

External Validity and Consistency over Time of Patient Segmentation Based on Disease Acceptance and Perceived Control in Inflammatory Bowel Disease

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ABSTRACT

Background & Aims: The patient segmentation model based on disease acceptance and perceived control may guide personalized care in inflammatory bowel disease (IBD). We aimed to investigate the external validity of the segmentation model and its consistency over time.

Methods: This is a multicenter longitudinal cohort study of adult IBD patients with questionnaires on disease acceptance and perceived control (6-items, 7-point Likert scale) and health-related quality of life (HRQoL) (Short IBD questionnaire, range 10-70). Segments were created based on mean scores (cut-off>5): (I) high acceptance, high control; (II) high acceptance, low control; (III) low acceptance, high control and; (IV) low acceptance, low control.

Results: The external validation cohort included 921 IBD patients. The acceptance and control scale were unidimensional and internally consistent. Segments differed significantly in gender, disease duration, IBD medication and clinical disease activity. High acceptance and/or high control were significantly associated with a higher HRQoL compared with low acceptance and low control (i.e., segment IV) (Beta (95%CI) segment I=11.7 (10.4-13.1), segment II=9.3 (7.7-10.9) and segment III=3.8 (1.6-6.0), $p \leq 0.001$). The follow-up cohort included 783 patients: 58% remained in the same segment while 42% differed in segment over time. Changes in segment were positively correlated with changes in HRQoL over time (Spearman rho 0.38, $p < 0.001$).

Conclusions: The patient segmentation model based on disease acceptance and perceived control was externally valid and showed consistency over time. The different segments were independently associated with HRQoL. Future interventions should aim to personalize care based on segments and improve disease acceptance and perceived control of IBD patients.

Key words: quality of life – subjective health – personalized care – Crohn's disease – ulcerative colitis.

Abbreviations: CD: Crohn's disease; CI: confidence interval; HBI: Harvey Bradshaw index; HRQoL: health-related quality of life; IBD: inflammatory bowel disease; IBD-U: inflammatory bowel disease unclassified; IQR: interquartile range; OR: odds ratio; SCCAI: simple clinical colitis activity index; SIBDQ: short inflammatory bowel disease questionnaire; UC: ulcerative colitis.

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INTRODUCTION

Crohn's disease (CD) and ulcerative colitis (UC) are chronic inflammatory bowel diseases (IBD) with a relapsing and remitting nature that often require long-term IBD medication and frequent monitoring of disease activity [1, 2]. Besides gastrointestinal symptoms, patients frequently experience symptoms of fatigue, anxiety, and depression [3, 4].

All in all, the disease has a major impact on health-related quality of life (HRQoL) of IBD patients [5]. The prevalence and healthcare expenditures of IBD are increasing [6, 7]. Therefore, personalized care strategies complementary to medical treatment – such as remote monitoring and psychosocial care – are needed to improve patient outcomes and confine healthcare costs.

In current IBD practice, care pathways are mostly based on disease- and treatment-related factors such as disease activity and IBD medication. But HRQoL, a core outcome of value-based care, is not solely determined by these factors [8, 9]. Clinical disease activity only explains a minority of the variance in HRQoL [10]. Psychological factors such as anxiety, depression, stress, and certain illness perceptions are other

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important determinants [11–14]. Aligning care strategies to psychological factors might help improve HRQoL.

Bloem [15] and Stalpers [16] developed a cross-disease segmentation model to guide actions and initiatives towards patients based on disease acceptance and perceived control. The model stratifies patients in four segments based on high or low scores on these determinants [17]. The segment provides direction to the kind of care and guidance that best fits the individuals' needs, complementary to medical treatment. For example, patients with high disease acceptance and perceived control might well self-manage their disease supported by e-health modalities for information and remote monitoring of disease [17]. On the other hand, patients with low disease acceptance and low perceived control might need intensified personal guidance, education and/or psychosocial counselling. This may help to increase their feeling that the health condition is acceptable, and their belief that the health condition can be influenced or controlled by themselves or others [17].

Recently, we first investigated the segmentation model in patients with IBD. This study suggested that the model is valid and distinguishes segments that differ in patient characteristics and outcomes [18]. Most importantly, high disease acceptance and high perceived control were independently associated with a better HRQoL. However, the study was performed in a single center limiting the generalizability of this association. Furthermore, it was a cross-sectional evaluation of the model. Therefore, it is unclear what happens to patients' level of disease acceptance and perceived control over time. Personalization of care based on the model may only be justified and implementable if segmentation is consistent. Thus, external validation and a longitudinal evaluation of the model is needed to support its use in IBD care.

This study has two primary objectives. First, to evaluate the external validity of the patient segmentation model and its association with HRQoL in a broader setting of three large IBD centers. Second, to assess the consistency of the segmentation model in course of time.

METHODS

Clinical Cohort

A longitudinal multicenter cohort study was performed in adult IBD patients monitored at three secondary care centers in the Netherlands including Jeroen Bosch Hospital, Medical Spectrum Twente and Rijnstate Hospital. The three study centers have a comparable care structure with IBD-dedicated gastroenterologists and nurses working in a multidisciplinary team including surgeons, dieticians, and medical psychologists. IBD patients were eligible for inclusion if they completed study questionnaires between September 2018 and May 2021. Two cohorts were created: 1) to evaluate the external validity of the model, and 2) to assess the segmentation model in course of time.

External Validation Cohort

The external validation cohort included patients that completed the segmentation questionnaire and the Short IBD Questionnaire (SIBDQ) at least once. Participants of the initial validation study at Rijnstate Hospital were excluded [18].

Follow-up Cohort

The follow-up cohort included patients that completed the segmentation questionnaire and the SIBDQ at least twice. The first segmentation questionnaire and SIBDQ were used as baseline assessment. Questionnaires completed after approximately one year ($\pm$ three months) were used as follow-up assessment.

Data Collection

Study questionnaires were part of patient-reported outcome measurements performed at study centers in the context of value-based healthcare programs. At Rijnstate Hospital, IBD patients were approached to complete study questionnaires once per year via e-mail using the web-based OnlinePROMs system. At Jeroen Bosch Hospital and Medical Spectrum Twente, patients were approached to complete questionnaires prior to their outpatient consultation using the IBDream registry [19]. Questionnaires could also be completed at own initiative or at request of the IBD nurse.

Clinical data was collected from the electronic medical records or using the IBDream registry data, including gender, age, smoking behavior, disease onset, the Montreal classification, current IBD medication, highest step-up in IBD medication, prior IBD-related bowel surgeries and IBD-related hospital admissions within one year prior to baseline. Clinical disease activity was assessed using the Harvey Bradshaw Index (HBI) for CD patients and the Simple Clinical Colitis Activity Index (SCCAI) for patients with UC or IBD-unclassified (IBD-U) [20, 21]. Clinical remission was defined as a HBI ≤ 4 or SCCAI ≤ 2 [22, 23]. Faecal calprotectin assessments were collected and a value $<250 \mu\text{g/g}$ was considered as biochemical remission [24]. Assessments of disease activity were only included if performed between 12 weeks before and 4 weeks after study questionnaires. A longer period before questionnaires was accepted as patients are instructed to contact their care provider if new symptoms occur. For the follow-up cohort, we also evaluated treatment with steroids, IBD-related hospital admission and surgery during follow-up. IBD medication at follow-up was compared with IBD medication at baseline to determine if a step-up occurred. A step-up in IBD medication was defined as the initiation of any IBD medication in addition to that used at baseline, switch to steroids or a next medication class (comparing no medication, mesalamines, immunomodulators and biologics) or switch to a different biologic or tofacitinib.

Measures

Subjective Health, Disease Acceptance and Perceived Control

Patients completed the segmentation questionnaire [15–17]. Subjective health, defined as an individual's experience of physical and mental functioning while living their life the way they want to, within the actual constraints and limitations of individual existence, was measured using a numerical, self-anchored, rating scale (0–10) illustrated as a ladder [15]. The lowest (=0) and highest (=10) step represent the patients' worst and best day in the past month. Patients are asked on which step they stand on the present day and on average in the past month. Disease acceptance is defined as the individual's

feeling that his health condition and the possible constraints on functioning resulting from it, are acceptable and fitting for him as a person [16]. Perceived control is defined as the individual's belief that his health condition can be influenced or controlled by himself or by others [16]. The level of disease acceptance and perceived control were assessed using three questions each (7-point Likert scale; 1=fully disagree, 7=fully agree). High disease acceptance and perceived control were defined by a mean score of more than 5 [25].

Health-related Quality of Life

HRQoL was measured using the SIBDQ [26, 27]. It consists of 10 items with a 7-point Likert scale resulting in a possible score range of 10–70. Higher scores imply better quality of life. At one of the three study centres (Rijnstate Hospital), HRQoL was measured with the 32-item IBD questionnaire. To allow combined analyses, the corresponding 10 items of the SIBDQ were selected and used in the present study.

Statistical Analysis

Validity Patient Segmentation Model

The validity of the patient segmentation model was evaluated using exploratory factor analysis, reliability testing (Cronbach's $\alpha > 0.7$ good internal consistency) and Spearman's correlation coefficients (ρ). We hypothesized that the subjective health, disease acceptance and perceived control were positively correlated with HRQoL (correlation coefficient > 0.4 , $p < 0.05$ were considered demonstrative of convergent validity).

Patients were stratified in four segments based on the mean disease acceptance and perceived control score (cut-off high scores > 5) (Fig. 1) [25]. Differences between segments were analyzed using one-way analysis of variance (ANOVA) for normally distributed variables, Kruskal-Wallis test for skewed data and Chi-square tests for categorical variables.

Multiple linear regression analysis was performed to assess if the different segments were independently associated with HRQoL. The following factors were included in the model: age, gender, smoking behavior, IBD subtype, disease duration, IBD medication, perianal disease, IBD-related bowel surgery, IBD-related hospital admission and clinical disease activity. Of these variables, clinical disease activity and smoking behavior

were missing in 18% and 5% of patients respectively. Possible selective missing was investigated by comparing patient characteristics and outcomes. We found no clinically relevant differences. Therefore, missing data were assumed to be missing at random. Clinical disease activity and smoking behavior were imputed using multiple imputation by chained equations with predictive mean matching. We performed 50 iterations per variable and created 10 datasets. The following variables were included in the imputation model: all aforementioned variables, fecal calprotectin assessments, SIBDQ scores, subjective health, disease acceptance and perceived control. Multiple regression analyses were performed for complete cases and for all cases including imputed data.

Patient Segmentation in Course of Time

For the follow-up cohort, the allocated segment of each patient at baseline was compared with the segment at follow-up. Differences in segments were summarized in the following four groups: 1) positive change (shift to a segment with higher acceptance and/or control, e.g., from segment III to II), 2) negative change (shift to a segment with lower acceptance and/or control), 3) patient segment I at both timepoints (with high acceptance and high control) and 4) patient segment II, III or IV at both timepoints (with low acceptance and/or low control).

The clinical outcomes and HRQoL of patients with positive, negative or no change in segment during follow-up were described and compared using Chi-square tests and Kruskal-Wallis tests. The relationship between differences in segment and the difference in SIBDQ scores between baseline and follow-up was evaluated using a scatterplot and Spearman's correlation coefficient (ρ).

Univariable logistic regression analysis was used to identify factors associated with positive, negative or no change in segment. The following factors were evaluated: age, gender, smoking behavior, IBD subtype, disease duration, perianal disease, IBD medication, IBD-related bowel surgery, IBD-related hospital admission and clinical disease activity. Factors with a p -value < 0.2 in the univariable analysis were included in the multivariable analysis. Clinical disease activity and smoking behavior were missing in 22% and 2% of patients respectively. In the multivariable model, only complete cases were included given the explorative character of the analysis.

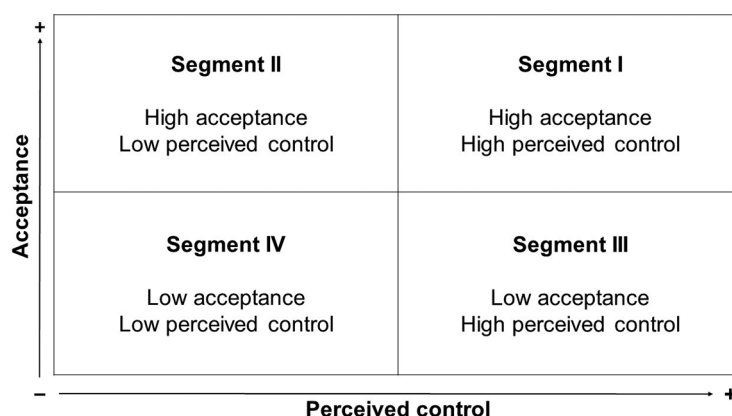


Fig. 1. The patient segmentation model based on disease acceptance and perceived control

Statistical analyses were performed using SPSS (version 25.0; IBM Corp, Armonk, NY, USA) and GraphPad Prism (version 8.0.2; GraphPad Software, San Diego, CA, USA).

Ethical Considerations

This is an observational study. The Radboud University Research Ethics Committee has confirmed that no ethical approval is required. All procedures performed were in accordance with the ethical standards of the 1964 Helsinki declaration and its later amendments.

RESULTS

External Validity Patient Segmentation Model

The external validation cohort included 921 IBD patients and was stratified in four segments (Fig. 2).

The disease acceptance and perceived control scale showed a unidimensional structure with 85% and 83% of the total variability explained by the first factor. Cronbach's α of the disease acceptance and perceived control scales were 0.92 and 0.90 respectively. Subjective health in the past month and on the present day, disease acceptance and perceived control were positively correlated with HRQoL (Spearman's rho 0.72, 0.67, 0.68 and 0.53 respectively, $p < 0.001$).

Of patients, 63% were diagnosed with CD, 38% used biologics and 81% were in clinical remission (Table I). The patients per segment differed significantly in gender, disease duration, current IBD medication, highest step-up in IBD medication and clinical disease activity. Also, HRQoL and subjective health differed significantly between segments. Patients in segment I – with high acceptance and high perceived control – scored highest with a median SIBDQ score of 62 (IQR 57–65) and a median score for subjective health on the present day and in the past month of 8 (IQR 7–9) and 8 (IQR 7–9) respectively.

Multiple regression analysis showed that high disease acceptance and/or high perceived control (i.e., segments I, II and III) were significantly associated with a higher HRQoL

compared with low acceptance and low control (i.e., segment IV) (Table II). The different segments were independently associated with HRQoL. Female gender, active smoking, steroid use and clinically active disease were negatively associated with HRQoL.

Patient Segmentation in Course of Time

The follow-up cohort included 783 IBD patients (Fig. 2). At baseline, 55% of patients were diagnosed with CD, 27% used biologics and 82% were in clinical remission (Table III). Patients were stratified in the four segments at baseline and after median 52 (IQR 51–53) weeks. The proportion of patients allocated to the different segments at baseline and at follow-up was comparable (Fig. 3).

In total, 58% remained in the same segment while 42% differed in segment over time (Fig. 3). In 23% of patients, disease acceptance and perceived control remained high (i.e., segment I). In 35% of patients, disease acceptance and/or perceived control remained low (i.e., segment II, III and IV). In 24% of patients, the level of disease acceptance or perceived control increased resulting in a positive change in segment. In 18% of patients, the level of disease acceptance or perceived control decreased resulting in a negative change in segment.

Clinical outcomes during follow-up are described in Supplementary Digital Content, Table I. The proportion of patients requiring a step-up in IBD medication and experiencing clinically active disease at baseline and at follow-up significantly differed between patient groups (Supplementary Digital Content, Table I). Patients with persistently low disease acceptance and/or low perceived control required a step-up in IBD medication most often (20%) and most frequently experienced clinically active disease at baseline (26%) and at follow-up (28%).

Health related quality of life differed between patients with a positive change, negative change and no change in patient segment (Fig. 4). The difference in HRQoL between patient groups was statistically significant at baseline, at follow-up and over time ($p < 0.001$).

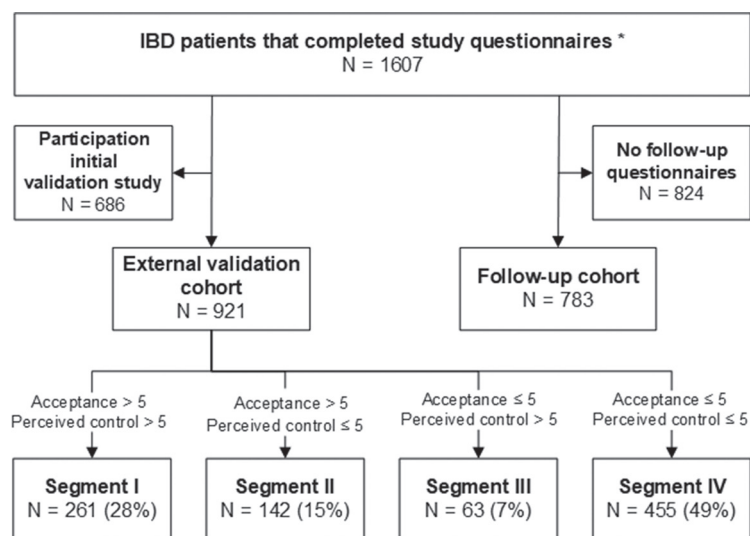


Fig. 2. Study inclusion and segmentation of external validation cohort. * The segmentation questionnaire and short inflammatory bowel disease questionnaire (SIBDQ) were collected during regular patient-reported outcome measurements.

Table I. Patient characteristics, a comparison between segment I, II, III and IV

	Total cohort N = 921	Segment I N = 261	Segment II N = 142	Segment III N = 63	Segment IV N = 455	p
Female gender	516 (56)	130 (50)	79 (56)	32 (51)	275 (60)	0.038
Age, years	45 ($\pm$ 15)	45 ($\pm$ 16)	45 ($\pm$ 16)	41 ($\pm$ 14)	44 ($\pm$ 15)	0.261
Current smoker*	148 (17)	38 (15)	19 (15)	13 (21)	78 (18)	0.628
IBD subtype						
Crohn's disease	583 (63)	159 (61)	95 (67)	41 (65)	288 (63)	0.761
Ulcerative colitis	315 (34)	94 (36)	46 (32)	20 (32)	155 (34)	
IBD-Unclassified	23 (3)	8 (3)	1 (1)	2 (3)	12 (3)	
Disease duration, years	9 [4 – 17]	11 [5 – 18]	11 [4 – 19]	6 [3 – 12]	9 [4 – 15]	0.001
Montreal classification UC						
E1 Ulcerative Proctitis	40 (13)	9 (10)	2 (4)	5 (25)	24 (15)	0.213
E2 Left-sided distal colitis	133 (42)	43 (46)	23 (50)	7 (35)	60 (39)	
E3 Extensive pancolitis	142 (45)	42 (45)	21 (46)	8 (40)	71 (46)	
Montreal classification CD, IBD-U*						
L1 Terminal ileum	189 (32)	43 (26)	29 (31)	16 (37)	101 (34)	0.470
L2 Colon	157 (26)	51 (31)	21 (22)	10 (23)	75 (25)	
L3 Ileocolon	253 (42)	72 (43)	44 (47)	17 (40)	120 (41)	
B1 Non-stricturing/penetrating	366 (60)	97 (58)	54 (56)	33 (77)	182 (61)	0.404
B2 Stricturing, non-penetrating	140 (23)	41 (25)	23 (24)	6 (14)	70 (23)	
B3 Stricturing, penetrating	100 (17)	29 (17)	19 (20)	4 (9)	48 (16)	
Perianal disease CD	88 (15)	23 (14)	19 (20)	3 (7)	43 (15)	0.287
Upper GI tract involvement CD	74 (13)	17 (11)	15 (16)	6 (15)	36 (13)	0.672
Current IBD medication						
No IBD medication	147 (16)	56 (22)	22 (16)	7 (11)	62 (14)	0.031
Mesalamines	256 (28)	87 (33)	36 (25)	19 (30)	114 (25)	0.098
Steroids	78 (8)	8 (3)	5 (4)	5 (8)	60 (13)	< 0.001
Immunomodulators	348 (38)	82 (31)	47 (33)	28 (44)	191 (42)	0.015
Biologics	350 (38)	92 (35)	56 (39)	17 (27)	185 (41)	0.134
Highest step-up IBD medication						
None, mesalamines or steroids	133 (14)	45 (17)	22 (16)	14 (22)	52 (11)	0.039
Immunomodulators	280 (31)	81 (31)	46 (32)	23 (37)	130 (29)	
Biologics	507 (55)	135 (52)	74 (52)	26 (41)	272 (60)	
IBD-related bowel surgery	164 (18)	44 (17)	28 (20)	5 (8)	87 (19)	0.155
Clinical disease activity†						
Remission (HBI $\leq$ 4, SCCAI $\leq$ 2)	614 (82)	192 (91)	106 (91)	45 (85)	271 (73)	< 0.001
Active (HBI > 4, SCCAI > 2)	127 (18)	20 (9)	10 (9)	8 (15)	101 (27)	
Faecal calprotectin‡						
< 250 μ g/g	520 (82)	131 (84)	78 (85)	34 (85)	277 (80)	0.485
$\geq$ 250 μ g/g	116 (18)	25 (16)	14 (15)	6 (15)	71 (20)	
IBD-related hospital admission	47 (5)	8 (3)	7 (5)	2 (3)	30 (7)	0.186
SIBDQ score (HRQoL)	55 [46 – 61]	62 [57 – 65]	59 [54 – 63]	53 [47 – 59]	47 [40 – 54]	< 0.001
Subjective health present day	7 [6 – 8]	8 [7 – 9]	8 [7 – 9]	7 [6 – 8]	6 [5 – 7]	< 0.001
Subjective health past month	7 [5 – 8]	8 [7 – 9]	8 [7 – 8]	7 [6 – 8]	6 [5 – 7]	< 0.001

Values expressed as number (percentage), mean ($\pm$ standard deviation) or median [interquartile range]. CD; Crohn's disease; GI; gastro-intestinal; HBI; Harvey Bradshaw Index; HRQoL: health-related quality of life; IBD: inflammatory bowel disease; IBD-U: IBD-unclassified; SCCAI: Simple Clinical Colitis Activity Index; SIBDQ: short IBD questionnaire; UC: ulcerative colitis. * Smoking behaviour reported for n = 876. † In 5 patients, disease was limited to the upper gastrointestinal tract and in 2 patients, disease limited to perianal disease (not categorized in L1/L2/L3). ‡ HBI and SCCAI reported for n = 753. Of patients without clinical disease activity data (n = 168), faecal calprotectin was available for 79 patients of which 67 (85%) were in biochemical remission (<250 μ g/g). § Faecal calprotectin reported for n = 636.

Table II. Multiple linear regression analysis of factors associated with health-related quality of life

Predictor variable *	Complete case analysis (N = 724)			Total cohort N = 921		
	B	95% CI	P-value	B	95% CI	p
Female gender [vs. male]	- 2.05	- 3.27; - 0.83	0.001	- 1.69	- 2.79; - 0.60	0.002
Smoking [vs. non-smoking]	- 2.40	- 4.03; - 0.77	0.004	- 2.09	- 3.67; - 0.62	0.005
Steroid use [vs. no steroid use]	- 2.56	- 4.71; - 0.42	0.019	- 2.88	- 4.89; - 0.87	0.005
Clinically active disease [vs. remission] *	- 8.61	- 10.20; - 7.01	< 0.001	- 8.47	- 10.19; - 6.76	< 0.001
Position in segmentation model [vs. segment IV]						
Segment I	11.00	9.55; 12.45	< 0.001	11.74	10.42; 13.06	< 0.001
Segment II	9.50	7.69; 11.31	< 0.001	9.28	7.70; 10.87	< 0.001
Segment III	3.36	0.99; 5.73	0.005	3.78	1.56; 6.00	0.001

R² model complete case = 45% and total cohort = 46%. B: regression coefficient; CI: confidence interval; IBD: inflammatory bowel disease. *The following factors were not significantly associated with health-related quality of life in both models: age, IBD subtype, disease duration, perianal disease, use of mesalamines, immunomodulators or biologics, prior IBD-related bowel surgery and IBD-related hospital admission one year prior to baseline. * Clinically active disease defined as a Harvey Bradshaw Index > 4 or a Simple Clinical Colitis Activity Index > 2.

Table III. Baseline patient characteristics of follow-up cohort

	N = 783
Female gender	435 (56)
Age, years	49 (±16)
Current smoker*	85 (11)
IBD subtype	
Crohn's disease	434 (55)
Ulcerative colitis	321 (41)
IBD-Unclassified	28 (4)
Disease duration, years	11 [4 – 19]
IBD medication at baseline	
No IBD medication	155 (20)
Mesalamines	285 (36)
Steroids	74 (10)
Immunomodulators	276 (35)
Biologics	210 (27)
Perianal disease CD	64 (15)
IBD-related bowel surgery	154 (20)
Clinical disease activity at baseline *	
Remission (HBI ≤ 4, SCCAI ≤ 2)	503 (82)
Active (HBI > 4, SCCAI > 2)	108 (18)
Faecal calprotectin at baseline †	
< 250 µg/g	397 (77)
≥ 250 µg/g	72 (23)

Values expressed as number (percentage), mean (± standard deviation) or median [interquartile range]. CD: Crohn's disease; HBI: Harvey Bradshaw Index; IBD: inflammatory bowel disease; SCCAI: simple clinical colitis activity index. *Smoking behaviour reported for n = 769. *Clinical disease activity reported for n = 611. Of patients without clinical disease activity data (n = 172), faecal calprotectin was available for 54 patients of which 51 (94%) were in biochemical remission (<250 µg/g). † Faecal calprotectin reported for n = 469.

In patients with a positive change in segment, HRQoL increased with median 3 (IQR 0–9) points. In patients with a negative change, HRQoL decreased with median 5 (IQR 0–11) points. Change in segment was positively correlated with

changes in HRQoL over time (Spearman rho 0.38, p < 0.001) (Supplementary Digital Content, Fig. 1).

Sociodemographic and clinical characteristics of patients were evaluated for associations with positive, negative and no change in segment (Supplementary Digital Content, Table II). Patients with a positive change in segment were less likely to have prior IBD-related bowel surgery compared with patients without a positive change in segment (OR=0.42; 95%CI: 0.23–0.77). Patients with a negative change in segment were less likely to have clinically active disease at baseline (OR=0.50; 95%CI: 0.26–0.97). In contrast, patients with persistently low disease acceptance and/or low perceived control were more likely to have prior IBD-related bowel surgery and clinically active disease at baseline (OR=1.87; 95%CI: 1.14–3.08 and OR=2.23; 95%CI: 1.43–3.48 respectively).

DISCUSSION

This multicenter study demonstrated that the patient segmentation model based on disease acceptance and perceived control is externally valid and shows consistency over time. The independent association between the different segments – with high or low disease acceptance and perceived control – and HRQoL was confirmed. After one-year follow-up, 58% of patients remained in the same segment while 42% of patients differed in segment over time. In one-third of patients, disease acceptance and perceived control scored persistently low and, in this group, HRQoL was lowest. A positive change in segment, resulting from increase in disease acceptance or perceived control, correlated with improvement of HRQoL.

The present study confirmed that the different segments are significantly associated with the HRQoL of IBD patients independent of clinical disease activity [18]. Disease acceptance was more strongly associated with HRQoL than perceived control. Compared with low acceptance and control (segment IV), high control (segment III), high acceptance (segment II) and high acceptance and control (segment I) were associated with a 4-, 9- and 12-point higher SIBDQ score. In comparison, active disease was associated with an 8.5-point lower SIBDQ score. Previous studies evaluated IBD patients' belief of control

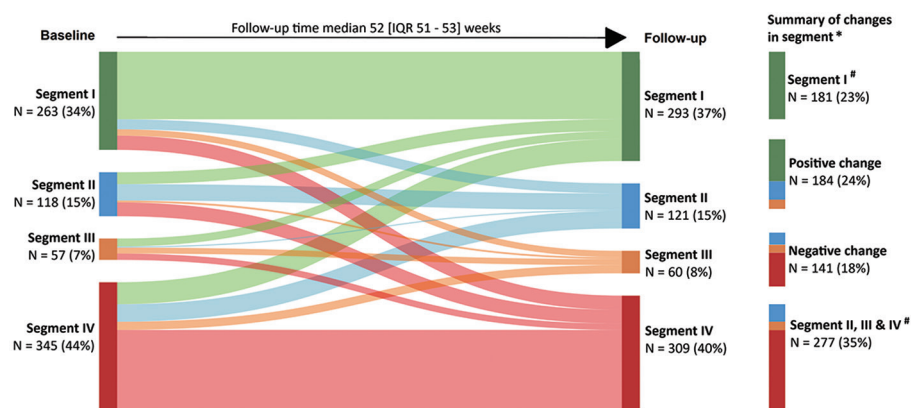


Fig. 3. A comparison between segmentation based on disease acceptance and perceived control at baseline and after one year follow-up. * Within subgroups, colours indicate segment at follow-up. # The same segment at baseline and follow-up.

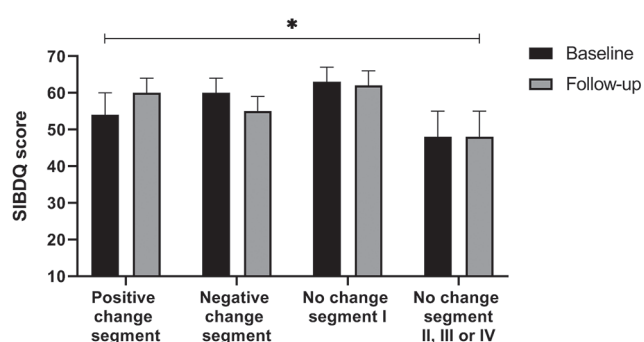


Fig. 4. A comparison of health-related quality of life (HRQoL) between patients with positive change, negative change or no change in segment. * The groups significantly differed in HRQoL at baseline, at follow-up and over time (i.e., the difference in HRQoL between baseline and follow-up), $p < 0.001$ using Kruskal-Wallis tests. SIBDQ: short inflammatory bowel disease questionnaire.

in the context of other illness perceptions, but most did not describe an association with HRQoL [12, 13, 28-31]. A possible explanation for this might be that illness perceptions focus on the disease itself and consider personal and treatment control as separate domains [16]. However, we evaluated the individual's belief that his overall health condition can be influenced or controlled in any way, by himself or by treatment. The association between disease acceptance and HRQoL has not been described previously as studies are limited and definitions of acceptance differ [32].

Our results demonstrated that the level of disease acceptance and perceived control of IBD patients can change over time. An improvement was observed in a quarter of patients and a decrease in about one-fifth of patients after one year. These changes seem only partially related to disease activity given the small decrease and increase in the proportion of patients with active disease during follow-up. In addition, only a quarter of patients with persistently low acceptance or control experienced clinically active disease. This finding is consistent with a prospective study reporting similar changes in IBD patients' sense of ability to influence the environment, and to achieve desired outcomes, despite differences in disease activity patterns over a 2-year period [33]. These findings raise

the question which other factors drive disease acceptance and perceived control in IBD patients.

Besides clinical disease activity, the established segments in this study differed in disease duration and IBD medication. This is in line with previous findings [18]. The lower disease duration in segments with low acceptance and control suggests a need for patient education and counselling at the early stage of the disease. When investigating changes in segment over time, we found prior IBD-related bowel surgery and clinically active disease were associated with a higher likelihood of persistently low acceptance or control. This may be related to failed attempts to achieve remission that can make a person feel worn down [34]. Besides that, literature suggests an association with psychological factors. Previous studies have shown a correlation between IBD patients' sense of control and symptoms of anxiety and depression [35, 36]. Moreover, differences exist between how individuals define an acceptable health condition as every person assesses their standard by comparing symptoms over time, in the context of their social environment [34]. Also, while some IBD patients may focus on the uncontrollability of the disease, others may focus more on aspects related to IBD they can control [37]. In future studies, the psychological profile of IBD patients in the different segments may be further investigated to help select appropriate care strategies for each segment.

In the majority of patients, the allocated segment was consistent over time. In almost a quarter of patients, disease acceptance and perceived control remained high after one year and their HRQoL scored consistently high. In the future, patients with high disease acceptance and perceived control might be efficiently and well supported by e-health modalities for information and remote monitoring of disease [38]. A larger group of patients scored low on disease acceptance or perceived control and, in one-third of all patients, scores remained low after one-year follow-up. This patient group may require a different approach involving more patient education or psychosocial counselling, for example provided by the IBD nurse or in a minority of cases by a medical psychologist. In order to provide such support within the possibilities of care facilities, available e-health modules or apps as well as services of patient associations may be used. The interventions should

aim to increase patients' level of disease acceptance and perceived control, thereby ultimately improving their HRQoL.

This study had several strengths including a large, multicenter patient cohort from non-academic teaching hospitals representative of the Dutch IBD population. In addition, the longitudinal study design allowed us to evaluate changes in disease acceptance and perceived control of IBD patients over time and to better understand their relationship with HRQoL. Moreover, the questionnaire that assesses disease acceptance and perceived control is brief and easy to use in clinical practice and these determinants of HRQoL provide direction to the kind of care individuals need. However, the study was limited by its observational character. Therefore, we cannot comment on the causality of the relationship. This needs to be further investigated in a prospective study. In addition, data on clinical disease activity close to study questionnaires was missing in 18 to 22% of patients despite the use of data from a prospective register and thorough searches in the electronic medical records. However, data was missing at random, and the different segments were associated with HRQoL in the total cohort and in complete case analysis.

CONCLUSIONS

The patient segmentation model based on disease acceptance and perceived control was externally valid and showed consistency over time. The different segments were independently associated with HRQoL. Future prospective studies are required to investigate whether personalized care strategies based on the level of disease acceptance and perceived control of IBD patients can improve HRQoL while confining health-care costs.

Conflicts of interest: The chair of professor S.B. at Nyenrode University is partially sponsored by Janssen Pharmaceuticals, Beerse, Belgium. T.R. has participated in advisory boards or as a speaker for Janssen, Takeda and Galapagos. L.v.E., P.T., M.G., M.R., and P.W. declare that they have no conflict of interest.

Authors' contribution: L.v.E., P.T., M.G., T.R. and P.W. contributed to the conception and design of the study. L.v.E. and P.T. performed the acquisition and analysis of data and all authors contributed to the interpretation of data. L.v.E. drafted the manuscript. All authors critically revised the manuscript, approved the final version to be published, and agree to be accountable for all aspects of the work.

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REFERENCES

1. Baumgart DC, Sandborn WJ. Crohn's disease. *Lancet* 2012;380:1590-605. doi:[10.1016/S0140-6736\(12\)60026-9](https://doi.org/10.1016/S0140-6736(12)60026-9)
2. Ordás I, Eckmann L, Talamini M, Baumgart DC, Sandborn WJ. Ulcerative colitis. *Lancet* 2012;380:1606-1619. doi:[10.1016/S0140-6736\(12\)60150-0](https://doi.org/10.1016/S0140-6736(12)60150-0)
3. Borren NZ, van der Woude CJ, Ananthakrishnan AN. Fatigue in IBD: epidemiology, pathophysiology and management. *Nat Rev Gastroenterol Hepatol* 2019;16:247-259. doi:[10.1038/s41575-018-0091-9](https://doi.org/10.1038/s41575-018-0091-9)
4. Barberio B, Zamani M, Black CJ, Savarino EV, Ford AC. Prevalence of symptoms of anxiety and depression in patients with inflammatory bowel disease: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2021;6:359-370. doi:[10.1016/S2468-1253\(21\)00014-5](https://doi.org/10.1016/S2468-1253(21)00014-5)
5. Knowles SR, Graff LA, Wilding H, Hewitt C, Keefer L, Mikocka-Walus A. Quality of Life in Inflammatory Bowel Disease: A Systematic Review and Meta-analyses—Part I. *Inflamm Bowel Dis* 2018;24:742-751. doi:[10.1093/ibd/izx100](https://doi.org/10.1093/ibd/izx100)
6. de Groof EJ, Rossen NG, van Rhijn BD, et al. Burden of disease and increasing prevalence of inflammatory bowel disease in a population-based cohort in the Netherlands. *Eur J Gastroenterol Hepatol* 2016;28:1065-1072. doi:[10.1097/MEG.0000000000000660](https://doi.org/10.1097/MEG.0000000000000660)
7. Pillai N, Dusheiko M, Maillard MH, et al; Swiss IBD Cohort Study Group. The Evolution of Health Care Utilisation and Costs for Inflammatory Bowel Disease Over Ten Years. *J Crohns Colitis* 2019;13:744-754. doi:[10.1093/ecco-jcc/jjz003](https://doi.org/10.1093/ecco-jcc/jjz003)
8. Kim AH, Roberts C, Feagan BG, et al. Developing a Standard Set of Patient-Centred Outcomes for Inflammatory Bowel Disease—an International, Cross-disciplinary Consensus. *J Crohns Colitis* 2018;12:408-418. doi:[10.1093/ecco-jcc/jjx161](https://doi.org/10.1093/ecco-jcc/jjx161)
9. Knowles SR, Keefer L, Wilding H, Hewitt C, Graff LA, Mikocka-Walus A. Quality of Life in Inflammatory Bowel Disease: A Systematic Review and Meta-analyses—Part II. *Inflamm Bowel Dis* 2018;24:966-976. doi:[10.1093/ibd/izy015](https://doi.org/10.1093/ibd/izy015)
10. van der Have M, van der Aalst KS, Kaptein AA, et al. Determinants of health-related quality of life in Crohn's disease: A systematic review and meta-analysis. *J Crohns Colitis* 2014;8:93-106. doi:[10.1016/j.crohns.2013.04.007](https://doi.org/10.1016/j.crohns.2013.04.007)
11. Stapersma L, van den Brink G, van der Ende J, et al. Illness Perceptions and Depression Are Associated with Health-Related Quality of Life in Youth with Inflammatory Bowel Disease. *Int J Behav Med* 2019;26:415-426. doi:[10.1007/s12529-019-09791-6](https://doi.org/10.1007/s12529-019-09791-6)
12. van der Have M, Brakenhoff LK, van Erp SJ, et al. Back/joint pain, illness perceptions and coping are important predictors of quality of life and work productivity in patients with inflammatory bowel disease: a 12-month longitudinal study. *J Crohns Colitis* 2015;9:276-283. doi:[10.1093/ecco-jcc/jju025](https://doi.org/10.1093/ecco-jcc/jju025)
13. Dorrian A, Dempster M, Adair P, et al. Adjustment to inflammatory bowel disease: the relative influence of illness perceptions and coping. *Inflamm Bowel Dis* 2009;15:47-55. doi:[10.1002/ibd.20583](https://doi.org/10.1002/ibd.20583)
14. Sainsbury A, Heatley RV. Review article: psychosocial factors in the quality of life of patients with inflammatory bowel disease. *Aliment Pharmacol Ther* 2005;21:499-508. doi:[10.1111/j.1365-2036.2005.02380.x](https://doi.org/10.1111/j.1365-2036.2005.02380.x)
15. Bloem S. Experience as a medicine: The development of a general subjective health instrument (in Dutch with English summary). Doctoral dissertation. Nyenrode Business University, 2008.
16. Stalpers J. Psychological Determinants of Subjective health. Doctoral dissertation. Nyenrode Business University. Nijenrode University Press Breukelen, 2009.
17. Bloem S, Stalpers J. Subjective Experienced Health As a Driver of Health Care Behavior. Nyenrode Research Paper Series; no. 12-01. doi:[10.2139/ssrn.2102513](https://doi.org/10.2139/ssrn.2102513)

18. van Erp LW, van Gerven J, Bloem S, Groenen MJM, Wahab PJ. Acceptance and perceived control are independently associated with quality of life in Inflammatory Bowel Disease: Introduction of a new segmentation model. *J Crohns Colitis* 2021;15: 1837–1845. doi:[10.1093/ecco-jcc/jjab082](https://doi.org/10.1093/ecco-jcc/jjab082)
19. de Jong ME, Smits LJT, van Ruijven B, et al. Increased discontinuation rates of anti-TNF therapy in elderly inflammatory bowel disease patients. *J Crohns Colitis* 2020;14:888–895. doi:[10.1093/ecco-jcc/jjaa012](https://doi.org/10.1093/ecco-jcc/jjaa012)
20. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. *Lancet* 1980;1:514. doi:[10.1016/S0140-6736\(80\)92767-1](https://doi.org/10.1016/S0140-6736(80)92767-1)
21. Walmsley RS, Ayres RC, Pounder RE, Allan RN. A simple clinical colitis activity index. *Gut* 1998;43:29–32. doi:[10.1136/gut.43.1.29](https://doi.org/10.1136/gut.43.1.29)
22. Best WR. Predicting the Crohn's disease activity index from the Harvey-Bradshaw Index. *Inflamm Bowel Dis* 2006;12:304–310. doi:[10.1097/01.MIB.0000215091.77492.2a](https://doi.org/10.1097/01.MIB.0000215091.77492.2a)
23. Turner D, Seow CH, Greenberg GR, Griffiths AM, Silverberg MS, Steinhart AH. A systematic prospective comparison of noninvasive disease activity indices in ulcerative colitis. *Clin Gastroenterol Hepatol* 2009;7:1081–1088. doi:[10.1016/j.cgh.2009.06.024](https://doi.org/10.1016/j.cgh.2009.06.024)
24. Reenaers C, Bossuyt P, Hindryckx P, Vanpoucke H, Cremer A, Baert F. Expert opinion for use of faecal calprotectin in diagnosis and monitoring of inflammatory bowel disease in daily clinical practice. *United European Gastroenterol J* 2018;6:1117–1125. doi:[10.1177/2050640618784046](https://doi.org/10.1177/2050640618784046)
25. Broekharst DSE, Bloem S, Groenland EAG, van Raaij WF, van Agthoven M. Differences between expert reported and patient reported burden of disease rankings. *Sci Rep* 2022;12:895. doi:[10.1038/s41598-021-04070-5](https://doi.org/10.1038/s41598-021-04070-5)
26. Guyatt G, Mitchell A, Irvine EJ, et al. A New Measure of Health Status for Clinical Trials in Inflammatory Bowel Disease. *Gastroenterology* 1989;96:804–810.
27. Irvine EJ, Zhou Q, Thompson AK. The Short Inflammatory Bowel Disease Questionnaire: a quality of life instrument for community physicians managing inflammatory bowel disease. CCRPT Investigators. Canadian Crohn's Relapse Prevention Trial. *Am J Gastroenterol* 1996;91:1571–1578.
28. Han SW, McColl E, Barton JR, James P, Steen IN, Welfare MR. Predictor's of quality of life in ulcerative colitis: The importance of symptoms and illness representations. *Inflamm. Bowel Dis* 2005;11:24–34. doi:[10.1097/00054725-200501000-00004](https://doi.org/10.1097/00054725-200501000-00004)
29. Van der Have M, Minderhoud IM, Kaptein AA, et al. Substantial impact of illness perceptions on quality of life in patients with Crohn's disease. *J Crohns Colitis* 2013;7:e292–e301. doi:[10.1016/j.crohns.2012.11.002](https://doi.org/10.1016/j.crohns.2012.11.002)
30. van Erp SJ, Brakenhoff LK, Vollmann M, et al. Illness Perceptions and Outcomes in Patients with Inflammatory Bowel Disease: Is Coping a Mediator? *Int J Behav Med* 2017;24:205–214. doi:[10.1007/s12529-016-9599-y](https://doi.org/10.1007/s12529-016-9599-y)
31. Rochelle TL, Fidler H. The importance of illness perceptions, quality of life and psychological status in patients with ulcerative colitis and Crohn's disease. *J Health Psychol* 2013;18:972–983. doi:[10.1177/1359105312459094](https://doi.org/10.1177/1359105312459094)
32. Hamama-Raz Y, Nativ S, Hamama L. Post-traumatic Growth in Inflammatory Bowel Disease Patients: The Role of Illness Cognitions and Physical Quality of Life. *J Crohns Colitis* 2021;15:1060–1067. doi:[10.1093/ecco-jcc/jjaa247](https://doi.org/10.1093/ecco-jcc/jjaa247)
33. Lix LM, Graff LA, Walker JR, et al. Longitudinal study of quality of life and psychological functioning for active, fluctuating, and inactive disease patterns in inflammatory bowel disease. *Inflamm Bowel Dis* 2008;14:1575–1584. doi:[10.1002/ibd.20511](https://doi.org/10.1002/ibd.20511)
34. Hall NJ, Rubin GP, Dougall A, Hungin AP, Neely J. The Fight for 'Health-related Normality': A Qualitative Study of the Experiences of Individuals Living with Established Inflammatory Bowel Disease (IBD). *J Health Psychol* 2005;10:443–455. doi:[10.1177/1359105305051433](https://doi.org/10.1177/1359105305051433)
35. Brooks AJ, Norman P, Peach EJ, et al. Prospective Study of Psychological Morbidity and Illness Perceptions in Young People with Inflammatory Bowel Disease. *J Crohns Colitis* 2019;13:1003–1011. doi:[10.1093/ecco-jcc/jjz028](https://doi.org/10.1093/ecco-jcc/jjz028)
36. Bennebroek Evertsz F, Sprangers MAG, de Vries LM, et al. I am a total failure: Associations between beliefs and anxiety and depression in patients with inflammatory bowel disease with poor mental quality of life. *Behav Cogn Psychother* 2020;48:91–102. doi:[10.1017/S1352465819000444](https://doi.org/10.1017/S1352465819000444)
37. Wolfe BJ, Sirois FM. Beyond standard quality of life measures: The subjective experiences of living with inflammatory bowel disease. *Qual Life Res* 2008;17:877–886. doi:[10.1007/s11136-008-9362-1](https://doi.org/10.1007/s11136-008-9362-1)
38. de Jong MJ, van der Meulen-de Jong AE, Romberg-Camps MJ, et al. Telemedicine for management of inflammatory bowel disease (myIBDcoach): a pragmatic, multicentre, randomised controlled trial. *Lancet* 2017;390:959–968. doi:[10.1016/S0140-6736\(17\)31327-2](https://doi.org/10.1016/S0140-6736(17)31327-2)