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Disease Uncertainty and Quality of Life Among Patients With Inflammatory Bowel Disease: The Mediating Role of Anxiety and Health Literacy

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ABSTRACT

Objective: This study aimed to examine the relationship between disease uncertainty and quality of life among Canadian adults with inflammatory bowel disease and to determine the mediating roles of anxiety and health literacy in this relationship.
Methods and Materials: This descriptive-correlational study was conducted using a cross-sectional predictive design. The study population consisted of adults with inflammatory bowel disease in Canada, and the final sample included 326 patients recruited from gastroenterology clinics, outpatient digestive disease centers, and patient support networks. Data were collected using a demographic and clinical information form, the Mishel Uncertainty in Illness Scale, the Inflammatory Bowel Disease Questionnaire, the Generalized Anxiety Disorder-7 scale, and the Health Literacy Questionnaire. Data were analyzed using SPSS and AMOS. Pearson correlation coefficients were used to examine relationships among the variables, and structural equation modeling was applied to test the direct and indirect effects of disease uncertainty on quality of life through anxiety and health literacy. The significance of indirect effects was examined using the bootstrap method with 5,000 resamples and 95% confidence intervals.
Findings: Disease uncertainty was significantly and negatively correlated with quality of life ($r = -0.61$, $p < 0.001$) and health literacy ($r = -0.49$, $p < 0.001$), and significantly positively correlated with anxiety ($r = 0.58$, $p < 0.001$). Anxiety was negatively associated with quality of life ($r = -0.67$, $p < 0.001$), while health literacy was positively associated with quality of life ($r = 0.52$, $p < 0.001$). The structural model showed acceptable fit. Disease uncertainty had significant direct effects on anxiety ($\beta = 0.58$, $p < 0.001$), health literacy ($\beta = -0.49$, $p < 0.001$), and quality of life ($\beta = -0.28$, $p < 0.001$). Anxiety ($\beta = -0.43$, $p < 0.001$) and health literacy ($\beta = 0.24$, $p < 0.001$) significantly predicted quality of life. Bootstrap analysis confirmed significant indirect effects through anxiety and health literacy.
Conclusion: Disease uncertainty was associated with poorer quality of life among patients with inflammatory bowel disease, and this relationship was partially mediated by increased anxiety and reduced health literacy.

Keywords: *Inflammatory bowel disease; disease uncertainty; quality of life; anxiety; health literacy; mediation model.*

1. Introduction

Inflammatory bowel disease (IBD), primarily including Crohn’s disease and ulcerative colitis, is a chronic, relapsing, and unpredictable immune-mediated condition that extends far beyond gastrointestinal inflammation and imposes complex biological, psychological, social, and functional consequences on patients’ lives. Although advances in diagnostic methods, pharmacological therapies, biologic agents, dietary management, telehealth services, and treat-to-target strategies have improved clinical outcomes, many patients continue to experience fluctuating symptoms, uncertainty regarding disease course, concerns about treatment risks, and persistent impairment in daily functioning. Contemporary IBD care increasingly recognizes that disease control cannot be evaluated solely through inflammatory markers, endoscopic healing, or symptom reduction; rather, patient-centered outcomes such as quality of life, psychological adjustment, self-care capacity, health literacy, and perceived control over illness are essential indicators of successful management (Napolitano et al., 2024; Sharara et al., 2026; Swaminathan et al., 2024). From this perspective, quality of life is not merely an additional outcome but a central dimension of the lived experience of IBD, reflecting the degree to which patients can maintain emotional stability, social participation, work functioning, sleep quality, nutritional confidence, interpersonal relationships, and a meaningful sense of autonomy while living with a chronic and often unpredictable condition (Nazarian et al., 2020; Thomann et al., 2021).

The burden of IBD on quality of life is multidimensional because the disease affects the body, mind, family system, and social roles simultaneously. Patients may experience abdominal pain, bowel urgency, fatigue, sleep disturbance, dietary restrictions, medication side effects, fear of relapse, work limitations, social withdrawal, and concerns about future complications. Studies focusing on physical, emotional, and social consequences have shown that quality of life can be impaired even when disease activity is clinically controlled, suggesting that the subjective burden of IBD may persist beyond observable inflammatory status (Herrera-deGuise et al., 2022; Starčević et al., 2025). Pain, fatigue, and bowel incontinence have been identified as particularly disruptive symptoms because they directly interfere with mobility, sleep, social confidence, employment, and personal dignity (Roukas et al., 2024). Sleep quality also appears to have a close relationship with quality of life, especially when it interacts with pain and symptom-related distress (Barnes et al., 2024). In addition, food-related quality of life is a major concern, as patients frequently modify diet, avoid social eating situations, or experience anxiety about triggering symptoms after meals (Cox et al., 2022; Peng et al., 2022). These findings collectively demonstrate that quality of life in IBD emerges from the interaction of symptoms, psychological responses, self-management demands, and the meaning patients assign to their illness.

Disease uncertainty is one of the most important subjective experiences in chronic illness and is especially relevant in IBD because the disease is characterized by periods of remission and relapse, variable treatment response, unpredictable symptom exacerbation, and complex therapeutic decision-making. Patients often face uncertainty about whether symptoms indicate inflammation or functional bowel disturbance, whether medications will remain effective, whether surgery may become necessary, and how the illness will affect employment, relationships, fertility, parenting, and long-term health. The increasing complexity of IBD therapies may also contribute to uncertainty, particularly when patients must weigh benefits and risks related to immunosuppressive or biologic treatments (Zayat et al., 2025). Recent clinical discussions emphasize that patients require clear communication regarding treatment risks, therapeutic expectations, and long-term disease management, because inadequate communication may increase ambiguity and reduce confidence in decision-making (Zayat et al., 2025). The challenge is not only medical but also cognitive and emotional: patients must continuously interpret bodily sensations, evaluate health information, anticipate possible relapse, and make decisions under incomplete certainty. Therefore, disease uncertainty may function as a psychological stressor that weakens quality of life by increasing perceived threat and reducing perceived control.

The biopsychosocial model provides a useful framework for understanding why uncertainty may be strongly associated with quality of life in IBD. According to this perspective, disease outcomes are shaped by the dynamic interplay of biological disease activity, psychological processes, behavioral adaptation, social resources, and environmental demands. Evidence from IBD research supports this view by showing that psychosocial factors are meaningfully related to quality of life, disease adjustment, and even future disease-related outcomes (Lang et al., 2023; Thomann et al., 2021). Positive affect has been examined as a potentially protective factor in relation to future disease activity, suggesting that emotional adaptation may have clinical relevance beyond subjective well-being (Lang et al., 2023). Conversely, psychological symptoms such as anxiety, depression, fatigue, and perceived disability have been repeatedly associated with poorer health-related quality of life in IBD (Mules et al., 2021; Seaman & Ferreira, 2024; Stroie et al., 2023). These findings support the assumption that uncertainty may influence quality of life not only through direct perceptions of illness burden but also through intermediate psychological mechanisms, particularly anxiety.

Anxiety is highly relevant in IBD because the unpredictable nature of symptoms can produce persistent worry, hypervigilance toward bodily sensations, fear of urgency or incontinence, concerns about public embarrassment, and apprehension about disease progression. Research on psychological symptoms in IBD has consistently shown that anxiety and depression are common and clinically meaningful correlates of quality of life (Bartocci et al., 2023; Kok et al., 2022). Multicenter studies have further demonstrated that psychological symptoms and sleep problems are closely linked to quality of life among patients with IBD across different geographical settings, highlighting the broad relevance of mental health in disease adjustment (Liu et al., 2024; Zhang et al., 2024). Even among patients with inactive disease, anxiety and depression remain important because fatigue and reduced health-related quality of life may persist in the absence of overt disease activity (Stroie et al., 2023). Gastrointestinal-specific anxiety and perceived disability are especially important because they capture illness-focused worry and the degree to which patients perceive IBD as limiting their daily roles (Seaman & Ferreira, 2024). Anxiety may therefore represent a key pathway through which disease uncertainty undermines quality of life: when patients cannot predict symptoms or understand the implications of disease changes, uncertainty may heighten anxiety, which in turn can impair emotional functioning, sleep, social participation, treatment confidence, and overall quality of life.

The importance of anxiety in IBD has also been reinforced by studies conducted during the COVID-19 pandemic, which created additional uncertainty regarding infection risk, access to medical care, immunosuppressive therapy, and disease management. Canadian and international studies showed that the pandemic had important implications for mental health and quality of life among patients with IBD (Graff et al., 2021; Hayes et al., 2021). Research from different countries similarly indicated that pandemic-related disruption was associated with changes in quality of life and psychological characteristics among IBD patients (Dávid et al., 2023; Gavrilescu et al., 2022). Clinically stable patients also experienced declines in health-related quality of life during the outbreak, suggesting that external uncertainty may intensify the psychological and functional burden of IBD even when disease status is not severely active (Herrera-deGuise et al., 2022). These findings are particularly relevant to the present study because they show that uncertainty, anxiety, and quality of life are closely connected under conditions in which patients perceive increased vulnerability and reduced control.

Health literacy is another central factor in the relationship between disease uncertainty and quality of life. In chronic illness, health literacy refers not only to the ability to read health information but also to the capacity to access, understand, evaluate, communicate, and apply health information in real-world decision-making. In IBD, health literacy may influence how patients interpret symptoms, understand test results, evaluate medication risks, communicate with gastroenterology teams, follow treatment plans, use digital resources, and participate in shared decision-making. When health literacy is limited, patients may experience greater confusion about disease mechanisms, more difficulty distinguishing flare symptoms from functional symptoms, and lower confidence in navigating treatment options. This may increase disease uncertainty and reduce quality of life by weakening self-management and perceived control. Current IBD care increasingly emphasizes self-care, patient engagement, caregiver contribution, and educational support, all of which depend on the patient’s ability to understand and use health information effectively (Napolitano et al., 2024; Sharara et al., 2026). The growing use of digital resources and telehealth-based psychological or mind–body interventions further increases the importance of health literacy because patients must engage with online platforms, interpret educational content, and apply behavioral guidance in everyday life (Chappell et al., 2025).

Health literacy may also interact with psychological adaptation because patients who understand their illness and treatment options may feel less threatened by symptoms and more capable of managing uncertainty. Conversely, patients with lower health literacy may be more vulnerable to misinformation, inconsistent risk perceptions, and avoidant coping. Coping strategies have been shown to play a meaningful role in quality of life among patients with IBD, indicating that the way patients respond to illness-related stress is strongly associated with adjustment (Wang et al., 2025). Cognitive functions, psychological disorders, and coping strategies have also been linked to quality of life and disease outcomes, emphasizing that patients' cognitive and emotional resources shape the experience of IBD (Almarzouki et al., 2024). Health literacy may therefore be conceptualized as a cognitive and behavioral resource that helps patients convert medical information into practical self-management behaviors. When this resource is weak, disease uncertainty may become more distressing and more damaging to quality of life. When it is strong, patients may be better able to communicate with clinicians, evaluate risks, anticipate disease changes, and maintain confidence in treatment.

Recent developments in IBD care further demonstrate the need to study health literacy alongside anxiety and quality of life. Patients are increasingly exposed to complex information about biologic therapies, biosimilars, small molecules, dietary interventions, functional gastrointestinal symptoms, microbiota, surgical outcomes, mental health care, and digital health resources. Managing IBS-like symptoms in IBD is clinically challenging because symptoms may persist even when inflammation is controlled, making it difficult for patients to interpret bodily sensations and determine the appropriate response (Wellens et al., 2024). Alterations in intestinal microbiota have also been associated with impaired psychological function among patients with IBD in remission, illustrating the biological complexity of the gut–brain relationship and the difficulty patients face when trying to understand symptom origins (Humbel et al., 2020). Such complexity may intensify uncertainty and increase dependence on clear, accessible, and actionable health information. In this context, health literacy may buffer the negative effects of uncertainty by helping patients understand that symptom experience, disease activity, psychological distress, and treatment response are interconnected but not always identical.

The social context of IBD also contributes to uncertainty and quality of life. IBD affects not only patients but also partners, caregivers, and family systems. Qualitative research has shown that partners may experience emotional, practical, and relational consequences when supporting someone with IBD (Thapwong et al., 2022). Caregivers may also experience burden and productivity loss, indicating that IBD has wider social and economic consequences beyond the individual patient (Zand et al., 2020). These relational burdens may feed back into patients' quality of life through guilt, dependence, communication difficulties, and concerns about being a burden to others. Work disability is another important aspect of quality of life, and anxiety has been associated with occupational consequences among patients with immune-mediated inflammatory diseases (Marcon et al., 2024). These findings suggest that disease uncertainty may have consequences across multiple life domains, including family relationships, work participation, and social functioning. Therefore, examining mechanisms such as anxiety and health literacy is clinically meaningful because both may influence how patients manage interpersonal and occupational demands.

Psychological and behavioral interventions for IBD and other gastrointestinal disorders have gained increasing attention, further underscoring the clinical significance of anxiety and health literacy as modifiable factors. Practical guides emphasize the need to recognize and manage psychological disorders in IBD as part of integrated care rather than treating mental health as separate from gastrointestinal disease (Kok et al., 2022). Systematic reviews and intervention protocols have examined psychological, behavioral, mindfulness-based, and acceptance-based approaches for reducing distress and improving adjustment in IBD and related gastrointestinal conditions (Avest et al., 2023; Evans et al., 2022; Sweeney et al., 2025). Antidepressant treatment has also been examined in relation to psychological comorbidities, disease activity, and quality of life, reflecting continued interest in the mental health dimension of IBD care (Wang et al., 2023). These intervention-oriented studies are important because they imply that the pathways linking uncertainty to quality of life may be clinically modifiable. If anxiety mediates the relationship between disease uncertainty and quality of life, then psychological interventions targeting worry, avoidance, acceptance, and illness-related threat appraisal may improve quality of life. If health literacy also mediates this relationship, then educational interventions, risk communication strategies, and self-management support may be equally important.

Despite growing evidence on psychological distress, coping, disease activity, and quality of life in IBD, several gaps remain. First, much of the literature has examined anxiety, depression, symptoms, or quality of life as parallel correlates rather than testing explanatory mechanisms linking disease uncertainty to quality of life. Second, although health literacy is increasingly relevant in modern

IBD care, it has received less direct attention as a mediator that may explain how uncertainty translates into poorer quality of life. Third, existing studies highlight the importance of psychological and social burden across different contexts, but there remains a need for integrated models that simultaneously consider emotional distress and informational capacity. Such models are particularly important in Canadian IBD populations, where patient-centered care, digital health resources, and shared decision-making require both psychological resilience and adequate health literacy. Research from Canada has already shown that poor quality of life in IBD is associated with multiple clinical and psychosocial factors, and national work has emphasized the mental health and quality-of-life impact of IBD during periods of heightened uncertainty (Graff et al., 2021; Nazarian et al., 2020). Building on this evidence, the present study positions disease uncertainty as a central predictor and examines anxiety and health literacy as two theoretically meaningful mediating pathways.

The aim of this study was to examine the relationship between disease uncertainty and quality of life among Canadian adults with inflammatory bowel disease and to determine the mediating roles of anxiety and health literacy in this relationship.

2. Methods and Materials

2.1. Study Design and Participants

This study was conducted as a descriptive-correlational study using a cross-sectional predictive design to examine the relationship between disease uncertainty and quality of life among adults with inflammatory bowel disease and to determine the mediating roles of anxiety and health literacy in this relationship. The study population consisted of adult patients diagnosed with inflammatory bowel disease in Canada. Participants were recruited from gastroenterology clinics, outpatient digestive disease centers, and patient support networks in Ontario, Quebec, British Columbia, and Alberta. The final sample included 326 adults with inflammatory bowel disease, of whom 174 had Crohn’s disease, 138 had ulcerative colitis, and 14 had inflammatory bowel disease-unclassified. Eligible participants were adults aged 18 years or older who had received a confirmed medical diagnosis of inflammatory bowel disease by a gastroenterologist at least six months before participation, were able to read and understand English, and were willing to provide informed consent. Patients were excluded if they reported a severe psychiatric disorder, cognitive impairment, active malignancy, hospitalization at the time of data collection, or any other severe medical condition that could independently affect quality of life. Participants were selected using convenience sampling, and data collection continued until the required sample size for mediation analysis was achieved. Before completing the questionnaires, all participants received information about the study objectives, voluntary participation, confidentiality of responses, and the right to withdraw at any stage without consequences for their medical care. Written informed consent was obtained from all participants.

2.2. Measures

Data were collected using a demographic and clinical information form and standardized self-report questionnaires measuring disease uncertainty, quality of life, anxiety, and health literacy. The demographic and clinical information form was designed by the researchers and included age, gender, marital status, educational level, employment status, type of inflammatory bowel disease, duration of diagnosis, disease activity status as reported by the participant, history of hospitalization, medication use, and history of surgery related to inflammatory bowel disease. Disease uncertainty was assessed using the Mishel Uncertainty in Illness Scale, which measures the extent to which patients perceive ambiguity, complexity, inconsistency, and unpredictability in relation to their illness. Higher scores indicate greater perceived uncertainty about the disease, treatment process, symptoms, and future health outcomes. Quality of life was assessed using the Inflammatory Bowel Disease Questionnaire, a disease-specific instrument designed to evaluate health-related quality of life among patients with Crohn’s disease and ulcerative colitis. This questionnaire assesses major dimensions of quality of life, including bowel symptoms, systemic symptoms, emotional functioning, and social functioning, with higher scores indicating better quality of life. Anxiety was measured using the Generalized Anxiety Disorder-7 scale, which evaluates the severity of anxiety symptoms during the previous two weeks. The scale includes items related to excessive worry, nervousness, restlessness, irritability, difficulty relaxing, and fear that something awful may happen, with higher scores indicating higher levels of anxiety. Health literacy was measured using the Health Literacy Questionnaire, which evaluates patients’ ability to access, understand, appraise, and use health-related information in the context of managing illness and communicating with health professionals. Higher scores indicate greater perceived health literacy and stronger capacity to engage in health-related decision-making. All instruments used in this study have been widely applied in clinical and health research, and their validity and reliability have been supported in previous studies. In the present study, internal consistency reliability was examined using Cronbach's alpha coefficients for all main variables before conducting inferential analyses.

2.3. Data Analysis

Data were analyzed using SPSS and AMOS statistical software. First, all questionnaires were screened for completeness, and missing data, outliers, and response patterns were examined. Cases with substantial missing responses were removed from the dataset, while minor missing values were managed using appropriate statistical procedures. Descriptive statistics, including mean, standard deviation, frequency, and percentage, were used to describe demographic and clinical characteristics of the participants and the main study variables. The assumptions of normality, linearity, multicollinearity, and homoscedasticity were examined before conducting inferential analyses. Skewness and kurtosis indices were used to assess the distribution of quantitative variables, and Pearson correlation coefficients were calculated to examine bivariate associations among disease uncertainty, anxiety, health literacy, and quality of life. Internal consistency of the measurement tools was assessed using Cronbach's alpha, with values of 0.70 or higher considered acceptable.

To test the hypothesized mediation model, structural equation modeling was performed. Disease uncertainty was entered as the independent variable, quality of life as the dependent variable, and anxiety and health literacy as parallel mediating variables. The direct effect of disease uncertainty on quality of life and the indirect effects through anxiety and health literacy were estimated simultaneously. Age, gender, disease duration, type of inflammatory bowel disease, and disease activity status were controlled in the model because of their potential association with quality of life. Model fit was evaluated using several indices, including the chi-square to degrees of freedom ratio, comparative fit index, Tucker–Lewis index, root mean square error of approximation, and standardized root mean square residual. A comparative fit index and Tucker–Lewis index greater than 0.90, a root mean square error of approximation below 0.08, and a standardized root mean square residual below 0.08 were considered indicators of acceptable model fit. The significance of indirect effects was examined using the bootstrap method with 5,000 resamples and 95% confidence intervals. Mediation was considered statistically significant when the bootstrap confidence interval for the indirect effect did not include zero. The level of statistical significance was set at $p < 0.05$ for all analyses.

3. Findings and Results

A total of 326 adults with inflammatory bowel disease participated in the study. The mean age of the participants was 39.84 years with a standard deviation of 12.26, and the age range was from 18 to 72 years. Regarding gender distribution, 188 participants were women, representing 57.7% of the sample, 132 were men, representing 40.5%, and 6 participants identified as non-binary or preferred not to disclose their gender, representing 1.8%. In terms of marital status, 167 participants were married or living with a partner, 113 were single, and 46 were divorced, separated, or widowed. Educationally, 59 participants had completed high school or less, 111 had a college diploma or vocational qualification, 109 had an undergraduate university degree, and 47 had completed postgraduate education. Employment status showed that 213 participants were employed either full-time or part-time, 52 were unemployed or on medical leave, and 61 were students, retired, or not currently in the labor force. With respect to clinical characteristics, 174 participants had Crohn's disease, 138 had ulcerative colitis, and 14 had inflammatory bowel disease-unclassified. The mean duration since diagnosis was 8.71 years with a standard deviation of 6.34. Based on self-reported current disease status, 86 participants described their disease as being in remission, 112 reported mild activity, 97 reported moderate activity, and 31 reported severe disease activity. In addition, 124 participants reported at least one previous hospitalization related to inflammatory bowel disease, and 78 reported a history of disease-related surgery. Medication patterns indicated that 152 participants were receiving biologic therapy, 84 were using immunomodulators, 129 were using aminosalicylates, and 58 reported current corticosteroid use. Overall, the sample represented a clinically heterogeneous group of Canadian adults living with inflammatory bowel disease, with sufficient variation in disease type, disease duration, and current disease activity to examine the psychological and health-literacy pathways associated with quality of life.

Table 1

Descriptive Statistics and Internal Consistency of the Main Study Variables

Variable	Possible Score Range	Observed Range	Mean	Standard Deviation	Skewness	Kurtosis	Cronbach’s Alpha
Disease uncertainty	1–5	1.42–4.86	3.14	0.72	0.18	-0.41	0.91
Anxiety	0–21	0–20	8.36	5.12	0.46	-0.38	0.89
Health literacy	1–5	1.61–4.92	3.28	0.67	-0.21	-0.29	0.88
Quality of life	32–224	72–211	145.63	30.47	-0.16	-0.52	0.93

As shown in Table 1, the participants reported a moderate level of disease uncertainty, with a mean score of 3.14, indicating that uncertainty about symptoms, treatment expectations, disease course, and future health consequences was a notable concern among the patients. The mean anxiety score was 8.36, suggesting that the overall level of anxiety symptoms was in the mild to moderate range, although the wide observed range indicated substantial individual differences in psychological distress. The mean health literacy score was 3.28, reflecting a moderate level of perceived ability to obtain, understand, evaluate, and use health-related information in managing inflammatory bowel disease. The mean quality of life score was 145.63, suggesting that participants experienced a moderate level of disease-specific quality of life, with considerable variability across the sample. The skewness and kurtosis values for all main variables were within acceptable limits, supporting the assumption of approximate normality for subsequent parametric and structural equation analyses. Cronbach’s alpha coefficients ranged from 0.88 to 0.93, demonstrating good to excellent internal consistency reliability for all instruments used in the study. These findings indicated that the measurement tools had adequate reliability in the present Canadian inflammatory bowel disease sample.

Table 2

Pearson Correlations Among Disease Uncertainty, Anxiety, Health Literacy, and Quality of Life

Variable	1	2	3	4
1. Disease uncertainty	1			
2. Anxiety	0.58***	1		
3. Health literacy	-0.49***	-0.42***	1	
4. Quality of life	-0.61***	-0.67***	0.52***	1

Table 2 presents the zero-order correlations among the main study variables. Disease uncertainty had a strong negative correlation with quality of life, indicating that patients who experienced greater ambiguity, unpredictability, and lack of clarity about their illness tended to report poorer disease-specific quality of life. Disease uncertainty was also positively and significantly associated with anxiety, showing that higher uncertainty was related to higher levels of worry, tension, and psychological distress. In addition, disease uncertainty was negatively associated with health literacy, suggesting that patients who perceived themselves as less able to access, understand, and use health information were more likely to experience uncertainty about their condition. Anxiety demonstrated the strongest bivariate association with quality of life, with higher anxiety being strongly related to lower quality of life. Health literacy was positively associated with quality of life, meaning that patients with stronger health-information skills and greater perceived capacity to navigate health-related decisions reported better quality of life. The correlation between anxiety and health literacy was negative and statistically significant, indicating that lower health literacy was associated with higher anxiety. Overall, the pattern of correlations supported the proposed mediation model by demonstrating that disease uncertainty was significantly related to both mediators and to quality of life, and that both anxiety and health literacy were significantly associated with quality of life.

Table 3

Standardized and Unstandardized Direct Effects in the Structural Equation Model

Path	B	Standard Error	β	Critical Ratio	p
Disease uncertainty → Anxiety	4.12	0.32	0.58	12.88	<0.001
Disease uncertainty → Health literacy	-0.46	0.05	-0.49	-9.20	<0.001
Anxiety → Quality of life	-2.55	0.24	-0.43	-10.63	<0.001
Health literacy → Quality of life	10.84	1.91	0.24	5.67	<0.001
Disease uncertainty → Quality of life	-11.94	2.08	-0.28	-5.74	<0.001
Disease activity → Quality of life	-8.46	1.55	-0.29	-5.46	<0.001
Age → Quality of life	0.12	0.09	0.05	1.36	0.174
Disease duration → Quality of life	-0.18	0.17	-0.04	-1.06	0.287

The structural equation model showed an acceptable fit to the observed data, indicating that the proposed mediation model was statistically appropriate for explaining quality of life among patients with inflammatory bowel disease. The model fit indices were within acceptable ranges: $\chi^2/df = 2.18$, comparative fit index = 0.96, Tucker–Lewis index = 0.94, root mean square error of approximation = 0.060, and standardized root mean square residual = 0.041. As shown in Table 3, disease uncertainty had a significant positive direct effect on anxiety, indicating that higher disease uncertainty predicted higher anxiety symptoms. Disease uncertainty also had a significant negative direct effect on health literacy, showing that patients with higher perceived uncertainty tended to report lower health literacy. In turn, anxiety had a significant negative direct effect on quality of life, meaning that higher anxiety predicted poorer quality of life after controlling for disease uncertainty, health literacy, disease activity, age, and disease duration. Health literacy had a significant positive direct effect on quality of life, indicating that stronger health literacy predicted better quality of life. The direct effect of disease uncertainty on quality of life remained significant and negative even after anxiety and health literacy were entered into the model, suggesting that disease uncertainty affected quality of life both directly and indirectly. Among the control variables, disease activity had a significant negative effect on quality of life, indicating that patients with more active symptoms reported poorer quality of life. Age and disease duration were not significant predictors of quality of life in the final model. The model explained 52% of the variance in anxiety, 24% of the variance in health literacy, and 61% of the variance in quality of life, demonstrating substantial explanatory power for the final outcome variable.

Table 4

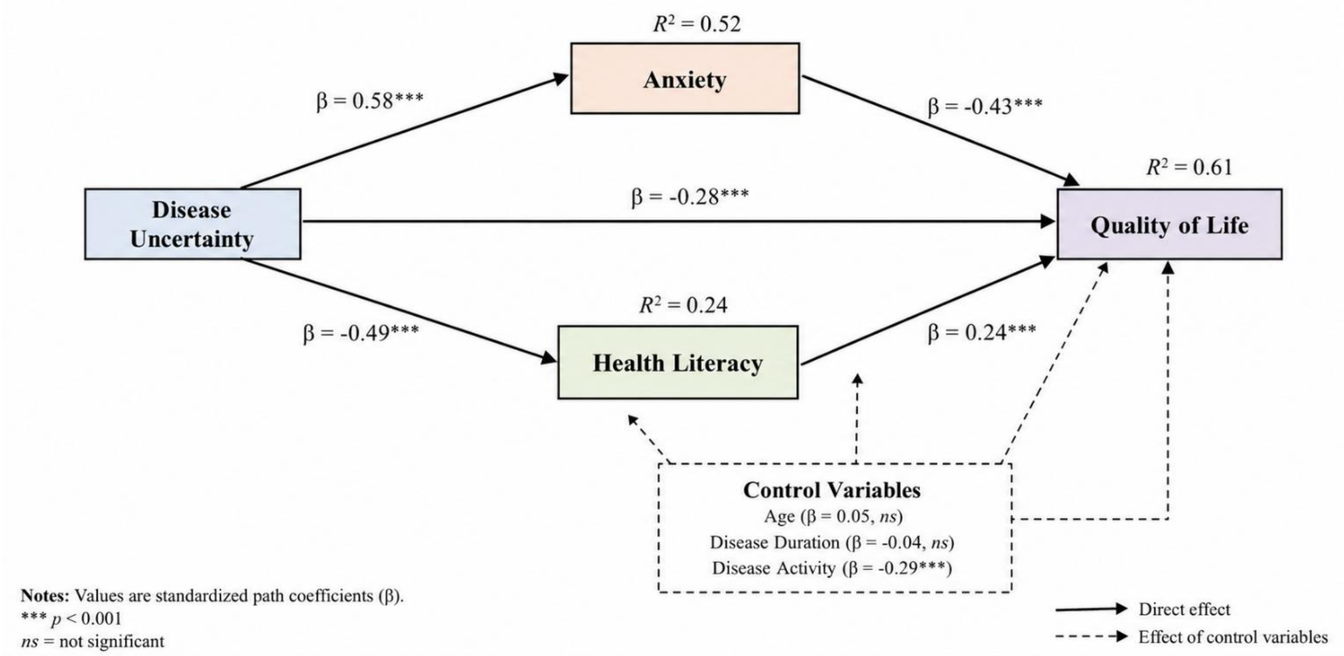
Bootstrapped Indirect Effects of Disease Uncertainty on Quality of Life Through Anxiety and Health Literacy

Effect	B	Standard Error	β	95% Bootstrap Confidence Interval	p
Disease uncertainty → Anxiety → Quality of life	-10.51	1.41	-0.25	-13.48 to -7.95	<0.001
Disease uncertainty → Health literacy → Quality of life	-4.99	1.23	-0.12	-7.62 to -2.80	<0.001
Total indirect effect	-15.50	1.82	-0.37	-19.25 to -12.24	<0.001
Direct effect	-11.94	2.08	-0.28	-16.03 to -7.86	<0.001
Total effect	-27.44	2.66	-0.65	-32.76 to -22.31	<0.001

Table 4 presents the bootstrapped indirect effects of disease uncertainty on quality of life through anxiety and health literacy. The indirect effect through anxiety was statistically significant, as the 95% bootstrap confidence interval did not include zero. This result indicated that higher disease uncertainty was associated with higher anxiety, which in turn was associated with poorer quality of life. In practical terms, anxiety functioned as an important psychological pathway through which uncertainty about inflammatory bowel disease reduced patients' quality of life. The indirect effect through health literacy was also statistically significant. This finding showed that greater disease uncertainty was associated with lower health literacy, and lower health literacy was subsequently associated with poorer quality of life. Therefore, health literacy also served as a meaningful explanatory mechanism in the association between disease uncertainty and quality of life. The total indirect effect was significant, confirming that anxiety and health literacy together explained a substantial part of the relationship between disease uncertainty and quality of life. However, the direct effect of disease uncertainty on quality of life also remained statistically significant, indicating partial mediation rather than full mediation. Approximately 56.5% of the total effect of disease uncertainty on quality of life was transmitted through anxiety and health literacy, while the remaining effect was direct. The anxiety pathway accounted for a larger portion of the indirect effect than the health literacy pathway, suggesting that emotional distress may be the stronger mechanism linking disease uncertainty to impaired quality of life in this sample.

Figure 1

Final Mediation Model of the Relationship Between Disease Uncertainty and Quality of Life Through Anxiety and Health Literacy



Notes: Values are standardized path coefficients (β).
*** $p < 0.001$
ns = not significant

The final mediation model showed that disease uncertainty had both direct and indirect associations with quality of life among patients with inflammatory bowel disease. The standardized path from disease uncertainty to anxiety was positive and strong, while the standardized path from anxiety to quality of life was negative and substantial. This indicated that uncertainty about the illness increased anxiety symptoms, and these symptoms were associated with a marked reduction in quality of life. The pathway from disease uncertainty to health literacy was negative, and the pathway from health literacy to quality of life was positive, indicating that uncertainty was linked to poorer perceived capacity to understand and use health information, while stronger health literacy was associated with better quality of life. The model therefore supported a dual-mediation mechanism in which psychological distress and health-information capacity operated simultaneously. The persistence of a significant direct path from disease uncertainty to quality of life suggested that uncertainty may also impair quality of life through additional mechanisms not examined in the present model, such as perceived control, coping style, treatment burden, symptom vigilance, or illness-related social limitations. Overall, the findings confirmed that disease uncertainty was an important risk factor for poorer quality of life in patients with inflammatory bowel disease and that anxiety and health literacy partially explained this association.

4. Discussion

The present study examined the relationship between disease uncertainty and quality of life among Canadian adults with inflammatory bowel disease and tested the mediating roles of anxiety and health literacy. The findings showed that patients reported moderate disease uncertainty, mild to moderate anxiety symptoms, moderate health literacy, and moderate disease-specific quality of life. Correlational findings indicated that disease uncertainty was negatively associated with quality of life and health literacy and positively associated with anxiety. Anxiety was strongly and negatively associated with quality of life, while health literacy was positively associated with quality of life. The structural equation model further confirmed that disease uncertainty had a significant direct negative effect on quality of life and significant indirect effects through both anxiety and health literacy. These findings suggest that patients who experienced higher uncertainty about the nature, course, symptoms, treatment, and consequences of IBD were more likely to experience anxiety and lower perceived ability to understand and use health information, which in turn contributed to poorer quality of life.

The significant negative association between disease uncertainty and quality of life is consistent with the broader biopsychosocial understanding of IBD, according to which quality of life is shaped not only by disease activity but also by patients' perceptions, coping resources, emotional responses, and social functioning. IBD is characterized by relapse-remission patterns, unpredictable symptom fluctuations, complex treatment decisions, and uncertainty about long-term complications. Therefore, patients may experience a persistent lack of control even when receiving regular medical care. This interpretation is aligned with studies showing that quality of life in IBD is influenced by physical, psychological, and social factors rather than by biological disease indicators alone (Sharara et al., 2026; Thomann et al., 2021). The present findings also correspond with evidence from Canadian IBD research indicating that poor quality of life is associated with a range of clinical and psychosocial factors, demonstrating that the Canadian IBD population may experience quality-of-life impairment through multiple interacting pathways (Graff et al., 2021; Nazarian et al., 2020). In this context, disease uncertainty can be understood as a central subjective burden that intensifies the impact of IBD on daily functioning, emotional stability, and perceived well-being.

The finding that disease uncertainty significantly predicted anxiety supports the assumption that uncertainty functions as a psychological stressor in IBD. When patients cannot confidently predict symptom recurrence, treatment response, disease progression, or the meaning of bodily changes, they may become more vigilant, worried, and emotionally reactive. This result is consistent with previous evidence showing that anxiety and depression are common among patients with IBD and are closely connected with health-related quality of life, disease adjustment, and perceived disease burden (Bartocci et al., 2023; Kok et al., 2022). The result also aligns with studies indicating that psychological symptoms remain important even in patients with inactive disease, suggesting that distress may persist beyond objective inflammatory activity (Stroie et al., 2023). Similarly, the Stress, Anxiety and Depression with Disease Activity study showed that disease activity is related to psychological symptoms and quality of life, supporting the view that clinical and psychological burdens are mutually reinforcing in IBD (Mules et al., 2021). Therefore, the present findings extend previous research by showing that disease uncertainty may be one of the cognitive-affective mechanisms through which anxiety emerges in patients with IBD.

The strong negative path from anxiety to quality of life was one of the most important findings of this study. Anxiety appears to reduce quality of life by increasing symptom monitoring, avoidance of social situations, fear of urgency or incontinence, sleep disruption, emotional fatigue, and reduced confidence in self-management. This interpretation is supported by multicenter studies showing that psychological symptoms are strongly associated with poorer quality of life among patients with IBD in different geographical contexts (Liu et al., 2024; Zhang et al., 2024). The finding also corresponds with research emphasizing gastrointestinal-specific anxiety and perceived disability as important factors in adjustment to IBD (Seaman & Ferreira, 2024). Anxiety may be particularly damaging in IBD because it is often focused on unpredictable gastrointestinal experiences, such as abdominal pain, urgency, bowel frequency, and fear of symptom occurrence in public settings. In addition, anxiety may contribute to occupational limitations and functional impairment, which is consistent with evidence linking anxiety with work disability in immune-mediated inflammatory diseases (Marcon et al., 2024). Thus, the current study confirms that anxiety is not merely a psychological comorbidity but a clinically meaningful pathway through which uncertainty can undermine quality of life.

The mediating role of anxiety was also consistent with evidence from the COVID-19 period, during which patients with IBD experienced additional uncertainty about infection risk, immunosuppressive therapy, health-care access, and disease management. Studies conducted during the pandemic showed that IBD patients experienced psychological distress and quality-of-life impairment under conditions of heightened uncertainty (Dávid et al., 2023; Gavrilescu et al., 2022). Canadian research similarly emphasized the mental health and quality-of-life consequences of COVID-19 for people with IBD (Graff et al., 2021). Moreover, the Common Sense Model was extended to show how fear related to COVID-19 affected quality of life in an international IBD cohort, reinforcing the idea that perceived threat and uncertainty are central to psychological adjustment (Hayes et al., 2021). The present study is consistent with these findings because it shows that uncertainty does not remain a neutral cognitive state; rather, it becomes clinically important when it is translated into anxiety, worry, and reduced emotional security.

Health literacy also emerged as a significant mediator between disease uncertainty and quality of life. The negative path from disease uncertainty to health literacy suggests that patients who perceive their disease as ambiguous, unpredictable, and difficult to interpret may also feel less capable of accessing, understanding, evaluating, and applying health-related information. The positive path from health literacy to quality of life indicates that patients with stronger informational capacity are more likely to experience better quality of life. This finding is particularly meaningful in IBD because patients must understand complex information about medications, dietary management, symptom monitoring, laboratory tests, endoscopy, biologic therapies, treatment risks, and long-term disease control. Effective risk communication is therefore essential, especially because patients are often required to make informed choices about therapies with both benefits and potential adverse effects (Zayat et al., 2025). In addition, contemporary IBD care increasingly emphasizes self-care, patient engagement, and caregiver contribution, all of which depend on the patient's ability to understand and use health information (Napolitano et al., 2024). The present findings therefore suggest that health literacy is a protective resource that may reduce the harmful effect of uncertainty on quality of life.

The health literacy pathway can also be interpreted in relation to the increasing complexity of IBD management. Modern IBD care involves treat-to-target strategies, disease severity assessment beyond symptoms, distinction between inflammatory and functional gastrointestinal symptoms, dietary recommendations, digital health resources, and shared decision-making. Recent reviews have emphasized the importance of measuring disease severity beyond conventional targets and understanding symptom burden in a more integrated way (Swaminathan et al., 2024; Wellens et al., 2024). Patients may also encounter conflicting information about diet, food triggers, low-FODMAP approaches, and food-related quality of life, which may increase confusion if health literacy is limited (Cox et al., 2022; Peng et al., 2022). In addition, research on microbiota and psychological function in IBD remission illustrates the complexity of the gut-brain relationship and may contribute to patients' difficulty in understanding why symptoms or distress persist despite clinical improvement (Humbel et al., 2020). Therefore, patients with better health literacy may be better equipped to interpret information, communicate with clinicians, make realistic treatment decisions, and maintain quality of life despite uncertainty.

The finding that disease uncertainty retained a significant direct effect on quality of life after accounting for anxiety and health literacy indicates partial mediation. This means that anxiety and health literacy explained a substantial portion of the relationship but did not fully account for it. Other mechanisms may also connect disease uncertainty to quality of life, including coping style, perceived control, fatigue, sleep quality, pain, social support, illness identity, treatment burden, and family functioning. This explanation is supported by studies showing that coping strategies are closely related to quality of life in IBD (Wang et al., 2025). Cognitive functions, psychological disorders, and coping strategies have also been associated with quality of life and disease outcomes, indicating that patients' adaptation depends on multiple psychological and behavioral resources (Almarzouki et al., 2024). Pain, fatigue, and bowel incontinence have been shown to impose major quality-of-life burden, while sleep quality may reduce quality of life through interaction with pain (Barnes et al., 2024; Roukas et al., 2024). Surgical history and treatment experiences may also affect quality of life through physical, emotional, and social consequences (Starčević et al., 2025). Therefore, uncertainty may impair quality of life both through anxiety and health literacy and through additional symptom-related and contextual pathways.

The present findings also have implications for integrated psychological and behavioral care in IBD. If anxiety mediates the relationship between uncertainty and quality of life, psychological interventions that reduce worry, avoidance, threat appraisal, and symptom-related fear may improve patient outcomes. Existing literature supports growing interest in psychological and behavioral treatments for gastrointestinal disorders and IBD, including acceptance-based, mindfulness-based, and telehealth-delivered interventions (Avest et al., 2023; Chappell et al., 2025; Evans et al., 2022; Sweeney et al., 2025). Evidence on antidepressants also suggests that addressing psychological comorbidities may be relevant to disease activity and quality of life in IBD (Wang et al., 2023). At the same time, the significant role of health literacy indicates that psychological care should not be separated from education, risk communication, and self-management support. Patients may benefit most from integrated care models that combine emotional support, clear medical explanations, digital resources, and practical guidance for symptom interpretation and treatment decision-making. Such an approach is consistent with the broader movement toward patient-centered support strategies for people living with IBD (Sharara et al., 2026).

5. Conclusion

Finally, the present findings should be interpreted within the social context of IBD. Disease uncertainty and poor quality of life do not affect only the patient as an isolated individual. IBD can influence partners, caregivers, family routines, employment, productivity, and interpersonal relationships. Qualitative evidence has shown that IBD affects partners emotionally and practically, while caregiver research has demonstrated significant burden and productivity loss (Thapwong et al., 2022; Zand et al., 2020). Therefore, uncertainty may reduce quality of life not only by increasing internal distress but also by disrupting social confidence, relationship security, and perceived independence. The finding that health literacy mediated the relationship between uncertainty and quality of life may also have a relational dimension, because patients with stronger health literacy may communicate more effectively with family members and health professionals. Overall, the present study contributes to the IBD literature by identifying anxiety and health literacy as two important explanatory mechanisms linking disease uncertainty to quality of life and by highlighting the need for care models that address both emotional and informational needs.

6. Limitations & Suggestions

This study had several limitations that should be considered when interpreting the findings. First, the cross-sectional design prevents causal conclusions about the relationships among disease uncertainty, anxiety, health literacy, and quality of life. Although the proposed mediation model was theoretically grounded and statistically supported, longitudinal data are required to determine whether disease uncertainty leads to later changes in anxiety, health literacy, and quality of life over time. Second, the study relied on self-report questionnaires, which may be influenced by response bias, recall bias, social desirability, and participants' current emotional state. Third, disease activity was assessed using self-reported disease status rather than objective clinical indicators such as biomarkers, endoscopic findings, or physician-rated indices. Fourth, the sample was recruited through clinics and patient support networks in selected Canadian provinces, which may limit generalizability to patients in rural regions, patients with limited access to specialty care, non-English-speaking patients, and individuals with lower digital access or lower willingness to participate in survey research. Finally, although anxiety and health literacy explained a substantial portion of the relationship between uncertainty and quality of life, other potentially important mediators, such as depression, coping style, perceived control, illness perception, social support, fatigue, pain, sleep disturbance, and treatment adherence, were not included in the model.

Future studies should use longitudinal and prospective designs to examine how disease uncertainty, anxiety, health literacy, and quality of life change across different stages of IBD, including diagnosis, remission, flare, treatment escalation, hospitalization, and post-surgical recovery. Future research should also combine self-report measures with objective clinical indicators, such as C-reactive protein, fecal calprotectin, endoscopic activity, medication class, and physician-rated disease severity, in order to clarify how subjective uncertainty interacts with biological disease activity. It is also recommended that future studies examine additional mediators and moderators, including depression, fatigue, pain, sleep quality, coping strategies, perceived control, social support, caregiver involvement, treatment adherence, and trust in health-care providers. Qualitative and mixed-methods studies could provide deeper insight into how patients describe uncertainty, how they seek and interpret health information, and how anxiety affects daily self-management decisions. Future studies should also compare different IBD subgroups, including Crohn's disease and ulcerative colitis, newly diagnosed and long-term patients, urban and rural populations, and patients from different linguistic and cultural backgrounds in Canada.

The findings of this study suggest that health professionals should routinely assess disease uncertainty, anxiety, health literacy, and quality of life as part of comprehensive IBD care. Gastroenterology teams should provide clear, consistent, and individualized explanations about disease course, treatment goals, medication risks, symptom monitoring, and relapse management in order to reduce avoidable uncertainty. Screening for anxiety should be integrated into routine care, and patients with clinically meaningful anxiety symptoms should be referred to appropriate psychological support, including cognitive-behavioral, mindfulness-based, acceptance-based, or other evidence-informed interventions. Health literacy should also be strengthened through plain-language education, structured self-management programs, decision aids, visual materials, digital resources, and repeated opportunities for patients to ask questions and confirm understanding. Clinicians should recognize that improving quality of life requires more than controlling inflammation; it also requires reducing uncertainty, supporting emotional adjustment, and helping patients develop the knowledge and confidence needed to manage IBD in everyday life.

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Declaration of Interest

The authors of this article declared no conflict of interest.

Ethical Considerations

The study protocol adhered to the principles outlined in the Helsinki Declaration, which provides guidelines for ethical research involving human participants.

Transparency of Data

In accordance with the principles of transparency and open research, we declare that all data and materials used in this study are available upon request.

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Authors' Contributions

All authors equally contributed to this article.

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