD patients*

The topic of anemia and osteoporosis in patients with IBD benefits from little attention when analyzing extra-intestinal disease complications. In our study, we observed that 92% of our patients have no anemia, which shows that the disease is controlled and the patients respond well to iron treatment, and only 9% of the patients, all women, had osteoporosis.

## Discussions

The results of this study focused on the psychological impact of IBD, demonstrating that although both men and women obtained high median scores according to the SIBDQ questionnaire, therefore having a general perception of an optimum QoL, the impact was higher for women, who obtained lower scores in comparison with men.

A study published in 2020 reports similar results: a lower QoL among women, compared to men diagnosed with IBD [10]. These findings correspond to the data observed in the general population, more precisely a higher rate of absenteeism from work and a more frequent use of healthcare services among women compared to men [10, 11]. Another important aspect that contributes to a reduced QoL is the presence of physical asthenia. Compared to men, women report a higher frequency and intensity of physical asthenia. This symptom is independent from the active state of the disease and the presence or absence of anemia, one of the causal factors [12-14].

However, a surprising feature pointed out by this study was that more than one third of the patients (36.1%) are unemployed, because of various reasons. Even though they are predominantly young adults, living with IBD is

definitely a challenge because work productivity and employment prospects are diminished, both directly by the symptoms and the complications of the disease, and, indirectly, by the psychological distress patients have to cope with, making it difficult to get and, especially, to keep a workplace.

A study conducted in Norway reports higher rates of unemployment and sick leave among patients diagnosed with IBD when compared to the general population [15]. Moreover, the unemployment rate was slightly higher in women compared to men (12.4% vs. 11.1%) [16]. The unemployment rate was higher in patients diagnosed with ulcerative colitis (13.2%) compared to those diagnosed with Crohn disease (8.7%) [15]. The mean unemployment age in patients with ulcerative colitis was 55.3 years, compared to 42.2 years in those with Crohn disease [15].

Even if fatigue and tiredness are more and more present among the general population due to a constant need to keep up with each other, especially in the working environment, it represents a daily burden for IBD patients, regardless of their gender [16]. According to the FACIT-F score, both women and men were severely affected, obtaining similar scores.

Numerous studies show that the QoL is impaired in these patients in comparison with the general population. Also, psychological distress does not always correlate with the activity and severity of the disease, because even during the clinical remission, patients may experience the impairment of the QoL [1-4].

Disease chronicity requires the development of self-management and coping skills over time; therefore, it is not surprising that IBD patients have an increased risk of mental health issues, including depression, which is an important problem that patients often experience; therefore, it is essential for the caregiver to recognize these diseases in the early stages. Recent studies show that the relationship between depression and chronic disease is bidirectional, with poor health leading to poor self-management, as well as poor self-management leading to poor health [17,18].

The ongoing problem depression and anxiety pose in IBD patients is outlined by this study by using the HADS anxiety and depression questionnaire, which showed that anxiety is more present in men than women, whereas depression was encountered more predominantly in women.

In addition to the huge impact that IBD has on the QoL, people living with IBD face other numerous challenges. These include social stigma of suffering from a chronic disease, affordability of medications, diminished employment prospects, difficulty with leisure time and travelling, limited community-based supports and inequitable access to health care specialists and services [16,18]. Reducing these difficulties should be a priority for

physicians and health care providers, to improve the QoL of their patients.

During flares, symptoms of IBD (both gastrointestinal and systemic symptoms) disrupt immediate activities and cause worry and embarrassment to patients. These immediate effects result in a plethora of impacts on the patient's life and psychological well-being, which continue to have consequences even during the clinical remission of the disease, but to a lower degree [19].

A 2016 systematic review analyzed 171 studies including 158,371 individuals and showed a prevalence rate of anxiety of approximately 20% and a prevalence rate of depression of 15% in patients with IBD [20]. Both mental disorders had a higher prevalence during the disease activity period compared to the remission period. The estimated anxiety prevalence in patients with IBD during the disease activity was 75.6%, compared to 20.5% in the general population. It is noteworthy that the anxiety prevalence has been shown to be higher in patients with active IBD compared to patients with diabetes or chronic obstructive pulmonary disease [20-22]. The estimated depression prevalence in patients with active disease was 40.7%, compared to 15.2% in the general population. Depressive disorders have also been diagnosed more frequently in patients with Crohn disease compared to those with ulcerative colitis [20].

Interestingly, we found that although both men and women obtained similar scores, men were more affected by anxiety, encountered more difficulties getting and, especially, keeping a workplace, which had a huge impact on their social life as well.

A key strength of this study was the evaluation of special issues women with IBD have, despite the maintenance of remission under biologic agents. Moreover, by using accessible and easy to understand and answer questionnaires, we were able to obtain clinical data, as it is experienced by each patient. An important limitation of this study is the small number of patients included, but the data obtained can be a starting point for further larger prospective multi-center studies.

Although women are more affected by depression and social stigma than men, they are more resilient and develop better coping mechanisms, therefore obtaining a better QoL than men.

These results correspond to the existing data that highlight the development of better coping mechanisms in women, compared to men diagnosed with IBD [23,24]. The data so far support a greater negative impact on the QoL of women with IBD compared to men diagnosed with the same conditions [25-27].

Nevertheless, we must highlight that, even during the sustained clinical remission, these patients, regardless of their gender, experience QoL impairment.

## Highlights

- ✓ Inflammatory bowel diseases (IBD) have a great impact on the quality of life (QoL).
- ✓ The QoL of patients with IBD is affected in many aspects, leading to the deterioration of their social and professional lives, regardless of their gender, even if the majority of patients regarded themselves as having a good QoL.
- ✓ The data show that there are differences between men and women.

## Conclusions

Our study results show that the QoL of patients with IBD is affected in many aspects, leading to the deterioration of their social and professional lives, regardless of their gender, even if the majority of patients regarded themselves as having a good QoL. Moreover, the data show that there are differences between men and women; when asking the question if women are really more affected than men, we observed that, although women encounter more difficulties, they have an overall better QoL than men. Nevertheless, future longitudinal studies on the psychological impact of patients with IBD are required in order to help us better understand their gender-specific needs, create better measurement tools and improve their QoL.

## Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

## Compliance with ethical standards

The ethical approval for this study was obtained from the ethics committee of the Emergency Clinical Hospital of Bucharest. All the subjects included in the study were informed about the purpose of the study and its involvement, subsequently signing an informed consent. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## References

1. Devlen J, Beusterien K, Yen L, Ahmed A, Cheifetz AS, Moss AC. The burden of inflammatory bowel disease: a patient-reported qualitative analysis and development of a conceptual model. *Inflamm Bowel Dis*. 2014; 20(3):545-52. doi: 10.1097/01.MIB.0000440983.86659.81
2. Liu R, Tang A, Wang X, Shen S. Assessment of Quality of Life in Chinese Patients With Inflammatory Bowel Disease and their Caregivers. *Inflamm Bowel Dis*. 2018;24(9):2039-2047. doi: 10.1093/ibd/izy099
3. Wilcox AR, Dragnev MC, Darcey CJ, Siegel CA. A new tool to measure the burden of Crohn's disease and its treatment: do patient and physician perceptions match? *Inflamm Bowel Dis*. 2010 Apr;16(4):645-50. doi: 10.1002/ibd.21094
4. Jones JL, Nguyen GC, Benchimol EI, Bernstein CN, Bitton A, Kaplan GG, Murthy SK, Lee K, Cooke-Lauder J, Otley AR. The Impact of Inflammatory Bowel Disease in Canada 2018: Quality of Life. *J Can Assoc Gastroenterol*. 2019 Feb;2(Suppl 1):S42-S48. doi: 10.1093/jcag/gwy048
5. Yang K, Girgis JS. Are women more likely than men are to care excessively about maintaining positive social relationships? A meta-analytic review of the gender difference in sociotropy. *Sex Roles*. 2019; 81:157-172. doi: 10.1007/S11199-018-0980-y
6. Jowett SL, Seal CJ, Barton JR, Welfare MR. The short inflammatory bowel disease questionnaire is reliable and responsive to clinically important change in ulcerative colitis. *Am J Gastroenterol*. 2001; 96(10):2921-8. doi: 10.1111/j.1572-0241.2001.04682.x
7. Smith E, Lai JS, Cella D. Building a measure of fatigue: the functional assessment of Chronic Illness Therapy Fatigue Scale. *PM R*. 2010 May;2(5):359-63. doi: 10.1016/j.pmrj.2010.04.017
8. Bernstein CN, Zhang L, Lix LM, Graff LA, Walker JR, Fisk JD, Patten SB, Hitchon CA, Bolton JM, Sareen J, El-Gabalawy R, Marriott J, Marrie RA; CIHR Team in Defining the Burden and Managing the Effects of Immune-mediated Inflammatory Disease. The Validity and Reliability of Screening Measures for Depression and Anxiety Disorders in Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2018 Aug 16;24(9):1867-1875. doi: 10.1093/ibd/izy068
9. Shen Y, Varma DS, Zheng Y, Boc J, Hu H. Age at menarche and depression: results from the NHANES 2005-2016. *PeerJ*. 2019 Jun 13;7:e7150. doi: 10.7717/peerj.7150
10. Greuter T, Manser C, Pittet V, Vavricka SR, Biedermann L; on behalf of Swiss IBDnet, an official working group of the Swiss Society of Gastroenterology. Gender Differences in Inflammatory Bowel Disease. *Digestion*. 2020;101 Suppl 1:98-104. doi: 10.1159/000504701
11. Häuser W, Janke KH, Klump B, Hinz A. Anxiety and depression in patients with inflammatory bowel disease: comparisons with chronic liver disease patients and the general population. *Inflamm Bowel Dis*. 2011 Feb;17(2):621-32. doi: 10.1002/ibd.21346
12. Saraiva S, Cortez-Pinto J, Barosa R, Castela J, Moleiro J, Rosa I, da Siva JP, Dias Pereira A. Evaluation of fatigue in inflammatory bowel disease - a useful tool in daily practice. *Scand J Gastroenterol*. 2019;54(4):465-470. doi: 10.1080/00365521.2019.1602669

13. Le Berre C, Peyrin-Biroulet L, Buisson A, Olympie A, Ravel MH, Bienenfeld C, Gonzalez F. Impact of inflammatory bowel diseases on working life: A French nationwide survey. *Dig Liver Dis*. 2019 Jul;51(7):961-966. doi: 10.1016/j.dld.2019.01.024
14. Van de Vijver E, Van Gils A, Beckers L, Van Driessche Y, Moes ND, van Rheeën PF. Fatigue in children and adolescents with inflammatory bowel disease. *World J Gastroenterol*. 2019 Feb 7;25(5):632-643. doi: 10.3748/wjg.v25.i5.632
15. Bernklev T, Jahnsen J, Henriksen M, Lygren I, Aadland E, Sauar J, Schulz T, Stray N, Vatn M, Moum B. Relationship between sick leave, unemployment, disability, and health-related quality of life in patients with inflammatory bowel disease. *Inflamm Bowel Dis*. 2006 May;12(5):402-12. doi: 10.1097/01.MIB.0000218762.61217.4a
16. Borren NZ, van der Woude CJ, Ananthakrishnan AN. Fatigue in IBD: epidemiology, pathophysiology and management. *Nat Rev Gastroenterol Hepatol*. 2019 Apr;16(4):247-259. doi: 10.1038/s41575-018-0091-9
17. Keefer L, Kane SV. Considering the Bidirectional Pathways Between Depression and IBD: Recommendations for Comprehensive IBD Care. *Gastroenterol Hepatol (N Y)*. 2017 Mar;13(3):164-169.
18. Egberg MD, Gulati AS, Gellad ZF, Melmed GY, Kappelman MD. Improving Quality in the Care of Patients with Inflammatory Bowel Diseases. *Inflamm Bowel Dis*. 2018 Jul 12;24(8):1660-1669. doi: 10.1093/ibd/izy030
19. 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. doi: 10.3748/wjg.v25.i38.5862
20. 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 Aug;87:70-80. doi: 10.1016/j.jpsychores.2016.06.001
21. Grigsby AB, Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. Prevalence of anxiety in adults with diabetes: a systematic review. *J Psychosom Res*. 2002; 53(6):1053-60. doi: 10.1016/s0022-3999(02)00417-8
22. Willgoss TG, Yohannes AM. Anxiety disorders in patients with COPD: a systematic review. *Respir Care*. 2013 May;58(5):858-66. doi: 10.4187/respcare.01862
23. Sarid O, Slonim-Nevo V, Pereg A, Friger M, Sergienko R, Schwartz D, Greenberg D, Shahar I, Chernin E, Vardi H, Eidelman L, Segal A, Ben-Yakov G, Gaspar N, Munteanu D, Rozental A, Mushkalo A, Dizengof V, Abu-Freha N, Fich A, Odes S; Israeli IBD Research Nucleus (IIRN). Coping strategies, satisfaction with life, and quality of life in Crohn's disease: A gender perspective using structural equation modeling analysis. *PLoS One*. 2017 Feb 28;12(2):e0172779. doi: 10.1371/journal.pone.0172779
24. McCombie AM, Mulder RT, Gearry RB. How IBD patients cope with IBD: a systematic review. *J Crohns Colitis*. 2013 Mar;7(2):89-106. doi: 10.1016/j.crohns.2012.05.021
25. Lee H, Mason D. Cultural and gender differences in coping strategies between Caucasian American and Korean American older people. *J Cross Cult Gerontol*. 2014 Dec;29(4):429-46. doi: 10.1007/s10823-014-9241-x
26. Huppertz-Hauss G, Høivik ML, Langholz E, Odes S, Småstuen M, Stockbrugger R, Hoff G, Moum B, Bernklev T. Health-related quality of life in inflammatory bowel disease in a European-wide population-based cohort 10 years after diagnosis. *Inflamm Bowel Dis*. 2015 Feb;21(2):337-44. doi: 10.1097/MIB.0000000000000272
27. Hauser G, Tkalcic M, Stimac D, Milić S, Sincić BM. Gender related differences in quality of life and affective status in patients with inflammatory bowel disease. *Coll Antropol*. 2011 Sep;35 Suppl 2:203-7.