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# WORK DISABILITY AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE: PREVALENCE AND PREDICTIVE FACTORS IN A CROSS-SECTIONAL STUDY

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### **ABSTRACT**

Background: Inflammatory bowel disease (IBD) is a lifelong illness usually diagnosed in early adulthood. It is characterized by unpredictable flare-ups and debilitating symptoms that can interfere with the patient's ability to work and could lead to professional disintegration and job loss. The aim of this study was to estimate the prevalence of work disability among IBD patients and to identify its predictive factors. Methods: Cross-sectional study including IBD patients exercising a professional activity, followed at the Gastroenterology B department of the Rabta hospital in Tunisia, between April and December 2019. The work ability was assessed by the «Work Ability Index (WAI)» questionnairy. Results: We included 45 patients: 80% Crohn's disease (CD) and 20% ulcerative colitis (UC). The mean age was 44 years with a M/F sex ratio of 0.73. Work ability assessed by the WAI was perceived as poor in 38% of patients, leading to an overall average absence of 49.6 days/year (p=0.001). The work disability was more important in workers (p=0.008), employees in private sector (p=0.017), workers with atypical schedules (p=0.034) and in case of a professional seniority higher than 16.5 years (p=0.009). Patientrelated factors were advanced age, low socio-economic conditions and low educational level. Disease-related factors were stricturing phenotype of CD, extensive UC, moderate to severe disease activity, presence of extraintestinal manifestations (EIM) and corticotherapy. In multivariate analysis, osteoarticular EIM (OR=21.9 [95% CI: 2.302 - 208.356]; p=0.007) and moderate to severe disease activity (OR=34.2 [95% CI: 3.585 - 327.269]; p=0.002) were predictive factors of impaired work ability. **Conclusion:** According to our study, IBD would cause work disability in 38% of cases. Moderate to severe disease activity and the presence of rheumatological EIM were both identified as independent predictors of work disability. Thus, the WAI can be used as a screening tool to identify the need for rehabilitation.

KEYWORDS: Inflammatory bowel disease, Work, Questionnaires, Absenteeism, Occupations, Ability.

#### BACKGROUND

Inflammatory bowel diseases (IBD) is a group of immune-mediated inflammatory conditions of the gastrointestinal tract. They are classified into two main categories: Crohn's disease (CD) and ulcerative colitis (UC), based on clinical, endoscopic and histological criteria. It is a lifelong illness that mainly affects young adults in working age. Increasingly frequent, IBD now affects more than 6.8 million people around the world. They have a limited impact on mortality but are responsible for a high level of morbidity.

The impact on employment is well known in certain chronic diseases, but very few data are available on the working life of IBD patients. Previous studies have found that IBD patients have higher rates of unemployment compared to the general population<sup>[3,4]</sup> Indeed, its fluctuating symptomatology, unpredictable flare-ups and absenteeism due to hospitalizations and

medical appointments are factors that can interfere with the patient's ability to work. This could lead to professional disintegration and job loss. Therefore, the study of the risk factors that influence work ability will allow the elaboration of a guideline to help the decision of aptitude in these patients in order to maintain them at work and thus improve their professional career.

The aim of our study was to estimate the prevalence of work disability among IBD patients and to identify its predictive factors according to the characteristics of the disease and professional status.

## **METHODS**

We conducted a cross-sectional, monocentric, observational study at the gastroenterology department B of "La Rabta" University Hospital in Tunisia, which is considered one of the leading governmental tertiary

hospitals in the region. Our study was conducted between April and December 2019.

We included patients with IBD (CD / UC) and exercising a professional activity for at least one year, who were in relapse or in remission and who presented to the outpatient consultation or who were hospitalized. We performed a survey among these patients using a self-report questionnairy on professional status, characteristics of the position held, and difficulties encountered during work. As for IBD characteristics, we collected clinical, evolutionary and therapeutic data using medical records. Furthermore, disease activity was assessed by calculating the Harvey Bradshaw Index (HBI) for CD and the Truelove and Witts for UC at the time of the interview.

For the evaluation of work capacity, we used the questionnairy "Work Ability Index (WAI)", which is a validated and commonly used practical tool. It is a short 7-item questionnairy, which classified work performance into four categories: poor (score between 7 and 27), moderate (28-36), good (37-43) and excellent (44-49).<sup>[5]</sup>

In order to determine the factors of disability at work, we divided our patients into two groups according to the WAI:

- Patients with work disability: patients who had poor work performance (WAI between 7 and 27)
- Patient with retained ability: patients who had moderate, good or very good work performance (WAI between 28 and 49)

A descriptive statistical study was initially performed to identify the main characteristics of the population. Then, we looked for factors associated with work disability by univariate analytical study and a logistic regression model. Statistical analysis was performed using Chi square test and student t test. In all statistical tests, p-value <0.05 was considered statistically significant.

#### RESULTS

#### **Baseline characteristics**

A total of 45 patients were included. The mean age was  $44 \pm 12$  years [extremes: 20-72 years] and the sex ratio M/F was 0.73. Patients were mostly living in urban areas (73%). The economic situation was considered moderate in 91% of the cases and poor in 9% of the cases. As for the instruction level, 38% of the patients had a university degree. Regarding smoking habits, 13% of the patients were regular smokers.

IBD was of type CD in 36 cases (80%) and UC in 9 cases (20%). The mean duration of the disease was 9 years [extremes: 1 - 18 years]. Location of CD was ileal in 41% of cases and perineal in 28% of patients. The phenotype was stricturing in 36% of cases and fistulizing in 14%. UC was extensive in 45% of patients. IBD was moderate to severe in 36% of cases. Eighteen patients (40%) had at least one extra-intestinal manifestation (EIM) associated with IBD. It was mainly osteoarticular type. The treatments received since the onset of the disease were aminosalicylates (44%), corticosteroids (69%), azathioprine (78%) or anti-TNFα (51%). Forty percent of patients underwent at least one surgical procedure during follow up.

Regarding the professional status, patients working in the private sector represented 67% of the cases and those in the public sector 33%. The predominant professional category was workers (51%). The professional seniority was 16.5 years. The mean number of working hours per week was  $38.8 \pm 11$  hours [extremes: 9 - 60 hours]. The majority of employees were working full time (85%) and on a fixed schedule during daytime (76%).

Table 1 summarizes the socio-demographic, clinical and occupational characteristics of the study population.

According to the WAI questionnaire, 38% of the patients (N=17) were assessed as suffering from poor work ability. The consequences of impaired work ability due to IBD were mainly absenteeism estimated at 49.6 days/year [extremes: 0 - 240 days].

Table 1: Baseline Demographic and Clinical characteristics of the study cohort (N=45).

e Demographic and Clinical characteristics of the study cohort (N=45).  Summary statistics,			
Baseline characteristics	mean ±SD or N (%)		
Demographics	mean ±9D of 1v (70)		
Mean age	$44 \pm 12$		
Female gender	26 (58)		
Urban habitation	12 (27)		
Low financial conditions	4 (9)		
University level of instruction	17 (38)		
Smoking	6 (13)		
Diagnosis	0 (13)		
Crohn's disease	36 (80)		
Ulcerative colitis	9 (20)		
	9 (20) 9 ± 7		
Disease duration (years)	9 ± /		
Disease location (CD)	15 (41)		
L1: Terminal ileal	15 (41)		
L2: Colonic	8 (23)		
L3: Ileo-colonic	12 (33)		
Upper GI	1 (3)		
Perianal disease (CD)	10 (28)		
Disease behavior (CD)			
B1: Inflammatory	20 (56)		
B2: Stricturing	13 (36)		
B3: Penetrating	5 (14)		
Disease extension (UC)			
E1. Ulcerative proctitis	2 (22)		
E2. Left sided UC	3 (33)		
E3. Pancolitis	4 (45)		
IBD severity			
Inactive or mild activity	29 (64)		
Moderate to severe activity	16 (36)		
EIMs	, , ,		
Rheumatological	16 (35)		
Ophthalmological	6 (13)		
Dermatological	1 (2)		
Hepatobiliary	3 (7)		
Medical treatment			
Salicylates	20 (44)		
Corticosteroids	31 (69)		
Azathioprine	35 (78)		
Anti-TNF	23 (51)		
Surgery	18 (40)		
Employment sector	18 (40)		
Public	15 (33)		
Private			
	30 (67)		
Laborers (Unskilled)	23 (51)		
Seniority of employment (years)	16.3		
Working hours per week (hours)	$38.8 \pm 11$		
Employment status	20 (05)		
Full-time	38 (85)		
Part-time	7 (15)		
Work schedule	24.77		
Daytime fixed	34 (76)		
Atypical schedule / night shift	11 (24)		
Previous year days of sick leave (days)	49,6		

SD – Standard deviation; CD – Crohn's disease; IBD – Inflammatory bowel disease; UC – Ulcerative colitis; EIMs – Extraintestinal manifestations; TNF – Tumour Necrosis Factor

#### Univariate analysis

Several factors have been shown to be associated with work disability in IBD patients. We identified these factors in univariate analysis and classified them into three types:

- Patient-related factors: age (r=0, 294; p=0.050) with a cut-off of 54.5 years, rural residence (p=0.034), bad economic conditions (p=0.016), and low educational level (p=0.030) [Table 2].
- Disease-related factors: stricturing phenotype of CD (p=0.011), extensive form of UC (p=0.048), moderate to severe disease activity (p=0.000),
- presence of ophthalmological EIMs (p=0.023), rheumatological EIMs (p=0.001), and hepatobiliary EIMs (p=0.048), and finally the need for corticotherapy (p=0.029) [Table 3].
- Occupational status-related factors: private sector (p=0.017), occupational category of manual workers (p=0.008), atypical working hours (p=0.034), professional seniority (r=0.386; p=0.009) with a cutoff of 16.5 years [Table 4].

Table 2: Univariate analysis of patients-related factors associated with work disability assessed by the WAI among IBD patients.

Variable	Retained ability (N=28) mean ± SD or N (%)	Disability (N=17) Mean ± SD or N (%)	P
Age	41,4 (± 10,1)	48,4 (± 13,2)	0,050
Gender			
Male	10 (53)	9 (47)	NS
Female	18 (69)	8 (31)	
Habitation			
Rural	4 (33)	8 (67)	0,034
Urban	24 (73)	9 (27)	
Financial conditions			
Good / Moderate	28 (68)	13 (32)	0,016
Poor	0	4 (100)	
Level of instruction			
Non-academic level	14 (50)	14 (50)	0,030
University level	14 (82)	3 (18)	
Smoking			
Yes	4 (67)	2 (33)	NS
No	24 (62)	15 (38)	
SD – Standard deviation; NS – Not Significant;			

Table 3: Univariate analysis of disease-related factors associated with work disability assessed by the WAI among IBD patients.

	Retained ability	Disability	
Variable	(N=28)	(N=17)	$\boldsymbol{P}$
	mean ± SD or N (%)	mean ± SD or N (%)	
Disease duration (years)	9 (± 6,3)	9,1 (± 9,2)	NS
Disease location (CD)			
L1: Terminal ileal	10 (67)	5 (33)	NS
L2: Colonic	6 (75)	2 (25)	No
L3: Ileo-colonic	7 (58)	5 (42)	
Upper GI			
Yes	0	1 (100)	NS
No	24 (69)	11 (31)	
Perianal disease (CD)			
Yes	9 (90)	1 (10)	NS
No	15 (58)	11 (42)	
Inflammatory phenotype of CD			
Yes	12 (60)	8 (40)	NS
No	12 (75)	4 (25)	
Stricturing phenotype of CD			
Yes	5 (38)	8 (62)	0,011
No	19 (83)	4 (17)	
Penetrating phenotype of CD	_	_	NS

Yes	4 (80)	1 (20)	
No	20 (65)	11 (35)	
Disease extension (UC)			
Distal form of UC (E1/E2)	4 (80)	1 (20)	0,048
Extended form of UC (E3)	0	4 (100)	
IBD severity			
Inactive or mild activity	24 (83)	5 (17)	0,000
Moderate to severe activity	4 (25)	12 (75)	
Rheumatological EIMs			
Yes	5 (31)	11 (69)	0,001
No	23 (79)	6 (21)	
Ophthalmological EIMs			
Yes	1 (17)	5 (83)	0,023
No	27 (69)	12 (31)	
Dermatological EIMs			
Yes	1 (100)	0	NS
No	27 (61)	17 (39)	
Hepatobiliary EIMs			
Yes	0	3 (100)	0,048
No	28 (67)	14 (33)	
Salicylates treatment			
Yes	14 (70)	6 (30)	NS
No	14 (56)	11 (44)	
Corticosteroids treatment			
Yes	16 (52)	15 (48)	0,029
No	12 (86)	2 (14)	
Azathioprine treatment			
Yes	22 (63)	13 (37)	NS
No	6 (60)	4 (40)	
Anti-TNF treatment			
Yes	15 (65)	8 (35)	NS
No	13 (59)	9 (41)	
Surgery			
Yes	11 (61)	7 (39)	NS
No	17 (63)	10 (37)	

SD – Standard deviation; NS – Not Significant; CD – Crohn's disease; IBD – Inflammatory bowel disease; UC – Ulcerative colitis; GI – Gastro-Intestinal; EIMs – Extraintestinal manifestations; TNF – Tumour Necrosis Factor

Table 4: Univariate analysis of work-related factors associated with work disability assessed by the WAI among IBD patients.

Variable	Retained ability (N=28)	Disability (N=17)	P	
	mean $\pm$ SD or N (%)	mean ± SD or N (%)		
Employment sector				
Public	13 (87)	2 (13)	0,017	
Private	15 (50)	15 (50)		
Professional category				
Professionals / Technicians	18 (81)	4 (19)	0,008	
Laborers	10 (43)	13 (57)		
Seniority of employment (years)	12,8 (± 8,4)	22,1 (± 14,3)	0,009	
Working hours per week (hours)	38,5 (± 12)	39,4 (± 10,9)	NS	
Employment status				
Full-time	24 (63)	14 (37)	NS	
Part-time	4 (57)	3 (43)		
Work schedule			_	
Daytime fixed	24 (73)	9 (27)	0,034	
Atypical schedule / night shift	4 (43)	8 (57)		
SD – Standard deviation; NS – Not	Significant;			

#### Multivariate analysis

The final multivariate regression model showed that the independent predictors of work disability were osteoarticular EIMs (OR=21.9 [95% CI: 2.302 -

208.356]; p=0.007) and moderate to severe disease activity (OR=34.2 [95% CI: 3.585 - 327.269]; p=0.002) [Table 5].

Table 5: Multivariate analysis of independent predictive factors of work disability assessed by the WAI among patients with IBD.

Variable	OR	95% CI		P
		Lower	Upper	
Rheumatological EIMs	21,898	2,302	208,356	0,007
Moderate to severe disease activity	34,255	3,585	327,269	0,002
OR – Odds Ratio; CI – Confidence interval; EIMs – Extraintestinal manifestations				

#### DISCUSSION

"Work ability" is defined as the physical and mental ability of a worker to perform his current job and in the near future, taking into account the work requirements he faces, his health and his skills. <sup>[6]</sup> In our study, 17 patients had a WAI score below 17, indicating a poor work ability, corresponding to a disability rate of 38%. In the published literature, the latter was assessed by different other scores, varied between 6.7% and 32.3%. <sup>[4,7,18]</sup>

Several studies have shown that age is a predictive factor of work disability. [13] which was in agreement with our study. The impact of age on work ability would be related to the increased incidence of comorbidities associated with IBD and to the age-related morbidity. This impairment of working ability with age is not specific to IBD and has been observed in several other chronic diseases. Regarding gender, In our study, it was not associated with work disability, while other authors have reported a higher probability of work impairment in women than in men. [8,9,15,18] This could be explained in part by gender inequalities in society, leading to higher demands and early burnout in this category. On the other hand, we have shown that bad economic conditions and rural residence were factors associated with work disability. Indeed, according to Walker C et al, [19] patients living below the level of poverty experienced more severe forms of illness requiring more frequent hospitalization and thus have higher absenteeism. As for the low level of instruction, it was also a factor associated with work disability in our study and according to several other authors. [13,15] This relationship would be notably due to the poor socio-economic conditions in this group of patients. About smoking, although it had no impact on work ability in our study, its effect on the natural history of IBD is well known. In fact, Vester-Andersen MK et al<sup>[4]</sup> found that smoking significantly increased the risk of work disability in UC up to 6 times. This may result from the association of smoking with other potentially disabling chronic diseases (cardiac, brochopulmonary...).

Regarding the disease-related factors, the presence of perineal lesions during CD was a risk factor for work disability according to some authors. [17,20] As for the phenotype of the disease, the fistulizing and stricturing forms seem to have a higher risk of causing an

impairment of work ability. This would be the result of the discomfort and symptoms caused by these forms, which are incompatible with the execution of professional activitie. [13,17,18] In our study, fistulizing phenotype was the only one associated with work disability. For UC, the extensive form was associated with work disability in our study and according to other authors.

Disease activity significantly increased work ability impairment in IBD patients. Siebert U et al showed that during UC, it increased the risk of work disability (OR=29.04 [95% CI: 2.36 - 357.41]; p < 0.010). [10] This same finding was reported by the French study of Williet N et al, in which moderate disease activity increased the risk of work disability by 10 times (OR=10.64 [95% CI: 7.03-16.11]; p <0.0001) and severe activity by 75 times (OR=75.68 [95% CI: 16.99-337.12]; p <0.0001). [16] In our study, moderate to severe disease activity was an independent predictor of work disability (OR=34.2 [95% CI: 3.585 - 327.269]; p=0.002).

According to some studies, the presence of EIMs increases the risk of work ability impairment. [15,17] This fact was confirmed by our study for the hepatobiliary and ocular EIMs. Among the osteoarticular type, we were able to identify in a multivariate analysis that it was an independent predictive factor of work disability (OR=21.9 [95% CI: 2.302 - 208.356]; p=0.007). This impaired work ability would be largely due to joint pain and stiffness associated with spondyloarthropathy. [21]

Regarding therapeutic profile, the need for corticotherapy, biotherapy and surgical intervention were predictive factors of work disability. [9,13,15,16] In fact, the use of such therapies would be more associated with more severe forms of IBD. In our population, although the need for medical or surgical treatment was higher than in the published literature, the use of corticosteroid therapy was the only one to be associated with work disability.

Concerning professional status, we have shown that employment in the private sector is more likely to lead to work disability. According to Virtanen M et al, [22] the more stable the employment conditions are, the better it is to maintain in work, which means a job that allows

patients to adapt their workplaces by making accommodations and thus maintain their income. Regarding occupational categories, manual workers were the most affected by work disability. This category often requires higher physical effort, which is sometimes incompatible with their illness.

Professional seniority is a parameter whose impact has not been studied in the literature. According to our study, it was positively correlated with work disability (r=0.386; p=0.009) with a cut-off of 16.5 years. Thus, in certain situations, the use of early retirement could be an effective solution.

Finally, concerning work schedules, the number of working hours per week was not associated with disability in our study, in contrary to the study reported by Van Gennep S et al, where weekly working hours exceeding 36h was positively correlated with low productivity at work. [23] On the other hand, atypical schedules or night shifts were factors of work disability in our study. In fact, according to several authors, circadian misalignment is an important possible risk factor for disease flare in IBD. It has been shown that night shift work is associated with an increase inflammation factors (TNF-a, IL1b, IL-6, serum cytokines) decreased resiliency of the colonic barrier and dysbiosis of the intestinal microbiota. [24,25]

## Limitation and outlook

The main limitation of the study was the relatively small number of participants. This limited the statistical analyses of the data collected. Larger numbers could have increased the reliability and significance of our results.

Another limitation is the monocentric nature of the study, conducted in a tertiary level hospital, where IBD is often more severe and may require more intensive medical care. This could lead to an overestimation of the negative impact of IBD on work ability.

The results of our research could also guide other studies. Larger, prospective, multicenter studies would be of great help in order to improve the management of these patients and their adaptation to their professional environment.

## CONCLUSION

According to our study, IBD would cause work disability in 38% of cases. We were able to define the most important factors that influence work ability. Moderate to severe disease activity and the presence of rheumatological EIM were both identified as independent predictors of work disability. We also demonstrated that the Work Ability Index (WAI) could be used as a screening tool to identify patients who require specific accommodations or workplace management in order to ensure better health care.

#### REFERENCES

- GBD 2017 Inflammatory Bowel Disease Collaborators. The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol, 2020; 5(1): 17–30.
- Ng SC, Shi HY, Hamidi N, Underwood FE, Tang W, Benchimol EI, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of populationbased studies. Lancet Lond Engl, 2017; 390(10114): 2769–78.
- 3. Mahlich J, Matsuoka K, Nakamura Y, Sruamsiri R. The relationship between socio-demographic factors, health status, treatment type, and employment outcome in patients with inflammatory bowel disease in Japan. BMC Public Health, 2017; 17: 623.
- Vester-Andersen MK, Prosberg MV, Vind I, Andersson M, Jess T, Bendtsen F. Low Risk of Unemployment, Sick Leave, and Work Disability Among Patients with Inflammatory Bowel Disease: A 7-year Follow-up Study of a Danish Inception Cohort. Inflamm Bowel Dis, 2015; 21(10): 2296–303.
- 5. Ilmarinen J. The Work Ability Index (WAI). Occup Med, 2006; 57(2): 160–160.
- 6. Ilmarinen JE. Aging Workers. Occup Environ Med, 2001; 58(8): 546–546.
- 7. Ananthakrishnan AN, Weber LR, Knox JF, Skaros S, Emmons J, Lundeen S, et al. Permanent work disability in Crohn's disease. Am J Gastroenterol, 2008; 103(1): 154–61.
- 8. Stjernman H, Tysk C, Almer S, Ström M, Hjortswang H. Unfavourable outcome for women in a study of health-related quality of life, social factors and work disability in Crohn's disease. Eur J Gastroenterol Hepatol, 2011; 23(8): 671–9.
- 9. Høivik ML, Moum B, Solberg IC, Henriksen M, Cvancarova M, Bernklev T, et al. Work disability in inflammatory bowel disease patients 10 years after disease onset: results from the IBSEN Study. Gut, 2013; 62(3): 368–75.
- 10. Siebert U, Wurm J, Gothe RM, Arvandi M, Vavricka SR, von Känel R, et al. Predictors of temporary and permanent work disability in patients with inflammatory bowel disease: results of the swiss inflammatory bowel disease cohort study. Inflamm Bowel Dis, 2013; 19(4): 847–55.
- 11. Mandel MD, Bálint A, Lovász BD, Gulácsi L, Strbák B, Golovics PA, et al. Work disability and productivity loss in patients with inflammatory bowel diseases in Hungary in the era of biologics. Eur J Health Econ HEPAC Health Econ Prev Care, 2014: 15. 1: S121-128.
- 12. Israeli E, Graff LA, Clara I, Walker JR, Lix LM, Targownik LE, et al. Low prevalence of disability among patients with inflammatory bowel diseases a

- decade after diagnosis. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc, 2014; 12(8): 1330-1337.e2.
- 13. van der Valk ME, Mangen MJJ, Leenders M, Dijkstra G, van Bodegraven AA, Fidder HH, et al. Risk factors of work disability in patients with inflammatory bowel disease--a Dutch nationwide web-based survey: work disability in inflammatory bowel disease. J Crohns Colitis., 2014; 8(7): 590-7.
- 14. Ramos A, Calvet X, Sicilia B, Vergara M, Figuerola A, Motos J, et al. IBD-related work disability in the community: Prevalence, severity and predictive factors. A cross-sectional study. United Eur Gastroenterol J, 2015; 3(4): 335–42.
- 15. Spekhorst LM, Oldenburg B, van Bodegraven AA, de Jong DJ, Imhann F, van der Meulen-de Jong AE, et al. Prevalence of- and risk factors for work disability in Dutch patients with inflammatory bowel disease. World J Gastroenterol, 2017; 23(46): 8182–92.
- Williet N, Sarter H, Gower-Rousseau C, Adrianjafy C, Olympie A, Buisson A, et al. Patient-reported Outcomes in a French Nationwide Survey of Inflammatory Bowel Disease Patients. J Crohns Colitis, 2017; 11(2): 165–74.
- 17. Everhov ÅH, Khalili H, Askling J, Myrelid P, Ludvigsson JF, Halfvarson J, et al. Sick Leave and Disability Pension in Prevalent Patients With Crohn's Disease. J Crohns Colitis, 2018; 12(12): 1418–28.
- 18. Chao CY, Lemieux C, Restellini S, Afif W, Bitton A, Lakatos PL, et al. Maladaptive coping, low self-efficacy and disease activity are associated with poorer patient-reported outcomes in inflammatory bowel disease. Saudi J Gastroenterol Off J Saudi Gastroenterol Assoc, 2019; 25(3): 159–66.
- 19. Walker C, Allamneni C, Orr J, Yun H, Fitzmorris P, Xie F, et al. Socioeconomic Status and Race are both Independently associated with Increased Hospitalization Rate among Crohn's Disease Patients. Sci Rep, 2018; 8(1): 4028.
- 20. Vollebregt PF, van Bodegraven AA, Markus-de Kwaadsteniet TML, van der Horst D, Felt-Bersma RJF. Impacts of perianal disease and faecal incontinence on quality of life and employment in 1092 patients with inflammatory bowel disease. Aliment Pharmacol Ther, 2018; 47(9): 1253–60.
- 21. van der Have M, Brakenhoff LKPM, van Erp SJH, Kaptein AA, Leenders M, Scharloo M, et al. Back/joint pain, illness perceptions and coping are important predictors of quality of life and work productivity in patients with inflammatory bowel disease: a 12-month longitudinal study. J Crohns Colitis, 2015; 9(3): 276–83.
- Virtanen M, Kivimäki M, Vahtera J, Elovainio M, Sund R, Virtanen P, et al. Sickness absence as a risk factor for job termination, unemployment, and disability pension among temporary and permanent employees. Occup Environ Med, 2006; 63(3): 212–7.

- 23. van Gennep S, de Boer NKH, Gielen ME, Rietdijk ST, Gecse KB, Ponsioen CY, et al. Impaired Quality of Working Life in Inflammatory Bowel Disease Patients. Dig Dis Sci, 2021; 66(9): 2916–24.
- 24. Reinhardt ÉL, Fernandes PACM, Markus RP, Fischer FM. Night work effects on salivary cytokines TNF, IL-1β and IL-6. Chronobiol Int, 2019; 36(1): 11–26.
- 25. Swanson GR, Kochman N, Amin J, Chouhan V, Yim W, Engen PA, et al. Disrupted Circadian Rest-Activity Cycles in Inflammatory Bowel Disease Are Associated With Aggressive Disease Phenotype, Subclinical Inflammation, and Dysbiosis. Front Med, 2022; 8: 770491.