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Trajectories of Psychological Stress in Youth Across the First Year of Inflammatory Bowel Disease Diagnosis

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Abstract

Objective: Youth newly diagnosed with inflammatory bowel diseases (IBD) may be physically impacted by their disease and experience increased psychological stress. Stress is known to relate to greater reported IBD symptoms, but little is known about the longitudinal experience of stress and clinical symptoms of youth newly diagnosed with IBD.

Methods: Fifty-seven children ($M_{age} = 14.26$, range 8–17 years) diagnosed with IBD completed measures assessing psychological stress (PROMIS Psychological Stress Experiences), depressive symptoms (Children's Depression Inventory-2), and clinical disease symptoms (Self-Report Disease Activity) within 45 days of diagnosis and at 6-month and 1-year follow-ups. Group-based trajectory modeling was used to describe trajectory patterns of psychological stress over the first year of diagnosis and logistic regression identified predictors of group membership. Results: Two distinct groups of psychological stress trajectories were identified: 1) low prevalence over the first year of diagnosis (51%) and 2) moderate and increasing prevalence (49%). Membership in the moderate and increasing psychological stress group was associated with female sex and greater IBD symptoms at diagnosis.

Conclusion: Findings suggest roughly half of youth newly diagnosed with IBD would likely benefit from multidisciplinary assessment and intervention to promote adaptive stress management, given moderate and increasing stress levels. Future research is needed to evaluate specific intervention techniques most helpful to youth with IBD.

Keywords

Inflammatory bowel disease; stress

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Inflammatory bowel diseases (IBD, i.e., Crohn's disease [CD] and ulcerative colitis [UC]) are characterized by chronic inflammation of the gastrointestinal tract (GI). For youth (<18 years old) diagnosed with IBD, the disease-related symptoms (e.g., abdominal pain, fever, fatigue, diarrhea, hematochezia, weight loss, and growth delays) can be impactful across multiple areas of functioning (Diefenbach & Breuer, 2006; Mackner et al., 2004). Youth newly diagnosed with IBD are physically impacted by their disease symptoms and associated treatments but are also at risk for increased psychological stress as they manage the demands of an unpredictable disease with relapsing and remitting symptoms and negative consequences such as missed school and activities. It is well recognized in adult samples that higher levels of perceived stress are associated with greater reporting of IBD symptoms, including abdominal pain, frequency of liquid stools, clinical relapse, and changes in IBD symptom activity (Bernstein et al., 2010; Langhorst et al., 2013; Targownik et al., 2015). Associations between perceived stress as a potentially modifiable factor and clinical disease course, underscore the need to better understand factors impacting patients' perceived stress following IBD diagnosis. Although associations between perceived stress and clinical symptoms have been observed in adult samples, these associations need to be empirically tested in longitudinal pediatric samples to know whether perceived stress is relevant to clinical disease course in youth.

In addition to associations with clinical symptoms, perceived psychological stress may be related to increased rates of depressive symptoms observed in pediatric patients with IBD (Greenley et al., 2010; Loftus et al., 2011; Reed-Knight et al., 2017). The relationship between higher rates of perceived stress and the development, course, and exacerbation of depression is well established (Pizzagalli, 2014). Stressors characterized by a perceived lack of control and inability to escape or resolve the situation are most associated with depressive symptoms (Pizzagalli, 2014), which may have particular relevance to patients newly diagnosed with a chronic, oftentimes unpredictable illness like IBD. The relationship between perceived stress and symptoms of depression has not been well studied in pediatric samples, but in adults with UC and CD diagnosed on average 13 years, higher perceived psychological stress was associated with greater symptoms of depression and anxiety (Goodhand et al., 2012). Though not specific to patients with IBD, growing neuroscience research indicates that the adolescent brain is sensitive to stress and that variability in the development of stress processing systems in adolescence may influence increased risk of stress-related psychopathology including depression (Eiland & Romeo, 2013; Roberts & Lopez-Duran, 2019). In addition to increased incidence of depressive symptoms observed in adolescence, there are known sex differences in stress-related symptoms (e.g., depression). Female youth have reported higher levels of perceived stress compared to males, suggesting that differences in stress susceptibility may be partially responsible for differences observed in rates of depressive symptoms (Bevans et al., 2018; Roberts & Lopez-Duran, 2019).

Prior literature has described the associations between perceived stress, clinical symptoms, and stress-related psychopathology in adult patients with IBD although gaps remain in the longitudinal experience of stress shortly following diagnosis and whether these findings are relevant to pediatric samples. Therefore, investigations are needed first to describe pediatric patients' experience of psychological stress, and to test the extent to which experiences of stress are related to relevant demographic factors and clinical symptoms. The current study

aimed to (1) test whether distinct classes of perceived stress trajectories could be identified in youth across the first 12-months of diagnosis with IBD and (2) identify the role of sex, clinical symptoms, and symptoms of depression at the time of diagnosis in predicting psychological stress trajectory group membership. It was hypothesized that female sex, greater clinical symptoms, and symptoms of depression would be predictive of membership in trajectories with elevated psychological stress.

Methods

Participants

Questionnaire data from fifty-seven children and adolescents recently diagnosed with IBD, and their caregivers were included in the current study based on the following inclusion criteria: (1) diagnosis with biopsy-confirmed IBD within the last 45 days, (2) child ages 8–17 years, (3) English language proficiency, and (4) accompanied by at least one caregiver to appointment. Exclusion criteria included documented history or caregiver reported (1) developmental disorder or non-verbal presentation impeding independent completion of questionnaires or (2) a chronic illness diagnosis in addition to IBD that could reasonably contribute to greater child distress or functional disability. Eighty-two caregiver-child dyads were sequentially approached to participate, of which 16 caregivers declined. An additional 9 dyads met inclusion criteria for recent diagnoses with IBD but were not eligible for the study due to remaining inclusion/exclusion criteria (i.e., caregiver did not have rights to consent for research [$n = 1$], caregiver did not speak English fluently [$n = 3$], child had history of additional complex medical condition(s) [$n = 3$], and child had developmental delay or cognitive impairment impeding completion of questionnaires [$n = 2$]). With the exception of caregiver-reported demographic data, only child reported data were utilized in this investigation.

Procedures

Study procedures were Institutional Review Board approved and part of a larger longitudinal investigation into psychosocial and physical functioning in youth with new IBD diagnoses. Informed consent and assent were obtained in writing from all participants. Research staff sequentially approached families at their outpatient gastroenterology clinic appointments and invited eligible youth and caregivers to complete questionnaires and physiological reactivity tasks within 45 days of the child's IBD diagnosis (Time 1). Families were also invited to complete questionnaires at 6-month (Time 2) and one-year (Time 3) follow-up assessments via in-person clinic visits, if a previously scheduled appointment aligned with research timeline, or via email or phone-call communication. Participants provided informed consent and completed questionnaires through REDCap, a HIPAA compliant data collection software (Harris et al., 2019) and were compensated for their time. Only questionnaire data are utilized in the present study. Trained research staff conducted chart review to extract physician-report of clinical disease activity at Time 1.

Measures

Demographics.—Caregivers completed a standard demographic questionnaire at Time 1 assessing caregiver (e.g., relationship to child, age, marital status, race/ethnicity, education,

income) and child characteristics (e.g., age, sex, diagnosis, race/ethnicity). Pre-determined response options were provided, as well as an “other” option followed by free response when indicated.

Psychological Stress

Psychological stress was measured at Time 1, Time 2, and Time 3 using the child-report versions of the Patient-Reported Outcomes Measurement Information System (PROMIS)—Psychological Stress Experiences short form, a sensitive and efficient measure of youth’s psychological stress, characterized by stress-related disruptions to cognitive processes, feeling overwhelmed, and lack of perceived control (Bevans et al., 2018). Factor analyses from the measure’s validation demonstrated that symptoms of psychological stress can be distinguished from sadness, nervousness, and worry and that youth can reliably report on their experiences of psychological stress (Bevans et al., 2018). This scale consists of 8 items examining stress-related thoughts and feelings (e.g., *I felt stressed; I felt unable to manage things in my life*) over the past 7 days. All items are summed together to yield a total score, which is then converted to a standardized T-score.

Depressive symptoms

Time 1 and Time 3 depressive symptoms were measured using the Children’s Depression Inventory-2 (CDI-2) (Kovacs, 2011). The CDI-2 is a 28-item child-report measure of physiological, behavioral, and emotional symptoms of depression. Each item contains three statements and children were asked to endorse one statement from each group of sentences that best applied to them over the past two weeks (e.g., *I am sad once in a while; I am sad many times; I am sad all the time*). Items are summed together to yield a total symptom severity score and converted to a standardized T-score.

Clinical Disease Activity

Physician-report of clinical disease activity at Time 1 was obtained via the Physicians Global Assessment (PGA), a global measure of disease severity completed at each medical appointment using clinical symptoms, examination, and labs as part of this site’s participation in ImproveCareNow (Crandall et al., 2011). Participants received a rating of quiescent (i.e., inactive), mild, moderate, or severe disease activity. At Time 1, child-reported symptoms of IBD were also obtained using the Self-Report Disease Activity (SRDA; Cushman et al., 2020). Participants rated abdominal pain frequency and intensity in the past week, number and type of bowel movements (i.e., solid, mushy, diarrhea), presence of nocturnal diarrhea, blood in stool, and impairment in daily activities. Higher SRDA scores indicate more clinical symptoms.

Analytic Plan

Data were analyzed using SAS 9.4 (Cary, NC) with two-tailed p-values < 0.05 considered statistically significant. To describe trajectory patterns of psychological stress across the first 12-months of diagnosis with IBD, group-based trajectory modeling via the TRAJ procedure was used (Jones & Nagin, 2007; Nagin & Odgers, 2010). We examined whether 2, 3, or 4 groups fit the data best, allowing linear, quadratic, and cubic terms for time in each group.

Starting with the least significant term in each group, higher order terms were eliminated one by one. Bayes Information Criterion (BIC) was used to select the number of distinct trajectory groups with the model producing the lowest BIC used for subsequent analyses. Next, logistic regression was used to identify predictors of psychological stress trajectory group membership while considering the potential effects of other variables. Selection of variables for inclusion in the logistic regression model was based on those found to be significantly, independently associated ($p < .05$) with group membership using mean difference (e.g., group differences in continuous variables, such as child age or reported symptoms) and Chi-square analyses (e.g., group differences in dichotomous variables, such as CD vs. UC diagnosis or child sex).

Results

Time 1 Characteristics

Table 1 displays Time 1 characteristics (i.e., characteristics at diagnosis) for the 57 youth with IBD. At Time 1, they were on average 14.26 years old ($SD = 2.35$) and had been diagnosed with IBD on average 26.6 days prior ($SD = 11.6$). Fifty-four percent of children were female, and the majority were diagnosed with Crohn's disease (79%). Fifty-seven youth participated at Time 1, 39 at Time 2, and 35 at Time 3, resulting in follow-up participation rates of 68% and 61%, respectively. Common reasons for attrition included inability to contact families for follow-up or disinterest in continuing to participate in the study. There were no significant differences in race or study variables across those completing all time points or those dropping out. Full sample characteristics and descriptive statistics for primary study variables are presented in Table 1.

Prevalence of Psychological Stress

Figure 1 graphically displays prevalence of psychological stress by assessment point for the entire sample. All mean T-scores fell in the average range.

Trajectories of Psychological Stress

Two distinct groups with linear trajectories for psychological stress across the first 12-months of diagnosis with IBD were identified within the sample (Figure 2). The two groups include 1) a group with a low prevalence of psychological stress over the first year of diagnosis (51%; Low Psychological Stress) and 2) a group with a moderate and increasing prevalence (49%; Moderate and Increasing Psychological Stress) over the first year of diagnosis. There was insufficient evidence to conclude that the slope of either group's linear trajectory was statistically significant using time as the only predictor, indicating no significant change across time in psychological stress for either group. However, changes in psychological stress symptoms for group 2 (Moderate and Increasing Psychological Stress) may represent a clinically meaningful increase in reported symptoms.

The groups differed significantly on child sex, such that a greater proportion of females were in the Moderate and Increasing Psychological Stress group ($n = 20$ females, $n = 8$ males) compared to the Low Psychological Stress group ($n = 11$ females, $n = 18$ males; $p = 0.01$), as well as child-reported disease symptoms (SRDA) of IBD at Time 1, with those in the

Moderate and Increasing Psychological Stress group reporting greater IBD symptoms ($M=14.44$, $SD=10.13$) compared to those in the Low Psychological Stress group ($M=5.86$, $SD=5.68$, $t=3.95$, $p<0.01$). The groups also differed on child-reported depressive symptoms at Time 1, with those in the Moderate and Increasing Psychological Stress group reporting greater levels of depressive symptoms ($M=59.74$, $SD=12.85$) compared to those in the Low Psychological Stress group ($M=48.14$, $SD=5.88$; $t=-4.39$, $p<.001$). The groups did not differ on child or parent age at Time 1, diagnosis of CD or UC, family income, child race, or PGA at Time 1 ($ps>0.05$).

Predictors of Psychological Stress Trajectories

Logistic regression was used to identify predictors of psychological stress trajectory group membership, specifically the likelihood of membership in the Moderate and Increasing Psychological Stress group (Table 2). The overall model was significant ($\chi^2=28.61$, $p<.0001$), and child sex and self-reported disease symptoms at Time 1 emerged as significant predictors of psychological stress trajectory group membership. Girls were more likely to be classified in the Moderate and Increasing Psychological Stress group ($n=20$ females, $n=8$ males) as compared to the Low Psychological Stress group ($n=11$ females, $n=18$ males; OR = 5.75, 95% CI: 1.20, 27.63). Higher levels of self-reported disease symptoms were also associated with higher odds of being classified in the Moderate and Increasing Psychological Stress group (OR = 1.15, 95% CI: 1.02, 1.31). Age and Time 1 depressive symptoms were not significant predictors of psychological stress trajectory group membership when included in the full model.

Discussion

The current study expands upon prior cross-sectional research by examining the longitudinal experience of psychological stress and its association with clinical disease symptoms among youth newly diagnosed with IBD. Two distinct groups emerged capturing clusters of individuals following similar trajectories of psychological stress symptoms over the first year of diagnosis. Approximately half of participants were characterized by consistently low psychological stress over one year while half were characterized by moderate and increasing psychological stress. In examining probability of trajectory membership with other sociodemographic or clinical symptoms, child sex and Time 1 child-reported disease activity were identified as clinically relevant factors. Findings demonstrate that the two clusters of individuals identified via trajectory analyses are associated with measurable differences and that those at greatest risk for experiencing psychological stress over the first year of diagnosis may be identified by these clinically relevant variables.

Psychological stress and stress more broadly have been most frequently investigated in adult patients with IBD, while pediatric investigations have focused more heavily on depression; however, these constructs are distinct. This is of particular importance given the clear association between stress and IBD disease activity and flares (Sun et al., 2019). A recent study among adolescents diagnosed with IBD 0 to 12 years prior to study participation identified several IBD-specific disease-related stressors, which were subsequently associated with symptoms and flares (Stellway et al., 2022). Though few investigations have studied

newly diagnosed patients in particular, the specific period leading up to and following a new diagnosis of IBD may be a time of particular stress, given the uncertainty of diagnostic testing and adjustment to a new diagnosis and medical regimen. In our newly diagnosed cohort, approximately half of participants followed a developmental trajectory of moderate and increasing psychological stress across the first year of diagnosis with IBD. While it is reassuring that not all youth newly diagnosed with IBD experienced elevated psychological stress, findings suggest that about half of patients newly diagnosed would likely benefit from assessment and intervention to promote adaptive stress management.

Female sex and higher child self-reported disease activity at diagnosis were associated with membership in the moderate and increasing psychological stress trajectory group. This is consistent with prior research conducted in pediatric IBD demonstrating higher IBD-specific stress among females compared to males and among those currently symptomatic or experiencing a flare (Stellway et al., 2022). Caregivers of youth with active disease states have also reported greater numbers of stressful life events during the past year compared to caregivers of youth in disease remission (Giannakopoulos et al., 2016). Though not specific to IBD, female adolescents have been shown to report higher perceptions of stress intensity and greater numbers of stressful life events compared to males (Jose & Ratcliffe, 2004). Findings from the current study are consistent with past research documenting sex differences in the experience of stress and stressful life events for healthy adolescents and those with IBD and extend these findings by demonstrating that female patients may be at greatest risk for psychological stress following diagnosis with IBD. Notably, depression symptoms at diagnosis and child age were not associated with trajectory group membership. Findings are consistent with a recent study finding that, although related, the experience of IBD-specific distress was distinct from both anxiety and depression (Stellway et al., 2022). Results also suggest that in conceptualizing patients' experiences of psychological stress, sex and self-reported disease activity may be the most relevant risk factors even in the context of measured depressive symptoms. Future research is needed to further characterize this association, as it is possible that the present study was underpowered to detect significant associations between symptoms of depression and stress.

The current study presents several clinical implications. First, practitioners working with pediatric patients with IBD should be aware that psychological stress may be present for at least half of newly diagnosed patients and that these symptoms do not seem to resolve with the passage of time alone across the first year of diagnosis. When considering which patients may be most at risk, females and those reporting higher levels of clinical symptoms of IBD should be considered for additional monitoring and possible intervention. Future research is needed to evaluate specific intervention techniques most relevant to patients with IBD, though youth reporting elevated levels of psychological stress may benefit from evidence-based stress management techniques including psychoeducation, diaphragmatic breathing, progressive muscle relaxation, and exercise planning (Mason et al., 2019). As symptoms of psychological stress were not found to decrease over time for the moderately stressed group, such interventions may be particularly beneficial early on in diagnosis to give patients foundational stress symptom identification and coping skills. Identifying and establishing coping skills and reinforcing their use as early as possible following diagnosis

has the potential to impact long-term IBD disease course, given the linkage between stress and disease symptoms across the lifespan (Langhorst et al., 2013; Sexton et al., 2017).

This study is not without limitations, which highlight several important future research directions. The current sample was small and recruited from one geographical region in the Southeastern United States. Multi-site collaborations across institutions serving pediatric GI patients would increase power to detect clinically and statistically significant associations between variables of interest to further elucidate predictors of psychological stress over time. Further, the current sample was predominately White and high income. Though consistent with other studies in this population, this may have contributed to lower overall stress levels in this sample. There is great need to further understand the experience of sociodemographically diverse youth with IBD, particularly for those who may experience greater life stressors resulting from systemic inequities. Further, while the present study examined child self-reported stress and symptoms, future research may seek to explore parents' own psychological stress and depressive symptoms over the first year of their child's IBD diagnosis. Additionally, while robust in identifying clusters of individuals experiencing similar trajectories of psychological stress and variables associated with group membership, these analyses are not able to identify causal relationships between variables. Thus, future research is needed to determine whether causal relationships exist between these variables, which will enhance opportunity for targeted clinical intervention within a multidisciplinary clinic setting. Additionally, it is not known whether participants were receiving any psychotherapy or medication interventions associated with stress, thus additional associations to inform clinical intervention may be identified with future examinations. Lastly, while an important expansion on cross-sectional research, the current study may not generalize to longer-term stress experiences among youth with IBD beyond one year. As such, future research may seek to examine how stress may shift or evolve long-term following diagnosis, particularly around other salient disease course periods including transition to adult healthcare.

A diagnosis with IBD can be a significant stressor for a child, and findings such as these point to the importance of providing multidisciplinary healthcare to newly diagnosed youth to address disease symptoms as well as emotional and cognitive consequences. Even aside from diagnosis with a chronic illness, adolescents in the United States are reporting increasing difficulties with symptoms of psychological stress, pointing to the need to provide particular attention and resources to those diagnosed with a chronic illness. Providers working with youth following an IBD diagnosis, particularly youth with potential risk factors for elevated stress, should consider assessing stress within the first year of diagnosis as a meaningful clinical symptom and providing brief, targeted intervention.

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Highlights

- Two stress trajectories over first year emerged: 1) low and 2) moderate/increasing.
- Moderate/increasing stress was associated with female sex and greater IBD symptoms.
- Assessment and intervention to promote adaptive stress management likely beneficial.

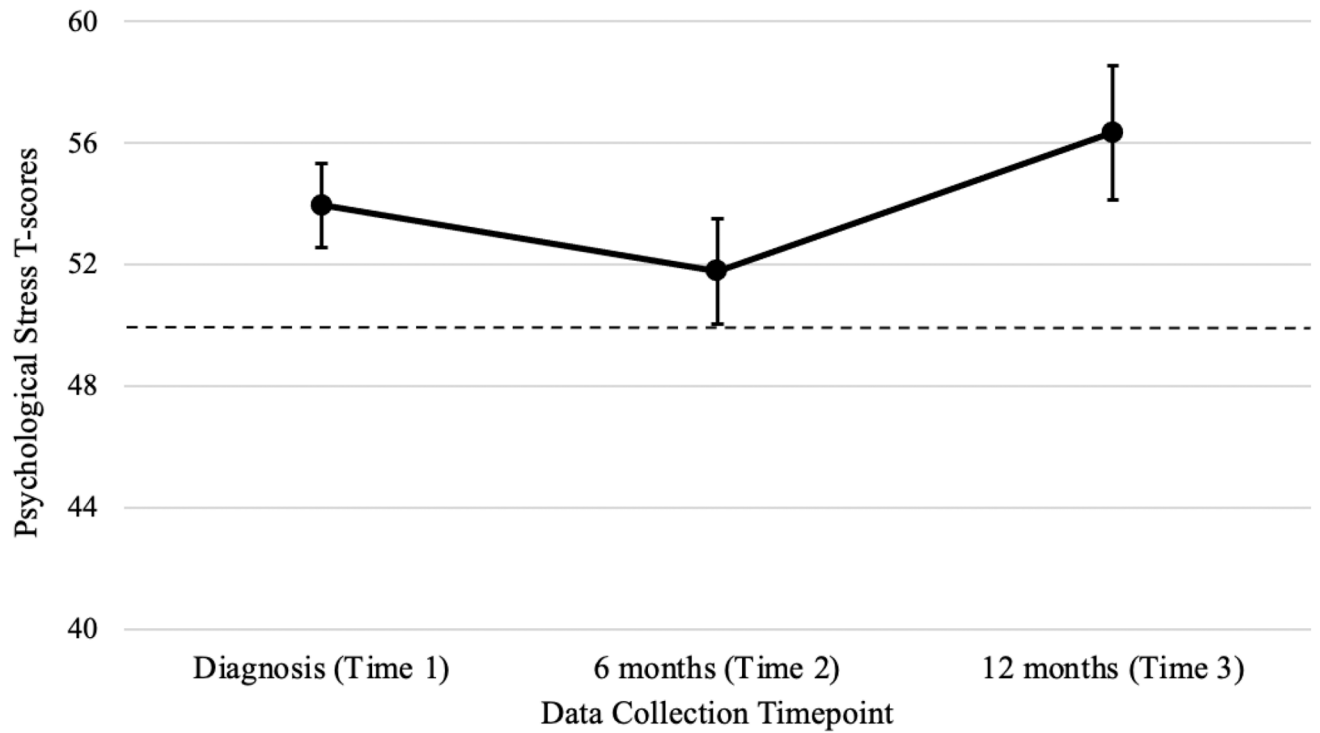


Figure 1.

Average Psychological Stress by Assessment Timepoint

Note. Psychological stress assessed via PROMIS T-scores (dashed line represents *T*-score norms $M = 50$, $SD = 10$). Error bars represent standard deviation of psychological stress by assessment timepoint.

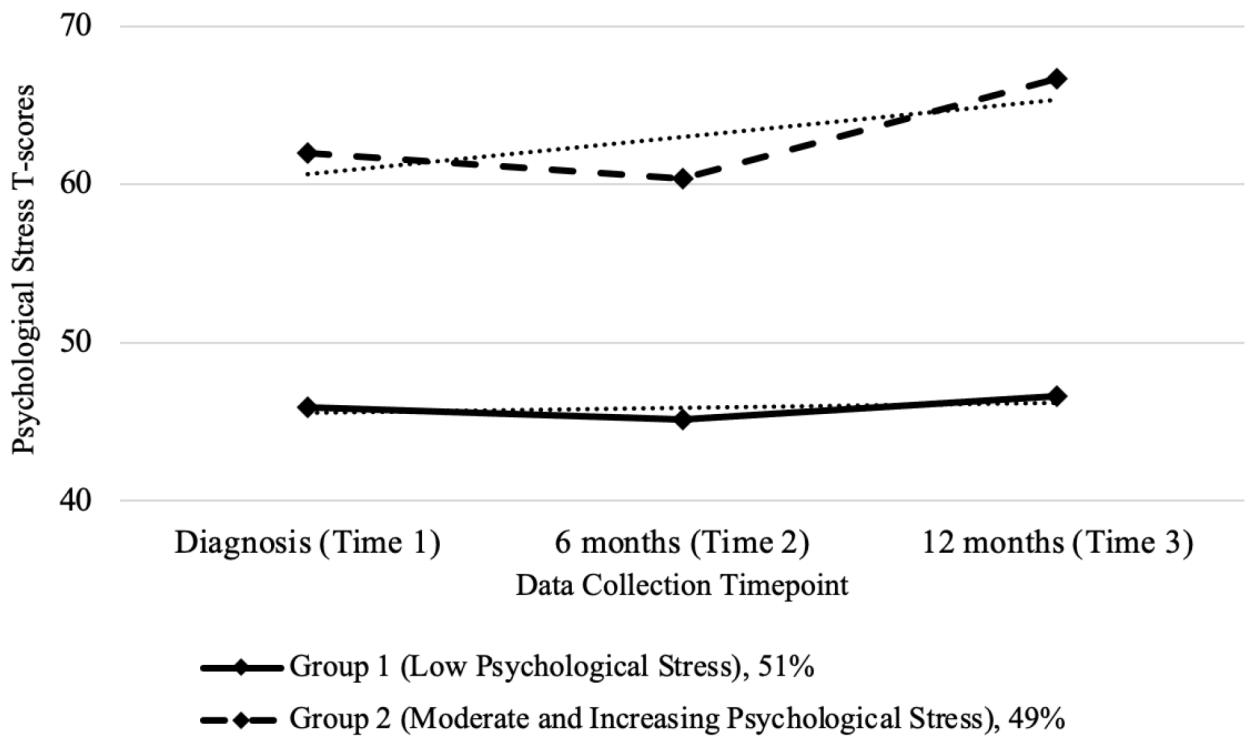


Figure 2.

Trajectory groups for psychological stress across the first year of IBD diagnosis

Note. Dotted lines indicate trajectory trendlines. Psychological stress assessed via PROMIS

T-scores (norms $M = 50$, $SD = 10$). Mean psychological stress by group and timepoint:

Moderate and Increasing Psychological Stress group (Time 1 = 61.9, Time 2 = 60.4, Time 3 = 66.7) and Low Psychological Stress group (Time 1 = 45.9, Time 2 = 45.1, Time 3 = 46.6).

Table 1.Sample characteristics ($N = 57$)

	Mean (SD) / n (%)	Range
Days since diagnosis at Time 1	26.6 (11.6)	11 – 46
Caregiver age (years)	45.21 (5.56)	30 – 57
Child age (years)	14.26 (2.35)	8.91 – 17.88
Child sex		
Female	31 (54%)	
Male	26 (46%)	
Child race/ethnicity		
White	41 (72%)	
Black/African American	11 (19%)	
Hispanic	2 (4%)	
Asian American	2 (4%)	
Missing	1 (1%)	
Child diagnosis		
Crohn's	45 (79%)	
Ulcerative colitis	10 (18%)	
Indeterminate colitis	2 (3%)	
Physician's Global Assessment		
Quiescent	21 (38%)	
Mild	24 (44%)	
Moderate	10 (18%)	
Child-reported disease symptoms at Time 1 ^a	10.26 (9.28)	0 – 40
Family income at Time 1		
Up to \$24,999	5 (9%)	
\$25,000 to \$49,999	3 (5%)	
\$50,000 to \$74,999	12 (21%)	
\$75,000 to \$99,999	7 (12%)	
\$100,000 to \$124,999	9 (16%)	
\$125,000 to \$149,999	6 (11%)	
Above \$150,000	11 (19%)	
Missing	4 (7%)	

Note. Physician's Global Assessment available for $n = 55$ participants.

^aHigher scores indicate more clinical symptoms, range 0–40

Table 2.

Summary of logistic regression analyses predicting psychological stress trajectory group membership

Predictor	β	SE β	OR (95% CI)
Age	0.22	0.16	1.25 (0.91, 1.70)
Sex (reference = female)	1.75*	0.80	5.75 (1.20, 27.63)
Self-reported disease activity (SRDA)	0.14*	0.07	1.15 (1.02, 1.31)
Depressive symptoms (CDI-2)	0.08	0.05	1.08 (0.98, 1.19)
χ^2	28.61***		

Note. The model estimated probability of membership in Group 2 (Moderate and Increasing Psychological Stress) and correctly classified 87% of cases. CDI-2 = Children's Depression Inventory, 2nd edition; CI = confidence interval; OR = odds ratio.

*
 $p < .05$.

**
 $p < .01$.

 $p < .001$.