



The role of resilience in mitigating depression and anxiety in patients with inflammatory bowel diseases

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ABSTRACT

Background: Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), often triggers psychological distress. Resilience, the ability to adapt to stress and trauma, may mitigate the psychological effects of chronic illnesses.

Aims: To determine whether higher psychological resilience is independently associated with reduced anxiety and depressive symptoms and whether it moderates the relationship between disease activity and these symptoms in IBD patients.

Methods: In this cross-sectional study, the Connor-Davidson Resilience Scale and the Hospital Anxiety and Depression Scale were administered to IBD outpatients. The disease activity was assessed using the Harvey-Bradshaw Index for CD and the Clinical Mayo Score for UC.

Results: A total of 458 patients were included. High resilience was associated with fewer symptoms of depression ($\beta = -0.726, p < .01$) and anxiety ($\beta = -0.668, p < .01$) in CD patients. Similar results were found among UC patients (depression: $\beta = -0.602, p < .01$; anxiety: $\beta = -0.490, p < .01$).

In CD, higher disease activity was associated with more depressive symptoms ($\beta = 0.098, p = .030$). Resilience moderated the association between CD activity and anxiety ($\beta = -0.125, p = .011$), whereas its moderating effect on depression did not reach statistical significance ($\beta = -0.086, p = .059$). Overall, disease severity was more strongly associated with higher levels of depression and anxiety symptoms among low resilience patients than among those with high resilience.

Conclusions: Resilience may play a protective role against depression and anxiety symptoms potentially tempering disease activity, making it a worthwhile focus in comprehensive IBD management, particularly in Crohn's disease. As a dynamic factor, these findings support integrating resilience-building interventions into personalized IBD care pathways.

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1. Introduction

Inflammatory bowel diseases (IBD), such as Crohn's disease (CD) and ulcerative colitis (UC), are chronic, relapsing conditions marked by relapsing-remitting gastrointestinal inflammation. UC is limited to the colonic mucosa, while CD affects the entire tract, primarily the terminal ileum and colon. Both involve fluctuating symptoms that adversely impact mental and physical health [1].

IBD severely impairs health-related quality of life [2] and causes significant psychological distress [3]. Debilitating symptoms and long-term complications like cancer risk and surgery can disrupt patients' social and professional lives [4]. Emotional difficulties caused by drug side effects and fluctuating disease courses impaired quality of life [2,5].

IBD patients show higher anxiety and depression rates than the general population, with odds ratios of 2.1–2.7 for depression and 2.2–2.5 for anxiety [6].

This psychological vulnerability is particularly pronounced in IBD due to the role of the gut-brain axis in modulating emotional processes. Chronic intestinal inflammation, altered intestinal permeability, and microbiota-gut-brain interactions contribute to dysregulated emotional responses, increasing the risk of disease-related anxiety and depression [7,8].

This interaction is bidirectional: psychological distress can, in turn, exacerbate disease activity, potentially via inflammatory and neuroendocrine pathways [8].

While the association between anxiety, depression and IBD has been well-documented, it remains unclear why some patients develop significant psychological symptoms whereas others maintain good emotional functioning despite similar disease burdens.

One potential protective factor is resilience, as individuals with higher levels of resilience often experience lower psychological distress in the face of illness-related challenges [9,10].

Resilience supports patients with chronic illnesses by reducing depression and enhancing quality of life, as seen in conditions like multiple sclerosis, arthritis, and Parkinson's disease [11]. Given IBD's rising prevalence [12] and its impact on health, identifying protective factors is crucial. In IBD, higher resilience is linked to lower disease activity, better quality of life [13], and less anxiety and depression [13,14], suggesting it helps manage both emotional and disease-related challenges. In this context, resilience is commonly described as having both promotive and protective functions in mental health [15]. Promotive factors are associated with more favorable psychological outcomes independently of the level of adversity, reflecting a general link between higher resilience and lower symptoms of anxiety and depression. IBD research on resilience has explored this role, showing its inverse relationship with emotional distress [13,14]. Protective factors, in contrast, are defined by their capacity to buffer the negative effects of specific risk exposures, such as elevated disease severity.

The distinction between promotive and protective effects allows for a more nuanced understanding of how resilience operates in the context of chronic illness. Its contribution may not be constant, but instead become particularly relevant when individuals are confronted with greater clinical or psychological challenges. Exploring this potential moderating function provides insight into the varying conditions under which resilience contributes to psychological adjustment, and may help identify patients for whom such psychological resources are especially consequential.

The current study investigates whether resilience acts as a *moderator*, specifically examining whether it buffers the impact of increased disease activity on psychological symptoms. This allows us to test whether the protective effect of resilience becomes more pronounced under conditions of greater clinical severity, which to our knowledge has not been directly examined in this context.

Traunmüller et al. [16] found that resilience moderated the link between COVID-19's psychological impact and anxiety symptoms. Similarly, a study on breast cancer patients showed resilience eased the

negative effects of anxiety and depression on post-traumatic growth [17]. Once considered a fixed trait, resilience is now seen as a dynamic process shaped by personal, social, and environmental influences [18,19].

Montpetit et al. [20] describe it as an evolving interaction between emotional responses and stressors, shaped by coping strategies, social support, therapy, and environmental factors.

Resilience's modifiability presents opportunities for targeted psychological interventions in IBD care. Incorporating resilience-enhancing programs into IBD management could significantly advance personalized care.

This study aims to investigate whether psychological resilience can both reduce overall symptoms of depression and anxiety (promotive effect), and buffer the negative psychological impact of increased IBD severity (protective effect). Although previous research has established association between resilience, and symptom of anxiety and depression in IBD, [13,14] the potential moderating role of resilience in the specific context of IBD severity and symptoms of psychological distress has not yet been directly tested. By addressing this gap, our study contributes to the growing interest in personalized, psychosocial approaches to chronic disease management, suggesting that resilience-enhancing interventions might help mitigate mental health risks in vulnerable IBD patients.

2. Materials and methods

2.1. Participants

In this cross-sectional study, consecutive IBD outpatients reaching IBD Center Digestive Disease Center - CEMAD, Fondazione Policlinico Universitario A. Gemelli IRCCS, were invited to participate in the study, from October 2019 to July 2024. After providing informed consent, patients were invited to complete the questionnaires in a quiet and comfortable setting with the support of a psychologist. Participation was voluntary, and patients were explicitly informed they could skip any question or withdraw from the study at any time without any consequence. The psychologist was available to clarify any question if needed but did not prompt or require completion of unanswered items.

Inclusion criteria were age between 18 and 75 years old, capacity to read and understand questionnaires, to sign informed consent in Italian, and diagnosis of IBD according to ECCO-ESGAR guidelines for 2019. Exclusion criteria were the presence of schizophrenia or other psychotic disorders, abuse of alcohol and/or other substances, and consumption of psychotropic drugs.

Exclusion criteria included psychotropics to minimize pharmacological confounding and observe the natural relationship between resilience and psychological symptoms. This conservative choice aligned with the study's goal of isolating underlying psychological mechanisms. While it improves interpretive clarity, it limits generalizability. A total of 476 IBD outpatients were initially screened for eligibility. Of these, 18 were excluded due to the presence of exclusion criteria, including ongoing treatment with psychotropic s ($n = 16$), and inability to provide informed consent due to language or cognitive barriers ($n = 2$). The study protocol was approved by the Ethics Committee of the Catholic University of Rome (prot. n. 2403, 10/01/2019) and was consistent with the European good clinical practice standards.

2.2. Measures

Participants were asked to complete a comprehensive questionnaire comprising three sections: (1) sociodemographic information, (2) psychological measures of resilience, depression, and anxiety, and (3) clinical assessments of disease activity. Sociodemographic data—including age, gender, marital status, educational level, and employment status—were collected via self-report as part of the initial section of the questionnaire. Medical history and observation were performed by internal medicine and gastroenterology specialists. In addition to the

psychometric assessments, relevant clinical data were collected from patients' medical records. These included current pharmacological treatments, classified as immunosuppressive agents, salicylates, steroids, antibiotics, and biologics.

- Resilience, defined as an individual's intrinsic and modifiable capacity to successfully adapt to changes [18], was assessed by the Connor-Davidson Resilience Scale [21]. The original scale contains 25 items, asking how the respondent has felt over the past month. The response scale has a 5-point Likert scale, ranging from 0 (not true at all) to 4 (true nearly all the time). The items tap five different facets: having high standards, tenacity, and competence, handling negative emotions, trusting one's instincts, and perceived benefits of stress, having a positive attitude to change and secure relationships, perceived control, and spirituality. However, the five-factor structure proposed in the original version of the scale [21] was not always confirmed in subsequent studies. In accordance with previous investigations [22], items 3, 9, and 20 were excluded, and a unidimensional model was adopted. Item scores on the remaining 22 items were summated to create an overall index ranging theoretically from 0 to 88, with higher scores indicating greater resilience.
- Depression and anxiety symptoms were defined as in Zigmond and Snaith (1983) [23] and measured by using the Hospital Anxiety and Depression Scale [23], one of the most frequently used questionnaires to assess psychological distress in both the general population and in individuals with medical conditions. The scale comprises 14 items, equally divided into two distinct subscales. The depression subscale (HADS-D) taps anhedonia-related symptoms. The anxiety subscale (HADS-A) is focused on symptoms of generalized anxiety. Items ask respondents how they felt or behaved in the past week, using a 4-point Likert scale ranging from 0 (not at all) to 3 (nearly all the time). For each subscale, the theoretical range was 0–21, with higher scores indicating higher levels of depressive or anxious symptoms.
 - The clinical disease activity of IBD patients was assessed by healthcare professionals during the same outpatient visit in which the survey was administered. These measures were extracted from the medical records and based on clinical evaluations performed within 24 h of questionnaire completion.

The clinical disease activity of IBD patients has been assessed according to the Harvey-Bradshaw index for CD patients [24], and the clinical Mayo Score for UC patients [25]. The Harvey-Bradshaw index considers five factors: general well-being, abdominal pain, number of liquid stools per day, abdominal mass, and complications. The clinical Mayo Score comprises three categories: bleeding, stool frequency, and physician assessment.

2.3. Statistical analysis

Hierarchical moderated regression analyses were used to investigate the relationship among the study variables. Two regressions were conducted for each group of IBD patients (CD and UC), with anxiety (Model 1) and depression (Model 2) as dependent variables, respectively. In each model, disease activity and resilience were entered in Step 1. Disease activity was assessed using the HBI for CD patients and the partial Mayo Score for UC patients. Gender (coded as 0 = female, 1 = male) and age (in years) were also entered as control variables. All continuous predictors were centered around the mean before entry in the regression [26]. Results from Step 1 provide insights into the unique contributions of resilience and disease activity on anxiety and depression, after controlling for gender and age.

To test the hypothesized protective role of resilience, an interaction term between disease activity and resilience was entered at Step 2. This analytic approach allowed us to assess whether the association between IBD severity and psychological distress was attenuated at higher levels

of resilience, consistent with theoretical models of protective psychological factors. The interaction was interpreted by examining the effect of disease activity on anxiety and depression at low (1 SD below the mean), average, and high (1 SD above the mean) resilience levels. Analyses were performed using the software IBM SPSS Statistics, version 27.

3. Results

3.1. Descriptive statistics

The study includes 458 IBD patients (CD: 242, 50 % females; UC: 216, 48 % females). No missing data were observed. The average age and standard deviation of the involved patients were 42.67.

± 14.91 (CD: 43.95 ± 14.82 ; UC: 41.23 ± 14.92). Among CD patients, 85 (35.1 %) were in remission, 70 (28.9 %) showed mild activity, 86 (35.5 %) showed moderate activity, and 1 (0.4 %) showed severe activity. Among UC patients, 88 (40.7 %) were in remission, while 73 (33.8 %), 37 (17.1 %), and 18 (8.3 %) showed mild, moderate, and severe activity, respectively.

The medications used were classified as immunosuppressive, salicylates, steroids, antibiotics, and biologics. The biological therapy was the most widely used type of treatment ($n = 176$, 72.8 %, for CD, $n = 141$, 65.4 %, for UC). A total of 15 (6.2 %) CD patients and 12 (5.6 %) UC patients were not on active treatment (Table S1, available in the online supplementary material, provides the full list of treatment regimens used in the sample of IBD patients).

Means, standard deviations, reliability coefficients, and intercorrelations among the study variables were calculated for each patient group and reported in Table 1. Resilience levels were slightly and significantly higher among CD than UC patients ($F(1, 456) = 6.545$, $p = .011$, $\eta^2 = 0.014$). No significant differences were found between CD and UC patients on the mean scores of the HADS subscales: (Anxiety: $F(1, 456) = 1.608$, $p = .205$, $\eta^2 = 0.004$; Depression: $F(1, 456) = 0.868$, $p = .352$, $\eta^2 = 0.002$). The two subscales were highly and positively correlated: $r = 0.73$ ($p < .01$) in CD patients, and $r = 0.62$ ($p < .01$) in the UC group. Based on a cut-off score of 11 [26], 54 CD patients (22.3 %) and 51 UC patients (23.6 %) were found to have probable clinically relevant anxiety symptoms, whereas 26 CD patients (10.7 %) and 25 UC patients (11.6 %) showed probable clinically relevant depression symptoms. The reliability coefficients of the scale scores, as measured by Cronbach's alpha, were all above the standard value of 0.70, indicating adequate levels of internal consistency.

3.2. Associations between disease severity, resilience and symptoms of depression and anxiety in Crohn's disease

Results of the moderated regression analyses for CD patients on the HADS subscales are presented in Table 2. Regarding depression (Model 1), disease activity was positively associated with depression scores in Step 1 ($b = 0.098$, $p = .030$), whereas resilience showed a strong negative association ($b = -0.729$, $p < .001$). Thus, patients with higher disease activity and lower levels of resilience reported more severe depressive symptoms. Age was uniquely associated with higher depression scores ($b = 0.140$, $p = .002$), with older patients reporting higher levels of depression symptoms. No significant association was found for gender. Overall, disease activity, resilience, and demographic variables accounted for 55 % of the variance in HADS–Depression scores ($p < .001$).

In Step 2, adding the interaction term between disease activity and resilience did not significantly improve the model ($\Delta R^2 = 0.007$, $p = .059$). Nonetheless, the observed pattern was consistent with theoretical expectations suggesting that the association between CD severity and depressive symptoms increased as resilience levels decreased ($\beta = -0.086$, $p = .059$). Simple slope analysis revealed a positive and significant effect of disease severity on depression among CD patients with

Table 1

Descriptive statistics, intercorrelations, and reliability coefficients for the study variables in samples of patients with Crohn’s Disease (CD, $n = 242$) and ulcerative colitis (UC, $n = 216$) patients.

	1.	2.	3.	4.	5.	6.
1. IBD activity		−0.02	0.15*	0.04	−0.19**	0.17**
2. CD-RISC – Resilience	0.13	<i>0.93</i>	−0.72**	−0.67**	0.06	0.12
3. HADS – Depression	0.17*	−0.59**	<i>0.79</i>	0.73*	−0.11	0.07
4. HADS – Anxiety	0.16*	−0.53**	0.62**	<i>0.86</i>	−0.17**	−0.04
5. Gender	−0.06	0.09	−0.11	−0.22**		−0.06
6. Age	−0.00	0.16*	0.05	−0.18**	0.10*	
M	4.62 (2.63)	64.78 (61.53)	5.21 (5.56)	6.97 (7.51)	0.50 (0.48)	43.95 (41.23)
SD	3.93 (2.46)	14.73 (12.16)	4.02 (3.89)	4.57 (4.56)	0.50 (0.50)	14.81 (14.92)

Note. Correlations for CD patients are reported above the diagonal; correlations for UC patients are below the diagonal. Cronbach’s alpha coefficients for the CD-RISC and the HADS subscales are shown in italics on the diagonal. Means and standard deviations for CD and UC patients are reported outside and within parentheses, respectively.

Table 2

Hierarchical moderated regression analyses predicting HADS scores in CD patients.

Predictors	Model 1 (Depression)			Model 2 (Anxiety)		
	<i>b</i>	<i>SE</i>	β	<i>b</i>	<i>SE</i>	β
<i>Step 1</i>						
Gender	−0.361	0.356	−0.045	−1.157**	0.440	−0.127
Age	0.038**	0.012	0.140	0.010	0.015	0.032
Disease activity	0.100*	0.046	0.098	−0.004	0.057	−0.004
Resilience	−0.199**	0.012	−0.729	−0.208**	0.015	−0.670
R ²	0.552			0.471		
F(df)	72.863 (4, 237)**			52.820 (4, 237)**		
<i>Step 2</i>						
Disease activity × Resilience	−0.006†	0.003	−0.086	−0.010*	0.004	−0.125
R ²	0.558			0.486		
ΔR^2	0.007			0.014		
$\Delta F(df)$	3.608 (1, 236)†			6.586 (1, 236)*		

Note. * $p < .05$; ** $p < .01$; † $p < .10$.

low ($b = 0.193, p = .004$) and average ($b = 0.104, p = .023$) resilience levels. In contrast, this association was not significant among highly resilient individuals ($b = 0.016, p = .803$).

Concerning anxiety (Model 2), resilience was inversely associated with anxiety scores in Step 1 ($\beta = -0.670, p < .001$), mirroring the pattern observed for depression. Gender was positively associated with anxiety symptoms ($b = -1.157, p = .009$), with females reporting higher rates of anxiety symptoms than males. In contrast, disease severity and age did not show significant unique contributions. Overall, the predictors entered in Step 1 accounted for 49 % of the variance in HADS–Anxiety scores ($p < .001$). Of interest, although the main effect of CD severity was not significant in Step 1, its relationship with anxiety differed as a function of resilience, as indicated by the significant interaction observed in Step 2 ($\beta = -0.125, \Delta R^2 = 0.014, p = .011$). As shown by simple slope analyses, the association between disease activity and anxiety did not reach statistical significance at low ($b = 0.149, p = .070$), average ($b = 0.002, p = .964$), or high ($b = -0.144, p = .066$) levels of resilience. Nevertheless, the observed pattern, showing a positive association only at low levels of resilience, may suggest a potential buffering effect, with less resilient individuals being more susceptible to anxiety symptoms in the face of disease activity.

3.3. Associations between disease severity, resilience and symptoms of depression and anxiety in ulcerative colitis

Results of the moderated regression analyses for UC patients are reported in.

Table 3. In Model 1, resilience ($\beta = -0.595, p < .001$) and age ($\beta = 0.156, p = .005$) were significantly associated with depression scores in Step 1, whereas the unique effects of disease activity and gender were not significant. Together, the predictors accounted for 37 % of the variance in HADS– Depression scores ($p < .001$). The interaction term entered in Step 2 was not significant ($\beta = 0.029, \Delta R^2 = 0.001, p = .598$).

In model 2, both gender ($b = -1.426, p = .007$) and resilience ($\beta =$

$-0.486, p < .001$) were significantly associated with anxiety, with higher symptoms level reported by female participants and those with lower resilience. Disease severity and age were not significantly associated with anxiety ($R^2 = 0.321, p < .001$). No significant interaction effect was observed in Step 2 ($\Delta R^2 = 0.000, p = .967$).

4. Discussion

The present study aimed to examine the beneficial role of psychological resilience in the symptoms of depression and anxiety in the IBD patient population. The study focused on two groups of adult patients with CD and UC, respectively. To the best of our knowledge, this is the first study to investigate the protective effect of resilience in this specific population.

Table 3

Hierarchical moderated regression analyses predicting HADS scores in UC patients.

Predictors	Model 1 (Depression)			Model 2 (Anxiety)		
	<i>b</i>	<i>SE</i>	β	<i>b</i>	<i>SE</i>	β
<i>Step 1</i>						
Gender	−0.531	0.425	−0.068	−1.426**	0.522	−0.157
Age	0.041**	0.014	0.156	−0.028	0.018	−0.090
Disease activity	0.139	0.087	0.088	0.165	0.106	0.089
Resilience	−0.190**	0.018	−0.595	−0.182**	0.022	−0.486
R ²	0.380			0.321		
$\Delta F(df)$	32.264 (4, 211)			24.960 (4, 211)**		
<i>Step 2</i>						
Disease activity × Resilience	0.004	0.007	0.029	−0.000	0.009	−0.002
R ²	0.380			0.321		
ΔR^2	0.001			0.000		
$\Delta F(df)$	0.279 (1,210)			0.002 (1, 210)		

Note. * $p < .05$; ** $p < .01$.

A first finding of the study was that CD patients with higher HBI scores reported more depressive symptoms compared to those with lower disease activity levels. This suggests that active disease may act as a potential risk factor for depression, consistent with prior studies highlighting associations between disease activity and depression in IBD patients [3].

Inflammatory bowel diseases are lifelong conditions characterized by a relapsing-remitting course, with relatively low levels of clinical response rate to treatments [27]. This potentially debilitating disease is often accompanied by several concerns and worries that can easily explain the psychological distress observed in IBD patients [3,5]. Additionally, patients affected by CD may experience symptoms of depression via the gut-brain axis, with serotonin as a key neurotransmitter in both the enteric and the central nervous system [27]. Indeed, the alterations in gastrointestinal function frequently occur together with central nervous system disorders [28]. Similarly, gastrointestinal symptoms are commonly associated with psychological symptoms and psychiatric diagnoses [29]. Brain imaging studies have highlighted these reciprocal interactions, showing that gut stimuli can trigger key brain regions involved in emotion regulation [30]. These findings highlight the distinctive nature of IBD among chronic diseases, where the psychological burden is not only reactive to illness stressors, but also intrinsically tied to biological mechanisms of inflammation, microbiota, and neuroimmune signaling.

Symptoms of anxiety, by contrast, were not significantly associated with CD disease activity. This finding, though unexpected, is consistent with a recent study showing that disease activity was positively related to depression but not to anxiety in a sample of CD patients [31]. It is also possible that anxiety symptoms in IBD are more trait-like, or influenced by anticipatory and contextual factors not fully captured by disease activity indices. Moreover, the instruments used (e.g., HADS) measure general psychological distress and not gut-specific anxiety, limiting interpretability in a brain-gut context.

As a further finding, the present study revealed that CD patients with low resilience levels reported more depressive symptoms than those with high resilience. This result aligns with prior research in the general population, which demonstrated the promotive role of resilience in reducing both the frequency and severity of depressive symptoms [32]. Resilience was also significantly associated with lower anxiety symptoms, corroborating evidence from prior studies of IBD patients [14]. Together, these results suggest that resilience acts as a promotive factor by reducing vulnerability to emotional distress in CD patients.

Of particular interest, disease severity was more strongly associated with higher levels of depression and anxiety symptoms in patients with low resilience compared to those with high resilience.

Although these differences were small and not always significant, the overall pattern of results may underscore the protective role of resilience against the adverse psychological impact of CD. These findings align with previous studies on resilience in chronic illness [16]. They support the notion that resilience is not only a promotive asset but also a buffer that can attenuate the influence of disease-related risk factors. The implication is clinically relevant: targeting resilience through structured interventions may reduce psychiatric morbidity and enhance quality of life in IBD.

In UC patients, higher resilience was similarly associated with fewer symptoms of depression and anxiety, further supporting its promotive role for mental health in physical illness contexts [33]. Similarly, a previous study revealed that resilience is inversely associated with perceived stress in UC patients, which, in turn, leads to increased anxiety and depression [34]. In light of this, the hypothalamic-pituitary-adrenal (HPA) axis likely plays a key role in this relationship. Stress-induced HPA axis dysregulation can exacerbate gastrointestinal inflammation, thereby compounding psychological distress and further influencing disease activity [35]. While resilience offers protection against this mental strain, more research is needed to explore its interaction with the HPA axis over time and its broader impact on IBD prognosis [13,14].

Likely, UC patients with higher resilience may build better stress-related coping strategies, thus preventing the development of depression and anxiety, two psychological disorders that have been associated with the clinical course of UC [3]. Nevertheless, the main effect of UC disease activity on both anxiety and depression was found to be nonsignificant. The interaction between resilience and disease activity was also absent. That is, no significant differences were found between high and low resilience in the relationship between UC activity and psychological distress. A potential explanation is that UC may result in a less severe burden of disease. Earlier studies have indeed reported that patients with CD are more vulnerable to psychological disorders compared to UC patients [36].

This study provides new understanding of how the gut-brain connection, mental strength, and IBD are related and it looks at how psychological resilience can help protect against mental health issues like depression and anxiety in people with IBD symptoms. It differs from previous studies by looking at how these factors work together instead of just focusing on individual body processes. This research contributes to a growing body of knowledge on the close ties between mental health and chronic illness management, indicating that the integration of psychological resilience into patient care may be promising. However, we acknowledge that the cross-sectional design significantly limits our ability to draw definitive conclusions about the causal direction of observed effects. Thus, longitudinal studies are essential to confirm the actual capacity of resilience to influence the temporal progression of psychological symptoms in IBD and further clarify the uniqueness and clinical relevance of these associations specifically within this disease context. The idea that resilience can be more than just a fixed quality, but something that can be developed to help improve patient outcomes, is a suggestion for future long-term studies to confirm.

This study has some limitations. First, in examining the effect of IBD severity on symptoms of depression and anxiety, we did not take into account all possible clinically relevant factors, such as disease duration and the history or effectiveness of medical interventions. These elements could influence the relationship between IBD severity and psychological distress. Also, the inclusion of IBD outpatients may limit the generalizability of our findings to those with more severe disease activity.

Notably, our participants were not selected based on a pre-existing diagnosis of anxiety or depression, aiming for a more generalizable understanding of the relationship between resilience and mental health outcomes in IBD patients. The study avoids potential selection bias and reflects a real-world scenario where patients may experience a range of mental symptoms that are not necessarily clinically diagnosed, but are still impactful. However, this might have attenuated the strength of the relationships among the variables under study.

Lastly, our reliance on self-reported measures for depression and anxiety, though widely used and valuable for large-scale screening, may not capture the clinical nuances that structured psychiatric interviews would provide. Future studies might consider incorporating clinical evaluations to provide a more comprehensive assessment of these complex psychological constructs.

This study focuses on anxiety and depression as indices of psychological discomfort, but resilient outcomes are not solely defined by their absence. Positive indicators, such as well-being, psychological growth, and coping skills, are also central to resilience. Future research should examine these aspects to provide a more holistic understanding of resilience in chronic illnesses.

Despite these limitations, findings from this study provide important insights into the promotive and protective effects of resilience as a factor that allows IBD patients to better cope with the unpredictable course of the disease. They have relevant clinical implications, suggesting the importance of implementing psychotherapeutic programs in order to promote resilience among IBD patients. Identifying individuals with low resilience may allow for individualized intervention to prevent or reduce the risk of negative psychological outcomes associated with IBD, such as depression and anxiety. In this regard, earlier studies have shown the

efficacy of several resilience trainings [37].

Longitudinal studies are needed to gain more insight into the protective role of resilience in preventing symptoms of anxiety and depression in a long-term perspective. We encourage scholars and clinicians to further address these important issues in future works.

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Author contribution

Daniele Ferrarese contributed equally to the conceptualization of the study and participated in reviewing and editing the manuscript. Michele Vecchione played a leading role in the methodological design, contributed equally to the conceptualization and formal analysis, and was also actively involved in reviewing and editing the manuscript. Giorgia Spagnolo provided supporting input to the formal analysis and contributed equally to the investigation. Antonio Mirijello also contributed in a supporting role to the formal analysis. Federica Di Vincenzo, Daniela Belella, Giovanni Camardese, Antonio Maria D'Onofrio, and Vincenzina Mora equally contributed to the investigation. Daniele Napolitano, Giovanni Cammarota, Franco Scaldaferrri, and Daniela Pia Rosaria Chieffo contributed equally to data curation and to the preparation of the original draft of the manuscript. Antonio Gasbarrini and Tommaso Dionisi provided equal contributions to validation and supervision, with Dionisi also involved in reviewing and editing the manuscript. Giovanni Addolorato led the supervision and project administration, contributed to validation, and participated equally in the review and editing of the manuscript. All authors have read and approved the final version of the manuscript.

Declaration of competing interest

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References

- [1] D.A. Gomez, M. Ahmad-Waqar, M.J. Brookes, A. Kumar, IBD-related mental health disorders: where do we go from here? *Frontline Gastroenterol.* 14 (6) (2023) 512–520, <https://doi.org/10.1136/flgastro-2023-102403>.
- [2] F. Farokhyar, J.K. Marshall, B. Easterbrook, E.J. Irvine, Functional gastrointestinal disorders and mood disorders in patients with inactive inflammatory bowel disease: prevalence and impact on health, *Inflamm. Bowel Dis.* 12 (1) (2006) 38–46, <https://doi.org/10.1097/01.mib.0000195391.49762.89>.
- [3] R. Neuendorf, A. Harding, N. Stello, D. Hanes, H. Wahbeh, Depression and anxiety in patients with Inflammatory Bowel Disease: A systematic review, *J. Psychosom. Res.* 87 (2016) 70–80, <https://doi.org/10.1016/j.jpsychores.2016.06.001>.
- [4] T.H. Taft, L. Keefer, A systematic review of disease-related stigmatization in patients living with inflammatory bowel disease, *Clin. Exp. Gastroenterol.* 9 (2016) 49–58, <https://doi.org/10.2147/CEG.S83533>.
- [5] A.J. Ferrari, F.J. Charlson, R.E. Norman, et al., Burden of depressive disorders by country, sex, age, and year: findings from the global burden of disease study 2010, *PLoS Med.* 10 (11) (2013) e1001547, <https://doi.org/10.1371/journal.pmed.1001547>.
- [6] G. Byrne, G. Rosenfeld, Y. Leung, et al., Prevalence of Anxiety and Depression in Patients with Inflammatory Bowel Disease, *Can J Gastroenterol Hepatol.* 2017 (2017) 6496727, <https://doi.org/10.1155/2017/6496727>.
- [7] E.J.L. Coley, E.A. Mayer, V. Osadchiv, et al., Early life adversity predicts brain-gut alterations associated with increased stress and mood, *Neurobiol. Stress.* 15 (2021) 100348, <https://doi.org/10.1016/j.yynstr.2021.100348>.
- [8] G. Addolorato, A. Mirijello, C. D'Angelo, et al., State and trait anxiety and depression in patients affected by gastrointestinal diseases: psychometric evaluation of 1641 patients referred to an internal medicine outpatient setting, *Int. J. Clin. Pract.* 62 (7) (2008) 1063–1069, <https://doi.org/10.1111/j.1742-1241.2008.01763.x>.
- [9] S.R. Knowles, S.I. Cook, D. Tribbick, Relationship between health status, illness perceptions, coping strategies and psychological morbidity: a preliminary study with IBD stoma patients, *J. Crohns Colitis.* 7 (10) (2013) e471–e478, <https://doi.org/10.1016/j.crohns.2013.02.022>.
- [10] K.L. Kumpfer, Factors and processes contributing to resilience, in: M.D. Glantz, J. L. Johnson (Eds.), *Resilience and Development*, Springer, 2002, pp. 179–224.
- [11] G.M. Kim, J.Y. Lim, E.J. Kim, S.M. Park, Resilience of patients with chronic diseases: A systematic review, *Health Soc. Care Community.* 27 (4) (2019) 797–807, <https://doi.org/10.1111/hsc.12620>.
- [12] A.E. M'Koma, Inflammatory bowel disease: an expanding global health problem, *Clin. Med. Insights Gastroenterol.* 6 (2013) 33–47, <https://doi.org/10.4137/CGast.S12731>.
- [13] P. Sehgal, R.C. Ungaro, C. Foltz, B. Iacoviello, M.C. Dubinsky, L. Keefer, High Levels of Psychological Resilience Associated With Less Disease Activity, Better Quality of Life, and Fewer Surgeries in Inflammatory Bowel Disease, *Inflamm. Bowel Dis.* 27 (6) (2021) 791–796, <https://doi.org/10.1093/ibd/izaa196>.
- [14] A. Philippou, P. Sehgal, R.C. Ungaro, et al., High Levels of Psychological Resilience Are Associated With Decreased Anxiety in Inflammatory Bowel Disease, *Inflamm. Bowel Dis.* 28 (6) (2022) 888–894, <https://doi.org/10.1093/ibd/izab200>.
- [15] M.A. Zimmerman, S.A. Stoddard, A.B. Eisman, C.H. Caldwell, S.M. Aiyer, A. Miller, Adolescent Resilience: Promotive Factors That Inform Prevention, *Child Dev. Perspect.* 7 (4) (2013), <https://doi.org/10.1111/cdep.12042>.
- [16] C. Traummüller, R. Stefitz, M. Schneider, A. Schwerdtfeger, Resilience moderates the relationship between the psychological impact of COVID-19 and anxiety, *Psychol. Health Med.* 28 (7) (2023) 1861–1872, <https://doi.org/10.1080/13548506.2021.1955137>.
- [17] L. Li, Y. Hou, F. Kang, X. Wei, The mediating and moderating roles of resilience in the relationship between anxiety, depression, and post-traumatic growth among breast cancer patients based on structural equation modeling: An observational study, *Medicine (Baltimore)* 99 (50) (2020) e23273, <https://doi.org/10.1097/MD.00000000000023273>.
- [18] M. Ungar, L. Theron, Resilience and mental health: how multisystemic processes contribute to positive outcomes, *Lancet Psychiatry* 7 (5) (2020) 441–448, [https://doi.org/10.1016/S22150366\(19\)30434-1](https://doi.org/10.1016/S22150366(19)30434-1).
- [19] S. Kuldas, M. Poody, Neither Resiliency-Trait nor Resilience-State: Transactional Resiliency/e, *Youth Soc.* 54 (8) (2022) 1352–1376, <https://doi.org/10.1177/0044118X211029309>.
- [20] M.A. Montpetit, C.S. Bergeman, P.R. Deboeck, S.S. Tiberio, S.M. Boker, Resilience-as-process: negative affect, stress, and coupled dynamical systems, *Psychol. Aging* 25 (3) (2010) 631–640, <https://doi.org/10.1037/a0019268>.
- [21] K.M. Connor, J.R. Davidson, Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC), *Depress. Anxiety* 18 (2) (2003) 76–82, <https://doi.org/10.1002/da.10113>.
- [22] V.B. Arias González, M.T. Crespo Sierra, B. Arias Martínez, A. Martínez-Molina, F. P. Ponce, An in-depth psychometric analysis of the Connor-Davidson Resilience Scale: calibration with Rasch-Andrich model, *Health Qual. Life Outcomes* 13 (2015) 154, <https://doi.org/10.1186/s12955015-0345-y>.
- [23] A.S. Zigmond, R.P. Snaith, The hospital anxiety and depression scale, *Acta Psychiatr. Scand.* 67 (6) (1983) 361–370, <https://doi.org/10.1111/j.1600-0447.1983.tb09716.x>.
- [24] R.F. Harvey, J.M. Bradshaw, A simple index of Crohn's-disease activity, *Lancet* 1 (8167) (1980) 514, [https://doi.org/10.1016/s0140-6736\(80\)92767-1](https://doi.org/10.1016/s0140-6736(80)92767-1).
- [25] J.D. Lewis, S. Chuai, L. Nessel, G.R. Lichtenstein, F.N. Aberra, J.H. Ellenberg, Use of the noninvasive components of the Mayo score to assess clinical response in ulcerative colitis, *Inflamm. Bowel Dis.* 14 (12) (2008) 1660–1666, <https://doi.org/10.1002/ibd.20520>.
- [26] L.S. Aiken, S.G. West, *Multiple Regression: Testing and Interpreting Interactions*, Sage Publications, 1991.
- [27] S. Singh, M.H. Murad, M. Fumery, P.S. Dulai, W.J. Sandborn, First- and Second-Line Pharmacotherapies for Patients With Moderate to Severely Active Ulcerative Colitis: An Updated Network Meta-Analysis, *Clin. Gastroenterol. Hepatol.* 18 (10) (2020) 2179–2191.e6, <https://doi.org/10.1016/j.cgh.2020.01.008>.
- [28] C. Bove, R.A. Travagli, Neurophysiology of the brain stem in Parkinson's disease, *J. Neurophysiol.* 121 (5) (2019) 1856–1864, <https://doi.org/10.1152/jn.00056.2019>.
- [29] A.C. Ford, B.E. Lacy, L.A. Harris, E.M.M. Quigley, P. Moayyedi, Effect of Antidepressants and Psychological Therapies in Irritable Bowel Syndrome: An Updated Systematic Review and Meta-Analysis, *Am. J. Gastroenterol.* 114 (1) (2019) 21–39, <https://doi.org/10.1038/s41395-018-02225>.
- [30] E.A. Mayer, Gut feelings: the emerging biology of gut-brain communication, *Nat. Rev. Neurosci.* 12 (8) (2011) 453–466, <https://doi.org/10.1038/nrn3071>.
- [31] I. Banovic, L. Montreuil, M. Derrey-Bunel, et al., Toward Further Understanding of Crohn's Disease-Related Fatigue: The Role of Depression and Emotional Processing, *Front. Psychol.* 11 (2020) 703, <https://doi.org/10.3389/fpsyg.2020.00703>.
- [32] M.P. Wermelinger Ávila, A.L. Lucchetti, G. Lucchetti, Association between depression and resilience in older adults: a systematic review and meta-analysis,

- Int. J. Geriatr. Psychiatr. 32 (3) (2017) 237–246, <https://doi.org/10.1002/gps.4619>.
- [33] F. Färber, J. Rosendahl, The Association Between Resilience and Mental Health in the Somatically Ill, *Dtsch. Arztebl. Int.* 115 (38) (2018) 621–627, <https://doi.org/10.3238/arztebl.2018.0621>.
- [34] W. Liu, J. Wang, H. Wang, X.Y. Chen, J.S. Li, *Zhonghua Nei Ke Za Zhi*. 57 (2) (2018) 107111, <https://doi.org/10.3760/cma.j.issn.0578-1426.2018.02.005>.
- [35] S. González Delgado, I. Garza-Veloz, F. Trejo-Vazquez, M.L. Martinez-Fierro, Interplay between Serotonin, Immune Response, and Intestinal Dysbiosis in Inflammatory Bowel Disease, *Int. J. Mol. Sci.* 23 (24) (2022) 15632, <https://doi.org/10.3390/ijms232415632>.
- [36] T.H. Taft, A. Bedell, M.R. Craven, L. Guadagnoli, S. Quinton, S.B. Hanauer, Initial Assessment of Post-traumatic Stress in a US Cohort of Inflammatory Bowel Disease Patients, *Inflamm. Bowel Dis.* 25 (9) (2019) 1577–1585, <https://doi.org/10.1093/ibd/izz032>.
- [37] S. Joyce, F. Shand, J. Tighe, S.J. Laurent, R.A. Bryant, S.B. Harvey, Road to resilience: a systematic review and meta-analysis of resilience training programmes and interventions, *BMJ Open* 8 (6) (2018) e017858, <https://doi.org/10.1136/bmjopen-2017-017858>.