Crohn's & Colitis 360, 2025, **7**, otaf011
https://doi.org/10.1093/crocol/otaf011
Advance access publication 18 March 2025
Observations and Research

US and European Patient and Health Care Professional Perspectives on Fatigue in Ulcerative Colitis and Crohn's Disease: Results From the Communicating Needs and Features of Inflammatory Bowel Disease Experiences Survey

Remo Panaccione, MD[*], Alison Potts Bleakman, PhD[†], Stefan SchreiberMD[‡], Simon Travis, MD[§], Marla Dubinsky, MD[¶], Toshifumi Hibi, MD, PhD[‖], Theresa Hunter Gibble, PhD[†], Tommaso Panni, PhD[†], Cem Kayhan, MD[†], Eoin J. Flynn, PhD[†], Angelo D. Favia, PhD[†], Christian Atkinson, BSc, MRes[**], and David T. Rubin, MD[††]

[*]Inflammatory Bowel Disease Unit, Division of Gastroenterology and Hepatology, University of Calgary, Calgary, AB, Canada
[†]Eli Lilly and Company, Indianapolis, IN, USA
[‡]Department of Internal Medicine I, University Hospital Schleswig-Holstein, Kiel, Germany
[§]Kennedy Institute and Translational Gastroenterology Unit, University of Oxford, Oxford, UK
[¶]Susan and Leonard Feinstein IBD Center, Icahn School of Medicine at Mount Sinai, New York, NY, USA
[‖]Center for Advanced IBD Research and Treatment, Kitasato University, Tokyo, Japan
[**]Adelphi Real World, Bollington, UK
[††]University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, IL, USA

Address correspondence to: Remo Panaccione, MD, Inflammatory Bowel Disease Unit, Division of Gastroenterology and Hepatology, University of Calgary, Calgary, AB T2N4N1, Canada (rpanacci@ucalgary.ca).

Background: Fatigue is a burdensome symptom of Crohn's disease (CD) and ulcerative colitis (UC). The Communicating Needs and Features of Inflammatory Bowel Disease Experiences (CONFIDE) study investigated how patients and health care professionals (HCPs) in the United States (US) and Europe (France, Germany, Italy, Spain, and the United Kingdom) perceived the experiences and impact of CD/UC-related symptoms.

Methods: Online, quantitative, cross-sectional surveys were conducted separately among patients with moderate-to-severe CD/UC (defined based on previous treatment, steroid use, and/or hospitalization) and HCPs who treated patients with CD/UC. US and Europe data are presented as descriptive statistics.

Results: Surveys were completed by 215 US and 547 European patients with CD, 200 US and 556 European patients with UC, and 200 US and 503 European HCPs. Overall, 35.8% US and 34.2% European patients with CD and 27.5% US and 20.9% European patients with UC reported currently experiencing fatigue (in past month). Most of these patients reported severe fatigue and indicated that CD/UC negatively affected their sleep, energy levels, and quality of life (QoL). The majority of patients currently experiencing but not discussing fatigue with their HCPs at every appointment wished they discussed it more frequently. However, most HCPs reported proactively discussing fatigue at routine appointments. Approximately 20% patients with CD/UC reported declining participation in work/school, social activities, and sports/physical exercise, and avoiding sexual activities due to fatigue.

Conclusions: US and European patients with CD/UC experienced severe burden of fatigue, which negatively affected their QoL. Assessing and discussing fatigue in routine appointments is critical for effectively managing this debilitating symptom.

Lay Summary

Fatigue is a common symptom of moderate-to-severe Crohn's disease and ulcerative colitis affecting patients' work/school, physical, social, and sexual activities. However, it is often underappreciated by physicians, highlighting the need to assess fatigue in clinical practice and develop management plans.

Key Words: fatigue, Crohn's disease, quality of life, ulcerative colitis

Introduction

Fatigue, often described as a persistent sense of exhaustion that is not relieved by rest, is a commonly reported symptom among patients with Crohn's disease (CD) or ulcerative colitis (UC).[1–4] Fatigue can significantly affect patients' health-related quality of life (HRQoL), social functioning, work productivity, and mental well-being.[1,5,6] In previous studies, fatigue has been reported to affect 72% to 86% of patients with active CD and UC, and 40% to 48% of those in remission.[5,7,8]

Received for publication: August 21, 2024. Editorial Decision: January 12, 2025

Etiologies of fatigue in patients with CD or UC include disease activity, anemia, medications, alterations to the gut-brain axis, psychological comorbidities, and micronutrient deficiencies, among others.[8,9] Although fatigue is one of the leading concerns for patients with CD and UC, current treatments focus on alleviating gastrointestinal (GI) symptoms (eg, diarrhea, rectal bleeding, and stool frequency), often overlooking and undertreating this debilitating symptom.[9–11] Exploratory studies have highlighted discrepancies in patients' and health care professionals' (HCPs') perceptions of CD- or UC-related fatigue.[12,13] In a survey comparing patients' feelings with physicians' beliefs, fatigue was reported as a daily concern by 66% of patients, but by only 36% of physicians.[14]

Given its subjective nature and the lack of a standardized assessment in clinical practice, the management of fatigue in inflammatory bowel disease (IBD) is often challenging and multifaceted. Due to this, the recognition of fatigue as a core assessment measure in clinical assessments and consultations is often poor.[1,10,15,16] Research to investigate interventions specifically to target IBD-related fatigue is limited and of low quality and reduction of fatigue has not been a primary outcome of CD or UC clinical trials.[16,17]

Previous surveys and qualitative studies of patients with CD or UC and/or HCPs have investigated the impact of IBD on patients' HRQoL.[18–20] However, there are discrepancies in the existing literature regarding the perceptions of fatigue and its impact among patients with UC or CD. It is also not known whether the findings of such studies are globally generalizable, as most studies are United States (US) based. Furthermore, there is a communication gap between patients and HCPs regarding the burden and impact of fatigue, hindering appropriate treatment.[21,22]

The Communicating Needs and Features of IBD Experiences (CONFIDE) study explored the burden and impact of IBD symptoms on patients' lives and elucidated the communication gaps between HCPs and patients in the US, Europe (France, Germany, Italy, Spain, and the United Kingdom [UK]), and Japan. The current study reports CONFIDE data on the experiences, perceptions, and impact of fatigue in patients with moderate-to-severe CD or UC and gastroenterology HCPs in the US and Europe.

Methods

The CONFIDE study was a noninterventional observational study comprising 2 online, quantitative, and point-in-time cross-sectional surveys: one for patients with CD or UC and another for prescribing HCPs managing CD and/or UC. This article includes results from surveys conducted among patients and HCPs from the US and Europe (France, Germany, Italy, Spain, and the UK). Previously published studies included details on survey development, content, and data collection.[23,24]

Study Population

Health care professionals and patients were recruited via online panels and screened online. They were also required to provide informed consent prior to screening. Eligible patients were adults (≥18 years) with a patient self-reported HCP diagnosis of moderate-to-severe active CD or UC. Moderate-to-severe disease was defined as having received 1 of the following within the last 12 months: anti-tumor necrosis factor, anti-integrin, Janus kinase inhibitor, anti-interleukin-12/23, or immunomodulator treatment, and/or having received steroid treatment for at least 1 month out of the last 12 months, and/or having been hospitalized for at least 4 consecutive weeks in the last 5 years. Patients who had undergone colectomy were excluded, and those with self-reported concomitant irritable bowel syndrome were restricted to no more than 20% of each country's sample size.

Gastroenterologists and internal medicine specialists with a GI focus, IBD nurse specialists (only in the UK), nurse practitioners (only in the US), and physician assistants (only in the US) were eligible to participate. Eligible HCPs spent ≥50% of their working time actively seeing patients, saw at least 5 patients with moderate-to-severe IBD per month, and were responsible for making prescribing decisions for at least 10 patients with UC or CD.

Survey Content

Data were collected via structured online surveys of ~30 minutes. The patient and HCP survey questions included in these analyses are provided as Appendix A. The first section of both the patient and HCP surveys collected demographic information. Additionally, the surveys included questions that examined the experience, severity, impact, and burden of fatigue on patients' lives, patient and HCP perceptions of fatigue on quality of life (QoL), productivity, and social health, as well as gaps and barriers to effective HCP–patient communication.

Patients were asked to select from a list of 30 symptoms those they were currently experiencing (suffered from in the last month) or those they had ever suffered. Among the symptoms ever experienced, patients were asked to rank the 5 symptoms with the greatest impact on them on a scale of 1-5 (1 = most impactful, 2 = second most impactful, etc.). Health care professionals were asked to rank the most common symptoms reported by patients on a scale of 1-3 (1 = most reported, 2 = second most reported, etc.). Health care professionals used a similar scale to rank top 5 symptoms with the greatest impact on patients from 1 to 5. Patient and HCP-reported rankings and mean impact ratings for fatigue are presented.

The Manitoba IBD Index[25] was used to assess patient-reported disease activity based on symptom persistence for the previous 6 months, using a 6-level response format (1: "constantly active, giving me symptoms every day," 2: "often active, giving me symptoms most days," 3: "sometimes active, giving me symptoms on some days (for instance 1 to 2 days/week)," 4: "occasionally active, giving me symptoms 1 to 2 days/month," 5: "rarely active, giving me symptoms on a few days in the past six months," and 6: "I was well in the past 6 months, what I consider a remission or absence of symptoms"). Disease was considered active if symptoms were experienced constantly to occasionally (responses 1-4), and inactive if symptoms were infrequent or absent (responses 5 or 6).[25]

The patient survey included validated patient-reported outcome measures, including the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale, to assess the severity and impacts of fatigue among patients over the past 7 days. Scores ranged from 0 to 52, with higher scores indicating lesser fatigue.[26,27]

Patients were also asked to rate their severity of fatigue from 1 to 7, where 1 indicated "not severe at all" and 7 indicated "worst imaginable severity." Patient- and HCP-reported impact of fatigue on QoL and impact of CD or UC on energy levels and sleep were reported on a scale of 1-7, where 1 indicated "no impact" and 7 indicated "high impact." Mean impact ratings are also presented.

Statistical Analysis

Data were presented using descriptive statistics; therefore, formal sample size estimations were not performed. Categorical variables were presented as number of observations (HCPs or patients), frequency, and percentage. Continuous variables (eg, age and time since diagnosis) were presented as number of observations (HCPs or patients), means, and standard deviations (SDs).

Ethical Considerations

All participants provided informed consent to participate in the study via an IRB-approved informed consent form. The protocol and supporting data collection materials were approved by the Western Institutional Review Board (study number: 1307697). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was consistent with Good Pharmacoepidemiology Practices and applicable laws and regulations of the countries where the study was conducted. Patients and HCPs were paid a nominal honorarium for completing the surveys.

Results

Demographics and Clinical Characteristics

Key demographics and characteristics of HCPs and patients with moderate-to-severe CD or UC are reported in Table 1. A total of 2706 patients with CD and 18 002 patients with UC were contacted. Surveys were completed by 215 US and 547 European patients with CD and 200 US and 556 European patients with UC between July 1, 2021 and September 9, 2021. Mean ages of US and European patients with CD were 40.9 and 38.0 years, respectively, and 54.9% of US and 55.4% of European patients were male. Among patients with UC, the mean ages were 40.4 and 38.9 years for US and Europe, respectively, and 61.5% and 57.4% were male. The proportions of patients receiving advanced therapies at the time of survey completion were 58.1% and 63.4%, respectively, among US and European patients with CD. Among patients with UC, the percentages were 76.5% and 54.1%, respectively. Most patients reported active disease, as assessed using the Manitoba IBD Index scores (CD, US:92.6% and Europe:87.4%; UC, US: 95.5% and Europe:91%).

A total of 840 HCPs were contacted, of whom 200 US and 503 European HCPs completed the surveys between May 28, 2021 and October 2, 2021. Most HCPs surveyed were male (78.0% US and 70.8% European) and gastroenterologists (88.0% US and 93.2% European). Demographics and characteristics of patients and HCPs in each European country are presented in Table S1.

Patient and HCP Perceptions of Fatigue

Among patients with CD, 45.6% US and 45.2% European patients reported *ever* suffering from fatigue, and 35.8% and 34.2% reported *currently* suffering (in the past month)

Table 1. Demographics and characteristics of patients and HCPs.

Patients with CD		
	US (*N* = 215)	Europe (*N* = 547)
Mean age, years (SD)	40.9 (11.4)	38.0 (9.7)
Sex, *n* (%)		
Male	118 (54.9)	303 (55.4)
Female	97 (45.1)	244 (44.6)
Ethnicity, *n* (%)		
White	175 (81.4)	515 (94.1)
Hispanic/Latino	21 (9.8)	1 (0.2)
African American	12 (5.6)	-
Other[a]	7 (3.3)	31 (5.7)
Time since diagnosis of CD (mean years [SD])	8.7 (8.6)	9.2 (8.5)
Current treatments, *n* (%)		
5-ASA	51 (23.7)	169 (30.9)
Corticosteroids	126 (58.6)	271 (49.5)
Immunomodulator	84 (39.1)	255 (46.6)
Anti-TNF biologic therapy	93 (43.3)	289 (52.8)
JAK inhibitor	18 (8.4)	47 (8.6)
Anti-IL-12/23 p40 biologic therapy	18 (8.4)	69 (12.6)
Anti-integrin biologic therapy	43 (20.0)	154 (28.2)
Patients receiving advanced therapies,[b], *n* (%)	125 (58.1)	347 (63.4)
Patients with concomitant IBS,[c] *n* (%)	42 (19.5)	91 (16.6)
Patient-reported disease activity (Manitoba IBD Index),[d] *n* (%)		
Active disease (experiencing symptoms constantly to occasionally)	199 (92.6)	478 (87.4)
Inactive disease (infrequent symptoms or feeling well)	16 (7.4)	69 (12.6)

Patients with UC		
	US (*N* = 200)	Europe (*N* = 556)
Mean age, years (SD)	40.4 (10.8)	38.9 (8.8)
Sex, *n* (%)		
Male	123 (61.5)	319 (57.4)
Female	77 (38.5)	236 (42.4)
Ethnicity, *n* (%)		
White	155 (77.5)	518 (93.2)
Hispanic/Latino	23 (11.5)	3 (0.5)
African American	18 (9.0)	-
Other[a]	4 (2.0)	35 (6.3)
Time since diagnosis of UC (mean years [SD])	7.9 (8.6)	7.9 (7.5)
Current treatments, *n* (%)		
5-ASA	27 (13.5)	283 (50.9)
Corticosteroids	81 (40.5)	347 (62.4)
Immunomodulator	49 (24.5)	214 (38.5)
Anti-TNF biologic therapy	93 (46.5)	300 (54.1)
JAK inhibitor	37 (18.5)	58 (10.4)
Anti-IL-12/23 p40 biologic therapy	19 (9.5)	60 (10.8)
Anti-integrin biologic therapy	61 (30.5)	118 (21.2)

Patients with UC		
	US (*N* = 200)	Europe (*N* = 556)
Patients receiving advanced therapies,[b] *n* (%)	153 (76.5)	301 (54.1)
Patients with concomitant IBS,[c] *n* (%)	40 (20.0)	95 (17.1)
Patient-reported disease severity (Manitoba IBD Index),[d] *n* (%)		
Active disease (experiencing symptoms constantly to occasionally)	191 (95.5)	506 (91.0)
Inactive disease (infrequent symptoms or feeling well)	9 (45.0)	50 (9.0)

HCPs		
	US (*N* = 200)	Europe (*N* = 503)
Sex, *n* (%)		
Male	156 (78.0)	356 (70.8)
Female	40 (20.0)	139 (27.6)
Prefer not to say	4 (2.0)	8 (1.6)
Primary specialty,[e] *n* (%)		
Gastroenterologist	176 (88.0)	469 (93.2)
Internal medicine with GI focus/specialization	2 (1.0)	3 (0.6)
IBD nurse specialist	0	31 (6.2)
Nurse practitioner	11 (5.5)	0
Physician assistant	11 (5.5)	0
Year of qualification, *n* (%)		
Before 1985	22 (11.0)	57 (11.3)
1985-2018	173 (86.5)	434 (86.3)
After 2018	5 (2.5)	12 (2.4)

Values are mean (SD) or *n* (%), unless otherwise indicated.
[a]Other races included Asian-Indian subcontinent, Asian-other, Japanese, Korean, Middle Eastern, Afro-Caribbean, Native American, Mixed race, South-East Asian, and other.
[b]Adalimumab (including biosimilars), infliximab (including biosimilars), golimumab, certolizumab pegol, vedolizumab, natalizumab, ustekinumab, and tofacitinib.
[c]Patients with self-reported concomitant irritable bowel syndrome were restricted to no more than 20% of each country's sample size.
[d]The Manitoba IBD Index was used to assess patient-reported disease activity. Patients were asked to describe their disease using the best response among the following: 1 = constantly active, giving me symptoms every day, 2 = often active, giving me symptoms most days, 3 = sometimes active, giving me symptoms on some days (for instance 1-2 days/week), 4 = occasionally active, giving me symptoms 1-2 days/month, 5 = rarely active, giving me symptoms on a few days in the past 6 months, and 6 = I was well in the past 6 months, what I consider a remission or absence of symptoms. Disease was considered active if symptoms were experienced constantly to occasionally (responses 1-4), and inactive if symptoms were infrequent or absent (responses 5 or 6).
[e]US HCPs included nurse practitioners and physician assistants; UK HCPs included IBD nurse specialists. Abbreviations: 5-ASA, 5-aminosalicylic acid; CD, Crohn's disease; GI, gastroenterology; HCP, health care professional; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome, IL, interleukin; JAK, Janus kinase; *N*, number of patients; *n*, number of patients in the subgroup; SD, standard deviation; TNF, tumor necrosis factor; UC, ulcerative colitis; UK, United Kingdom; US, United States.

from fatigue. In the subset of patients with CD receiving advanced therapies, 47.2% US and 45.5% European patients reported ever suffering from fatigue and 36.0% and 34.3% reported currently suffering from fatigue. The percentages of patients with UC who reported ever or currently experiencing fatigue in the US were 40.0% and 27.5%, respectively, and 30.6% and 20.9%, respectively, in Europe. Similar results were observed among patients with UC receiving advanced therapies: 35.9% and 25.5% in the US and 28.6% and 19.9% in Europe (Figure 1A and B). Among patients with concomitant irritable bowel syndrome (Table 1), 50% US and 42% European patients with CD reported ever experiencing fatigue and 48% US and 34% European patients reported currently experiencing fatigue. Among patients with UC and concomitant irritable bowel syndrome, the related percentages were 38% in the US and 33% in Europe for ever experiencing fatigue and 30% in the US and 27% in Europe for currently experiencing fatigue. Fatigue was the fourth most common currently experienced symptom reported by patients with CD but was not among the top 5 most common symptoms reported by patients with UC (Figure S1). Among patients with CD currently experiencing fatigue, greater than 90% of patients described their disease as active on the Manitoba IBD Index (US: 93.5% and Europe: 92.5%). Among patients with UC currently suffering from fatigue, 98.1% US and 92.2% European patients indicated that their disease status was active (Figure 1C).

Among symptoms reported as ever experienced, 53.1% US and 44.5% European patients with CD and 37.5% US and 55.3% European patients with UC ranked fatigue among the top 5 symptoms with the greatest impact on them (Figure 1D). Approximately 20% of patients ranked fatigue among the top 3 symptoms with the greatest impact on them. Fatigue was reported among the top 5 symptoms with the greatest impact by a minority of HCPs in the US and Europe (CD, US: 22.0% and Europe: 34.0%; UC, US: 11.5% and Europe: 22.7%). Similar trends were observed for HCP-perceived top 3 symptoms with the greatest impact on patients (Figure 1E). In contrast, less than 25% of HCPs ranked fatigue among the top 3 most commonly reported symptoms in both US and European patients with CD (US: 10.5%, Europe: 23.5%). For patients with UC, only 4.5% US HCPs and 10.1% European HCPs ranked fatigue to be among the top 3 most commonly reported symptoms (Figure 1F).

Experience and Burden of Fatigue

Mean (SD) FACIT-Fatigue scores were 26.8 (10.8) and 27.4 (11.3), respectively, for US and European patients with CD; and 26.2 (11.3) and 29.4 (10.0), respectively, for US and European patients with UC (Figure 2A). Among the patients who reported currently experiencing fatigue, mean (SD) FACIT-Fatigue scores were 26.1 (10.9) and 24.3 (10.8), respectively, for US and European patients with CD; and 24.5 (11.5) and 26.0 (10.6), respectively, for US and European patients with UC (Figure 2B).

Most patients with CD or UC experiencing fatigue in the past month rated its severity as high (scores ranging from 4 to 7) using a 7-point scale (mean [SD] rating: CD, US: 4.9 [1.5] and Europe: 5.0 [1.6]; UC, US: 5.1 [1.6] and Europe: 4.7 [1.5]) (Figure 2C). Among US (*n* = 98) and European (*n* = 247) patients with CD who had ever experienced fatigue, most patients (US: 79.6%, Europe: 67.6%) reported experiencing fatigue at least once a week over the past 3 months. Similarly, among US (*n* = 80) and European (*n* = 170) patients with UC who had ever experienced fatigue, 70.0% US patients and 66.5% European patients reported experiencing fatigue at least once a week over the past 3 months (Figure 2D).

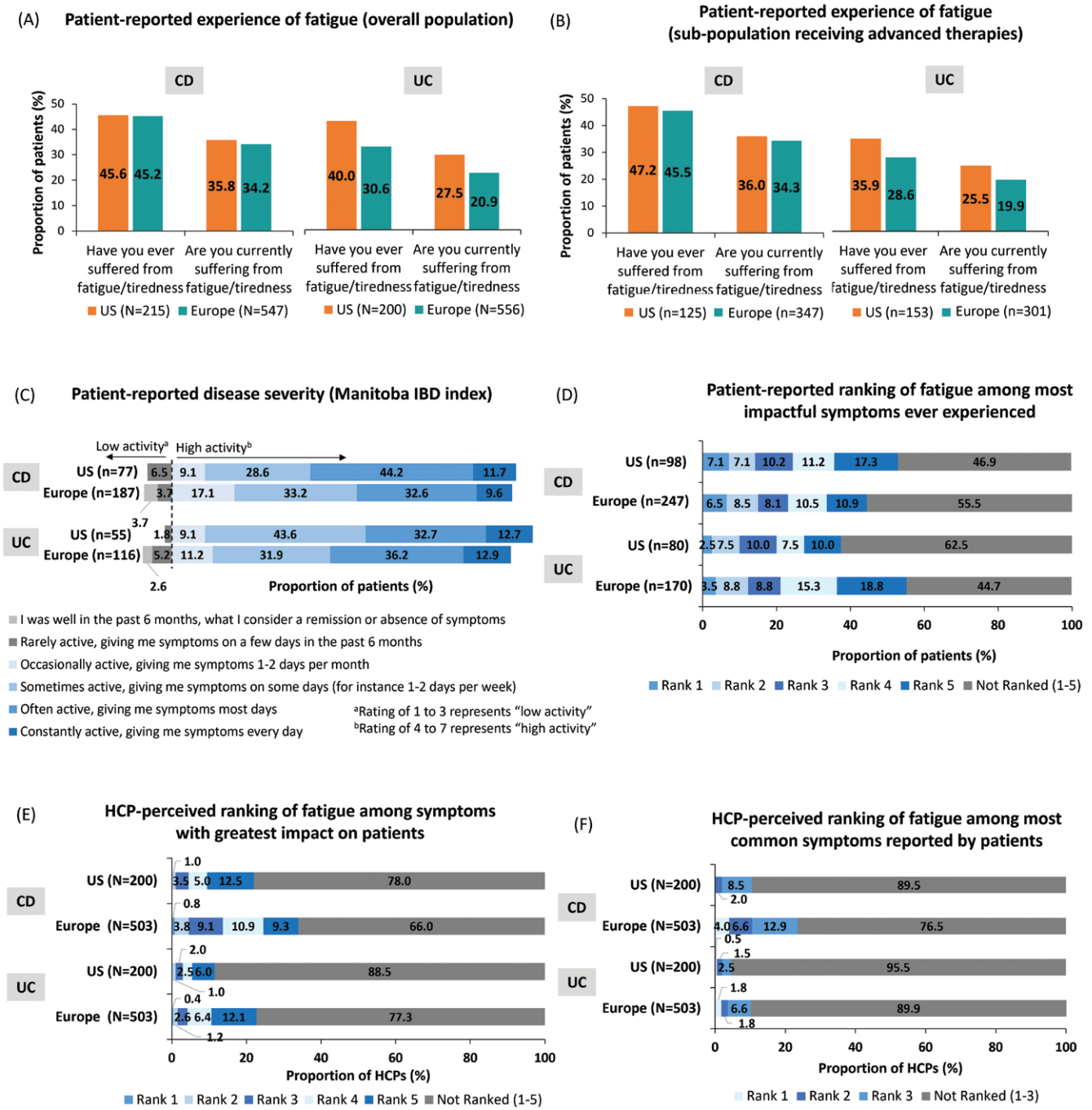

Figure 1. Patient and HCP perceptions of CD- or UC-related fatigue. (A) Proportion of patients who reported ever and currently suffering from fatigue. Patients were asked which symptoms they have ever suffered from and currently suffer from (ie, in the last month). Symptoms were selected from a list of 30 options. (B) Proportion of patients who reported ever and currently suffering from fatigue in the subset of patients receiving advanced therapies. (C) Patient-reported disease activity among those currently experiencing fatigue (Manitoba IBD index). (D) Patient-reported ranking of fatigue when asked about most impactful symptoms ever experienced. (E) HCP-perceived ranking of fatigue when asked about symptoms with the greatest impact on patients. (F) HCP-perceived ranking of fatigue when asked about most common symptoms reported by patients.Abbreviations: CD, Crohn's disease; HCP, health care professional; IBD, inflammatory bowel disease; *N*, number of patients; UC, ulcerative colitis; US, United States.

Impact of Fatigue on HRQoL of Patients With CD or UC

Approximately 20% of the CD or UC patient population reported fatigue as a reason for declining participation in work/school, social activities, and sports/physical exercise in the past 3 months (Figure 3A). Among patients with CD who reported that they had avoided or decreased their sexual activity in the last 3 months due to their CD (US: 148, Europe: 305), 37.8% US patients and 29.5% European patients reported fatigue/tiredness due to CD as the reason. A total of 126 US and 292 European patients with UC reported decreased sexual activity in the last 3 months, of whom 28.6% US and 17.8% European patients attributed it to fatigue due to their UC.

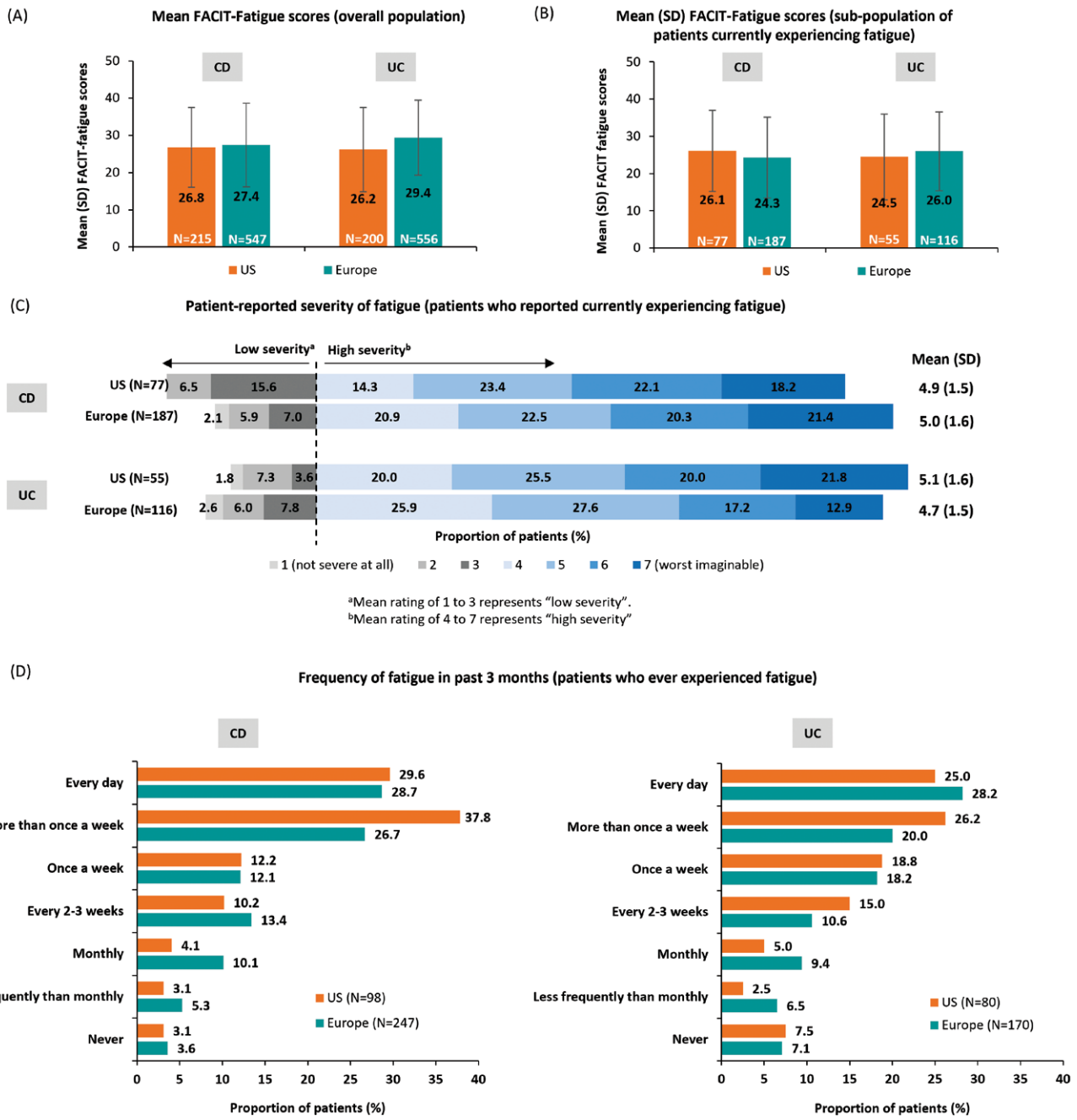

Figure 2. Patient experience of CD- or UC-related fatigue. (A) Mean (SD) FACIT-Fatigue scores (range: 0-52, where higher the score, the lesser the fatigue experienced) among patients with CD or UC. (B) Mean (SD) FACIT-Fatigue scores among patients who reported currently experiencing fatigue. (C) Patient-reported severity of fatigue among patients who reported experiencing fatigue in the past month, on a scale of 1-7, where 1 indicates "not severe at all" and 7 indicates "worst imaginable severity." Mean ratings (SD) of severity are presented. (D) Frequency of patients' experience of fatigue in the past 3 months among patients who reported ever experiencing fatigue. Abbreviations: CD, Crohn's disease; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; *N*, number of patients; SD, standard deviation; UC, ulcerative colitis; US, United States.

Among patients with CD who had ever experienced fatigue, 46.9% US and 40.5% European patients reported that it negatively affected their working hours. Similarly, among patients with UC, these percentages were 41.2% and 42.4% for US and European populations, respectively. Approximately a third of patients with CD or UC reported that they stopped working for the day sooner than planned (CD, US: 32.7% and Europe: 32.4%; UC, US: 38.8% and Europe: 34.1%) (Figure 3B).

High impact of CD and UC (scores ranging from 4 to 7) on sleep was reported by most patients: CD (US: 79.1%, Europe: 75.1%) and UC (US: 83.5%, Europe: 78.8%); mean (SD) rating of impact: CD (US: 4.7 [1.8], Europe: 4.6 [1.7]) and UC (US: 5.0 [1.6], Europe: 4.7 [1.6]) (Figure 3C). More than 80% of patients also indicated a negative impact on energy levels due to CD or UC: CD (US: 84.2% and Europe: 80.1%) and UC (US: 88.0% and Europe: 81.1%). Mean (SD) rating of impact was 4.9 (1.6) for US and 4.9 (1.7) for European

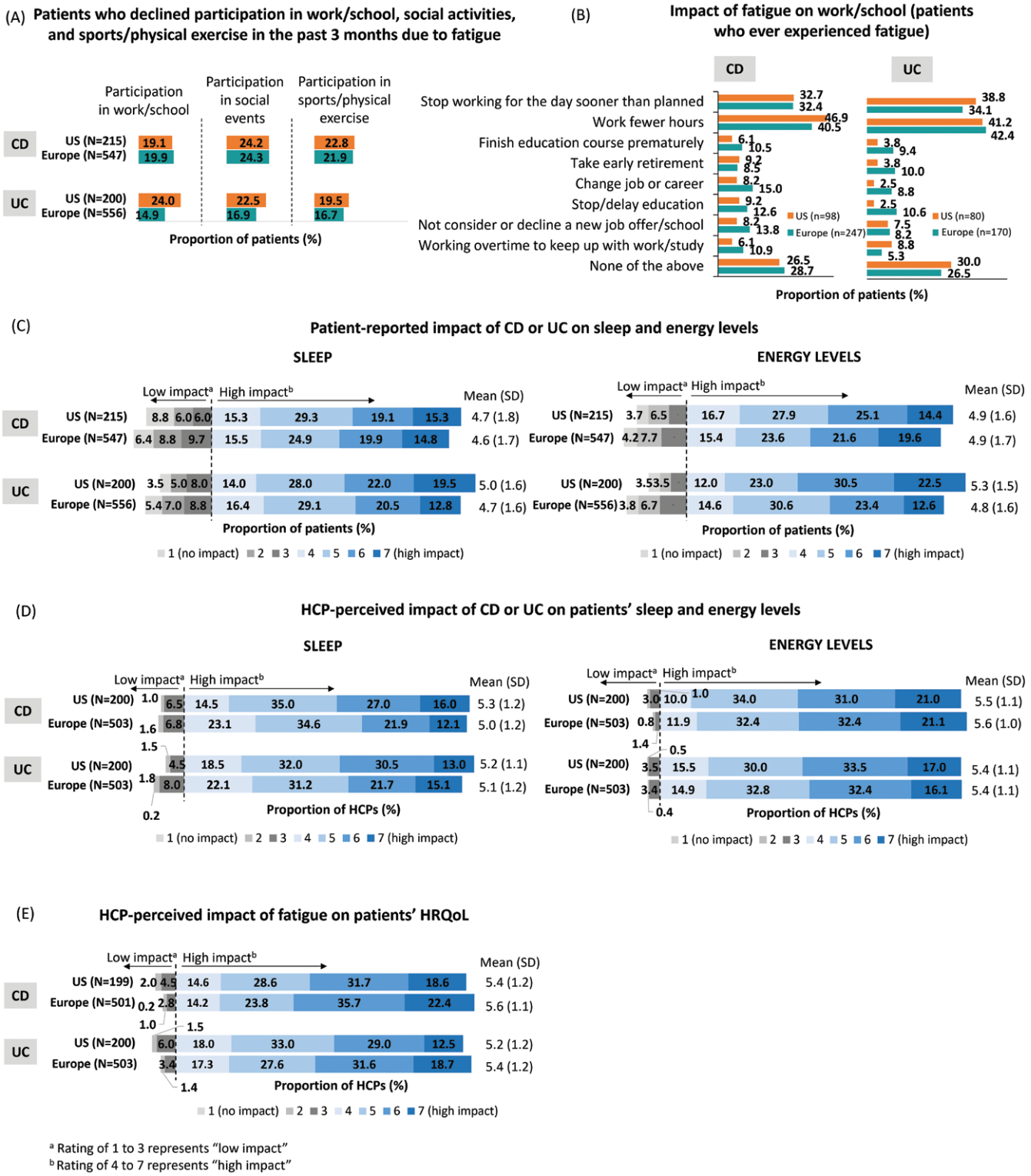

Figure 3. Impact of fatigue on HRQoL of patients with CD or UC. (A) Patients who declined participation in work/school, social activities, and sports/physical exercise in the past 3 months due to CD- or UC-related fatigue. (B) Impact of CD/UC-related fatigue on work/school (among patients who reported ever experiencing fatigue). Patients were asked to choose from a list of possible reasons pertaining to work/school (among patients who reported ever experiencing fatigue). (C) Patient-reported impact of CD or UC on sleep and energy levels. Patients reported the impact on a scale of 1-7, where 1 indicates "no impact" and 7 indicates "high impact." Mean ratings (SD) of impact are presented. (D) HCP-perceived impact of CD or UC on patients' sleep and energy levels. HCPs reported the impact on a scale of 1-7, where 1 indicates "no impact" and 7 indicates "high impact." Mean ratings (SD) of impact are presented. (E) HCP-perceived impact of fatigue on patients' HRQoL. HCPs reported the impact on a scale of 1-7, where 1 indicates "no impact" and 7 indicates "high impact." Mean ratings (SD) of impact are presented. Abbreviations: CD, Crohn's disease; HCP, health care professional; HRQoL, health-related quality of life; *N*, number of patients; QoL, quality of life; SD, standard deviation; UC, ulcerative colitis.

patients with CD, and 5.3 (1.5) for US and 4.8 (1.6) for European patients with UC (Figure 3C). Furthermore, more than 90% HCPs reported a high impact on patients' sleep and energy levels due to CD or UC, as well as their general QoL, due to CD- or UC-related fatigue, among both US and European patients. Mean (SD) rating of HCP-perceived impact for sleep, energy levels, and QoL ranged from 5.0 (1.2) to 5.6 (1.0) for CD and 5.1 (1.2) to 5.4 (1.1) for UC (Figure 3D and E).

HCP–Patient Communication

When asked about the frequency of discussing fatigue with their HCPs, more than one-third of US and European CD and UC patients currently experiencing fatigue reported discussing it frequently: CD (US: 37.7%, Europe: 41.2%) and UC (US: 41.8%, Europe: 44.0%) (Figure 4A). Among patients who did not discuss fatigue with their HCPs at every appointment, the majority mentioned that they would like to discuss it more frequently with their HCPs: CD (US: 67.3%, Europe: 75.6%) and UC (US: 66.7%, Europe: 74.4%). Yet, more than half of HCPs self-reported proactively discussing fatigue with their patients: CD (US: 59.5%, Europe: 69.4%) and UC (US: 59.0%, Europe: 64.6%) (Figure 4B). Among HCPs not proactively discussing fatigue with their patients with CD or UC during routine appointments, more than 30% revealed that they expected patients to bring it up during a consultation if it was an issue (Figure 4C).

Discussion

This study from the CONFIDE survey provides valuable insights into the burden and experience of fatigue among patients with CD or UC, as well as HCP perceptions of its prevalence and impact.

Previous cross-sectional and survey-based studies have highlighted fatigue as a persistent and troublesome symptom affecting patients with UC or CD.[4,5,21] Consistent with these reports, our results suggest that fatigue was experienced by a substantial proportion of patients with UC or CD in both US and European populations. Among patients who had ever experienced fatigue, most patients reported experiencing it at least once a week over the past 3 months and identified it as an impactful symptom affecting their overall HRQoL.

European and US patients with CD or UC reported more severe fatigue (mean FACIT-fatigue score range: 26-29 out of a total score of 52; higher scores indicate lesser fatigue) compared with the general healthy population (mean score in general population: 43/52[28]; scores < 30/52 indicate severe fatigue[29]). Most patients with CD or UC who reported currently experiencing fatigue self-reported active disease and indicated a high burden of fatigue (as assessed using FACIT-Fatigue scale), similar to previous studies reporting the association of fatigue with disease activity.[10] Importantly, mean FACIT-Fatigue scores among patients currently experiencing fatigue were similar to those of the overall population, which included patients who did not report currently experiencing fatigue. This could be due to patients getting so used to experiencing fatigue that they viewed their current health as the "new normal," often dismissing it as an inevitable part of their disease.[30,31] Similarly, although >80% of patients with CD or UC reported a negative effect on energy levels, <36% patients identified fatigue as a current symptom. Fatigue is often considered "inferior" to other IBD symptoms, with patients feeling that "fatigue is just a part of the disease" and "nothing can be done about fatigue," thereby underestimating or underreporting this important symptom.[22,32]

More than a third of patients identified fatigue among the top 5 most impactful symptoms that they had ever experienced. Nevertheless, a lower proportion of HCPs considered it among the top 5 most impactful symptoms. Such misalignment in patient and HCP perceptions of fatigue on patients' HRQoL was previously identified by the IBD-Global Assessment of Patient and Physician Unmet Needs Survey (IBD-GAPPS) survey, conducted among patients with CD and UC in the US and Europe.[21] Interestingly, compared with patients, HCPs perceived a greater impact of CD or UC symptoms on sleep and energy levels of patients in the current study.

Altogether, these findings indicate a mismatch between the patient and HCP perceptions of the experience and burden of fatigue. Similar misalignment in patient and HCP perceptions was evident from previous qualitative studies, where HCPs had a limited understanding of fatigue as a troublesome symptom, whereas patients felt unsupported, with their reports of fatigue not addressed by HCPs.[12,13] Such patients' and HCPs' perceptions, behaviors, and knowledge related to fatigue play a major role in seeking and providing fatigue-related care.

Among the patients with CD or UC who reported currently experiencing fatigue, more than one-third discussed it frequently. Most of those who did not discuss fatigue with their HCPs expressed a desire to do so more frequently. However, most HCPs self-reported discussing fatigue during routine clinical appointments. When asked about the reason for not routinely discussing fatigue, the most common reason was that the patients were expected to bring it up if it is an issue. Furthermore, patients with CD or UC reported frequently experiencing fatigue, with a majority experiencing it at least once every week. However, HCPs believed that fatigue was not a commonly reported symptom among either US or European patients with CD or UC. This highlights an important communication gap between patients and HCPs and underappreciation of fatigue when treating patients with CD or UC.[13]

A considerable impact of UC or CD symptoms on sleep and energy levels of patients was observed in both US and European populations studied. These findings corroborate previous reports, where fatigue and sleep disturbances were identified as a common source of distress in patients with CD and UC.[4,33] Additionally, a correlation or association between sleep disturbances and fatigue in patients with IBD had often been reported.[4,5,34] Furthermore, sleep disturbances could also be a possible cause of CD- or UC-related fatigue in these patients, as previously reported.[9]

Patients with CD or UC commonly report reduced sexual activity due to their symptoms.[35] Fatigue was among the symptoms most commonly associated with reduced sexual activity in patients with IBD.[36,37] In agreement with these findings, our results suggest reduced sexual activity in many patients with CD or UC, with more than a third citing "fatigue/tiredness" as a reason.

Fatigue has been strongly associated with work productivity loss and in patients with UC or CD. In this study, most patients experiencing fatigue reported stopping work for the

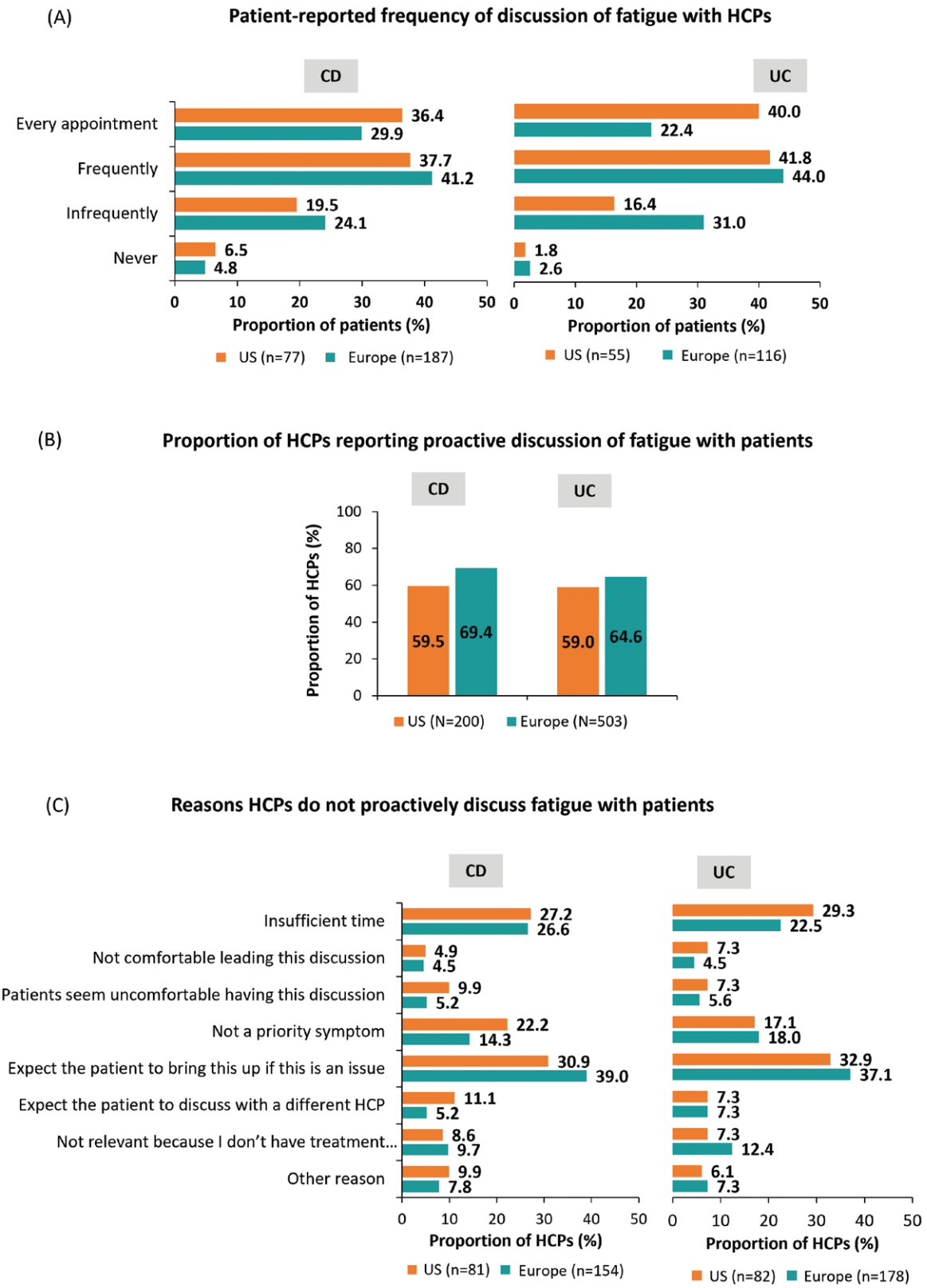

Figure 4. HCP–patient communication regarding CD- or UC-related fatigue. (A) Patient-reported frequency of discussion of fatigue as a symptom with HCPs, among patients who reported currently experiencing fatigue. (B) Proportion of HCPs reporting proactive discussion of fatigue with patients at a routine appointment. (C) Reasons for HCPs to not proactively discuss fatigue/tiredness in routine appointments (among HCPs who do not proactively discuss fatigue). HCPs were asked to choose from a list of possible reasons. Abbreviations: CD, Crohn's disease; HCP, health care professional; *N*, number of patients; UC, ulcerative colitis; US, United States.

day sooner than planned or working fewer hours due to CD- or UC-related fatigue, potentially impacting their productivity. Patients reported declining participation in sports/physical exercise, social events, and work/school due to fatigue related to their IBD. Similar effects of fatigue on patients' daily activities and work have previously been reported. In a qualitative study conducted in the UK, patients with CD or UC reported that their employers and work colleagues did not understand the debilitating impacts of fatigue and had inflexible, unsupportive, and unhelpful attitudes.[38]

Overall, the experience and symptomatic burden of fatigue were largely similar in patients with CD or UC across US and European populations. A numerically greater proportion of patients with CD reported currently experiencing fatigue compared with those with UC. Similarly, previous case control and survey-based studies have reported a numerically higher prevalence of fatigue in patients with CD compared with those with UC.[3,21] This can be attributed to the more severe symptoms and worse QoL reported in patients with CD compared with those with UC.[39,40]

Even among patients with improved GI symptoms and adequate disease control, fatigue continues to be a factor contributing to poor QoL. There remains an unmet need in addressing and understanding fatigue.[41] Despite the burdensome and debilitating nature of fatigue in IBD patients, there are no interventions that specifically target fatigue management. Given its complex nature and multiple etiologies, including inflammation, pain, nutritional deficiencies, disturbed sleep, emotional stress, anemia, and medication,[8,9] management of fatigue is challenging, as several factors need to be considered when developing treatment strategies.[9] Therefore, there is a need for the evaluation of pharmacological interventions for management of IBD-related fatigue.[16,42]

Limitations

This study had several limitations. First, back translations of the CONFIDE patient and HCP surveys were not performed. Prior to the survey launch, a translation agency performed the translations, which were validated by comparing with the original English version by native speakers with a specialty in the medical field. Second, patient eligibility, diagnosis of concomitant irritable bowel syndrome, and survey responses were patient self-reported and were primarily based on their retrospective assessment. This may have resulted in recall bias and adversely affect data reliability. Furthermore, treatment guidelines may be updated following study initiation, which is a common limitation of observational studies. To mitigate this, the definition of moderate-to-severe CD and UC was developed in collaboration with expert gastroenterologist advisors. Third, only the patients and HCPs who completed the survey were included. Due to this, the results might have been biased to include patients who were more active in managing their disease and communicating with HCPs or those who were not satisfied with their disease management and may not reflect the general population with moderate-to-severe CD or UC. Similarly, HCPs who pay more attention to patients' perspectives could be more likely to participate in the survey compared with those who may be less aware of patients' needs. Fourth, direct comparisons between data from patients with UC and CD were not conducted in this study but will be considered for future analyses. Last, this study was limited to patients with "moderate-to-severe" CD or UC in the US and Europe with mostly white race and non-Hispanic/Latino ethnicity. Therefore, the results may not represent the global UC or CD population and do not fully represent different racial and ethnic populations.

Conclusions

Fatigue is commonly reported by patients with UC or CD and presents with high severity and burden even among those receiving advanced therapies. However, the impacts of this important symptom are often underappreciated by HCPs. Although many HCPs reported discussing fatigue proactively, some patients expressed a desire to discuss fatigue more frequently, indicating a gap in communication. The findings emphasize the importance of routinely discussing and assessing CD- or UC-related fatigue during clinic visits and developing a multidimensional approach to treat this debilitating symptom.

Supplementary Data

Supplementary data is available at *Crohn's & Colitis 360* online.

Acknowledgments

Sonal Saxena and Mythili Ananth, employees of Eli Lilly Services India Private Limited, provided medical writing support.

Author Contributions

T.H.G., A.P.B., C.K., and T.P. contributed to conception, design, and interpretation of data. M.C.D., D.R., A.D.F., E.J.F., R.P., S.T., S.S., and T.H. contributed to design and interpretation of data. C.A. contributed to design, acquisition, and interpretation of data. A.P.B., T.H., and T.P. were involved in data analyses. All the authors were involved in critical revision of the intellectual content.

Funding

This study and the journal's article processing fee are funded by Eli Lilly and Company.

Conflict of Interest

R.P., Consultant for: Abbott, AbbVie, Abbivax, Alimentiv (formerly Robarts), Amgen, AnaptysBio, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly, Ferring, Galapagos, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Shire, Sublimity Therapeutics, Spyre Therapeutics, Takeda Pharmaceuticals, Theravance Biopharma, Trellus, Union Biopharma, Viatris, Ventyx, UCB; Speaker's Fees for: AbbVie, Amgen, Arena Pharmaceuticals, Bristol-Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Gilead

Sciences, Janssen, Merck, Organon, Pfizer, Roche, Sandoz, Shire, Takeda Pharmaceuticals; Advisory Boards for: AbbVie, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Roche, SandozShire, Sublimity Therapeutics, Takeda Pharmaceuticals, and Ventyx. S.S., Consultancy fees: AbbVie, Arena, Biogen, Bristol-Myers Squibb, Celgene, Celltrion, Falk, Fresenius, Gilead Sciences, IMAB, Janssen, Eli Lilly and Company, Hikma, MSD, Mylan, Pfizer Inc, Protagonist, Provention Bio, Takeda, Ventyx, and Theravance. S.T., Grants: AbbVie, ECCO, Eli Lilly and Company, Helmsley Trust International, International Organization for the Study of Inflammatory Bowel Disease, Norman Collision Foundation, Pfizer, Takeda, UCB Pharma, UKIERI, Vifor Pharma; Honoraria: Ferring Pharmaceuticals, Takeda, Eli Lilly and Company, Bristol Myers Squibb, Janssen, Violicom; Travel grants: AbbVie, Eli Lilly and Company, Janssen, Pfizer, Takeda, Ferring Pharmaceuticals, Amgen, Biogen; Consultancy fees: AbbVie, Allergan, Amgen, Apexian, Bioclinica, Biogen, Bristol Myers Squibb, ChemoCentryx, Cosmo Pharmaceuticals, Endpoint Health, Eli Lilly and Company, Enterome, Equillium, Ferring Pharmaceuticals, Genentech/Roche, GlaxoSmithKline, Immunocore, Immunometabolism, Janssen, Merck, Merck Sharp & Dohme, Mestag Therapeutics, Novartis, Pfizer, Protagonist Therapeutics, Proximagen, Receptos, Roche, Sanofi, Satisfai Health, Sensyne Health, Sorriso Pharmaceuticals, Takeda, UCB Pharma, VHsquared, Vifor Pharma. M.C.D., Consultancy fees: AbbVie, Abivax, Astra Zeneca, Boehringer Ingelheim International GmbH, Bristol Myers Squibb, Celgene Corporation, Eli Lilly and Company, F. Hoffman-La Roche Ltd, Genentech Inc., Gilead Sciences, Janssen, LLC, Merck, Pfizer, Prometheus Biosciences, Takeda Pharmaceuticals USA, Inc., and UCB; Stock options: TrellusHealth Inc.; Research support: AbbVie, Janssen, LLC, Pfizer, and Prometheus Labsa; and licensing fees: Takeda. T.H., Personal fees: Abbvie GK, EA Pharma, Janssen Pharmaceutical K.K, JIMRO, Mitsubishi-Tanabe, Mochida Pharmaceutical, Pfizer Japan, Sandoz K.K, Takeda Pharmaceutical, Zeria Pharmaceutical, Celltrion Healthcare Japan, Eli Lilly Japan, Gilead Sciences, Miyarisan Pharmaceutical, Alfresa Pharma Corporation, Kyorin Pharmaceutical; Grants: JIMRO, Mochida Pharmaceutical, Zeria Pharmaceutical, Miyarisan Pharmaceutical, Alfresa Pharma Corporation, and Kyorin Pharmaceutical. C.A., Employment: Adelphi Real World. D.R., Grant support: Takeda; Consultant: Abbvie, Altrubio, Apex, Avalo Therapeutics, Bristol-Myers Squibb, Buhlmann Diagnostics Corp, Celgene, Connect BioPharma, Intouch Group, Iterative Health, Janssen Pharmaceuticals, Lilly, Pfizer, Samsung Neurologica, and Takeda. Board of Trustees: Crohn's & Colitis Foundation; Board of Directors: Cornerstones Health. A.P.B., T.H.G., T.P., C.K., E.J.F., and A.D.F. are employees and shareholders of Eli Lilly and Company.

Data Availability

The datasets analyzed during the current study are not publicly available due to proprietary reasons and are intellectual properties of Eli Lilly and Company.

Appendix A

Patient survey questions

All patients were asked:

- What is your age?
- Which of the following are you currently diagnosed with?
  - Crohn's disease (CD)
  - Ulcerative colitis (UC)
  - Irritable Bowel Syndrome (IBS)
  - Diverticulitis
  - Endometriosis
  - Dyspepsia
  - Heartburn or gastrointestinal reflex disease (GERD)
  - None of the above
- What was your sex at birth?
  - Male
  - Female
  - Prefer not to say
- What is your ethnic origin?
  - White/Caucasian
  - African American
  - Native American
  - Asian-Indian subcontinent
  - Asian—other
  - Chinese
  - Japanese
  - Korean
  - Hispanic/Latino
  - Middle Eastern
  - Mixed race
  - Other
- In what year were you diagnosed with CD/UC?
- What medicines are you currently taking for your CD/UC?
  - Non-Biologics:
    - 5-ASA (for example SALOFALK, PENTASA)
    - Corticosteroids: Methylprednisolone, budesonide, prednisolone, prednisone
    - Azathioprine, methotrexate
    - Mercaptopurine
  - Biologics:
    - Adalimumab (HUMIRA)
    - Infliximab (REMICADE)
    - Golimumab (SIMPONI)
    - Certolizumab-pegol (CIMZIA)
    - Vedolizumab (ENTYVIO)
    - Natalizumab (TYSABRI)
    - Ustekinumab (STELARA)
  - Biosimilars:
    - Infliximab biosimilar (REMSIMA, INFLECTRA, FLIXABI, RENFLEXIS, IXIFI, ZESSLY)
    - Adalimumab biosimilar (AMJEVITA/AMGEVITA, SOLYMBIC, IMRALDI, HADLIMA, HYRIMOZ, CYLTEZO, HALIMATOZ, HEFIYA, HULIO, IDACIO, KROMEYA, ABRILADA)
  - JAK Inhibitor:
    - Tofacitinib (XELJANZ)
  - Enteral nutrition (food or drug administration via tube)
    - Enteral nutrition—exclusive
    - Enteral nutrition—supplemental

  - Parenteral nutrition
    - Parenteral nutrition—exclusive
    - Parenteral nutrition—supplemental
  - Pain relief treatments
    - Acetaminophen (for example paracetamol, Tylenol, ibuprofen)
    - Codeine
    - Lidocaine
    - Morphine
    - Oxycodone
    - Medical cannabis
    - Tramadol
    - Other
  - Antibiotics
  - Calcineurin inhibitors
    - Cyclosporine
    - Tacrolimus
    - Other
- Not currently receiving treatment for CD/UC
- *Below is a list of possible symptoms caused by your CD/UC.*
  a) Which symptoms have you ever suffered from?
  b) Which symptoms do you currently suffer from (that is in the last month)?
  c) Rank the 5 symptoms that have the greatest impact on you

Symptom list:

Diarrhea; blood in stool; increased stool frequency (more bowel movements than normal); bowel urgency (sudden and immediate need to have a bowel movement); bowel urgency related accidents (cannot make it to the bathroom in time); bowel movement accidents that occur without your control or any warning; fecal seepage/unnoticed leakage of stool resulting in stained undergarments/sheets; needing to have a bowel movement shortly after eating; waking up at night due to bowel movement; waking up at night due to pain; loud stomach gurgling/rumbling; fistula-related symptoms around the anus/rectum (eg, recurrent drainage or pain around the anus); abdominal pain before bowel movement; persistent abdominal pain; stricture-related pain (pain related to scarring of the bowel); bloating; passing of mucus; constipation; passing of wind/gas (flatulence); fear of passing wind due to concerns as to whether will also pass a stool, mucous, and/or blood; feeling of constantly needing to have a bowel movement despite an empty bowel; *fatigue/tiredness*; joint pain; joint swelling; back pain; vomiting/nausea; loss of appetite; weight loss; night sweats; fever; no symptoms.

- *In the past 6 months my disease has been:*
  - Constantly active, giving me symptoms every day.
  - Often active, giving me symptoms most days.
  - Sometimes active, giving me symptoms on some days (for instance 1-2 days per week).
  - Occasionally active, giving me symptoms 1-2 days per month.
  - Rarely active, giving me symptoms on a few days in the past 6 months.
  - I was well in the past 6 months, what I consider a remission or absence of symptoms.
- *Of the symptoms you have experienced in the last month, how would you rate the severity of fatigue on a scale of 1 to 7, where 1 indicates "not severe at all" and 7 indicates "worst imaginable severity."*
- *Among the symptoms you indicated you are currently experiencing; how often do you discuss fatigue with your HCP?*
  - Never
  - Infrequently
  - Frequently
  - Every appointment?
- *Among the symptoms you indicated you do not discuss at every appointment with your HCP, would you like to discuss fatigue more frequently with your HCP?*
  - Yes
  - No
- *In the last three months, have you declined participating in < A/B/C > due to fatigue?*
  (A) Work/School (for example, academic, professional work)
  (B)Social events (for example meeting with friends or family)
  (C) Sports/physical exercise
- *In the last 3 months, have you avoided or decreased sexual activity because of your CD/UC?*
  - Yes
  - No
- *If yes, for what reason[s] have you avoided sexual activity in the last three months?* Data for patients who selected "due to tiredness/fatigue due to my CD/UC" as the reason are presented.
- *How often did CD/UC-related fatigue occur in the past 3 months?*
  - Every day
  - More than once a week
  - Once a week
  - Every two/three weeks
  - Monthly
  - Less frequently than monthly
  - Never
- *Has your CD/UC-related fatigue meant that you have had to*
  - Stop working for the day sooner than planned
  - Work fewer hours
  - Finish education course prematurely
  - Take early retirement
  - Change job or career
  - Stop/delay education
  - Not consider or decline a new job offer/school
  - Working overtime to keep up with work/study
  - None of the above
- *FACIT-Fatigue questionnaire*

	Not at all	A little bit	Somewhat	Quite a bit	Very much
I feel fatigued	○	○	○	○	○
I feel weak all over	○	○	○	○	○
I feel listless ("washed out")	○	○	○	○	○

	Not at all	A little bit	Somewhat	Quite a bit	Very much
I feel tired	○	○	○	○	○
I have trouble starting things because I am tired	○	○	○	○	○
I have trouble finishing things because I am tired	○	○	○	○	○
I have energy	○	○	○	○	○
I am able to do my usual activities	○	○	○	○	○
I need to sleep during the day	○	○	○	○	○
I am too tired to eat	○	○	○	○	○
I need help doing my usual activities	○	○	○	○	○
I am frustrated by being too tired to do the things I want to do	○	○	○	○	○
I have to limit my social activity because I am tired	○	○	○	○	○

- *Overall, how does your CD/UC impact your*
  - Sleep
  - Energy levels (fatigue/tiredness related to your CD/UC)

HCP survey questions

All HCPs were asked:

- What is your primary specialty?
  - Gastroenterologist
  - IBD nurse specialist
  - Nurse practitioner
  - Internal medicine with GI focus
  - Physician assistant (US Only)
  - Other
- In a typical month, how many patients in total do you see and make prescribing decisions for with each of the following conditions?
- What percentage of these patients would you categorise as having moderate or severe disease?
- What percentage of your practice time is spent actively seeing patients as opposed to performing other activities such as academic/teaching duties?
- What is your biological sex?
  - Male
  - Female
  - Prefer not to say
- In what year did you qualify as a (primary speciality selected above)?
  - Before 1984
  - 1984–1996
  - 1997-2006
  - 2007-2017
  - After 2017
- *Below is a list of possible symptoms related to CD/UC* (see symptom list above on page 2). Please indicate:
  a) Which symptom[s] do you proactively discuss with your patients with moderate/severe CD/UC at a routine appointment?
  b) The top five symptoms you think have the greatest impact on your patients with moderate/severe CD/UC
  c) The top three symptoms most reported by your patients with moderate/severe CD/UC

Fatigue-related data for the above questions were presented.

- *HCPs who do not proactively discuss fatigue were asked: You stated that you do not routinely discuss fatigue. Why is that?*
  - Insufficient time
  - Not comfortable leading this discussion
  - Patients seem uncomfortable having this discussion
  - Not a priority symptom
  - Expect the patient to bring this up if this is an issue
  - Expect the patient to discuss with a different HCP
  - Not relevant because I don't have treatment available to treat the symptom
  - Other reason
- When present, what impact do you think fatigue has on the quality of life of patients with moderate/severe CD/UC? (on a scale of 1 to 7, where 1 indicates "no impact" and 7 indicates "greatest possible impact")
- What impact do you believe moderate/severe CD/UC has on each of the following aspects of a patient's quality of life?
  - Sleep
  - Energy levels (fatigue/tiredness related to patients' CD/UC)

REFERENCES

1. Uhlir V, Stallmach A, Grunert PC. Fatigue in patients with inflammatory bowel disease-strongly influenced by depression and not identifiable through laboratory testing: a cross-sectional survey study. *BMC Gastroenterol.* 2023;23(1):288. doi:10.1186/s12876-023-02906-0
2. Farrell D, McCarthy G, Savage E. Self-reported symptom burden in individuals with inflammatory bowel disease. *J Crohns Colitis.* 2016;10(3):315-322. doi:10.1093/ecco-jcc/jjv218
3. Grimstad T, Norheim KB, Isaksen K, et al. Fatigue in newly diagnosed inflammatory bowel disease. *J Crohns Colitis.* 2015;9(9):725-730. doi:10.1093/ecco-jcc/jjv091
4. Regueiro M, Hunter T, Lukanova R, et al. Burden of fatigue among patients with ulcerative colitis and Crohn's disease: results from a global survey of patients and gastroenterologists. *Adv Ther.* 2023;40(2):474-488. doi:10.1007/s12325-022-02364-2
5. D'Silva A, Fox DE, Nasser Y, et al. Prevalence and risk factors for fatigue in adults with inflammatory bowel disease: a systematic review with meta-analysis. *Clin Gastroenterol Hepatol.* 2022;20(5):995-1009.e7. doi:10.1016/j.cgh.2021.06.034
6. Casati J, Toner BB, de Rooy EC, Drossman DA, Maunder RG. Concerns of patients with inflammatory bowel disease: a review of emerging themes. *Dig Dis Sci.* 2000;45(1):26-31. doi:10.1023/a:1005492806777
7. van Langenberg DR, Gibson PR. Systematic review: fatigue in inflammatory bowel disease. *Aliment Pharmacol Ther.* 2010;32(2):131-143. doi:10.1111/j.1365-2036.2010.04347.x
8. Aluzaite K, Al-Mandhari R, Osborne H, et al. Detailed multidimensional assessment of fatigue in inflammatory bowel disease. *Inflamm Intest Dis* 2019;3(4):192-201. doi:10.1159/000496054
9. Nocerino A, Nguyen A, Agrawal M, Mone A, Lakhani K, Swaminath A. Fatigue in inflammatory bowel diseases: etiologies and management. *Adv Ther.* 2020;37(1):97-112. doi:10.1007/s12325-019-01151-w

10. Lee HH, Gweon T, Kang S, et al. Assessment of fatigue and associated factors in patients with inflammatory bowel disease: a questionnaire-based study. *J Clin Med* 2023;12(9):3116. doi:10.3390/jcm12093116
11. Czuber-Dochan W, Ream E, Norton C. Review article: description and management of fatigue in inflammatory bowel disease. *Aliment Pharmacol Ther.* 2013;37(5):505-516. doi:10.1111/apt.12205
12. Czuber-Dochan W, Dibley LB, Terry H, Ream E, Norton C. The experience of fatigue in people with inflammatory bowel disease: an exploratory study. *J Adv Nurs.* 1999;69(9):1987. doi:10.1111/jan.12060
13. Czuber-Dochan W, Norton C, Bredin F, Darvell M, Nathan I, Terry H. Healthcare professionals' perceptions of fatigue experienced by people with IBD. *J Crohns Colitis.* 2014;8(8):835-844. doi:10.1016/j.crohns.2014.01.004
14. Lesage AC, Hagège H, Tucat G, Gendre JP. Results of a national survey on quality of life in inflammatory bowel diseases. *Clin Res Hepatol Gastroenterol.* 2011;35(2):117-124. doi:10.1016/j.gcb.2009.08.015
15. Hindryckx P, Laukens D, D'Amico F, Danese S. Unmet needs in IBD: the case of fatigue. *Clin Rev Allergy Immunol.* 2018;55(3):368-378. doi:10.1007/s12016-017-8641-4
16. Farrell D, Artom M, Czuber-Dochan W, Jelsness-Jørgensen LP, Norton C, Savage E. Interventions for fatigue in inflammatory bowel disease. *Cochrane Database Syst Rev.* 2020;4(4):CD012005. doi:10.1002/14651858.CD012005.pub2
17. Emerson C, Barhoun P, Olive L, et al. A systematic review of psychological treatments to manage fatigue in patients with inflammatory bowel disease. *J Psychosom Res.* 2021;147(Article 110524). doi:10.1016/j.jpsychores.2021.110524
18. Matos R, Lencastre L, Rocha V, et al. Quality of life in patients with inflammatory bowel disease: the role of positive psychological factors. *Health Psychol Behav Med.* 2021;9(1):989-1005. doi:10.1080/21642850.2021.2007098
19. Charabaty A, Schneider B, Zambrano JA, Keefer L. Living with inflammatory bowel disease: online surveys evaluating patient perspectives on treatment satisfaction and health-related quality of life. *Crohns Colitis 360.* 2022;4(3):otac035. doi:10.1093/crocol/otac035
20. Moradkhani A, Beckman LJ, Tabibian JH. Health-related quality of life in inflammatory bowel disease: psychosocial, clinical, socioeconomic, and demographic predictors. *J Crohns Colitis.* 2013;7(6):467-473. doi:10.1016/j.crohns.2012.07.012
21. Rubin DT, Sninsky C, Siegmund B, et al. International perspectives on management of inflammatory bowel disease: opinion differences and similarities between patients and physicians from the IBD GAPPS survey. *Inflamm Bowel Dis.* 1953;27(12):1942-1953. doi:10.1093/ibd/izab006
22. Bredero Q, ter Avest MM, Fleer J, Dijkstra G, Schroevers MJ. P693 Care needs and reasons for (not) seeking care among fatigued patients with inflammatory bowel disease: a qualitative study. *J Crohns Colitis.* 2024;18(1):i1313-i1313. doi:10.1093/ecco-jcc/jjad212.0823
23. Travis S, Potts Bleakman A, Dubinsky MC, et al. The communicating needs and features of IBD experiences (CONFIDE) study: US and European patient and health care professional perceptions of the experience and impact of symptoms of moderate-to-severe ulcerative colitis. *Inflamm Bowel Dis.* 2023;30(6):939-949. doi:10.1093/ibd/izad142
24. Schreiber S, Hunter Gibble T, Panaccione R, et al. Patient and health care professional perceptions of the experience and impact of symptoms of moderate-to-severe Crohn's disease in us and Europe: results from the cross-sectional CONFIDE Study. *Dig Dis Sci.* 2024;69(7):2333-2344. doi:10.1007/s10620-024-08434-5
25. Clara I, Lix LM, Walker JR, et al. The manitoba IBD index: evidence for a new and simple indicator of IBD activity. *Am J Gastroenterol.* 1763;104(7):1754-1763. doi:10.1038/ajg.2009.197
26. Yellen SB, Cella DF, Webster K, Blendowski C, Kaplan E. Measuring fatigue and other anemia-related symptoms with the functional assessment of cancer therapy (FACT) measurement system. *J Pain Symptom Manage.* 1997;13(2):63-74. doi:10.1016/s0885-3924(96)00274-6
27. Loftus EV, Ananthakrishnan AN, Lee W-J, et al. Content validity and psychometric evaluation of the functional assessment of chronic illness therapy–fatigue (FACIT–Fatigue) in patients with Crohn's disease and Ulcerative colitis. *PharmacoEcon Open.* 2023;7(5):823-840. doi:10.1007/s41669-023-00419-w
28. Eek D, Ivanescu C, Corredoira L, Meyers O, Cella D. Content validity and psychometric evaluation of the functional assessment of chronic illness therapy-fatigue scale in patients with chronic lymphocytic leukemia. *J Patient Rep Outcomes.* 2021;5(1):27. doi:10.1186/s41687-021-00294-1
29. Saraiva S, Cortez-Pinto J, Barosa R, et al. 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
30. Norton BA, Thomas R, Lomax KG, Dudley-Brown S. Patient perspectives on the impact of Crohn's disease: results from group interviews. *Patient Prefer Adherence.* 2012;6(-):509-520. doi:10.2147/PPA.S32690
31. Radford SJ, Moran GW, Czuber-Dochan W. The impact of Inflammatory Bowel Disease related fatigue on health-related quality of life: a qualitative semi-structured interview study. *J Res Nurs.* 2022;27(8):685-702. doi:10.1177/17449871211061048
32. Dhálaigh DN, Greaney AM, Farrell D. 'It's just part of the disease': a qualitative study exploring help-seeking behaviours for fatigue in inflammatory bowel disease. *Gastrointest Nurs* 2021;19(5):40-48. doi:10.12968/gasn.2021.19.5.40
33. Canakis A, Qazi T. Sleep and fatigue in IBD: an unrecognized but important extra-intestinal manifestation. *Curr Gastroenterol Rep.* 2020;22(2):8. doi:10.1007/s11894-020-0746-x
34. Artom M, Czuber-Dochan W, Sturt J, Norton C. Targets for health interventions for inflammatory bowel disease-fatigue. *J Crohns Colitis.* 2016;10(7):860-869. doi:10.1093/ecco-jcc/jjw029
35. Roseira J, Magro F, Fernandes S, et al. Sexual quality of life in inflammatory bowel disease: a multicenter, National-level study. *Inflamm Bowel Dis.* 2020;26(5):746-755. doi:10.1093/ibd/izz185
36. Pires F, Martins D, Ministro P. A survey on the impact of IBD in sexual health: Into intimacy. *Medicine (Baltimore).* 2279;101(52):e32279. doi:10.1097/md.0000000000032279
37. Marín L, Mañosa M, Garcia-Planella E, et al. Sexual function and patients' perceptions in inflammatory bowel disease: a case–control survey. *J Gastroenterol.* 2013;48(6):713-720. doi:10.1007/s00535-012-0700-2
38. Dibley L, Khoshaba B, Artom M, et al.; and members of the IBD-BOOST PPI team. Patient strategies for managing the vicious cycle of fatigue, pain and urgency in inflammatory bowel disease: impact, planning and support. *Dig Dis Sci.* 3342;66(10):3330-3342. doi:10.1007/s10620-020-06698-1
39. Seyedian SS, Nokhostin F, Malamir MD. A review of the diagnosis, prevention, and treatment methods of inflammatory bowel disease. *J Med Life.* 2019;12(2):113-122. doi:10.25122/jml-2018-0075
40. Bernabéu Juan P, Cabezos Sirvent P, Sempere Robles L, van-der Hofstadt Gomis A, Rodríguez Marín J, van-der Hofstadt Román CJ. Differences in the quality of life of patients recently diagnosed with Crohn's disease and ulcerative colitis. *Int J Environ Res Public Health.* 2023;20(16):6576. doi:10.3390/ijerph20166576
41. Keefer L, Bedell A, Norton C, Hart AL. How should pain, fatigue, and emotional wellness be incorporated into treatment goals for optimal management of inflammatory bowel disease? *Gastroenterology.* 1451;162(5):1439-1451. doi:10.1053/j.gastro.2021.08.060
42. Kreijne JE, Lie MR, Vogelaar L, van der Woude CJ. Practical guideline for fatigue management in inflammatory bowel disease. *J Crohns Colitis.* 2016;10(1):105-111. doi:10.1093/ecco-jcc/jjv168