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Psychological adaptation and health-related quality of life in inflammatory bowel disease: a 5-year follow-up study

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Abstract

Inflammatory bowel disease (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), is a chronic immune-mediated gastrointestinal condition in which long-term care increasingly involves patient-reported health, emotional functioning, and psychological adaptation. Because psychological adaptation may not parallel clinical remission, this 5-year longitudinal study examined changes in psychopathological symptoms, alexithymia, coping strategies, and health-related quality of life (HR-QoL) in 73 outpatients receiving maintenance medical treatment. We expected no uniform mean-level improvement or deterioration and hypothesised that increases in depressive and anxiety symptoms, alexithymia, and avoidance coping would be associated with poorer HR-QoL outcomes and that increases in positive attitude coping would be associated with better outcomes. Participants were reassessed during clinical remission using validated measures, and psychological changes were analysed in relation to follow-up quality of life outcomes, adjusting for baseline levels and disease duration. Mean-level changes were limited across depressive symptoms, overall anxiety, alexithymia, most coping dimensions, and HR-QoL indices. Somatic anxiety increased over time (p=.03), whereas social support coping decreased consistently in the overall sample and within both diagnostic subgroups (p<.01). Increases in depressive symptoms were associated with poorer mental health and lower disease-specific HR-QoL (both p<.001), while increases in alexithymia were associated only with poorer disease-specific HR-QoL (p<.05). In the multivariate model, depressive change independently predicted follow-up physical health (p=.02), mental health (p<.001), and disease-specific HR-QoL (p<.001). These findings suggest that psychological vulnerability may remain clinically relevant even during remission and identify depressive symptoms as a key correlate of long-term patient-reported functioning. The results support the integration of psychological assessment and multidisciplinary care within routine gastroenterological follow-up and highlight the potential value of psychologically informed interventions aimed at preserving HR-QoL and long-term adaptation.

Key words: inflammatory bowel disease, health-related quality of life, psychopathology, depression, alexithymia, coping strategies, longitudinal study.

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Introduction

Inflammatory bowel disease (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), is a chronic, relapsing-remitting, immune-mediated disorder of the gastrointestinal tract associated with substantial long-term morbidity and progressive functional impairment (Podolsky, 2002; Yang *et al.*, 2026). UC is characterised by continuous mucosal inflammation extending proximally from the rectum and typically presents with bloody diarrhoea, bowel urgency, and tenesmus. By contrast, CD is characterised by discontinuous, transmural inflammation that may affect any segment of the gastrointestinal tract and commonly presents with abdominal pain and chronic diarrhoea; strictures, fistulas, abscesses, and perianal disease may occur in more complicated cases. Systemic symptoms, including fatigue and weight loss, may be present in both conditions. The clinical course is heterogeneous, ranging from prolonged periods of remission interrupted by occasional relapses to persistent or recurrent disease activity requiring treatment escalation, hospitalisation, or surgery (Chang, 2020). Over recent decades, the epidemiology of IBD has undergone a marked transition from a predominantly Western disease to a global health concern. Although incidence rates have stabilised in some high-income regions, the prevalence continues to increase due to earlier diagnosis and improved survival, and has now exceeded 0.5% in several countries, with projections approaching 1% of the general population in the future (Kaplan & Ng, 2017; Ng *et al.*, 2017). This epidemiological transition has

reinforced the need to examine the long-term psychological and patient-reported consequences of living with IBD, with particular attention to the emotional and regulatory processes that may shape psychological adaptation and perceived functioning over time.

From a pathophysiological perspective, IBD is currently conceptualised as the result of a dysregulated immune response to intestinal antigens in genetically susceptible individuals, shaped by environmental exposures, alterations in the gut microbiota, and impairment of epithelial barrier function (Chang, 2020; de Souza *et al.*, 2017; Khor *et al.*, 2011). The gut-brain axis model has extended this framework by emphasising reciprocal communication between the gastrointestinal tract and the central nervous system (Günther *et al.*, 2021; Konturek *et al.*, 2011; Schneider *et al.*, 2023). During mucosal immune activation, pro-inflammatory cytokines, including tumour necrosis factor alpha and interleukin-6, may exert effects beyond the intestinal compartment, influencing neuroendocrine and glial processes involved in stress sensitivity, visceral perception, and affective regulation. In parallel, dysbiosis may alter the availability of microbial-derived metabolites with immunoregulatory properties, particularly short-chain fatty acids, thereby influencing intestinal homeostasis and potentially contributing to gut-brain communication pathways. In IBD, these neuroimmune and microbial pathways provide a mechanistic basis for the observed associations between disease activity, stress reactivity, symptom perception, psychopathological morbidity, and broader processes of psychological adaptation (Gracie *et al.*, 2018; Gracie *et al.*, 2019; Peppas *et al.*, 2021).

Among the psychological outcomes linked to the gut-brain axis, internalising symptoms have received the greatest empirical attention. Systematic reviews have consistently indicated clinically relevant anxiety and depressive symptoms across the IBD course, including during remission (Mikocka-Walus *et al.*, 2016; Neuendorf *et al.*, 2016). Meta-analytic estimates indicate pooled prevalences of 32.1% for anxiety symptoms and 25.2% for depressive symptoms. Compared with inactive disease, active disease is associated with 2.5-fold higher odds of anxiety and 3.1-fold higher odds of depressive symptoms (Barberio *et al.*, 2021). Longitudinal meta-analyses further support temporal associations in both directions. An IBD diagnosis is associated with 48% and 55% higher subsequent risks of anxiety and depression, respectively (Bisgaard *et al.*, 2023); conversely, a history of depression is associated with subsequent CD and UC, with pooled relative risks of 1.17 and 1.21 (Piovani *et al.*, 2024). Among patients with established IBD, active disease is associated with relative risks of 2.24 for later anxiety and 1.49 for later depressive symptoms (Fairbrass *et al.*, 2022), while depression is associated with more frequent disease flares, a greater need for surgical intervention, and treatment escalation, with pooled estimates ranging from 1.37 to 1.38 (Ji *et al.*, 2024). Taken together, these findings support a bidirectional relationship in which disease activity may increase psychological vulnerability, while internalising symptoms may contribute to poorer clinical outcomes and long-term adaptation.

This perspective is directly relevant to patient-reported outcomes. In IBD, inflammatory markers, physician-rated disease activity, and remission status capture only part of the burden experienced by patients. Health-related quality of life (HR-QoL) refers to patients' appraisal of the extent to which illness and treatment affect physical functioning, emotional well-being, social participation, and overall adaptation to daily life with a chronic condition (Caputo *et al.*, 2022; Guyatt *et al.*, 1993; Testa & Simonson, 1996). Empirical work has linked poorer HR-QoL to active disease and relapse history, as well as to fatigue, pain, treatment burden, healthcare use, work impairment and psychological distress (Graff *et al.*, 2006; Knowles, Graff, *et al.*, 2018; Lix *et al.*, 2008; Olsen *et al.*, 2023). Thus, meta-analytic comparisons indicate markedly poorer HR-QoL during active than inactive disease, with pooled standardised mean differences of −1.29 for disease-specific and −1.19 for generic total measures. The effect was larger for mental than physical health (−1.34 *vs.* −0.71), although heterogeneity across studies was substantial (Knowles, Keefer, *et al.*, 2018). Longitudinal evidence further suggests that reductions in anxiety and depressive symptoms are accompanied by improvements in HR-QoL independently of clinical disease activity (Farbod *et al.*, 2021). This observation is particularly relevant in chronic conditions such as IBD, where subjective well-being may not necessarily parallel objective indicators of disease activity. Taken together, these findings have suggested that HR-QoL in IBD is shaped by both disease-related and psychological factors, supporting its relevance not only as a patient-reported outcome but also as a clinically meaningful indicator of long-term psychological adaptation to chronic illness.

Beyond general measures of psychological distress, increasing attention has been devoted to more specific dimensions of emotional and regulatory functioning. Alexithymia refers to difficulties in identifying and describing feelings, an externally oriented thinking style, and reduced differentiation between affective states and bodily sensations (Bagby *et al.*, 1994; Nemiah & Sifneos, 1970; Sifneos, 2000). Within psychosomatic and chronic illness research, these features have been linked to the recognition and interpretation of somatic signals, thereby shaping illness experience and symptom communication (Kano & Fukudo, 2013; Martino *et al.*, 2021; Merlo *et al.*, 2025; Silvestro *et al.*, 2023). These characteristics may be particularly relevant in chronic gastrointestinal disorders, where the interpretation of bodily sensations and illness-related signals plays a central role in everyday disease management. Evidence in IBD remains nuanced, as patients cannot be considered uniformly alexithymic, although higher levels of this trait have been associated with psychological distress, somatic preoccupation, and poorer patient-reported outcomes (Iglesias-Rey *et al.*, 2012; Martino, Caputo, *et al.*, 2020; Porcelli *et al.*, 1996; Viganò *et al.*, 2018). Alexithymia is therefore relevant not as a general descriptor of patients with IBD, but as a potential vulnerability factor within the broader process of psychological adaptation to chronic illness.

Coping offers a complementary perspective on the way patients manage illness-related demands. Within the transactional model of stress, coping denotes the cognitive and behavioural efforts used to deal with situations appraised as taxing or exceeding available resources (Lazarus & Folkman, 1984). In IBD, passive, avoidant, emotion-focused, and disengaged responses have been associated with higher psychological distress, poorer adjustment, and less favourable patient-reported outcomes, whereas active coping, acceptance, perceived control, self-efficacy, and support-seeking have generally been linked to more favourable outcomes (Chao *et al.*, 2019; Kantidakis *et al.*, 2021; McCombie *et al.*, 2015; van Erp *et al.*, 2021). The interpretation of this evidence is complicated by substantial heterogeneity in theoretical frameworks, assessment instruments, and outcome measures. Moreover, recent reviews indicate that most available studies remain cross-sectional, providing limited insight into how coping responses evolve and contribute to long-term psychological adaptation in IBD (McCombie *et al.*, 2013; Popa *et al.*, 2024). Understanding

whether coping strategies remain stable or change across the disease course may therefore provide important information about patients' adjustment to chronic illness beyond traditional clinical indicators.

Prospective studies have clarified selected aspects of psychological adjustment in IBD. These include the relationship between HR-QoL and disease activity, the clinical relevance of anxiety and depressive symptoms, the relative temporal stability of alexithymia, and the contribution of coping-related responses to functional outcomes (Farbod *et al.*, 2021; Lix *et al.*, 2008; Porcelli *et al.*, 1996; van der Have *et al.*, 2015). However, most longitudinal investigations have focused on isolated psychological constructs or specific outcomes, limiting a comprehensive understanding of how emotional distress, alexithymia, coping processes, and HR-QoL evolve together over time. Consequently, it remains unclear whether these psychological dimensions remain stable, improve, or deteriorate over time, and how their longitudinal trajectories relate to patient-reported outcomes. This limitation is particularly relevant in IBD, a lifelong condition in which psychological adaptation may evolve gradually and may not necessarily parallel objective indicators of disease activity or clinical remission. Examining intra-individual change may therefore provide a more informative perspective on long-term adaptation than cross-sectional comparisons alone.

To address this gap, the present study adopted a 5-year longitudinal design in a previously characterised cohort of patients with IBD (Martino *et al.*, 2023). Specifically, it aimed to: i) examine changes in psychopathological symptoms, alexithymia, coping strategies, and HR-QoL indices over time; ii) investigate whether longitudinal changes in psychological variables were associated with changes in HR-QoL; and iii) evaluate whether changes in psychological functioning accounted for variance in HR-QoL at follow-up after controlling for baseline HR-QoL levels. Accordingly, we expected no uniform improvement or deterioration in psychological functioning and HR-QoL over the 5-year interval, given the limited and heterogeneous longitudinal evidence reviewed above (H1). We further hypothesised that increases in depressive and anxiety symptoms, alexithymia, and avoidance coping would be associated with declines in HR-QoL and that increases in positive attitude coping would be associated with improvements in HR-QoL (H2). Finally, we expected changes in depressive symptoms, alexithymia, positive attitude coping, and avoidance coping to account for additional variance in HR-QoL at follow-up beyond that explained by baseline HR-QoL and disease duration (H3). Clarifying these longitudinal associations may contribute to a more comprehensive biopsychosocial understanding of psychological adaptation in IBD and support integrated models of care in which psychological assessment and clinically informed psychotherapeutic interventions are incorporated into long-term gastroenterological follow-up.

Materials and Methods

Study design and procedure

This study was conducted as a prospective longitudinal follow-up of a previously characterised cohort of patients with IBD (Martino *et al.*, 2023). The baseline assessment was carried out in 2020, and all participants were subsequently invited to take part in a follow-up evaluation conducted in 2025, corresponding to a 5-year interval between assessments. All participants received detailed information about the study procedures and provided renewed written informed consent before participation. The study was conducted in accordance with the Declaration of Helsinki and its later amendments (World Medical Association, 2013) and was approved by the Ethics Committee of the University, Hospital "G. Martino" of Messina (protocol no. 2533, January 30, 2020). Psychological assessments were conducted by an experienced clinical psychologist in a private setting and included a clinical interview and the administration of validated self-reported measures. Clinical and sociodemographic data were obtained through medical record review and structured patient interviews.

Participants

At baseline, 84 consecutive outpatients were recruited at the IBD Unit of the Department of Clinical and Experimental Medicine, University, Hospital "G. Martino", Messina, Italy . Inclusion and exclusion criteria were defined in the baseline study (Martino *et al.*, 2023) and were verified at follow-up to ensure consistency with the original study design. Briefly, eligible participants were adults aged 18 years or older with a confirmed diagnosis of CD or UC established at least 6 months before enrolment and receiving maintenance medical treatment. Clinical remission was required for inclusion at baseline and for reassessment at follow-up. At both assessment points, remission status was confirmed by the treating gastroenterologists during routine specialist visits, based on clinical evaluation and patients' medical records. Exclusion criteria included alcohol or substance abuse, known psychiatric disorders, current use of psychotropic medications, moderate to severe respiratory, renal, or hepatic failure, heart failure with New York Heart Association class ≥II, endocrine disorders, and active malignancy. Of the original cohort, 73 patients (86.9%) completed the follow-up assessment. Eleven participants did not participate: 10 were no longer attending the gastroenterology outpatient clinic, and one declined further participation. No additional participants were recruited. Among the 73 patients reassessed at follow-up, 30 had CD, and 43 had UC. All diagnoses were confirmed by gastroenterologists.

The statistical sensitivity of the available follow-up sample was evaluated using G*Power 3.1.9.7 (Faul *et al.*, 2009), assuming α=.05, 80% power, and two-tailed tests where applicable. The minimum detectable effects were a Cohen's d of 0.33 for paired-sample comparisons and an absolute correlation of .32. For comparisons between the CD and UC groups, the corresponding minimum detectable effects were Cohen's d=0.68 for continuous variables and Cohen's w=0.33-0.40 for categorical variables. For the univariate models following the multivariate test, the sample permitted the detection of an incremental effect of Cohen's f^2=0.17 for the four psychological change variables beyond the covariates included in the models.

Participant flow through the study is shown in Figure 1.

Instruments

The assessment battery was selected to ensure comparability with the baseline evaluation of the same cohort (Martino *et al.*, 2023). All scores were analysed as continuous variables.

Disease-specific HR-QoL was assessed using the Short Inflammatory Bowel Disease Questionnaire (SIBDQ) (Irvine *et al.*, 1996). For administration in Italian, the wording of the corresponding 10 items was drawn from the validated Italian version of the IBDQ (Ciccocioppo *et al.*, 2011). The Italian validation study

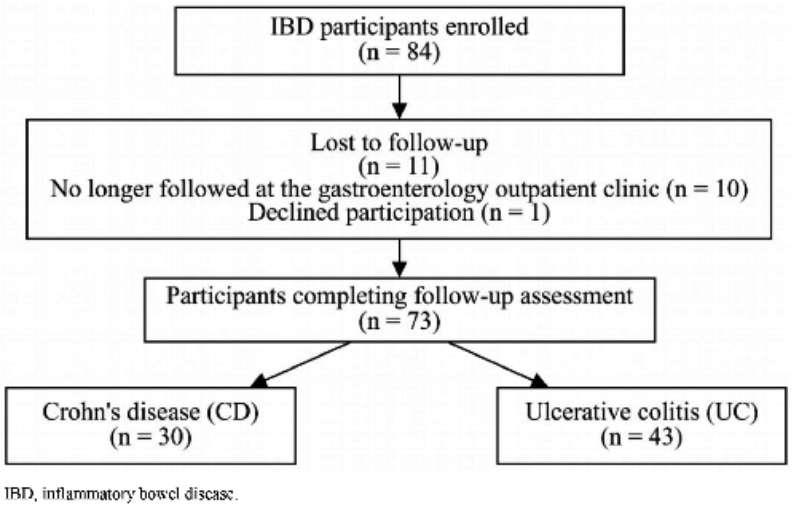

Figure 1. Study of patients with IBD, divided into CD and UC.

demonstrated excellent internal consistency, with Cronbach's α coefficients of 0.96 for the overall scale, 0.87 for the Bowel Symptoms factor, 0.91 for the Emotional Function factor, 0.84 for the Systemic Symptoms factor, and 0.90 for the Social Function factor, consistent with previous findings in the literature. Furthermore, the instrument demonstrated good test-retest reliability, with a Pearson's correlation coefficient (r) of 0.81. The questionnaire encompasses bowel and systemic symptoms together with emotional and social functioning. Responses are provided on a 7-point scale and summed into a total score ranging from 10 to 70, with higher values denoting better disease-specific HR-QoL.

General physical and mental health were evaluated using the 12-Item Short Form Health Survey (SF-12; Gandek *et al.*, 1998). The questionnaire consists of 12 items with response formats ranging from two to six categories and yields norm-based Physical (PCS-12) and Mental Component Summary (MCS-12) scores. Both scores are expressed on a 0-100 metric and centred at 50 with a standard deviation of 10 in the reference population; higher values represent better perceived health. The Italian validation study reported acceptable internal consistency, with Cronbach's α coefficients of 0.69 for the PCS-12 and 0.84 for the MCS-12 (Ruotolo *et al.*, 2021).

Depressive symptoms were assessed using the Beck Depression Inventory-II (BDI-II; Beck *et al.*, 1996; Sica & Ghisi, 2007). The questionnaire is composed of 21 items rated from 0 to 3 and summed into an overall score ranging from 0 to 63, with higher values indicating greater depressive symptom severity. Conventional ranges are 0-13 for minimal, 14-19 for mild, 20-28 for moderate, and 29-63 for severe symptoms. Only the total score was used in the present analyses. The Italian validation studies and supporting evidence (Maggi *et al.*, 2023; Montano & Flebus, 2006; Sica & Ghisi, 2007) demonstrated good psychometric properties for the BDI-II. Internal consistency, assessed using Cronbach's α, was 0.80, while one-month test-retest reliability was r=0.76. Furthermore, the instrument demonstrated good convergent validity with the Depression Questionnaire (r=0.77) and satisfactory divergent validity with the State-Trait Anxiety Inventory (r=0.66).

Anxiety symptoms were assessed using the Hamilton Anxiety Rating Scale (HAM-A; Hamilton, 1959), administered in Italian. The scale contains 14 items rated from 0 to 4 and summed into a total score ranging from 0 to 56, with higher values indicating greater anxiety severity. Two established component scores were also calculated from the same items (Maier *et al.*, 1988): psychic anxiety, reflecting cognitive-affective symptoms and comprising items 1-6 and 14, and somatic anxiety, reflecting physical and autonomic symptoms and comprising items 7-13. Each component ranges from 0 to 28, with higher values indicating greater severity in the corresponding domain. For clinical orientation, total scores of 0-7, 8-14, 15-23, and ≥24 have been proposed to indicate minimal, mild, moderate, and severe anxiety, respectively (Matza *et al.*, 2010). The HAM-A has demonstrated satisfactory internal consistency and concurrent validity in its original psychometric evaluation (Maier *et al.*, 1988).

Emotional functioning was evaluated with the Italian version of the Toronto Alexithymia Scale-20 (TAS-20; Bagby *et al.*, 1994; Italian validation provided by Bressi *et al.*, 1996). The questionnaire includes 20 items rated from 1 to 5 and provides an overall score and three-dimensional scores: difficulty identifying feelings (7 items; range 7-35), difficulty describing feelings (5 items; range 5-25), and externally oriented thinking (8 items; range 8-40). The total score ranges from 20 to 100, with higher scores indicating greater alexithymia; scores ≥61 conventionally indicate alexithymia. The original validation of the TAS-20 demonstrated good internal consistency, with a Cronbach's α coefficient of 0.81 for the overall scale and coefficients of 0.78, 0.75, and 0.66 for the Difficulty Identifying Feelings, Difficulty Describing Feelings, and Externally Oriented Thinking subscales, respectively. Similarly, the Italian validation confirmed satisfactory internal consistency, reporting Cronbach's α coefficients of 0.82 for the overall scale, 0.79 for the first factor, 0.68 for the second factor, and 0.54 for the third factor.

Coping strategies were assessed using the Coping Orientation to Problems Experienced New Italian Version-25 (Foà *et al.*, 2015). The questionnaire consists of 25 items rated from 1 to 6 and organised into five dimensions: positive attitude (6-36), social support (5-30), problem orientation (5-30), transcendent orientation or turning to religion (4-24), and avoidance (5-30). Higher scores indicate more frequent use of the corresponding coping strategy. The Italian validation study demonstrated good internal consistency across all subscales, with Cronbach's α coefficients of 0.80 for Social Support, 0.72 for Avoidance Strategies, 0.90 for Positive Attitude, 0.86 for Problem Solving, and 0.96 for Turning to Religion.

In the present sample, internal consistency was acceptable to good across the scores examined; the corresponding coefficients are reported in *Supplementary Table 1*.

Statistical analysis

Statistical analyses were conducted using JASP (version 0.97.0) and the Statistical Package for the Social Sciences (SPSS; version 25). Descriptive statistics were performed to characterise the sample. Continuous variables are reported as means and standard deviations, and categorical variables as frequencies and percentages. Between-group differences (CD *vs.* UC) were examined using independent samples *t*-tests for continuous variables and chi-square tests for categorical variables. Sex-related differences in psychological and HR-QoL outcomes at follow-up were examined using independent-samples *t*-tests. Mean-level longitudinal changes in psychological features, psychopathological symptoms, and HR-QoL indices were examined using paired-samples *t*-tests, both in the overall sample and within diagnostic subgroups. Cohen's *d* was calculated as an effect-size estimate for mean comparisons. To quantify longitudinal change, absolute change scores (Δ) were calculated as the difference between follow-up and baseline values (Δ=follow-up−baseline), thereby capturing within-individual variation over time. Pearson's correlation coefficients were used to assess associations between changes in psychological variables and HR-QoL indices. To examine whether changes in psychological functioning predicted HR-QoL outcomes at follow-up, a multivariate general linear model (GLM) was conducted, with follow-up HR-QoL indices (PCS, MCS, and SIBDQ) entered jointly as dependent variables. Baseline PCS, MCS, and SIBDQ scores were included as covariates to adjust for initial HR-QoL levels, thereby accounting for baseline individual differences and potential regression to the mean effects. Disease duration (years) was also included as a covariate. Changes in depressive symptoms, alexithymia, positive attitude coping, and avoidance coping were entered as predictors, based on their theoretical relevance to psychological adaptation in chronic illness. Following the multivariate test (Pillai's Trace), univariate linear models were examined to characterise the specific contribution of each predictor to individual HR-QoL outcomes. Explained variance (R^2) was reported for each univariate model.

Model assumptions were evaluated through inspection of residual plots, including assessment of linearity, homoscedasticity, and normality of residuals. Multicollinearity was examined using variance inflation factors (all <2), and influential observations were assessed using Cook's distance (all values <1). No formal correction for multiple testing was applied because each longitudinal analysis addressed a distinct, prespecified hypothesis rather than repeatedly testing the same hypothesis across multiple comparisons. Statistical significance was set at $p<.05$ (two-tailed).

Results

Sample characteristics

Demographic and clinical characteristics of the follow-up cohort are presented in Table 1. The follow-up sample comprised 73 patients, including 30 with CD and 43 with UC. The overall mean age was 46.1±15.9 years, and 53.4% of participants were male. No statistically significant differences between diagnostic groups were observed in sex distribution, body mass index, educational level, or employment status (all $p>.05$). However, patients with CD were significantly older than those with UC ($p=.01$) and had a longer disease duration ($p=.04$).

Psychological outcomes at follow-up and longitudinal changes

At the 5-year follow-up, no statistically significant differences were observed between patients with CD and UC in depressive symptoms, anxiety severity, alexithymia, coping strategies, or HR-QoL measures (all $p>.05$). Results are presented primarily for the overall cohort, while longitudinal analyses within each diagnostic subgroup are also reported.

Sex-related differences were observed at follow-up. Women reported higher levels of depressive symptoms than men (BDI-II: 14.3±7.1 *vs.* 9.1±6.3; $t(71)=3.35$, $p=.001$, $d=0.79$) and greater anxiety severity on the HAM-A total score (26.9±11.7 *vs.* 19.4±9.6; $t(71)=3.02$, $p=.003$, $d=0.71$). This difference was evident for both the psychic (13.4±5.2 *vs.* 9.5±4.7; $t(71)=3.38$, $p=.001$, $d=0.79$) and somatic (13.4±6.9 *vs.* 9.9±5.3; $t(71)=2.44$, $p=.017$, $d=0.57$) anxiety

Table 1. Main sociodemographic and clinical characteristics of participants with IBD.

Variables	IBD (n=73)	CD (n=30)	UC (n=43)	p
Age, years	46.1±15.9	51.6±15.8	42.2±14.9	.01
Gender, male (%)	39 (53.4)	19 (63.3)	20 (46.5)	.16
BMI, kg/m²	25.4±4.4	24.6±3.1	25.9±5.2	.22
Disease duration, years	16.2±9.6	18.9±10.6	14.4±8.4	.04
Education, n (%)				.19
Primary school	1 (1.4)	1 (3.3)	0 (0)	
Secondary school	13 (17.8)	8 (26.7)	5 (11.6)	
High school	38 (52.0)	13 (43.3)	25 (58.1)	
Bachelor's degree	20 (27.4)	7 (23.3)	13 (30.2)	
PhD or specialisation	1 (1.4)	1 (3.3)	0 (0)	
Employment status, n (%)				.16
Full time	42 (57.5)	18 (60.0)	24 (55.8)	
Unemployed	13 (17.8)	2 (6.7)	11 (25.6)	
Retired	13 (17.8)	7 (23.3)	6 (14.0)	
Other	5 (6.8)	3 (10.0)	2 (4.7)	

IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; BMI, body mass index. Continuous variables are presented as mean ± standard deviation; categorical variables as n (%). The "Other" employment status category included participants primarily engaged in household and family care.

dimensions. Women also reported poorer mental health, as reflected by lower SF-12 MCS scores (38.4±9.8 *vs.* 45.9±8.6; $t(71)=-3.48$, $p<.001$, $d=-0.82$). No additional sex differences emerged across the remaining measures (all $p>.05$). Complete descriptive statistics and between-sex comparisons are reported in *Supplementary Table 2*. Overall, this pattern was consistent with that observed at baseline (Martino *et al.*, 2023).

Longitudinal changes from baseline to follow-up are summarised in Table 2. Overall, psychological functioning and HR-QoL showed limited mean-level change across the 5-year observation period. Significant changes were limited to an increase in somatic anxiety ($t(72)=-2.22$, $p=.03$, $d=-0.26$) and a reduction in social support coping ($t(72)=5.78$, $p<.01$, $d=0.68$). Although not reaching conventional levels of statistical significance, trends toward lower depressive symptoms ($p=.08$), higher disease-specific HR-QoL ($p=.05$), greater positive attitude coping ($p=.05$), and

Table 2. Baseline to follow-up changes in psychological outcomes and HR-QoL indices of participants with IBD, divided into CD and UC.

Variables	IBD (n=73)	CD (n=30)	UC (n=43)	p (IBD)	p (CD)	p (UC)
Depressive symptoms						
Baseline	13.1±7.9	13.0±8.3	13.1±7.7			
Follow-up	11.5±7.2	11.8±8.1	11.3±6.5	.08	.42	.11
Anxiety symptoms						
Baseline	21.6±11.6	23.6±13.4	20.3±10.0			
Follow-up	22.9±11.2	22.1±11.6	23.4±11.0	.26	.33	.05
Psychic anxiety						
Baseline	11.6±5.7	12.4±6.6	11.1±5.0			
Follow-up	11.3±5.3	11.1±5.7	11.4±5.1	.51	.07	.64
Somatic anxiety						
Baseline	10.0±6.3	11.1±7.2	9.2±5.6			
Follow-up	11.5±6.3	10.9±6.3	11.9±6.3	.03	.86	.01
Physical component summary						
Baseline	45.9±9.4	45.7±9.6	46.1±9.3			
Follow-up	46.5±9.6	46.9±8.9	46.2±10.3	.63	.43	.97
Mental component summary						
Baseline	41.4±10.9	40.5±11.1	41.9±10.9			
Follow-up	42.4±9.8	42.0±10.5	42.6±9.4	.32	.42	.57
Alexithymia						
Baseline	51.3±14.5	50.3±15.2	52.1±14.1			
Follow-up	52.7±17.6	53.5±19.8	52.2±16.2	.41	.17	.95
Difficulty identifying feelings						
Baseline	17.6±7.1	16.8±7.3	18.2±6.9			
Follow-up	16.8±7.4	17.0±8.2	16.7±6.9	.32	.87	.22
Difficulty describing feelings						
Baseline	13.9±5.1	13.1±4.9	14.4±5.2			
Follow-up	14.8±5.4	14.2±5.5	15.2±5.3	.19	.30	.40
Externally oriented thinking						
Baseline	19.7±5.5	20.3±6.0	19.3±5.2			
Follow-up	21.1±7.2	22.4±7.9	20.2±6.6	.05	.07	.32
Positive attitude						
Baseline	25.6±4.7	25.3±5.0	25.9±4.6			
Follow-up	26.7±5.1	26.5±5.0	26.9±5.2	.05	.20	.13
Social support						
Baseline	20.1±5.6	20.4±5.3	19.9±5.8			
Follow-up	16.1±5.7	16.8±5.2	15.7±6.1	< .01	< .01	< .01
Problem orientation						
Baseline	22.6±4.5	21.7±5.4	23.2±3.6			
Follow-up	22.2±4.5	21.3±4.1	22.7±4.7	.50	.72	.56
Turning to religion						
Baseline	13.9±7.1	13.8±7.7	14.0±6.8			
Follow-up	13.9±7.8	14.3±8.1	13.7±7.6	1.00	.82	.73
Avoidance						
Baseline	12.4±5.6	13.9±6.6	11.4±4.5			
Follow-up	13.3±5.4	13.8±6.1	13.0±4.9	.15	.89	.05
Disease-specific HR-QoL						
Baseline	49.8±9.0	49.2±11.4	50.3±6.9			
Follow-up	52.0±10.2	50.9±11.8	52.7±9.1	.05	.34	.08

IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; HR-QoL, health-related quality of life.

higher externally oriented thinking scores (p=.05) were also observed. All remaining measures showed no significant variation over time, with effect sizes ranging from negligible to small in magnitude ($|d|$=0.00-0.24).

Subgroup analyses revealed a similar pattern of change across diagnostic groups. In patients with CD, no significant longitudinal changes were observed, except for a reduction in social support coping ($t(29)$=3.43, p<.01, d=0.63). Among patients with UC, somatic anxiety increased ($t(42)$=−2.88, p=.01, d=−0.44), and social support coping decreased ($t(42)$=4.61, p<.01, d=0.70), whereas all other measures showed no statistically significant changes across the follow-up period.

The relationship between psychological change and health-related quality of life

Pearson correlations between change scores (Δ) are reported in Table 3. Overall, increases in psychological distress were associated with poorer patient-reported outcomes, particularly in the domains of mental health and disease-specific quality of life. Increases in depressive symptoms were moderately associated with declines in mental health (ΔMCS; r=−.47, p<.001) and disease-specific HR-QoL (ΔSIBDQ; r=−.38, p<.001). Similarly, increases in anxiety symptoms were associated with poorer perceived mental health (ΔMCS; r=−.26, p<.05), although no significant relationships emerged with physical health or disease-specific HR-QoL.

Changes in alexithymia were negatively associated with changes in disease-specific HR-QoL (r=−.26, p<.05), while no significant associations were observed with the general health indices. Among coping dimensions, only positive attitude was positively related to mental health (ΔMCS; r=.26, p<.05). No significant associations emerged between the remaining coping dimensions and HR-QoL indices. Disease duration and BMI were not significantly associated with any of the psychological change scores.

Additional analyses revealed a coherent pattern linking coping responses and psychological distress. Increases in avoidance coping were associated with increases in depressive symptoms (r=.24, p=.04), anxiety symptoms (r=.31, p<.01), and alexithymia (r=.30, p<.01). Conversely, greater positive attitude coping was associated with reductions in depressive symptoms (r=−.27, p=.02). No further significant associations were observed among the remaining coping dimensions.

Results of the multivariate GLM are reported in Table 4. A significant overall effect of changes in depressive symptoms emerged on follow-up HR-QoL indices, controlling for baseline HR-QoL and disease duration (Pillai's Trace=.28, $F(3,62)$=8.13, p<.001, η^2p=.28). The model accounted for a substantial proportion of variance in follow-up HR-QoL outcomes, explaining 44% of the variance in physical health, 58% in mental health, and 52% in disease-specific HR-QoL. Univariate analyses indicated that longitudinal increases in depressive symptoms were independently associated with poorer follow-up outcomes across HR-QoL domains. Specifically, each 1-point increase in depressive symptoms over time was associated with a .48-point decrease in mental health, a

Table 3. Pearson correlations of psychological change scores with HR-QoL change scores and clinical characteristics of patients with IBD (N=73).

Variables (Δ)	Δ PCS	Δ MCS	Δ SIBDQ	Disease duration	BMI
Δ Depressive symptoms	−.21	−.47**	−.38**	.09	.07
Δ Anxiety symptoms	−.16	−.26*	−.14	.01	−.17
Δ Alexithymia	−.10	−.02	−.26*	.14	.00
Δ Positive attitude	−.05	.26*	.01	−.05	.08
Δ Social support	.06	−.09	−.13	.16	.16
Δ Problem orientation	−.04	.21	−.02	−.09	.08
Δ Turning to religion	−.03	.11	.00	.08	−.07
Δ Avoidance	−.03	−.21	−.12	.07	−.05

PCS, Physical Component Summary; MCS, Mental Component Summary; SIBDQ, Short Inflammatory Bowel Disease Questionnaire; BMI, body mass index; *p<.05; **p<.001.

Table 4. Multivariate models of follow-up HR-QoL outcomes controlling for baseline HR-QoL and disease duration in patients with IBD (N=73).

Predictor	PCS B (SE) (Follow-up)	p	MCS B (SE) (Follow-up)	p	SIBDQ B (SE) (Follow-up)	p
PCS (baseline)	.49 (.12)	<.001	.04 (.11)	.72	.18 (.12)	.13
MCS (baseline)	.27 (.10)	.01	.56 (.09)	<.001	.33 (.10)	<.001
SIBDQ (baseline)	−.05 (.14)	.74	.13 (.13)	.32	.34 (.14)	.02
Δ Depressive symptoms	−.35 (.14)	.02	−.48 (.13)	<.001	−.53 (.14)	<.001
Δ Alexithymia	−.05 (.08)	.53	.11 (.07)	.11	.01 (.08)	.88
Δ Positive attitude	−.23 (.21)	.27	.34 (.19)	.08	−.25 (.21)	.22
Δ Avoidance	−.04 (.18)	.85	−.16 (.16)	.31	−.10 (.18)	.59
Disease duration	−.16 (.10)	.10	.05 (.09)	.54	−.11 (.10)	.27

PCS, Physical Component Summary; B, unstandardised regression coefficient; SE, standard error; MCS, Mental Component Summary; SIBDQ, Short Inflammatory Bowel Disease Questionnaire.

.53-point decrease in disease-specific HR-QoL, and a .35-point decrease in physical health. No significant effects emerged for changes in alexithymia, avoidance coping, or disease duration (all $p>.05$). Positive attitude coping showed a trend-level association with mental health at follow-up ($p=.08$), although this effect did not reach statistical significance.

Discussion

This 5-year follow-up study examined psychological functioning and HR-QoL in patients with IBD reassessed during clinical remission. The predominant finding was the limited mean-level change in psychological functioning and patient-reported outcomes over time. Depressive symptoms, overall anxiety, alexithymia, most coping dimensions, and HR-QoL indices remained largely unchanged across the 5-year observation period. In contrast, somatic anxiety increased and social support coping decreased, representing the only consistent longitudinal changes observed. The corresponding effect sizes indicated a small increase in somatic anxiety and a moderate reduction in social support coping. Despite this pattern, changes in depressive symptoms emerged as the only psychological factor independently associated with physical health, mental health, and disease-specific HR-QoL at follow-up after controlling for baseline HR-QoL and disease duration.

Taken together, these findings suggest that psychological adaptation in this cohort is characterised more by continuity than by generalised deterioration. At the same time, the results indicate that clinically relevant psychological vulnerability may persist during clinical remission. This distinction between clinical status and patient-perceived functioning is consistent with contemporary treat-to-target approaches in IBD, which increasingly recognise HR-QoL and functional outcomes as important long-term therapeutic goals alongside symptom control and mucosal healing (Turner *et al.*, 2021). Accordingly, the present findings support the view that biological disease control and subjective adaptation represent related, but non-equivalent, dimensions of long-term IBD management.

Within this broader perspective, depressive symptoms deserve particular attention. In the present study, changes in depressive symptoms emerged as the only psychological factor independently associated with physical health, mental health, and disease-specific HR-QoL at follow-up, even after adjustment for baseline HR-QoL and disease duration, with a multivariate effect size of $\eta^2p=.28$. This finding suggests that depressive symptoms capture a clinically meaningful component of long-term adaptation that is not fully explained by initial perceived health status or illness duration.

This observation is consistent with a large body of evidence showing that depression is among the strongest psychological contributors to reduced health status, disability, treatment burden, and impaired subjective functioning across chronic medical conditions (Guarino *et al.*, 2025; Martino, Catalano, *et al.*, 2020; Meduri *et al.*, 2026; Ricciardi *et al.*, 2024). Population-based studies have further demonstrated that depression substantially worsens perceived health beyond the effect of chronic disease alone (Moussavi *et al.*, 2007). The relevance of this relationship is particularly evident in IBD, where depressive symptoms are common, may persist during remission, and are consistently associated with poorer patient-reported outcomes (Barberio *et al.*, 2021; Mikocka-Walus *et al.*, 2016; Neuendorf *et al.*, 2016). Longitudinal studies have similarly shown that changes in depressive symptoms are accompanied by corresponding changes in HR-QoL independently of disease activity, while recent evidence in UC confirms the long-term relevance of internalising symptoms for patient-reported functioning (Farbod *et al.*, 2021; Oh *et al.*, 2025).

Although causal direction cannot be inferred, several mechanisms may explain this association. Depressive worsening may contribute to poorer HR-QoL through reduced vitality, diminished agency, negative illness expectations, social withdrawal, and lower engagement in everyday activities. Conversely, poorer perceived health may exacerbate depressive symptoms, particularly in the presence of pain, treatment burden, subclinical inflammation, stressful life events, or fear of relapse (Bisgaard *et al.*, 2023). Together, these findings support the view that depressive symptoms represent a clinically relevant longitudinal correlate of perceived functioning in IBD among patients assessed during clinical remission.

The selective increase in somatic anxiety adds a complementary dimension to the overall pattern of longitudinal mean-level changes observed in this study. While total anxiety and psychic anxiety remained substantially unchanged over the 5-year follow-up, the somatic component increased, particularly among patients with UC. This finding suggests that anxiety-related burden may persist primarily through bodily arousal, visceral vigilance, muscular tension, and heightened attention to physical sensations rather than through overt cognitive or emotional symptoms of anxiety.

In chronic gastrointestinal disorders, bodily sensations may acquire illness-related significance through previous disease flares, uncertainty regarding relapse, and learned associations between physical discomfort and disease recurrence (Merlo *et al.*, 2026; Rochelle & Fidler, 2013). Within the gut-brain framework, visceral signals are not processed merely as sensory events but may become emotionally salient cues shaped by prior illness experiences and symptom-related uncertainty (Ge *et al.*, 2022). Consistent with this interpretation, evidence from patients with IBD in clinical remission supports the relevance of interoceptive processes for emotional functioning (Atanasova *et al.*, 2021), while recent experimental findings suggest that fear-related responses to internal bodily sensations may remain altered even in the absence of active inflammation (Lanters *et al.*, 2024; Öhlmann *et al.*, 2026).

Although this finding should be interpreted cautiously, given its relatively isolated nature within the overall pattern of results, the increase in somatic anxiety may reflect a persistent tendency to attribute threat value to bodily sensations. This interpretation is consistent with the broader observation that psychological adaptation in IBD may remain vulnerable to illness-related bodily concerns even during periods of clinical remission.

A further longitudinal change concerned social support coping, which decreased consistently across the overall cohort and within both diagnostic groups. Together with the increase in somatic anxiety, this represented one of the few domains showing measurable variation over time against a background of broad psychological and HR-QoL stability. The finding suggests that the relational dimension of coping may remain more dynamic than other aspects of psychological functioning during long-term adaptation to IBD.

Previous research indicates that support-seeking behaviours may evolve over the course of chronic illness as patients develop more established patterns of disease management and self-regulation (McCombie *et al.*, 2015). In this context, the observed reduction may reflect a reorganisation of coping strategies rather than a direct reduction in available interpersonal resources. At the same time, given the well-established association between social support and better psychological and patient-reported outcomes in IBD (Fu *et al.*, 2020; Kamp *et al.*, 2019; Maguire *et al.*, 2021), this finding should not be assumed to represent a uniformly adaptive process. Future studies should directly assess both perceived support availability and support utilisation to clarify the clinical significance of this longitudinal change.

Alexithymia and coping provided additional information

regarding the processes through which patients adapted to chronic illness over time. Consistent with previous longitudinal evidence, alexithymia remained largely stable across the 5-year follow-up, supporting its conceptualisation as a relatively enduring vulnerability dimension in IBD (Porcelli *et al.*, 1996). Although changes in alexithymia did not independently predict HR-QoL outcomes in the multivariate model, increases in alexithymia were associated with poorer disease-specific HR-QoL at the correlational level. This finding suggests that difficulties in identifying and communicating emotional states may continue to influence the subjective experience of illness even when they do not emerge as primary longitudinal predictors of perceived health. Such an interpretation is consistent with previous studies linking alexithymia to psychological distress, somatic preoccupation, and poorer patient-reported outcomes in IBD (Iglesias-Rey *et al.*, 2012; Martino, Caputo, *et al.*, 2020; Viganò *et al.*, 2018).

A similar pattern emerged for coping. Changes in coping strategies were not independently associated with follow-up HR-QoL in the multivariate analyses, although the observed correlational pattern was theoretically coherent. Increases in avoidance were associated with increases in depressive symptoms, anxiety, and alexithymia, whereas greater positive attitude coping was associated with lower depressive symptoms and better perceived mental health. Positive attitude coping also showed a trend-level association with mental health in the multivariate model, although this effect did not reach statistical significance. Overall, these findings are consistent with evidence indicating that avoidant and disengaged coping strategies are associated with poorer adjustment in IBD, while more constructive and adaptive coping responses tend to be linked to better psychological functioning and patient-reported outcomes (Chao *et al.*, 2019; McCombie *et al.*, 2013; McCombie *et al.*, 2015; Popa *et al.*, 2024).

Taken together, these results suggest that alexithymia and coping may contribute less as direct predictors of long-term HR-QoL than as regulatory processes through which emotional burden is organised, amplified, or contained over time.

The absence of relevant differences between CD and UC at follow-up further supports a process-oriented interpretation of the findings. Although patients with CD were older and had a longer disease duration, the two diagnostic groups did not differ in depressive symptoms, anxiety, alexithymia, coping strategies, or HR-QoL indices. This pattern suggests that, within the cohort assessed during clinical remission, the psychological dimensions examined in the present study may operate across IBD phenotypes rather than being specific to a particular diagnostic subgroup. Concerning HR-QoL, these findings are also broadly consistent with the pooled differences previously reported between CD and UC for generic and disease-specific total scores, with standardised mean differences of −0.12 and −0.08, respectively (Knowles, Keefer, *et al.*, 2018).

In contrast, sex differences showed a clearer and more consistent pattern. Women reported higher depressive symptoms, greater anxiety severity, higher levels of both psychic and somatic anxiety, and poorer perceived mental health ($|d|$=0.57-0.82). These findings are consistent with recent meta-analytic evidence documenting higher risks of anxiety and depression among women with IBD (relative risk [RR]=0.73 and RR=0.80, respectively), whereas men may be at greater risk for selected adverse clinical outcomes, including surgery and early mortality (Salem *et al.*, 2024). The persistence of these differences in a cohort assessed during clinical remission suggests that sex-related psychological vulnerability may remain relevant even when the disease is clinically stable. Accordingly, emotional distress and anxiety symptoms may warrant particular attention during long-term follow-up, especially among women reporting persistent psychological burden despite satisfactory clinical control.

These longitudinal findings refine the interpretation of the baseline study conducted in the same cohort. The previous cross-sectional investigation demonstrated that psychopathological symptoms, alexithymia, coping strategies, and HR-QoL were closely interrelated in patients with IBD (Martino *et al.*, 2023). The present follow-up extends these observations by showing that, although few group-level differences emerged across the 5-year interval, within-person variation in depressive symptoms emerged as the most consistent correlate of subsequent patient-reported functioning. At the same time, alexithymia and coping appeared to contribute primarily to the broader regulatory context within which illness-related distress and adaptation were organised. Together, these findings highlight the importance of distinguishing between cross-sectional associations and longitudinal predictors when examining psychological adaptation in chronic illness.

The clinical implications of these findings primarily concern the importance of routinely monitoring depressive symptoms as part of long-term IBD management. Periodic assessment of depressive symptoms may help identify patients whose physical, mental, and disease-specific HR-QoL remains vulnerable despite clinical remission, in line with recent consensus statements emphasising the need to screen and manage psychopathological risk as part of routine IBD care (Hinnant *et al.*, 2025). At the same time, the increase in somatic anxiety, the reduction in social support coping, and the observed associations involving alexithymia and coping suggest that psychological adaptation in IBD extends beyond the presence or absence of depressive symptoms alone. Although these variables did not emerge as independent predictors of follow-up HR-QoL in the multivariate model, they appear to reflect broader regulatory processes through which patients interpret bodily sensations, organise emotional experience, mobilise interpersonal resources, and respond to the ongoing demands of chronic illness. These findings therefore support the value of a comprehensive psychological assessment that includes both emotional distress and the regulatory dimensions shaping patients' adaptation to disease.

In this perspective, clinically informed psychological and psychotherapeutic interventions may complement gastroenterological treatment by addressing emotional awareness, bodily vigilance, coping flexibility, and interpersonal functioning, thereby contributing to the preservation of HR-QoL and long-term adjustment. Rather than positioning psychological care as separate from medical management, these findings support a patient-tailored, multidisciplinary model in which gastroenterological and psychological expertise jointly address the clinical and subjective dimensions of IBD. This perspective is particularly relevant because recent evidence suggests that psychological interventions may improve HR-QoL and reduce depressive and anxiety symptoms in patients with IBD, although effects remain heterogeneous and appear to depend on intervention type, outcome selection, and integration within clinical care pathways (Riggott *et al.*, 2023; Wang *et al.*, 2025).

Some limitations should be acknowledged. Although clinical remission was confirmed by the treating gastroenterologists, the study did not include longitudinal inflammatory indices. Further studies should consider longitudinal inflammatory markers, such as C-reactive protein and faecal calprotectin, endoscopic assessments, disease relapse frequency, treatment regimens and their modifications over time, as well as relevant life events, to provide a more comprehensive understanding of the factors influencing perceived HR-QoL. The findings should therefore be interpreted cautiously. Sample size and the observational design limit causal inferences and generalisability. Future studies should integrate repeated psychological assessments with longitudinal clinical data in larger multicentre cohorts.

Conclusions

This 5-year follow-up study indicates that psychological adaptation in IBD remains clinically relevant even in patients assessed during clinical remission. The predominant finding was the overall stability of psychological functioning and patient-reported outcomes, suggesting that long-term adaptation may be characterised more by continuity than by progressive deterioration. Within this generally stable pattern, changes in depressive symptoms emerged as the psychological factor most consistently associated with subsequent physical health, mental health, and disease-specific HR-QoL.

These findings reinforce the importance of distinguishing clinical remission from patient-perceived functioning. While the disease may be clinically controlled, psychological vulnerability can persist and continue to influence quality of life and everyday functioning. From a clinical perspective, routine assessment of depressive symptoms and broader psychological functioning may help identify patients at risk of poorer long-term adaptation.

Overall, the present findings support the integration of psychological assessment within multidisciplinary IBD care and contribute to a patient-centred biopsychosocial model in which emotional functioning is recognised as an integral component of long-term disease outcomes.

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Online supplementary material:

Supplementary Table 1. Internal consistency (Cronbach's α) of study measures at follow-up.

Supplementary Table 2. Sex-related differences in psychological functioning and HR-QoL at follow-up.

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Availability of data and materials: the raw data supporting the conclusions of this article will be made available by the authors, without undue reservation. Correspondence and requests for materials should be addressed to the corresponding author.