Self-reported Disability in Patients with Inflammatory Bowel Disease Largely Determined by Disease Activity and Illness Perceptions

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Background: The inflammatory bowel disease (IBD) disability index has recently been introduced to measure patients' physical, psychological, familial, and social limitations associated with IBD. We assessed factors related to self-reported disability and the relationship between disability and direct health care costs.

Methods: A large cohort of patients with Crohn's disease (CD) and ulcerative colitis (UC) was prospectively followed for 2 years by 3 monthly web-based questionnaires. At 2 years, patients completed the IBD disability index, with lower score indicating more disability. Linear regression analysis was used to examine the impact of demographics, clinical characteristics, and illness perceptions on self-reported disability. Trends in direct health care costs across the disability severity groups minimal, mild, moderate, and severe, were tested.

Results: A total of 554 patients with CD and 424 patients with UC completed the IBD disability index (response rate, 45%). Both clinical characteristics and illness perceptions significantly contributed to self-reported disability (45%–47%, $P = 0.000$ and 8%–12%, $P = 0.000$, respectively). Patients with CD scored lower on the self-reported IBD disability index than patients with UC (0.255 versus 3.890, $P < 0.000$), indicating more disability in patients with CD. Factors independently associated with higher self-reported disability rates were increased disease activity, illness identity (higher number of symptoms attributed to IBD), and stronger emotional response. Disease duration and disease phenotype were not associated with self-reported disability. Direct health care costs increased with the worsening of self-reported disability ($P = 0.000$).

Conclusions: More disability was reported by patients with CD than by UC. Self-reported disability in IBD was mainly determined by clinical disease activity and illness perceptions but not by disease duration or disease phenotype.

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Key Words: IBD disability index, illness perceptions, determinants, health care costs

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The natural history of Crohn's disease (CD) and ulcerative colitis (UC) is characterized by periods of relapse and remission, potentially leading to intestinal damage, and surgery over time.[1,2] This may induce a wide spectrum of physical, psychological, familial, and social problems.[3,4] Both widely used symptom-assessment tools and quality of life (QOL) questionnaires cannot provide a reliable assessment of these problems.[5,6] Therefore, Peyrin-Biroulet et al recently developed the inflammatory bowel disease (IBD) disability index to objectively and comprehensively cover the range of functional limitations in IBD.[7] This tool is thought to be useful for clinical practice, disease modification trials, and health reporting in IBD.[7,8]

The IBD disability index is based on the WHO's International Classification of Functioning, Health, and Disability.[9] This classification describes the impact of illness on a patient as a dynamic interaction between illness, personal, and environmental factors. Functioning is subdivided into the activity and the participation component, including regulating defecation, interpersonal activities, and work. The health-related component consists of body structures, such as blood in stool and arthritis/arthralgia, and body functions, such as energy, sleep, and body image. Personal and environmental factors are recognized as mediating factors for the association between these 2 components.

Important mediating factors are the patient's illness perceptions. According to the Common Sense Model,[10] these illness perceptions or patient beliefs may attenuate the impact of clinical characteristics on clinical outcomes, including disability, QOL, and distress.[11–13]

In contrast to other chronic illnesses, such as rheumatoid arthritis,[14] data on disability in IBD are scarce. Most studies in IBD on this topic have a retrospective design,[15,16] are small, or are focused on work disability.[17,18] In a prospective validation study of 166 participants, the interview-based IBD disability index has been reported to be reliable, reproducible, sensitive for detecting disability, with a good correlation with the Crohn's Disease Activity Index, Mayo index, and Inflammatory Bowel Disease Questionnaire.[19]

This study aimed to assess: (1) the severity of self-reported disability and functional limitations, (2) determinants of self-reported disability, (3) the impact of self-reported disability on direct health care costs (DHC) and QOL in a nationwide cohort of patients with IBD.

METHODS

Patient Population and Study Design

The Costs Of Inflammatory bowel disease In the Netherlands ("COIN") cohort was established in 2010. This is an ongoing study of adult patients with CD and UC from 7 general and 8 university hospitals in the Netherlands who were identified between 2007 and 2010, using Diagnosis-Treatment-Combination codes. Patients completed 3 monthly web-based questionnaires including questions about demographics, clinical characteristics, and resource utilization. The cohort is described in more detail in a previous report.[20] The study was centrally approved by the Ethics Committee of the University Medical Center Utrecht, Utrecht.

The primary outcome of interest, self-reported disability (hereafter referred to as "disability"), was measured with the IBD disability index 24 months after study entry. Most information on demographic and clinical and behavioral determinants of disability was collected concurrently. Data concerning smoking, education, comorbid conditions, and disease localization were assessed at baseline. Of the 3015 patients who were included in the COIN study, 505 (17%) were lost to follow-up. Patients who were lost to follow-up were more likely to be female ($P = 0.021$), smoker ($P = 0.000$), and had a lower education level ($P = 0.000$) than those patients with IBD who were not lost to follow-up.

Determinants

Determinants of disability were based on previous studies on factors independently associated with work disability or a disabling disease course, encompassing stricturing or penetrating disease, requiring abdominal surgery or immunomodulators (see Table, Supplemental Digital Content 1, http://links.lww.com/IBD/A674).

Demographic determinants included gender, age, smoking status (current smoker, exsmoker, nonsmoker), and education level (low versus high). Low education included no education, primary education, secondary education, and technical or professional school, whereas high education included higher vocational education and university.

Clinical determinants included comorbid conditions (self-reported depression, joint complaints, chronic back pain), age at diagnosis, disease duration, localization at enrollment for CD (ileal, colonic, ileocolonic), penetrating disease course for CD (defined as perianal fistula or other fistula), previous IBD-related surgery, stoma, pouch, and medical treatment at enrollment (mesalazine, corticosteroids, immunomodulators, anti-TNF agents). Previous IBD-related surgery compromised intestinal resections and perianal operations.

Behavioral determinants included illness perceptions, which were assessed with the Brief Illness Perception Questionnaire.[21] This 9-item questionnaire explores the cognitive and emotional representations of illness across 8 dimensions: Consequences, Timeline, Personal Control, Treatment Control, Identity, Concerns, Understanding, and Emotional Response. Items are assessed on an 11-point Likert scale; e.g., "How much does your illness affect your life?": 0 ["not at all"]–10 ["severely affects my life"].

IBD Disability Index

The IBD disability index consists of 28 questions, exploring limitations across 5 International Classification of Functioning, Health, and Disability domains: Overall Health, Body Functions (sleep/energy, affect, body image, pain, diarrhea, body mass index, weight loss), Activities and Participation (regulating defecation, looking after one's health, interpersonal activities, and work/education), Body Structures (blood in stool, arthralgia/arthritis), and Environmental Factors (exacerbating effect of medication, food, family, and health care professional).[7]

A validated scoring system was used to measure the presence and severity of disability in the previous week with lower or negative scores indicating greater disability (see Data, Supplemental Digital Content 2, http://links.lww.com/IBD/A675).[19] The total score on the IBD disability index ranges between −80 (maximum degree of disability) and 22 (no disability). The severity of disability was categorized into minimal (>−10), mild (−10 to −19), moderate (−20 to −35), and severe (≤−35).[19] The majority of questions are scored by patients on a 5-point Likert scale ("no," "mild," "moderate," "severe or extreme limitations"), whereas other questions included a dichotomous answer ("yes" or "no").

DHC and QOL

DHC included costs related to outpatient hospital visits, diagnostic procedures medication use, stoma appliance use, IBD-related hospitalizations, and IBD-related surgeries. DHC were calculated by multiplying self-reported units of resource utilization by their unit costs.[22]

QOL was measured by the validated Dutch translation of the Inflammatory Bowel Disease Questionnaire-32, encompassing 32 items, with a graded response range of "worst" (1) to "best" (7) and a possible total score of 32 to 224.[6,23]

Statistical Analysis

Data analyses were performed using SPSS 20.0 and SAS 9.2. Descriptive statistics were used to characterize patients with CD and UC. Means and medians were reported with a SD and interquartile range, respectively. Comparisons between CD and UC were analyzed with Student's *t* test for continuous variables and $\chi 2$ or Fisher's exact test for dichotomous variables. The IBD disability index was translated into the self-reported IBD disability index by 4 authors (B.O., H.H.F., A.A.K., M.H.), following the forward-backward-forward technique. Two randomly selected groups of 10 outpatients with IBD filled out the self-reported IBD disability index, followed 1 week later by an interview-based IBD disability index (group 1) or vice versa (group 2). The reproducibility of the IBD disability index was assessed with the reliability coefficient by Bland and Altman.[24] Correlation analyses were performed to assess associations between demographic, clinical and behavioral determinants, and the IBD disability score (see Table, Supplemental Digital Content 3, http://links.lww.com/IBD/A678). Variables that reached at least a borderline statistical significance ($P < 0.10$) in the correlation analyses were included in the hierarchical linear regression analysis, which is based on the Common Sense Model.[10] Tests for trends in DHC across the categories minimal, mild, moderate, and severe disability were conducted by using the median value in each category as a continuous variable in the linear regression models.

RESULTS

Patient Population

In total, 1108 patients with IBD (response rate: 45%) were enrolled, including 554 patients with CD (50%), 424 patients with UC (38%), and 130 patients with "IBD-unknown/unclassified" (12%) (Fig. 1). Patients with "IBD-unknown/unclassified" were excluded from further analyses.

Table, Supplemental Digital Content 4, http://links.lww.com/IBD/A676 shows data on baseline demographic and clinical characteristics in both the responders (CD: n = 554 and UC: n = 424) and nonresponders (CD: n = 726 and UC: n = 479). There were no relevant statistical significant differences between both groups.

Patients with CD were more likely to be female (58% versus 45%, $P = 0.000$), smoker (20% versus 7%, $P = 0.000$), had a lower age at diagnosis (30.7 versus 36.0 yr, $P = 0.000$), a higher probability of having a stoma (14% versus 5%), and a lower probability of having a pouch (2% versus 9%, $P = 0.000$) as compared with patients with UC. Patients with CD were more frequently treated with immunomodulators (31% versus 21%, $P = 0.000$) and/or anti-TNF agents (21% versus 4%, $P = 0.000$) as compared with patients with UC.

Self-reported IBD Disability Index: Internal Consistency, Reproducibility

The internal consistency/reproducibility (Cronbach's α) for the 5-point Likert questions was 0.872. The total scores showed a good reproducibility between the patient-reported and interview-based IBD disability index, with a 95% probability that the total score on the second IBD disability index fell within the Bland and Altman coefficient of repeatability. Reproducibility was comparable for group 1 and group 2.

Severity of Disability and Functional Limitations

Patients with CD scored significantly lower on the self-reported IBD disability index as compared with patients with UC

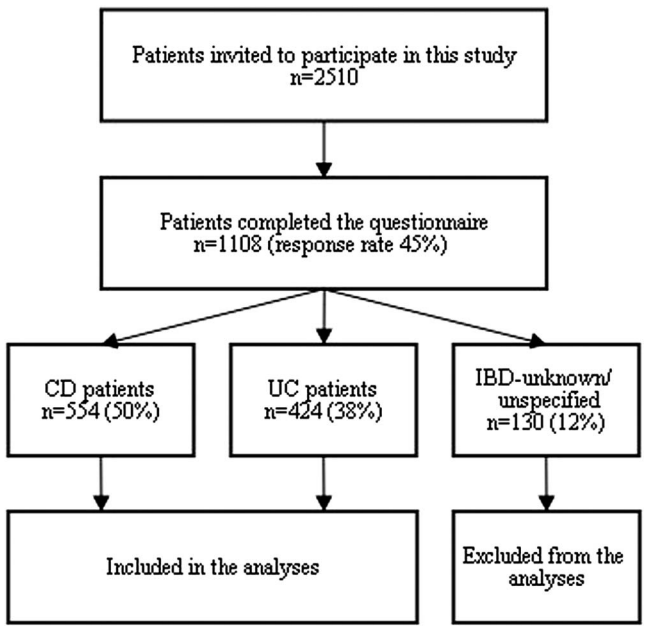


FIGURE 1. Study flow-chart.

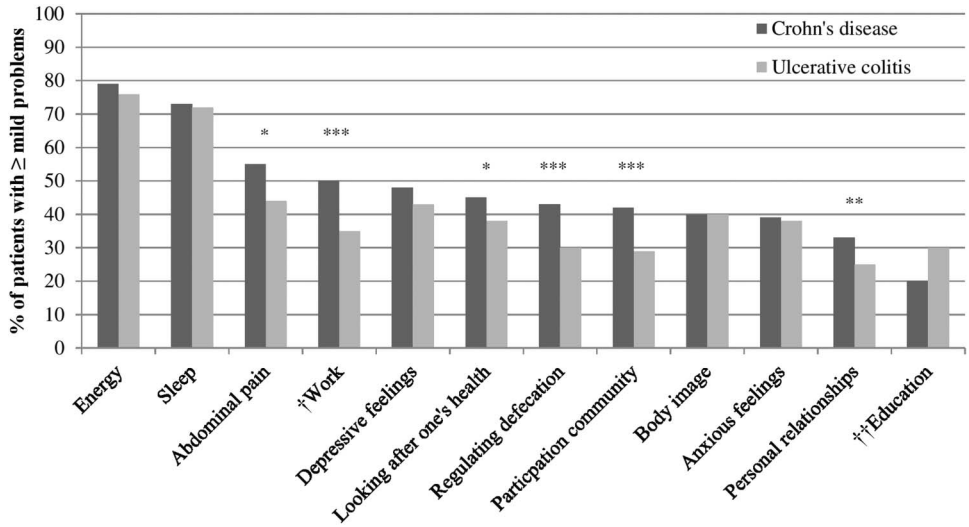
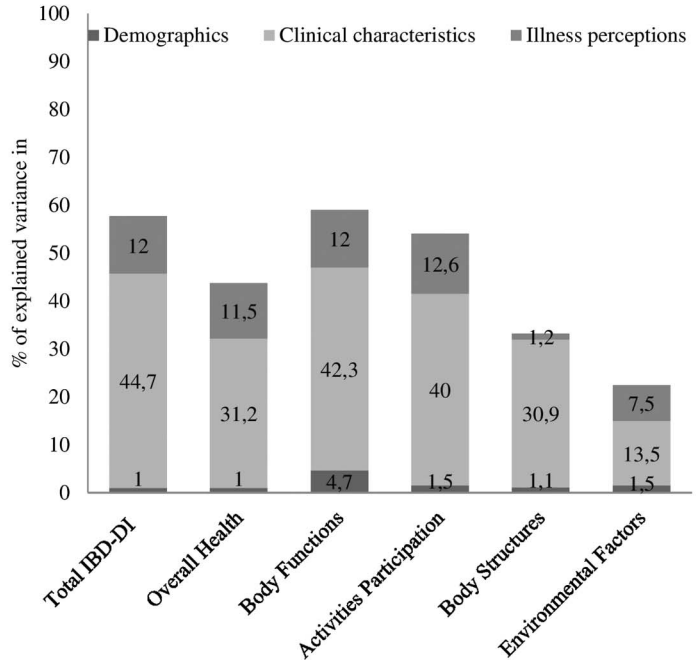


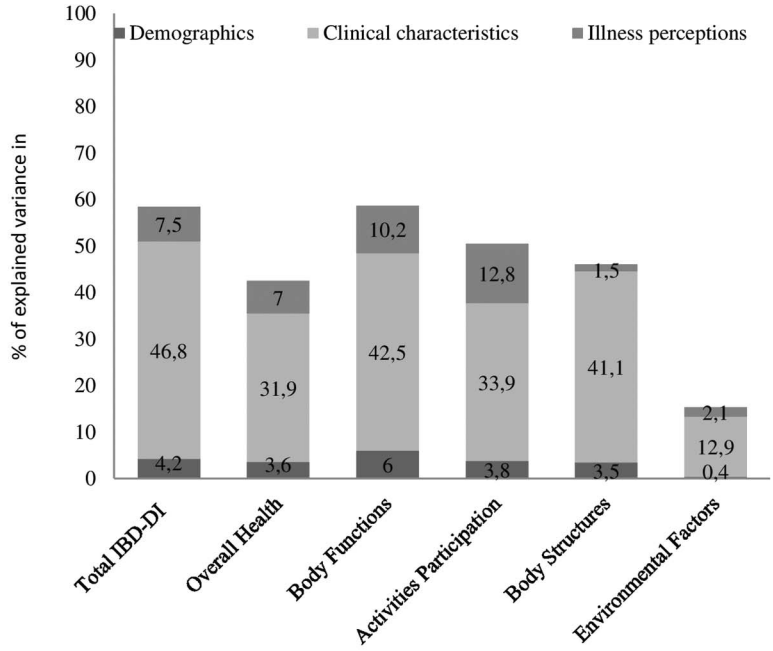
FIGURE 2. Functional limitations in patients with CD (n = 554) and UC (n = 424). †Patients with CD (333) and UC (274) were used or partially disabled. ††Patients with CD (20) and UC (10) were student. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

(0.255 versus 3.890, $P < 0.000$), indicating a greater disability in CD. Problems that were most frequently reported by both CD and UC patients were related to sleep and abdominal pain (Fig. 2). Patients with CD reported significantly more problems related to abdominal pain (55% versus 44%, $P = 0.022$), regulating defecation (43% versus 30%, $P = 0.027$), looking after one's health (45% versus 38%, $P = 0.000$), participation in the community (42% versus 29%, $P = 0.000$), personal relationships (33% versus 25%, $P = 0.005$), and work (50% versus 35%, $P = 0.000$) as compared with patients with UC.



IBD-DI = self-reported IBD disability index. Demographics contributed to a significant proportion of the variance in total IBD-DI ($p<0.05$) and domain sub-scores ($p<0.000$), except for Overall Health ($p=0.061$). Clinical characteristics and illness perceptions contributed to a significant proportion of the variance in IBD-DI and domain sub-scores ($p<0.000$).

FIGURE 3. Percentages of variance in self-reported disability total and domain subscores by demographic (step 1), clinical (step 2), and behavioral variables (step 3) in patients with CD (n = 554).



IBD-DI = self-reported IBD disability index. Demographics contributed to a significant proportion of the variance in total IBD-DI (p<0.000) and domain sub-scores (p<0.000), except for Environmental Factors (p=0.472). Clinical characteristics and illness perceptions contributed to a significant proportion of the variance in IBD-DI and domain sub-scores (p<0.000).

FIGURE 4. Percentages of variance in self-reported disability and domain subscores by demographic (step 1), clinical (step 2), and behavioral variables (step 3) in patients with UC (n = 424).

Determinants of Disability

Multiple hierarchical regression analyses were performed to assess the contributory role of demographic (step 1), clinical (step 2), and behavioral (e.g., illness perceptions) determinants (step 3) in determining the IBD disability index total and its domain subscores. In patients with CD, demographic, clinical, and behavioral determinants contributed towards a significant proportion of explained variance in total IBD disability score, namely 1.0% ($P < 0.05$), 44.7% ($P < 0.001$), and 12.0% ($P < 0.001$), respectively (Fig. 3). Factors that were independently associated with greater disability included clinical disease activity ($\beta = -5.696$; 95% CI, -8.763 to -2.629), previous CD-related surgery ($\beta = 2.279$; 95% CI, 0.647–3.912), self-reported depression ($\beta = -5.696$; 95% CI, -8.763 to -2.629), and the illness perceptions Personal Control ($\beta = 0.354$; 95% CI, 0.047–0.661), identity ($\beta -0.940$; 95% CI, -1.464 to -0.416), and Emotional response ($\beta = -0.522$; 95% CI, -0.949 to -0.094) (Table 2). In patients with UC, demographic, clinical, and behavioral determinants contributed towards a significant proportion of explained variance in total IBD disability score, namely 4.2% ($P < 0.001$), 46.8% ($P < 0.001$), and 7.5% ($P < 0.001$), respectively (Fig. 4). Factors that were independently associated with greater disability included clinical disease activity ($\beta = -2.891$; 95% CI, -3.385 to -2.396) and the illness perceptions Identity ($\beta = -0.643$; 95% CI, -1.218 to -0.067), and Emotional response ($\beta = -0.497$; 95% CI, -0.926 to -0.068) (Table 2).

Relationship Between Mean DHC, QOL, and Self-reported IBD Disability Severity

Of the total 1108 patients with IBD, minimal, mild, moderate, and severe disability were present in 901 (81.3%), 129 (11.6%), 70 (6.3%) and 8 (0.7%) patients, respectively (see Fig., Supplemental Digital Content 5, http://links.lww.com/IBD/A677). A statistically significant increasing linear trend ($P = 0.000$) in DHC as disability increased was demonstrated. In addition, a statistically significant decreasing linear trend ($P = 0.000$) in mean QOL scores as disability increased was demonstrated.

DISCUSSION

In this Dutch nationwide cohort, we observed that disability was mainly determined by clinical disease activity and illness perceptions. Typical characteristics of a complicated disease course, including disease duration, penetrating disease, ileal involvement, or surgery, were not associated with disability. Additionally, we found that greater disability was associated with higher DHC and a lower QOL.

TABLE 1. Demographic and Clinical Characteristics of the Study Population

	CD (n = 554)	UC (n = 424)	*P*
Demographic characteristics			
Male gender (%)	232 (42)	234 (55)	0.000
Age (±SD), yr	55.0 (13.4)	56.4 (12.6)	0.100
Current smoker (%)	108 (20)	28 (7)	0.000
Low education (%)	345 (62)	232 (55)	0.114
Clinical characteristics			
Comorbid conditions (%)			
Depression	46 (8)	31 (7)	0.789
Joint complaints	160 (28)	91 (21)	0.030
Chronic back pain	59 (11)	37 (9)	0.316
Age at diagnosis (±SD), yr	30.7 (12.7)	36.0 (13.5)	0.000
Disease duration, median (IQR)	19.5 (10.5–31.5)	16.5 (9.5–24.2)	0.000
Disease localization (%)			
Large bowel	165 (30)		
Small bowel	119 (22)		
Both large and small bowel	255 (46)		
Unknown	15 (3)		
Penetrating disease course (%)	283 (51)		
Previous IBD-related surgery	313 (57)	74 (18)	0.000
Stoma (%)	76 (14)	21 (5)	0.000
Pouch (%)	13 (2)	40 (9)	0.000
Medication use (%)			
Mesalazine	131 (24)	281 (66)	0.000
Steroids	47 (9)	27 (6)	0.225
Immunosuppressant	170 (31)	87 (21)	0.000
Anti-TNFα agents	115 (21)	15 (4)	0.000

To our knowledge, this is the largest study to date, assessing functional disability in patients with IBD with the recently introduced IBD disability index. This index has previously demonstrated to be reliable, reproducible, and sensitive for detecting disability.[19] It has also shown to have a good correlation with existing symptom-assessment tools and with the Inflammatory Bowel Disease Questionnaire. However, as the IBD disability index needs to be completed by a physician, implementation into clinical practice is challenging. Therefore, we studied the agreement between the patient-reported and interview-based IBD disability index and found a good reproducibility (repeatability coefficient ≥0.95) between these 2 indices.

It seems plausible that a complicated disease course in IBD—characterized by strictures, fistulas, and surgeries—leads to intestinal dysfunction, surgery, and a progressive deterioration of the functional status.[25] Yet, in line with previous studies,[15,26] we found that disability was mainly determined by clinical disease activity and illness perceptions but not by characteristics of a complicated disease course.

In a small pilot study of 38 patients with IBD, it has been found that perceived disability (as measured with the Perceived Disability Scale) was moderately to strongly associated with bowel health, systemic health, more abdominal pain, less engagement in daily activities, higher perceived stress, and a higher number of gastroenterologist visits.[15] Perceived disability was not significantly associated with disease duration, hospitalizations, and history of surgeries. In a recent study among 244 patients with long-term IBD from the population-based Manitoba Cohort study, it has been found that disability (as measured with World Health Organization Disability Assessment Schedule) was associated with long-term clinical disease activity and a history of major depression but not with disease duration, previous IBD surgeries, or disease phenotype.[26]

In addition, we found that disability was strongly associated with several illness perceptions. Illness perceptions accounted for 1% to 13% of the explained variance in disability, in addition to demographic (1%–5%) and clinical characteristics (13%–47%). This finding is in line with the results of a previous study that showed that illness perceptions accounted for 23% of the explained variance in disability (as measured with the Functional Limitations Profile), in addition to demographic variables (23%) and coping (6%).[16] Our findings corroborate the Common Sense Model, in which it is stated that individual's personal beliefs about IBD play a major role in the adjustment to the illness.[10,27]

In both CD and UC patients, illness identity was strongly and independently associated with disability. This indicates that patients with IBD who associate a wide range of symptoms to their illness experience a greater disability. It has been postulated that patients misattribute unrelated symptoms to IBD, leading to a perception of greater disease activity and subsequently to disability.[10] Our findings are in line with previous studies in IBD and other immune-mediated inflammatory diseases demonstrating illness identity to be strongly associated with increased disability (IBD[16]; RA[11,28] and psoriasis[12,28]), reduced QOL (IBD[29,30]; RA[28] and psoriasis[12]), and psychological distress (RA[31]). Emotional response was also strongly and independently associated with disability in patients with CD and UC. The latter finding concurs with previous studies in patients with IBD[15,29,30] and indicates that negative beliefs about the effects of illness on the patient's emotional status (in terms of anxiety and depression) result in the perception of a greater disability.

Personal control was strongly and independently associated with disability in patients with CD but not in UC. This suggests that patients with CD with less personal controllability of their illness experience a greater disability. The fact that personal controllability was not statistically significantly associated with disability in UC might be explained by the fact that patients with CD were more likely to have a stoma. Patients with a stoma can be expected to have specific problems and concerns, such as leakage, and inability to control gas, which may compromise their

TABLE 2. Independent Determinants of Self-reported Disability in Patients with CD (n = 554) and UC (n = 424)

	CD			UC		
	β	95% CI	*P*	β	95% CI	*P*
Demographics						
Gender	0.938	−0.669 to 2.545	0.252	−0.399	−2.000 to 1.202	0.625
Current smoker	0.688	−1.314 to 2.690	0.500	−3.019	−6.101 to 0.064	0.055
Clinical determinants						
Age at diagnosis	−0.006	−0.071 to 0.058	0.847			
Clinical disease activity	−5.696	−8.763 to −2.629	0.000	−2.891	−3.385 to −2.396	0.000
Previous CD-related surgery	2.279	0.647 to 3.912	0.006			
Pouch	1.887	−3.492 to 7.265	0.491			
Depression	−5.696	−8.763 to −2.629	0.000	−0.440	−3.505 to 2.624	0.778
Back pain				0.206	−2.473 to 2.885	0.880
Arthralgia	−0.622	−2.481 to 1.237	0.511	−0.895	−2.883 to 1.093	0.377
Steroids				−0.142	−3.343 to 3.059	0.930
Anti-TNF agents	0.015	−1.822 to 1.851	0.987	0.139	−4.291 to 4.570	0.951
Illness perceptions						
Consequences	−0.401	−0.862 to 0.06	0.088	−0.399	−0.894 to 0.097	0.114
Personal control	0.354	0.047 to 0.661	0.024	0.155	−0.135 to 0.444	0.294
Treatment control	0.171	−0.135 to 0.477	0.273	0.274	−0.046 to 0.594	0.094
Identity	−0.940	−1.464 to −0.416	0.000	−0.643	−1.218 to −0.067	0.029
Concerns	−0.420	−0.855 to 0.016	0.059	−0.160	−0.623 to 0.302	0.496
Understanding	0.0450	−0.300 to 0.389	0.799	−0.004	−0.337 to 0.329	0.981
Emotional response	−0.522	−0.949 to −0.094	0.017	−0.497	−0.926 to −0.068	0.023

control over the illness.[32] It may also be possible that the impact of personal control on disability in UC is canceled out by other factors, including the relapse rate. In our cohort, the relapse rate during 2 years of follow-up was significantly higher in patients with UC compared with CD (data not shown).

Finally, we have demonstrated that mean DHC increased and mean QOL scores decreased significantly with increasing of disability in patients with IBD. These findings strongly suggest that preventing disability in IBD may be a useful strategy to reduce future direct and indirect health care costs and burden to society.

This study has several strengths. First, the self-reported IBD disability index showed a good reliability and agreement with the interview-based disability index. Therefore, the self-reported IBD disability index can be used in web-based questionnaires, which may facilitate clinical research. Second, the large sample size enabled us to assess a large panel of potential determinants of disability. Third, patients were included from both university and general hospitals, thereby in our view, reliably representing the average patient with IBD in the Netherlands.

Several limitations of this study need to be addressed as well. First, an inherent limitation to the web-based design of this study is sampling bias. Although one might assume that disabled patients are more willing to fill out the questionnaires, we did not observe statistically significant differences between responders and nonresponders regarding relevant demographics, disease characteristics, and DHC. Second, self-reported data on comorbid conditions (e.g., depression) may be inaccurate. Third, potential determinants of functional disability, including endoscopic and laboratory markers of disease activity (CRP, fecal calprotectin), were not available. Fourth, as we performed a cross-sectional analysis, correlations between demographic, clinical, and behavioral variables and disability do not imply causality. For example, the inverse correlation that was found between anti-TNF treatment and disability may be caused by confounding by indication. Fifth, although we assessed the agreement between the patient-reported and interview-based IBD disability index, additional studies are required to determine the construct validity, discriminant ability, test–retest reliability, and responsiveness of the patient-reported IBD disability index.

Our findings underscore the importance of addressing and understanding patients' symptoms and perceptions of IBD. This relevant information allows clinicians to guide counseling and tailoring medical and biopsychosocial interventions to a patient's specific needs, potentially resulting in less disability, lower health care costs and a higher QOL. Previous studies have already shown that behavioral interventions based on the Common Sense Model of self-regulation can change illness perceptions of patients after myocardial infarction and patients with end-stage renal disease and thereby improve major components of QOL (i.e., return to work).[33,34]

In conclusion, our results clearly show that disability in IBD is associated with clinical disease activity and illness perceptions but not with a longer disease duration or an unfavorable disease phenotype. Greater disability is associated with higher costs and lower QOL. Because illness perceptions are potentially modifiable factors, they may provide a relevant target for interventions aimed at improving disability and other health outcomes. Future studies should focus on the additional value of the IBD disability compared with current symptom-assessment tools.

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