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Original Article

Prevalence and Determinants of Fatigue in Patients with IBD: A Cross-Sectional Survey from the GETAID

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Abstract

Background: Fatigue is commonly reported by patients with inflammatory bowel disease [IBD], but the determinants of IBD-related fatigue have yet to be determined.

Aims: To identify the factors associated with fatigue in a large population of patients with IBD.

Patients and Methods: Fatigue and nine other IBD-related disability dimensions were assessed in a cohort of 1704 consecutive patients with IBD using the IBD-disk questionnaire in a cross-sectional survey of 42 French and Belgian centres. Fatigue and severe fatigue were defined as energy subscores >5 and >7, respectively. Determinants of fatigue were assessed using univariate and multivariate analyses (odds ratios [ORs] are provided with 95% confidence intervals).

Results: The prevalence rates of fatigue and severe fatigue were 54.1% and 37.1%, respectively. Both fatigue and severe fatigue were significantly higher in patients with active disease than in patients with inactive disease [64.9% vs 44.7% and 47.4% vs 28.6%, respectively; $p < 0.001$ for both comparisons]. In the multivariate analysis stratified by age, sex, type of IBD and IBD activity, fatigue was associated with age >40 years (OR = 0.71 [0.54–0.93]), female sex (OR = 1.48 [1.13–1.93]) and IBD-related sick leave (OR = 1.61 [1.19–2.16]), and joint pain (OR = 1.60 [1.17–2.18]), abdominal pain (OR = 1.78 [1.29–2.45]), regulating defecation (OR = 1.67 [1.20–2.32]), education and work (OR = 1.96 [1.40–2.75]), body image (OR = 1.38 [1.02–1.86]), sleep (OR = 3.60 [2.66–4.88]) and emotions (OR = 3.60 [2.66–4.88]) subscores >5.

Conclusion: Determinants of fatigue are not restricted to IBD-related factors but also include social factors, sleep and emotional disturbances, thus supporting a holistic approach to IBD patient care.

Key Words: Crohn's disease; ulcerative colitis; inflammatory bowel disease; disability; fatigue

1. Introduction

Inflammatory bowel diseases [IBDs], including Crohn's disease [CD] and ulcerative colitis [UC], are chronic relapsing and remitting inflammatory diseases affecting the gastrointestinal tract.[1,2] IBD is responsible for significant disability.[3–5] Disability is an umbrella term encompassing impairments, activity limitations and participation restrictions, thus summarizing the functional dimension of the handicap.[6,7] Disability can be studied using two validated tools [the IBD-disability index and the IBD-disk] that assess ten dimensions of disability, including joint pain, abdominal pain, regulation of defecation, interpersonal interactions, education and work, sleep, energy, emotions, body image, and sexual functions.[3–5]

Fatigue is one of the most prevalent and burdensome symptoms reported by patients with IBD.[8] Recently, a systematic review with meta-analysis estimated the prevalence of fatigue in 12 025 patients with IBD to be 47%, with no difference between CD and UC.[9] Active IBD, anxiety and depression, sleep disturbances and anaemia were the most commonly reported fatigue-associated factors. That study found high heterogeneity depending on the definition of fatigue and on the various datasets of patient characteristics. Indeed, fatigue is a multifactorial and multimodal symptom that could be linked not only to inflammation and micronutrient deficits but also to psychosocial and sleep disturbances as well as to exercise deconditioning.[10,11]

The aim of the present study was to identify the determinants of fatigue in a large population of patients with IBD.

2. Patients and Methods

2.1. Study population

Between November 26 and 30, 2018, all consecutive outpatients with IBD who were seen at the outpatient clinic or infusion unit were asked to participate in a cross-sectional multicentre survey.[4,12] Participating centres were all affiliated with the Groupe d'Etude Therapeutique des Affections Inflammatoires du tube Digestif [GETAID] in France or Belgium. This study was conducted in accordance with French ethical and legal principles through reference methodology MR-004 [Institut National des Donnees de Sante registration number 2210131].

2.2. Survey instrument

All patients completed the IBD-disk assessing ten dimensions of IBD-related disability: joint pain, abdominal pain, regulation of defecation, interpersonal interactions, education and work, sleep, energy, emotions, body image, and sexual functions [Supplementary Table S1 and Figure S1]. For each dimension of disability, patients had to score their level of agreement with a specific statement on a 0–10 visual analog scale [VAS; 0 = no burden; 10 = maximal burden]. Fatigue was assessed according to the energy statement of the IBD-disk ['I have not felt rested and refreshed during the day and have felt tired and without energy']. According to the original instructions, any subscore >5 represents a significant disability for each IBD-disk component.[13] Fatigue was defined as an IBD-disk energy subscore >5, and severe fatigue was defined as >7.

The recorded data included patient demographics, occupational status, weight and height, type of IBD, age at diagnosis of IBD, duration of IBD, history of surgical treatment of IBD, current treatment, patient-global assessment of clinical remission, IBD-related sick leave rate, IBD daily life burden [0–10 visual analog scale], frequency of appointments with a gastroenterologist, and perceived need for other healthcare professionals such as a dietician, a psychotherapist, a sexologist, a sports coach, an IBD nurse or a social worker. Current treatments included 5-aminosalicylates, conventional immunosuppressants [namely thiopurine or methotrexate], anti-tumour necrosis factor [anti-TNF] agents [namely adalimumab, infliximab, certolizumab pegol or golimumab], vedolizumab, ustekinumab, tofacitinib or any other treatment.

2.3. Study objectives

The aim of the present study was to assess the prevalence of fatigue and severe fatigue among a large cohort of outpatients with IBD and to identify factors associated with fatigue and severe fatigue.

2.4. Statistical analysis

The data are expressed as numbers [%] for qualitative data and as the mean ± standard deviation [SD] or median (interquartile range [IQR]) for quantitative data. In the case of a partially incomplete IBD-disk questionnaire [six or more out of ten completed items], missing data were generated using multiple imputations based on sociodemographic data and

Table 1. Demographic, disease and medication characteristics of the study population

Characteristic	Overall population [n = 1704]
Age, years (median [IQR])	39.0 [29.0-51.0]
Male gender, no. [%]	802 [47.1%]
BMI, kg/m² [mean ± SD]	24.3 ± 5.1
Duration of IBD, years (median [IQR])	10.5 [5.5–18.5]
Age at diagnosis, years (median [IQR])	24.6 [18.6–34.6]
Type of IBD, [%]	
Crohn's disease	1109 [67.7%]
Ulcerative colitis	595 [32.3%]
History of intestinal resection, no. [%]	763 [44.8%]
Occupational status, %	
Employed	1070 [62.8%]
Homemaker	145 [8.5%]
Unemployed	154 [9.0%]
Student	137 [8.0%]
Retired	198 [11.6%]
Perceived need for healthcare professionals	
Dietician	423 [24.8%]
Psychologist	240 [14.1%]
Sexologist	150 [8.8%]
Sports coach	363 [21.3%]
IBD nurse	107 [6.3%]
Social worker	141 [8.3%]
Current treatment	
None	108 [6.3%]
5-ASA	147 [8.6%]
Immunomodulator alone	178 [10.4%]
Anti-TNF	933 [54.8%]
Vedolizumab	235 [13.8%]
Ustekinumab	111 [6.5%]
Fatigue	922 [54.1%]
Severe fatigue	633 [37.1%]
IBD-disk subscores	
Joint pain	3.9 ± 3.2
Abdominal pain	4.2 ± 3.1
Regulating defecation	3.8 ± 3.4
Interpersonal interactions	2.5 ± 3.0
Education and work	4.0 ± 3.4
Sleep	4.9 ± 3.4
Energy	5.7 ± 3.2
Emotions	4.5 ± 3.3
Body image	3.9 ± 3.4
Sexual functions	2.9 ± 3.2

5-ASA: 5-aminosalicylic acid; BMI: body mass index; IBD: inflammatory bowel disease; IQR: interquartile range.

Table 2. Pearson's correlation coefficient R^2 assessing the convergent validity of fatigue and other IBD-disk subscores evaluating other dimensions of IBD-related disability

	Fatigue
Joint pain	0.381
Abdominal pain	0.504
Regulating defecation	0.456
Interpersonal interactions	0.407
Education and work	0.593
Sleep	0.624
Emotions	0.633
Body image	0.416
Sexual functions	0.393
Overall IBD-disk score	0.758
IBD daily life burden	0.453

The p values for each Pearson's correlation coefficient were <0.001.
IBD: inflammatory bowel disease.

available IBD-disk subscores. Multiple imputations consisted of the generation of 50 different complete datasets finally combined in a pooled dataset. Patients with five or more IBD-disk missing items were excluded from the present study. Spearman's rho correlation coefficient was determined to identify correlations between fatigue and other variables. To identify predictors of fatigue and severe fatigue, univariate analysis using the χ^2-test was performed. Subsequent multivariate analysis using binary logistic regression models was performed and adjusted for using the above-mentioned variables. Variables with $p < 0.10$ in the univariate analysis were considered potential adjustment variables for the multivariate analysis. Multivariate analysis was stratified by age, sex, type of IBD and IBD activity. All analyses were two-tailed, and p values <0.05 were considered significant. All statistics were calculated using SPSS statistical software [SPSS Inc., v23].

3. Results

3.1 Study population

We included 1704 patients in 42 tertiary care centres in the present study (802 [47.1%] males, median age of 39.0 years [IQR 29.0–51.0]; 67.7% of Crohn's disease). Table 1 summarizes the main characteristics of the study population. The median duration of IBD was 10.5 years [IQR 5.5–18.5]. Current treatment included 5-aminosalicylates in 8.6% of the cases, conventional immunosuppressants alone in 10.4%, anti-TNF agents in 54.8%, vedolizumab in 13.8% and ustekinumab in 6.5%, and for 6.3% of the cases, no treatment was currently prescribed.

3.2 Prevalence of fatigue and severe fatigue in the study population

The mean overall fatigue VAS was 5.7 ± 3.2 [Table 1]. The prevalence of fatigue was 54.1%, and the prevalence of severe fatigue was 37.1%. The patient global assessment of clinical remission was missing in 205 out of 1704 patients. The prevalence of fatigue was significantly higher in patients with active disease according to the patient global assessment [64.9% vs 44.7%, $p < 0.001$]. The prevalence of severe

fatigue was significantly higher in patients with active disease according to the patient global assessment [47.4% vs 28.6%, $p < 0.001$].

3.3 Correlations between fatigue and other variables

Significant correlations were observed between fatigue and all the other dimensions of IBD-related disability assessed by the IBD-disk [Table 2]. The strongest correlations were observed between fatigue and sleep disturbances [$R^2 = 0.624$] and between fatigue and emotional disturbances [$R^2 = 0.633$]. In patients with fatigue, sleep and emotional disturbances were significantly higher compared with those without fatigue [69.7% vs 20.1% and 61.5% vs 14.0%, respectively, $p < 0.001$ for both comparisons].

3.4 Predictors of fatigue and severe fatigue in the study population

In the multivariate analysis stratified by age, gender type of IBD and IBD activity, fatigue was significantly increased in female patients (odds ratio [OR] = 1.48, 95% confidence interval, CI [1.13–1.93], $p = 0.004$), age >40 years (OR = 0.71, 95% CI [0.54–0.93], $p = 0.01$), IBD-related sick leave (OR = 1.61 95% CI [1.19–2.16], $p = 0.002$), joint pain subscore >5 (OR = 1.52, 95% CI [1.12–2.07], $p < 0.001$), abdominal pain subscore >5 (OR = 1.78, 95% CI [1.29–2.45], $p < 0.001$), regulating defecation subscore >5 (OR 1.67, 95% CI [1.20–2.3], $p = 0.002$), education and work subscore >5 (OR = 1.96, 95% CI [1.40–2.75], $p < 0.001$), sleep subscore >5 (OR = 3.77, 95% CI [2.86–4.88], $p < 0.001$), emotions subscore >5 (OR = 3.60, 95% CI [2.66–4.88], $p < 0.001$) and body image subscore >5 (OR = 1.38, 95% CI [1.02–1.86], $p = 0.04$) [Table 4].

In the multivariate analysis stratified by age, sex, type of IBD and IBD activity, severe fatigue was significantly increased in female patients (OR = 1.37, 95% CI [1.04–1.79], $p = 0.02$), and in patients with joint pain subscore >5 (OR = 1.45, 95% CI [1.09–1.93], $p = 0.01$), abdominal pain subscore >5 (OR = 1.79, 95% CI [1.30–2.47], $p < 0.001$), regulating defecation subscore >5 (OR = 1.43, 95% CI [1.06–1.94], $p < 0.001$), education and work subscore >5 (OR = 2.21, 95% CI [1.63–3.01], $p < 0.001$), sleep subscore >5 (OR = 3.73, 95% CI [2.82–4.95], $p < 0.001$) and emotions subscore >5 (OR = 3.65, 95% CI [2.75–4.83], $p < 0.001$) [Table 5].

4. Discussion

Fatigue is a burdensome, multidimensional and multifactorial symptom implying a lack of energy or exhaustion that is out of proportion to physical exertion, that limits daily activities and that is not relieved by rest.[14] In this large multicentre study, we showed that fatigue was influenced by age, sex and many impaired dimensions assessed by the IBD-disk, mostly emotional and sleep disturbances. In parallel, fatigue was associated with IBD-related sick leave and clinical symptoms, such as joint and abdominal pain, and difficulties in regulating defecation.

Sleep disturbances are commonly reported in the general population and are linked with worsening of health-related quality of life.[15] Sleep disturbances have also been widely reported in patients with IBD, mostly with questionnaire-based tools rather than with polysomnography. In a recent meta-analysis, patients with IBD had poorer sleep quality than controls.[16] Sleep disturbances and IBD activity are mutually impacted through the brain–gut axis. Indeed, in another meta-analysis, poor sleep quality was associated with an increased risk for disease activity without any clue to a potential causal relationship.[17] In the present study, we also observed a high prevalence of sleep disturbances [sleep subscore >5] and severe sleep disturbances [emotion subscore >7] in 47.0% and 30.9% of patients, respectively. Patients with active IBD had more sleep disturbances than those without active IBD [56.0% vs 38.6%, $p < 0.001$].

Many patients with IBD may experience symptoms of common mental disorders such as anxiety or depression.[18,19] Such an association may be either fortuitous or induced by systemic inflammation, chronicity of symptoms and reduced social functioning. In a recent meta-analysis, the pooled prevalence of anxiety and depression in patients with IBD was 32.1% [28.3–36.0%] and 25.2% [22.0–285.5%], respectively, without any difference between CD and UC and with a higher prevalence in women. In the present study, emotional disturbances, including anxiety and depression, were observed in 39.7% of patients with IBD [emotion subscore >5].

The association of fatigue, sleep disorders, and anxiety and depression has been previously reported in the general population as well as in patients with IBD.[15,20,21] Indeed, sleep disturbances have often been linked to most mental health conditions, including anxiety and depression.[15] In a

Table 3. Proportion of patients with IBD-disk subscore >5 according to the presence of fatigue and severe fatigue

Proportions of patients with IBD-disk subscores >5	Fatigue [$n = 924$]	Absence of fatigue [$n = 780$]	p	Severe fatigue [$n = 633$]	Absence of severe fatigue [$n = 1071$]	p
Joint pain >5	43.4%	17.6%	<0.001	48.0%	21.8%	<0.001
Abdominal pain >5	52.1%	16.0%	<0.001	59.4%	21.5%	<0.001
Regulating defecation >5	47.1%	15.6%	<0.001	52.3%	21.1%	<0.001
Interpersonal interactions >5	26.8%	8.8%	<0.001	30.6%	11.5%	<0.001
Education and work>5	53.2%	12.3%	<0.001	61.8%	18.4%	<0.001
Sleep >5	69.7%	20.1%	<0.001	77.3%	29.1%	<0.001
Emotions >5	61.5%	14.0%	<0.001	70.5%	21.6%	<0.001
Body image >5	47.1%	19.2%	<0.001	50.4%	24.8%	<0.001
Sexual functions >5	36.6%	13.1%	<0.001	40.9%	16.9%	<0.001

IBD: inflammatory bowel disease.

Table 4. Predictors of fatigue in our study population of 1704 patients

	OR [95% CI] on univariable analysis	*p*	OR [95% CI] on multivariable analysis	*p*
Age >40 years	0.90 [0.74–1.08]	0.26	0.71 [0.54–0.93]	0.01
Female gender	2.17 [1.79–2.64]	<0.001	1.48 [1.13–1.93]	0.004
Clinical remission assessed by patient global assessment	0.44 [0.35–0.54]	<0.001	—	NS
IBD-related sick leave	1.89 [1.52–2.34]	<0.001	1.61 [1.19–2.16]	0.002
Perceived need for healthcare professionals				
Psychotherapist	2.00 [1.49–2.67]	<0.001	—	NS
Sexologist	2.09 [1.44–2.79]	<0.001	—	NS
Sports coach	1.48 [1.16–1.87]	0.001	—	NS
Social worker	1.54 [1.08–2.21]	0.02	—	NS
IBD-disk subscores				
Joint pain >5	3.60 [2.87–4.50]	<0.001	1.60 [1.17–2.18]	0.003
Abdominal pain >5	5.68 [4.52–7.14]	<0.001	1.78 [1.29–2.45]	<0.001
Regulating defecation >5	4.81 [3.80–6.06]	<0.001	1.67 [1.20–2.32]	0.002
Interpersonal interactions >5	3.77 [2.84–5.03]	<0.001	—	NS
Education and work >5	8.13 [6.33–10.42]	<0.001	1.96 [1.40–2.75]	<0.001
Sleep >5	9.09 [7.30–11.36]	<0.001	3.77 [2.86–4.88]	<0.001
Emotions >5	9.80 [7.69–12.50]	<0.001	3.60 [2.66–4.88]	<0.001
Body image >5	3.73 [2.99–4.65]	<0.001	1.38 [1.02–1.86]	0.04
Sexual functions >5	3.83 [2.99–4.90]	<0.001	—	NS

OR: odds ratio; CI: confidence interval; NS: not significant. Odds ratios [ORs] with 95% confidence intervals [CIs] were estimated using binary logistic regression.

Table 5. Predictors of severe fatigue in our study population of 1704 patients

	OR [95% CI] on univariable analysis	*p*	OR [95% CI] on multivariable analysis	*p*
Female gender	2.05 [1.68–2.51]	<0.001	1.37 [1.04–1.79]	0.02
Active worker and student	0.76 [0.62–0.94]	0.01	—	NS
Clinical remission assessed by patient global assessment	0.45 [0.36–0.55]	<0.001	—	NS
IBD-related sick leave	1.51 [1.20–1.90]	<0.001	—	NS
Perceived need for healthcare professionals				
Psychotherapist	1.86 [1.41–2.44]	<0.001	—	NS
Sexologist	1.73 [1.24–2.43]	0.001	—	NS
Sports coach	1.65 [1.12–2.45]	0.01	—	NS
Social worker	1.55 [1.09–2.19]	0.01	—	NS
IBD-disk subscores				
Joint pain >5	3.30 [2.67–4.08]	<0.001	1.45 [1.09–1.93]	0.01
Abdominal pain >5	5.35 [4.31–6.62]	<0.001	1.85 [1.38–2.49]	<0.001
Regulating defecation >5	4.10 [3.31–5.08]	<0.001	1.43 [1.06–1.94]	0.02
Interpersonal interactions >5	3.40 [2.65–4.39]	<0.001	1.43 [1.01–2.04]	<0.001
Education and work >5	7.14 [5.75–8.93]	<0.001	2.21 [1.63–3.01]	<0.001
Sleep >5	8.26 [6.58–10.42]	<0.001	3.73 [2.82–4.95]	<0.001
Emotions >5	8.70 [6.94–10.87]	<0.001	3.65 [2.75–4.83]	<0.001
Body image >5	3.08 [2.49–3.79]	<0.001	—	NS
Sexual functions >5	3.40 [2.72–4.27]	<0.001	—	NS

OR: odds ratio; CI: confidence interval; NS: not significant. Odds ratios [ORs] with 95% confidence intervals [CIs] were estimated using binary logistic regression.

large randomized controlled trial including 3755 patients, improving sleep using digital cognitive behavioural therapy was associated with an improvement of psychiatric symptoms.[22] However, this triple association is not easy to manage and is much more a multidirectional association between fatigue, sleep and emotional disturbances. Although not specific to IBD, those symptoms should be prospectively evaluated to lower the IBD-related burden irrespective of the specific management of IBD.

In the present study, the presence of IBD-related sick leave was associated with a higher rate of fatigue. Similarly, active workers and students had lower rates of fatigue than unemployed workers, remote workers and retired patients, but only in the univariate analysis. Many studies have evaluated the impact of IBD on work productivity. Recently, a pan-European study estimated that the mean annual cost of absenteeism ranged from €1253 to €7915.[23] Patients in clinical remission had a lower annual indirect cost than those with active IBD. The authors suggest that the cost of absenteeism should be prospectively screened as an indirect marker of IBD-related disability.

Our study has several limitations. First, this cross-sectional study was not designed to specifically study fatigue and its determinants but to more broadly study IBD-related disability. Thus, we did not use a specific questionnaire and indices of fatigue but a 0–10 VAS included in the IBD-disk questionnaire. Second, being an anonymous study, our dataset did not include an objective assessment of systemic inflammation, such as C-reactive protein or faecal calprotectin, or nutritional status, such as haemoglobin or albumin. It is conceivable that malnutrition, anaemia and systemic inflammation may have an impact on perceived fatigue. Third, such a cross-sectional study provides limited evidence concerning changes over time and the opportunity to lower fatigue through the management of IBD. As such, it is conceivable that we underestimate the impact of clinical symptoms on the emergence of IBD-related fatigue. Last, looking at outpatients, we did not ask specifically for current use of prednisone and/or prednisolone in the treatment list. However, very few patients reported taking steroids as 'other treatment'. The absence of a specific box for steroids in our questionnaire may have underestimated the proportion of patients with ongoing steroids.

In conclusion, fatigue is a highly common symptom in patients with IBD that contributes to disability even in patients who report being in clinical remission. We identified a vicious cycle implicating fatigue, sleep disorders and emotional disturbances such as anxiety and depression. The management of IBD must involve a multidisciplinary team, including psychotherapists and sleep specialists. Further studies are needed to better assess ways of dealing with fatigue in patients with IBD to improve the health-related quality of life of patients with IBD.

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Conflict of Interest

Aurelien Amiot has received consulting fees from Abbvie, Hospira, Takeda, Gilead and Biocodex as well as lecture fees and travel accommodations from Abbvie, Janssen, Biocodex, Hospira, Ferring, Takeda and MSD. This author has also received advisory board fees from Gilead, Takeda and Abbvie. Yoram Bouhnik has received lecture and consulting fees from Abbvie, Biogaran, Boehringer-Ingelheim, CTMA, Ferring, Gilead, Hospira, ICON, Inception IBD, Janssen, Lilly, Mayoli Spindler, Merck, MSD, Norgine, Pfizer, Robarts Clinical Trials, Roche, Sanofi, Shire, Takeda, UCB and Vifor Pharma. This author has also stock ownership of Inception IBD, San Diego, CA, USA. Melanie Serrero has received lecture or consulting fees from Abbvie, Ferring, Amgen, Celltrion, Janssen, Ferring, Takeda and Tillotts. Jerome Filippi has received lecture and consulting fees from Abbvie, Amgen, Biogen, Ferring, HAC Pharma, Janssen, MSD, Pfizer, Sandoz and Takeda. Xavier Roblin reported a relationship with MSD, Abbvie, Amgen, Sandoz, Pfizer, Takeda and Janssen. Guillaume Bouguen has received lecture fees from Abbvie, Ferring, MSD, Takeda and Pfizer and consultancy fees from Takeda and Janssen. Denis Franchimont is research director of FNRS; he has received educational grants from Abbvie, Takeda and MSD, and has received honoraria fees for lectures or consultancy from Ferring, Falk, Chiesi, Abbvie, MSD, Centocor, Pfizer, Amgen, Janssen, Mundipharma, Takeda and Hospira. Guillaume Savoye has received lecture fees from Vifor Pharma, Takeda, Pfizer, HAC Pharma, Abbvie, MSD and Ferring France. This author has also received travel accommodations from Ferring, Abbvie and MSD France as well as a research grant from Ferring. Anthony Buisson has received research funding from Pfizer, lecture fees from Abbvie, Ferring, Hospira, MSD, Janssen, Sanofi-Aventis, Takeda and Vifor Pharma and consulting fees from Abbvie, Biogen, Janssen, Pfizer and Takeda. Edouard Louis has received fees for: research grant: Takeda, Pfizer; educational grant: Abbvie, Takeda, Janssen; speaker fees: Abbvie, Ferring, MSD, Falk, Takeda, Hospira, Janssen, Pfizer, Celgene; advisory board: Abbvie, Ferring, MSD, Takeda, Celgene, Hospira, Janssen; consultant: Abbvie. Stephane Nancey has received consulting fees from Merck, Abbvie, Takeda, Ferring, Norgine, Vifor Pharma, Novartis, Janssen Cilag, Hospira, Takeda and HAC Pharma. Vered Abitbol has received lecture fees from Amgen, Biogen, Mylan, Sandoz, Pfizer, Takeda, Janssen, Tillots, Gilead and Ferring. Jean-Marie Reimund has received consulting fees from Hospira and Pfizer. This author has also received lecture fees from Abbvie, Biocodex, Ferring, Janssen Cilag, Pfizer and Takeda, as well as travel accommodations from Ferring, Abbvie, MSD, Janssen Cilag, Pfizer, Hospira and Takeda. Olivier DeWit declares counselling, boards, transport or personal fees from Abbvie, BMS, Celltrion, Ferring, Galapagos, Janssen, Mylan, Pfizer and Takeda. Lucine Vuitton has received lecture fees from Abbvie, MSD, Takeda, Ferring, Janssen and Pfizer, and research grants from MSD, Takeda and Pfizer. Nicolas Mathieu has received consulting fees from Celltrion, Mylan, MSD, Gilead and Sandoz, and lecture fees from Abbvie, Amgen, Biogen, Janssen, MSD, Pfizer and Takeda. Laurent Peyrin-Biroulet has received consulting fees from Merck, Abbvie, Janssen, Genentech, Ferring, Norgine, Tillots, Vifor, Shire, Therakos, Pharmacosmos, Pilège, BMS, UCB-Pharma, Hospira, Celltrion, Takeda, Biogaran, Boerhinger-Ingelheim, Lilly, Pfizer and HAC-Pharma. This author has also received lecture fees from Merck, Abbvie, Takeda, Janssen Cilag, Ferring, Norgine, Tillots, Vifor, Therakos, HAC-Pharma and Mitsubishi. Cyrielle Gilletta has received lecture fees from Abbvie, Takeda, Pfizer and Janssen, and consulting fees from Abbvie, Janssen and Takeda. Matthieu Allez has received

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Author Contributions

Conception and design of the study: AM, SC, MN, DL, LPB. Generation, collection, assembly, analysis and/or interpretation of data: SC, JT, MN, YB, MS, JF, XR, AB, GB, DF, GS, AB, EL, SN, VA, JMR, OdW, LV, NM, LPB, CG, MA, SV, CLB, ND, HB, MB, LP, RA, MF, LC, DL, AA. Drafting or revision of the manuscript: JT, SC, MN, YB, MS, JF, XR, AB, GB, DF, GS, AB, EL, SN, VA, JMR, OdW, LV, NM, LPB, CG, MA, SV, CLB, ND, HB, MB, LP, RA, MF, LC, DL, AA. Approval of the final version of the manuscript: JT, SC, MN, YB.

Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Supplementary Data

Supplementary data are available online at *ECCO-JCC* online.

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