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Parental and child coping in pediatric IBD: an analysis of the behavioral and clinical outcomes in a longitudinal cohort of children with newly diagnosed IBD

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Thesis

PARENTAL AND CHILD COPING IN PEDIATRIC IBD: AN ANALYSIS OF THE BEHAVIORAL AND CLINICAL OUTCOMES IN A LONGITUDINAL COHORT OF CHILDREN WITH NEWLY DIAGNOSED IBD

by

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DEDICATION

I would like to dedicate this work to all those who have supported me thus far: my parents, siblings, friends, and mentors.

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To Dr. Rufo and Dr. Zimmerman, thank you for your support and mentorship this past year. I appreciate all the feedback and lessons (both academic and life-related!) learned throughout our meetings.

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PARENTAL AND CHILD COPING IN PEDIATRIC IBD: AN ANALYSIS OF THE BEHAVIORAL AND CLINICAL OUTCOMES IN A LONGITUDINAL COHORT OF CHILDREN WITH NEWLY DIAGNOSED IBD

IMAN IQBAL

ABSTRACT

BACKGROUND: Chronic illness in children is highly disruptive to both the affected child and their parent(s). Recent literature largely supports the impact of psychosocial factors on the onset and progression of IBD. Our study aims to investigate how psychosocial factors involved in parental and child coping, such as anxiety or depression, may predict the clinical and psychological outcomes of children with newly diagnosed IBD. **METHODS**: We recruited and administered questionnaires to parents and children (aged 9-17) with newly diagnosed IBD. Questionnaires were administered at enrollment and at follow-up visits about one year later. The children completed four questionnaires, including IMPACT-III (measure for quality of life), SCARED (screens for anxiety), and CDI and PHQ-9 (screens for depression). The parents completed three questionnaires, including HADS (screens for anxiety and depression), PIP (assesses the burden of parental stress related to caring for an ill child), and a healthcare utilization survey (quantifies the need for medical support). Clinical data were extracted from the Boston Children's Hospital's electronic medical records to assess clinical outcomes. **RESULTS**: We recruited a total of 86 parent/child pairs. Of the 31% of children screening positive for anxiety, 61% had parents that also screened positive for anxiety ($p = 0.007$). However, the same relationship was not observed for depressed children and

their parents. Children with anxious parents reported a significantly worse quality of life than children with non-anxious parents (119.61 vs. 137.33; $p < 0.001$). Although the same mean differences were not observed for children with depressed parents, there was an association between parents that scored higher for depression and children who scored lower for quality of life ($r = -0.287$; $p < 0.010$). Quality of life scores were significantly lower in children above 12 years old than in children under 12 years old (126.6 vs 137.67; $p = 0.021$). Furthermore, children with worse disease severity (assessed by PUCAI or PCDAI scores) also reported worse quality of life. No significant associations were observed between disease severity and parental anxiety/depression or between disease severity and child anxiety/depression. Greater healthcare utilization was significantly correlated with greater parental anxiety ($r = 0.269$; $p = 0.017$) and greater parental depression scores ($r = 0.324$; $p = 0.004$). Over a one-year period, paired survey data revealed decreased parental stress, healthcare utilization, and child anxiety. There were no significant differences in parental anxiety, parental depression, or child depression, while a significant improvement was observed in child quality of life over a one-year period. **CONCLUSIONS**: Greater parental anxiety, depression, and stress correlated with worse quality of life in children with newly diagnosed IBD. Similarly, higher anxiety and depression scores in children were associated with decreased quality of life. Interestingly, this association was not seen for disease severity. While this may indicate a stronger relationship with parent and child coping and a child's behavioral outcomes rather than the child's clinical outcome, additional studies are needed, as the PUCAI and PCDAI scores for disease severity were the only measurements for clinical

outcomes. In addition, while we identified significant findings at one year, the study sample size for those who completed follow-up was relatively small. Larger studies are necessary to further investigate the longitudinal outcomes of coping in pediatric IBD. Overall, our data supports a more holistic approach to addressing the behavioral, emotional, and physical needs of both parents and children with newly diagnosed pediatric IBD.

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LIST OF ABBREVIATIONS

ASA..... Aminosalicylic Acid

BMI..... Body Mass Index

CAT/CR..... Center for Ambulatory Infusion and Therapeutics/Clinical Research

CD..... Crohn's Disease

CDI..... Children's Depression Inventory

CPT..... Calprotectin

CRP..... C-Reactive Protein

EEN..... Exclusive Enteral Nutrition

ESR..... Erythrocyte Sedimentation Rate

FLA..... Fecal Lactoferrin

HADS..... Hospital Anxiety and Depression Scale

HADS-A..... Hospital Anxiety and Depression Scale - Anxiety

HADS-D..... Hospital Anxiety and Depression Scale - Depression

HCT..... Hematocrit

HIPAA..... Health Insurance Portability and Accountability Act

HUS..... Healthcare Utilization Survey

IBD..... Inflammatory Bowel Disease

IRB..... Institutional Review Board

PCDAI..... Pediatric Crohn's Disease Activity Index

PHQ-9..... Patient Health Questionnaire

PIP..... Pediatric Inventory for Parents

PIP-D.....Pediatric Inventory for Parents - Difficulty

PIP-F ..... Pediatric Inventory for Parents – Frequency

PUCAI.....Pediatric Ulcerative Colitis Activity Index

REDCap .....Research Electronic Data Capture

SCARED.....Screen for Child Anxiety Related Emotional Disorders

TNF ..... Tumor Necrosis Factor

UC.....Ulcerative Colitis

6MP.....Mercaptopurine

INTRODUCTION

Chronic illnesses can significantly impact a person's life. For children, the implications can be debilitating, including impaired social and physical functioning, academic underperformance, delays in linear growth and sexual maturity, and mental health disorders[1]. Inflammatory bowel disease (IBD) includes a family of chronic gastrointestinal disorders with increasing incidence in children and adolescents worldwide[2]. Patients with IBD typically report symptoms such as weight loss, abdominal pain, and bloody diarrhea[3]. The clinical course of pediatric-onset cases is often more severe and complicated than that observed in patients with adult-onset disease; thus, pediatric cases typically require more comprehensive care[4,5].

IBD is generally divided into two subtypes based on symptoms and endoscopic findings: ulcerative colitis (UC) and Crohn's disease (CD). There is also a third subtype in which patients are categorized as having indeterminate colitis (IC), as they present with symptoms and endoscopic findings consistent with both UC and CD[4]. The inflammation observed in patients with UC is typically limited to the mucosa, begins in the rectum, and extends in a contiguous fashion to include some or all of the large intestine[3,4]. In contrast, the inflammation observed in patients with CD involves the whole wall of the intestine, occurs in any region of the gastrointestinal tract, and can be discontinuous in nature[3,4]. CD is the more prevalent of the two main IBD subtypes. It makes up around 70% of cases, with patients with UC comprising most of the remaining 30% of cases[4].

Both CD and UC can significantly impact a child's quality of life. For instance, Bernstein et al. (2019) found significant psychiatric comorbidity in pediatric patients with IBD[6]. In their study, they found that children with IBD were more likely to suffer from anxiety, depression, and bipolar disorders than children without IBD[6]. These psychosocial symptoms, as well as clinical symptoms of IBD negatively impact other parts of a child's life, including attending school, going on outings, or engaging in hobbies[7]. The resulting decrease in social engagement limits opportunities for mental and interpersonal development and significantly decreases quality of life and emotional well-being[7]. Thus, while IBD is primarily a disease of the gastrointestinal tract, its effects can be utterly debilitating to so many different parts of a child's life. As such, it's important to better understand the onset and clinical course of pediatric patients with IBD to provide the most effective and high-quality prospective clinical care.

IBD typically results from an interplay of genetic and environmental factors that result in an impaired immune response to what appears to be a patient's normal intestinal microbiome[8]. The resulting inflammation generally leads to a disruption in the mucosal barrier that lines and protects the gastrointestinal tract[3,8]. Current therapies for pediatric IBD vary greatly, and all agents address some component(s) of the dysregulated immune response. Initial therapies include corticosteroids and amino-salicylates, which are more effective at treating symptoms rather than underlying aberrant physiology[3]. Newer therapies, including anti-TNF drugs (e.g., infliximab), are more specific and target the mechanisms driving the chronic illness[3]. In addition, recent research efforts involve studying the impact of psychological and social factors on the clinical course and

management of pediatric patients with IBD. Environmental exposures that impact disease onset and severity in pediatric-onset IBD include psychological stress, diet, tobacco smoke exposure, anxiety, mood disorders, and antibiotic use[9]. However, the exact causes and mechanisms underlying IBD remain poorly understood[3].

Clinical and Environmental Factors Involved in Pediatric IBD

Recent investigations into the interaction of biological, environmental, and psychosocial factors in IBD have heightened awareness of a "gut-brain-microbiota axis" that could play a role in its pathogenesis[10,11,12,13]. This theory posits a bidirectional communication between the gut and the brain, as shown in Figure 1. This demonstrates how cytokines and neuroactive molecules from the immune and enteric nervous systems act on the gastrointestinal system and vice-versa[14]. As such, the intermittent inflammation observed in patients with IBD could be initiated by acute damage to the mucosal barrier lining the gastrointestinal tract by stress-related inflammatory cytokines, cortisol, or adrenaline, as described in Figure 2[14].

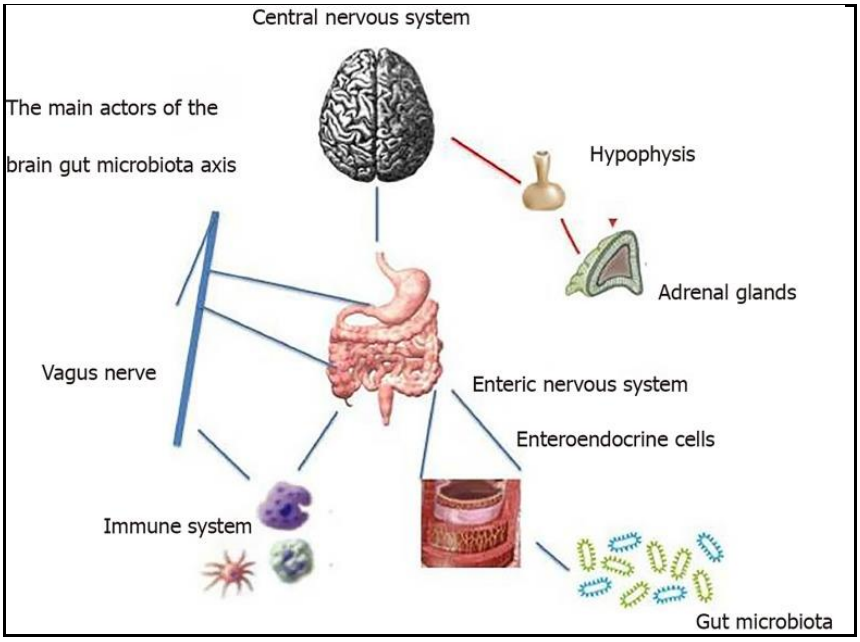

Figure 1. The Gut-Brain-Microbiota Axis[14]. Bidirectional communication between the gut and the brain through complex interaction of the central nervous system, enteric nervous system, and the immune system.

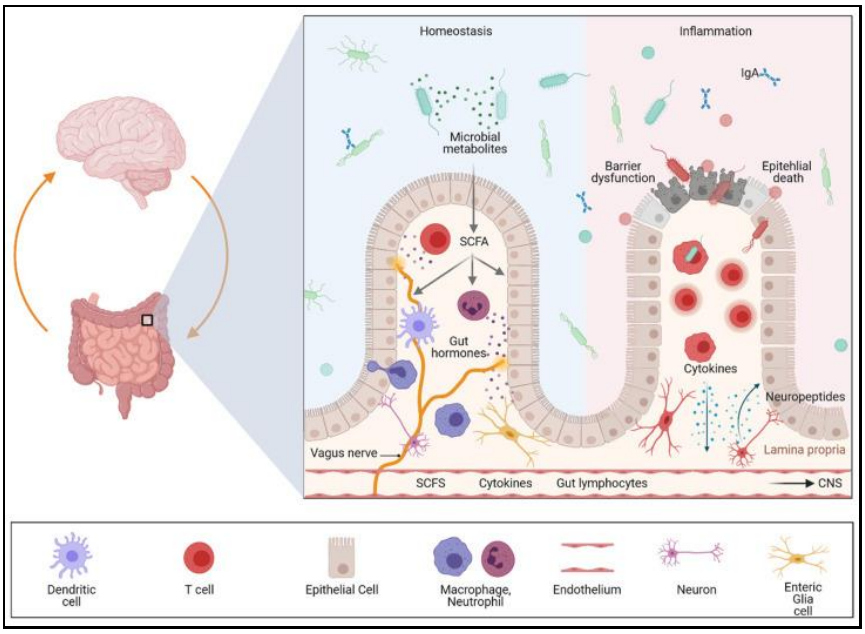

Figure 2. The Intestinal Barrier[10]. A comparison between a healthy gut mucosal barrier and an inflamed barrier during pediatric IBD.

Data from several studies have also demonstrated that psychosocial factors, including anxiety or depression, may influence the onset and progression of IBD in children[7,13,15]. Micocka-Walus et al. (2016) found a significant association between depression and worse clinical outcomes in children with IBD[16]. This association can be explained by the bidirectional gut-brain-microbiota axis theory, in which the cytokine products of stress damage the gastrointestinal system directly. However, the association may also be explained by indirect effects, in that behavioral factors related to mood disorders (i.e., anxiety or depression) increase the likelihood of nonadherence to treatment plans. This can result in poorer clinical outcomes[13,16]. However, it is difficult to denote any casual relationships, so mood disorders are often seen as comorbidities, as mentioned previously in the research by Bernstein and colleagues[6].

Furthermore, other environmental or psychosocial factors like a difficult family life or distressing events can increase stress. Giannakopoulos et al. (2016) noted that children with active IBD reported significantly more stressful life events than children in remission[17]. Increased stress may make children more susceptible to gastrointestinal infection. This could result from an imbalance in stress-related hormones, such as corticotropin-releasing factor, which can suppress the immune system and increase inflammation in the gastrointestinal tract[14,18]. However, given the bi-directionality of the gut-brain axis, and the complex interaction between these contributing factors, a causal inference cannot be drawn between stress and IBD. Instead, we can only appreciate the association between environmental, behavioral, and psychosocial factors and worsening disease progression.

The feedback loop involving the outcome of stressors in managing chronic disease is complex. While a stressful environment will negatively impact a child, that child is likely to induce stress in those around them, which can subsequently rebound to further impact the child. A meta-analysis conducted by Cousino and Hazen (2013) found that parenting stress was significantly worse in parents or caregivers of children with an active chronic illness[19]. Interestingly, higher parental stress scores correlated with poorer psychological adjustment in their child's condition, indicating how coping mechanisms or strategies may contribute to different outcomes[19]. Coping strategies can vary from seeking social support to relying on drug use, and the more maladaptive the coping behavior, the more likely it is to impact an already taxed situation negatively[20]. For instance, anxiety can impact a parent or guardian's ability to support their child best as they cope with the challenges of managing a chronic disease[19]. Children may internalize anxious behaviors modeled by their parents, and these learned negative coping strategies can permanently impact their approach to managing their disease[21]. A study done by Murphy et al. (2020) found that greater protective parental responses and anxious behavior predicted worse disease severity in children with IBD, demonstrating a potential link between parental coping behavior and the clinical course of their children's IBD management[22].

However, only a handful of studies have evaluated the impact of parental stress and coping mechanisms on the behavior and clinical outcomes of children with IBD[23,24]. It is thus important to understand the relationship between caregiver and child when studying the epidemiology of chronic illnesses in children, including IBD.

A recent study by Bramuzzo et al. 2020 and colleagues investigated the impact of parental well-being on child well-being in pediatric patients with IBD[23]. They administered questionnaires to children with IBD that collected data concerning quality of life and their perception of their parent's behaviors, including "distress, anxiety, depression, and pain catastrophizing"[23]. They found that high levels of parental distress correlated with a lower quality of life in their children[23]. However, they found no significant correlation between parental anxiety and depression and their child's IBD despite previous studies finding an association[19]. This may be due to biases in the questionnaires or limited sample size. Nonetheless, conflicting findings reported in the scant literature make it difficult to reach evidence-based conclusions or recommendations. Further research is necessary to understand better how parental psychosocial factors impact disease progression and outcomes in children with IBD.

Specific Aims

Our study aims to investigate how parental and child coping affects the clinical and psychological outcome of a child with newly diagnosed IBD. With respect to clinical outcome, we will assess the relationship between parent and child mood disorders, anxiety and depression, and disease severity. We are also interested in investigating the interplay between parental and child anxiety and depression. Furthermore, we will assess how a child's quality of life is impacted by parental anxiety and depression. Lastly, we aim to follow children and their parents over a one-year period to gain an understanding of how measured parameters of anxiety and depression change over time.

The longitudinal data collected in this study should help to fill the knowledge gap existing concerning our understanding of the impact of environmental and psychosocial factors on the progression of IBD. This should better inform physicians and caretakers of risk factors that may predict worse disease severity. In gaining this knowledge, we hope to more readily identify and support the most vulnerable children and families with more timely supportive interventions.

METHODS

Our study population included children with IBD and their parents recruited from the Gastroenterology Department at Boston Children's Hospital. Participants were approached in the GI clinic or the Center for Ambulatory Infusion and Therapeutics/Clinical Research (CAT/CR) at the Longwood location, and at the Infusion Clinic at the Waltham location.

Children were eligible for the study if they had been diagnosed with IBD within six months, as defined by the date of the child's initial diagnostic endoscopy. The age range for eligibility was 9-18. Parental measures were completed by the parent or caregiver accompanying the child to their medical visit.

Moreover, the primary GI physicians and Social Workers associated with eligible patients were contacted to ensure that there was no contraindication to a patient/parent participating in a study of this nature. Patients and caregivers were then approached in an ambulatory setting, and informed consent was completed at the bedside. Each child and parent pair were then administered a series of questionnaires. One year following this baseline visit, children and their parents were approached again to complete the same questionnaires as a follow-up.

Child Measures

Each child participating in our study was given four questionnaires to complete. These questionnaires were administered only if a social worker and a nurse practitioner were present to ensure safety. In addition, two of the surveys for the children, the PHQ-9

and CDI, included questions regarding suicidal ideations. Based on their answers to these questions, any child at risk was referred to the psychiatric team on call.

IMPACT-III Questionnaire

The IMPACT-III questionnaire has been validated to assess the quality of life in children and young adults with IBD. There are a total of 35 questions, and the children respond using a 5-point Likert scale. Thus, the total composite score for this questionnaire can range from 35 to 175. A higher score indicates a better health-related quality of life. The IMPACT-III score is further broken down along six domains, including bowel symptoms (7 questions), systemic symptoms (3 questions), social functioning (12 questions), body image (3 questions), treatment/interventions (3 questions), and emotional functioning (7 questions)[25].

Screen for Child Anxiety Related Emotional Disorders (SCARED) Questionnaire

The SCARED questionnaire has been validated to assess anxiety in children over the last three months. The metric includes 41 questions, the responses to each of which range from 0 (Not True or Hardly Ever True) and 2 (Very True or Often True). The total composite score for this questionnaire thus ranges from 0 to 82. A score of 25 or more indicates an anxious state, with higher indicating greater anxiety[26]. There are five domains in this questionnaire, including generalized anxiety (9 questions), separation anxiety (8 questions), panic or somatic disorder (13 questions), social anxiety disorder (7 questions), and significant school avoidance (4 questions)[26].

Children's Depression Inventory (CDI) Questionnaire

The CDI assesses symptoms of depression and dysthymia in children over the previous two weeks. A total of 27 questions are answered, with responses ranging from 0 to 2. The maximum score is 54, and scores of 20 are indicative of depression[27]. Higher scores indicate more severe depressive or dysthymic symptoms. There are five domains in this questionnaire, including negative mood (6 questions), interpersonal problems (4 questions), ineffectiveness (4 questions), anhedonia (8 questions), and negative self-esteem (5 questions)[27].

Patient Health Questionnaire (PHQ-9)

The PHQ-9 screens for depressive symptoms present in the past two weeks. This questionnaire is not age specific. There are a total of 9 questions, and each is scored from 0 to 3. Higher scores indicate greater depressive symptoms, and a score greater than or equal to 10 indicates depression[28].

Parent/Caregiver Measures

Parents or caregivers accompanying the child participating in this study completed three questionnaires.

Pediatric Inventory for Parents (PIP)

The PIP assesses the degree of stress experienced by a parent of a child with a chronic illness. There are a total of 42 questions, and each is answered using a 1 to 5

Likert scale. For each question, parents choose a score for both difficulty and frequency, so there are a total of 84 responses. Frequency scores range from 1 (never) to 5 (very often), and difficult scores range from 1 (not at all) to 5 (extremely). The questions are drawn from four domains, including communication (9 questions), emotional distress (15 questions), medical care (8 questions), and role function (10 questions)[29]. Higher difficulty and frequency scores indicate greater stress levels felt by the parent or caregiver.

Hospital Anxiety and Depression Scale (HADS)

The HADS questionnaire screens for parental anxiety and depression. There are 14 questions, split into two sets of 7 items along two dimensions, including anxiety and depression. Each question is scored from 0 to 3, so total scores range from 0 to 21 for each subscale[30]. Scores of 8 or greater on either subscale indicate the presence of anxiety or depression[30]. Higher scores indicate greater severity of anxiety or depression.

Healthcare Utilization Survey (HUS)

The Healthcare Utilization Survey evaluates how often the parent and child have used healthcare resources within the past month. There are six items in the survey that ask about hospitalizations, emergency room visits, pediatrician, or gastroenterologist visits, as well as calls to pediatricians or gastroenterologists. The higher the score, the greater the healthcare utilization.

Data Management and Analysis

The data used in this study were collected from January 2017 to January 2023. All questionnaire responses were inputted into Research Electronic Data Capture (REDCap), a HIPAA-compliant, browser-based software. In addition to the questionnaires, participant demographics and clinical outcomes were abstracted from the Boston Children's Hospital's Electronic Medical Records and inputted into REDCap. The clinical outcomes included parameters such as the Pediatric Ulcerative Colitis Activity Index (PUCAI) and Pediatric Crohn's Disease Activity Index (PCDAI), which are scores for disease severity. In addition, medications or surgeries that were part of the child's treatment plan, as well as IBD-related inflammatory markers, such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), were also inputted into REDCap. This information was abstracted from initial and follow-up visits to assess for changes over time.

The data were exported from REDCap to Microsoft Excel (Version 16.66.1) and SPSS (Version 27) for analysis. Prior to analysis, data cleaning was done using a set of exclusion criteria. For each questionnaire, if either participant (child or parent) was missing more than 10% of responses, their response was excluded from data analysis. If more than none but less than 10% of responses were missing, the missing values were imputed using the mean score for each question.

After data cleanup, the data were analyzed using Fisher's exact test, independent t-test, paired t-test, and ANOVA. The test used was dependent on the type of data available and the type of comparison needed.

Ethical Approval

This study protocol was reviewed and approved by the Institutional Review Board (IRB) at Boston Children's Hospital (Protocol number IRB-P00023915).

RESULTS

Demographics and Participant Enrollment

Participant enrollment is outlined in Figure 3. We consented and enrolled 86 parent/child pairs, and each of these pairs consented and completed all baseline study questionnaires. Data from participants that consented but did not provide data or withdrew from the study were excluded from the final analysis. Of the 86 pairs that filled out the initial surveys, 27 completed follow-up surveys. An additional 21 pairs are scheduled to complete follow-up surveys. 38 pairs have been lost to follow-up or declined to complete follow-up study questionnaires.

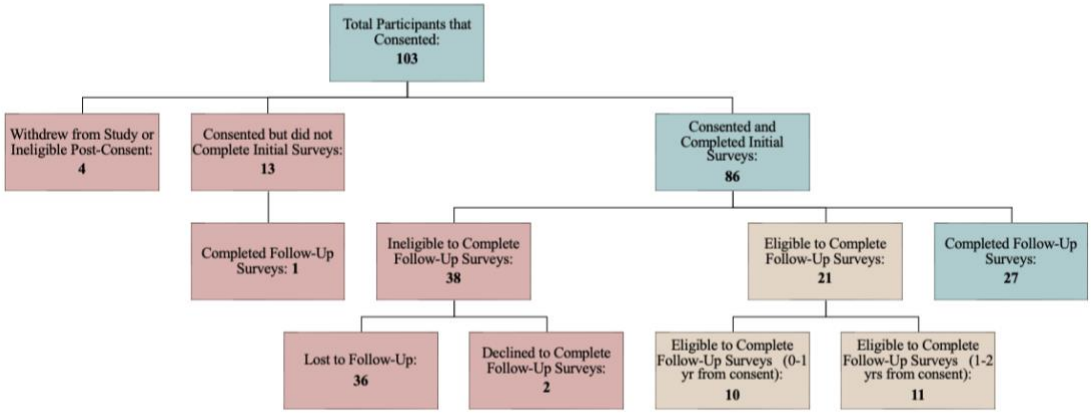

Figure 3. Participant Enrollment Diagram. **A flowchart of the child and parent pairs in the study as of February 2023.**

Tables 1, 2, and 3 describe the demographics and clinical information of our baseline study population. Of the 86 children participating in this study, 40.7% were female and 59.3% were male. A large percentage of these children also reported their race as White (73.2%). The majority (68.6%) of the children were diagnosed with

Crohn's Disease, 25.6% had Ulcerative Colitis, and the remaining 5.8% were classified as having Indeterminate Colitis. Most study participants were receiving steroids (55.8%) and TNF inhibitors (61.6%) for the management of their IBD. 48.8% of participants were also receiving medications that fell into the "Other" category, including cholecalciferol (Vitamin D3) and proton pump inhibitors (ex: omeprazole, omeprazole). Study participants were recruited almost equally across inpatient (37.2%), outpatient (26.7%), and ambulatory infusion (33.7%) centers. Most children (79.1%) were accompanied by their mother at the baseline encounter, while 18.6% were accompanied by their father, and the remaining 2.3% by an unknown caregiver or relative.

Table 1. Participant Demographics. Demographics of children participating in this study. Data was extracted from Boston Children's Hospital's Electronic Medical Records and was inputted into REDCap.

Participant Demographics (*n* = 86)	***n***	**%**
Gender		
Female	35	40.7
Male	51	59.3
Type of IBD		
Crohn's Disease	59	68.6
Ulcerative Colitis	22	25.6
Indeterminate Colitis	5	5.8
Race		
White	63	73.2
Black / African American	3	3.5
Asian	0	0
Native American / Alaskan Native	0	0
Native Hawaiian / Other Pacific Islander	0	0
Other	8	9.3
Unknown	1	1.2
Decline to Answer	11	12.8
Ethnicity		
Not Hispanic/Latino	74	86.1
Hispanic/Latino	5	5.8
Decline to Answer	7	8.1
Medications		
Acetylsalicylic acid (ASA)	7	8.1
Steroids	48	55.8
TNF Inhibitors	53	61.6
Vedolizumab	0	0
Mercaptopurine (6MP)	1	1.2
Methotrexate	16	18.6
Stelara	1	1.2
Tacrolimus	1	1.2
Exclusive enteral nutrition (EEN)	1	1.2
Other	42	48.8
Location		
Inpatient	32	37.2
Outpatient	23	26.7
CAT-CR/Infusions	29	33.7
Unknown	2	2.3
Parent/Caregiver Role		
Mother	68	79.1
Father	16	18.6
Unknown	2	2.3

Clinical parameters, including disease activity scores and inflammatory markers, are displayed in Table 2. The median PUCAI score was 25.0 ± 22.3, and the median PCDAI score was 10.0 ± 11.1. Data for each participant's hematocrit (HCT), C-reactive protein level (CRP), and erythrocyte sedimentation rate (ESR) were reported from testing done on or within two months of the patient's baseline encounter. The median values for HCT, CRP, and ESR were 36.5 ± 4.3, 0.3 ± 1.5, and 17.0 ± 16.1, respectively. Median baseline fecal calprotectin and lactoferrin values were 1067.0 ± 921.5 and 281.7 ± 542.4, respectively.

Table 2. Participant Clinical Parameters. Clinical parameters, including disease activity scores and inflammatory markers for study participants.

Clinical Parameters	***n***	**Median**	**SD**
Disease Activity Score			
PUCAI	25	25.0	22.3
PCDAI	61	10.0	11.1
Inflammatory Markers			
Hematocrit (HCT)	84	36.5	4.3
C-Reactive Protein (CRP)	84	0.3	1.5
Erythrocyte Sedimentation Rate (ESR)	83	17.0	16.1
Calprotectin (CPT)	39	1067.0	921.5
Fecal Lactoferrin (FLA)	12	281.7	542.4

Additional anthropomorphic and clinical data were extracted from the electronic medical records, including height, weight, body mass index (BMI), age, and time since diagnosis. The median height, weight, BMI, and age were 159.8 ± 15.7, 52.7 ± 15.9, 19.8 ± 4.5, and 15 ± 2.6, respectively. The median time since diagnosis was 1.09 months, defined as the interval between a patient's diagnostic endoscopy and their baseline study encounter.

Table 3. Participant Clinical Demographics. Clinical demographics for study participants. Data was extracted from Boston Children's Hospital's Electronic Medical Records and was inputted into REDCap. Time since diagnosis was calculated as the time between the diagnostic endoscopy and the first encounter.

Clinical Demographics	***n***	**Median**	**SD**
Height	86	159.8	15.7
Weight	86	52.7	15.9
Body Mass Index (BMI)	86	19.8	4.5
Age	86	15	2.6
Time Since Diagnosis	86	1.09	1.74

Children participating in this study completed the IMPACT-III, SCARED, PHQ-9, and CDI questionnaires at baseline and one year later. The parent or caregiver accompanying the child at each encounter completed the HADS, PIP, and Healthcare Utilization questionnaires. The HADS questionnaire reports scores for parental anxiety and depression, and the PIP questionnaire reports frequency and difficulty scores. Tables 4 and 5 display the number of survey responses used for data analysis along with each

questionnaire's median score and SD. Responses missing greater than 10% of the answers are not included. Two of the parent questionnaires, the HADS and PIP questionnaires, reported two different scores. Thus, there are two different medians displayed in Tables 4 and 5.

Table 4. Survey Summary at First Encounter. Parental and child responses received for each questionnaire, with the median score and SD of each survey.

Questionnaires	***n***	**Median**	**SD**
IMPACT-III	83	131.0	19.9
SCARED	84	14.5	12.5
PHQ-9	82	3.5	3.7
CDI	84	4.0	5.7
HADS (Anxiety)	86	6.0	4.6
HADS (Depression)	86	2.0	3.7
PIP (Frequency)	77	96.0	28.7
PIP (Difficulty)	77	92.0	28.5
Healthcare Utilization	85	5.0	4.7

Table 5. Survey Summary at Follow-Up Encounter. Parental and child responses received for each questionnaire, with the median score and SD of each survey.

Questionnaires	*n*	Median	SD
IMPACT-III	26	144.0	14.9
SCARED	25	15.0	22.6
PHQ-9	25	4.0	3.8
CDI	26	5.0	4.8
HADS (Anxiety)	24	6.0	3.8
HADS (Depression)	24	1.5	3.3
PIP (Frequency)	21	74	20.3
PIP (Difficulty)	21	68	30.6
Healthcare Utilization	23	2.0	2.1

Quality of Life and Behavioral Outcomes

We first investigated the relationship between IMPACT-III and HADS scores for parental anxiety and depression. The IMPACT-III was administered to the children in our study to assess their quality of life. As shown in Figures 3 and 4, there were significant negative correlations between both HADS-Anxiety (HADS-A) and IMPACT-III scores ($r = -0.498$; $p < 0.001$), as well as HADS-Depression (HADS-D) and IMPACT-III scores ($r = -0.287$; $p = 0.010$), respectively. Higher parental anxiety and depression scores thus correlated with lower quality of life in children with IBD.

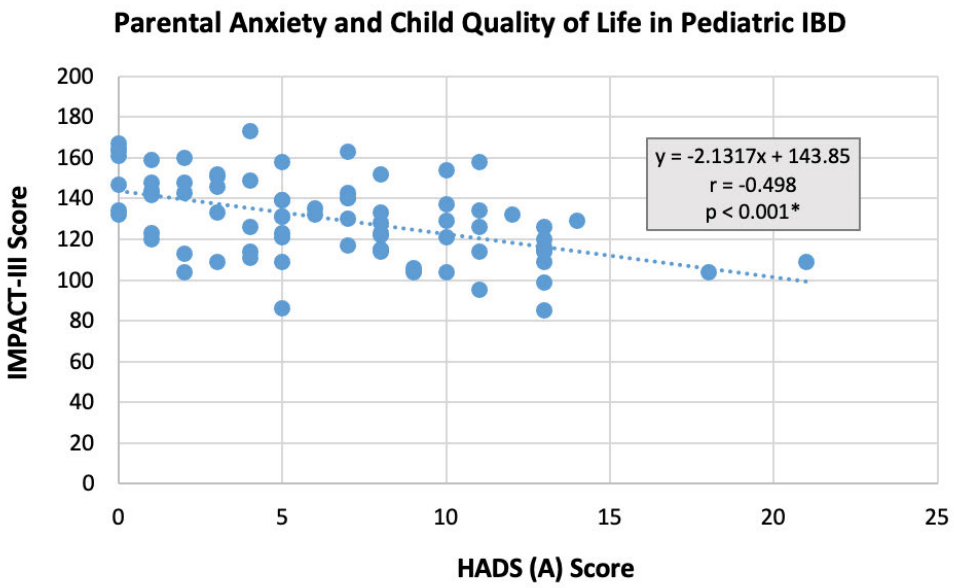

Figure 3. Parental Anxiety and Child Quality of Life in Pediatric IBD. The relationship between HADS-A scores for parental anxiety and the IMPACT-III scores for child quality of life. Data shows a significant, negative, moderate correlation ($r = -0.498$; $p < 0.001$).

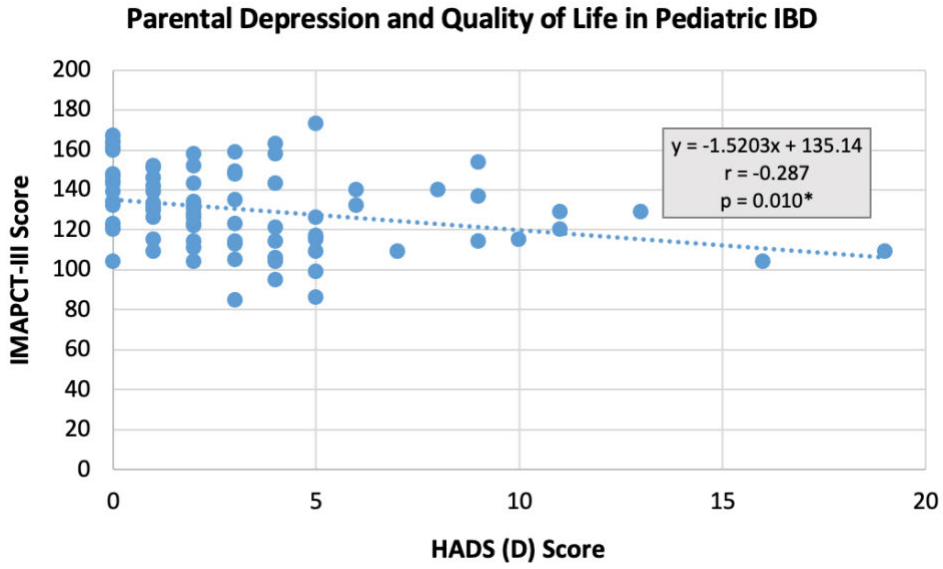

Figure 4. Parental Depression and Child Quality of Life in Pediatric IBD. The relationship between HADS-D scores for parental depression and the IMPACT-III scores for child quality of life. Data shows a significant, negative, weak correlation ($r = -0.287$; $p < 0.010$).

To further understand the relationship between parental anxiety/depression and the quality of life in children newly diagnosed with IBD, we performed an independent t-test with the HADS and IMPACT-III questionnaires. In particular, we compared groups of children who had parents with anxiety/depression to those without. A cutoff score of 8 for the HADS-A and HADS-D total scores was used to determine whether the parent had anxiety and/or depression. 46 parents had a HADS-A score above 8 (testing positive for anxiety), whereas only 10 scored above 8 in HADS-D (testing positive for depression). As shown in Table 6, using an independent t-test, there is a significant difference in the mean IMPACT-III score of children with parents who have anxiety (119.61) and children with parents without anxiety (137.33), with a p-value less than 0.001. However, there is no significant difference in the mean IMPACT-III scores of children with parents who have depression (125.10) and children with parents without depression (130.62), with a p-value of 0.416.

Table 6. Quality of Life of Children with Parents with Anxiety and Depression. Mean IMPACT-III scores of children with parents with anxiety and without anxiety. Mean IMPACT-III scores of children with parents with depression and without depression. HADS-A score > 8 and HADS-D score > 8 were used as the cut-off for parental anxiety and depression.

HADS	Mean IMPACT-III Score	p-value
Parental Anxiety (n = 46)	119.61	<0.001*
No Parental Anxiety (n = 33)	137.33	
Parental Depression (n = 10)	125.10	0.416
No Parental Depression (n = 69)	130.62	

**p < 0.05 is significant*

A visual depiction of this difference in mean IMPACT-III scores can be seen in Figures 5 and 6. The data illustrated in the box plots in Figure 5 indicate a significant difference between the mean IMPACT-III scores of children with anxious parents versus children without anxious parents. In contrast, statistical significance was not observed in the IMPACT-III scores for the children of parents with and without depression.

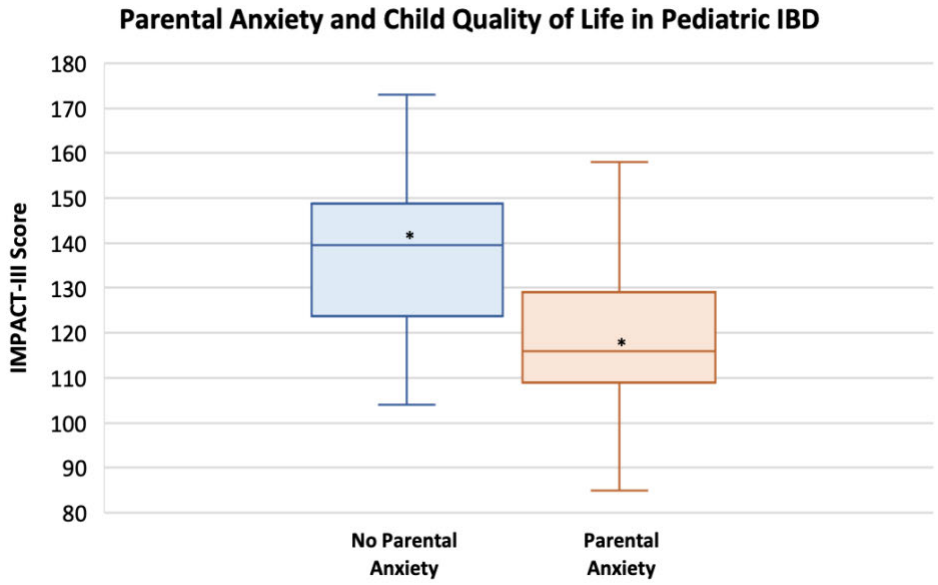

Figure 5. IMPACT-III Scores of Children with Parents with Anxiety vs. without Anxiety. There is no overlap in the mean lines of children with parents with anxiety (minimum = 85; maximum = 158) and of those with parents without anxiety (minimum = 104; maximum = 173), indicating significance.

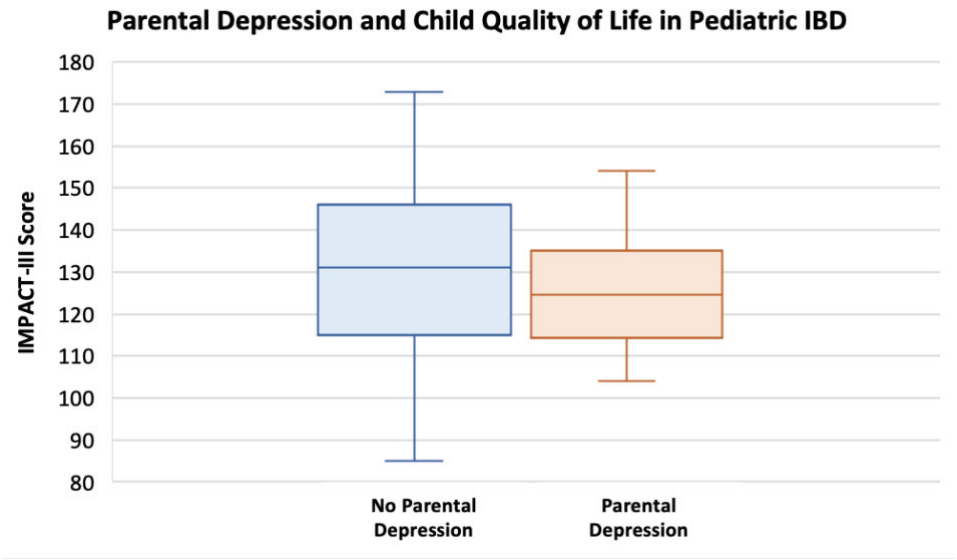

Figure 6. IMPACT-III Scores of Children with Parents with Depression vs. without Depression. There is an overlap in the mean lines of children with parents with depression (minimum = 104; maximum = 154) and of those with parents without depression (minimum = 85; maximum = 173, indicating no significant difference.

The IMPACT-III questionnaires can also be analyzed as subdomains, including Bowel Symptoms, Systemic Symptoms, Social Functioning, Body Image, Treatment/Interventions, and Emotional Functioning. Tables 7 and 8 display the mean IMPACT-III scores for each subdomain in children of anxious versus non-anxious parents and children of depressed versus nondepressed parents after conducting a one-way ANOVA test. In children of anxious parents, the mean IMPACT-III scores of all subdomains, except Systemic Symptoms ($p = 0.108$), were significantly lower than those of children without anxious parents. No significant difference was seen between children of parents with depression and children of parents without depression.

Table 7. Mean IMPACT-III Subdomain Scores for Children with Anxious Parents and Children without Anxious Parents. The IMPACT-III domains for bowel symptoms, social function, body image, treatment/interventions, and emotional functioning had mean IMPACT-III scores in children with anxious parents (n = 46) that were lower than the mean IMPACT-III scores in children without anxious parents (n = 33). Analysis was done using one-way ANOVA.

IMPACT-III Domain	Parental Anxiety (n=46)	No Parental Anxiety (n=33)	p-value
Bowel Symptoms	21.64	25.76	0.002*
Systemic Symptoms	9.64	10.65	0.108
Social Functioning	22.73	27.50	<0.001*
Body Image	9.97	11.13	0.028*
Treatment/Interventions	10.21	12.26	<0.001*
Emotional Functioning	22.73	27.50	<0.001*

**p < 0.05 is significant*

Table 8. Mean IMPACT-III Subdomain Scores for Children with Depressed Parents and Children without Depressed Parents. The IMPACT-III domains for bowel symptoms, systemic symptoms, social function, body image, treatment/interventions, and emotional functioning had mean IMPACT-III scores in children with depressed parents (n = 10) that were not significantly different than the mean IMPACT-III scores in children without depressed parents (n = 69). Analysis was done using one-way ANOVA.

IMPACT-III Domain	Parental Depression (n=10)	No Parental Depression (n=69)	p-value
Bowel Symptoms	23.60	24.10	0.807
Systemic Symptoms	9.80	10.29	0.604
Social Functioning	44.90	48.57	0.078
Body Image	10.20	10.71	0.520
Treatment/Interventions	11.50	11.39	0.905
Emotional Functioning	25.10	25.57	0.811

We examined the relationship between demographic data and quality of life in patients newly diagnosed with IBD. First, we examined the association between age and the child's quality of life. For this study, the age of 12 at the time of consent was used as the cutoff between young children and older adolescents. Using an independent t-test, children under 12 had a significantly higher mean IMPACT-III score (137.67) than children above 12 (126.55), with a p-value of 0.021. The data in Table 9 illustrates how the mean IMPACT-III scores varied between these two groups.

Table 9. Mean IMPACT-III Scores in Children of Different Ages with IBD. Children were divided into two age groups, below and above 12, before an independent t-test was done to compare mean IMPACT-III scores.

Age Group	**Mean IMPACT-III Score**	**p-value**
Below 12 (n = 24)	137.67	0.021*
Above 12 (n = 55)	126.55	

**p < 0.05 is significant*

We next investigated associations between the biological gender of children with IBD and their quality of life. As described in Table 10, there was no significant difference in the mean IMPACT-III scores of female (127.06) versus male children (132.61), with a p-value of 0.213.

Table 10. Mean IMPACT-III Scores in Male and Female Children with IBD. An independent t-test was done to analyze the mean IMPACT-III scores in female children (n=34) versus male children (n=49) with IBD.

Gender	Mean IMPACT-III Score	p-value
Female (n = 34)	127.06	0.213
Male (n = 49)	132.61	

We investigated interactions between a child's age and their parent's levels of anxiety or depression. This was done by comparing the mean HADS-A and HADS-D in participants below and above the age of 12. We found no significant differences in the mean parental anxiety score (HADS-A) in children below 12 (5.96) and children above 12 (6.78), with a p-value of 0.473 (Table 11). The same result was observed concerning parental depression, as there is no significant difference in mean parental depression scores (HADS-D) in children below 12 (3.08) versus children above 12 (3.58), with a p-value of 0.591 (Table 12).

Table 11. Mean HADS-A Scores in Children of Different Ages with IBD. Children were divided into two age groups, below and above 12, before an independent t-test was done to compare mean HADS-A scores of parental anxiety.

Age Group	Mean HADS-A Score	p-value
Below 12 (n = 24)	5.96	0.473
Above 12 (n = 55)	6.78	

Table 12. Mean HADS-D Scores in Children of Different Ages with IBD. Children were divided into two age groups, below and above 12, before an independent t-test was done to compare mean HADS-D scores of parental depression.

Age Group	Mean HADS-D Score	p-value
Below 12 (n = 24)	3.08	0.591
Above 12 (n = 55)	3.58	

To further understand the relationship between parental coping and the quality of life in a child with IBD, we examined how a child's quality of life varied with parental stress. We compared scores measured in the PIP and IMPACT-III questionnaires. The PIP questionnaire was filled out by the parents and assessed the difficulty and frequency of stressful events relating to their child. Two scores are generated: PIP-Frequency (PIP-F) and PIP-Difficulty (PIP-D). A significant negative correlation was observed (Figure 7) between PIP-F scores and IMPACT-III scores ($r = -0.540$; $p < 0.001$). Thus, as the parental stress frequency increased, the quality of life of children with newly diagnosed IBD decreased. A similar inverse correlation was observed between PIP-D and IMPACT-III scores (Figure 8). As PIP-D scores for parental stress difficulty increased, the IMPACT-III scores of children decreased ($r = -0.460$; $p < 0.001$). Overall, we found a clear negative association between parental stress and the quality of life in children with IBD.

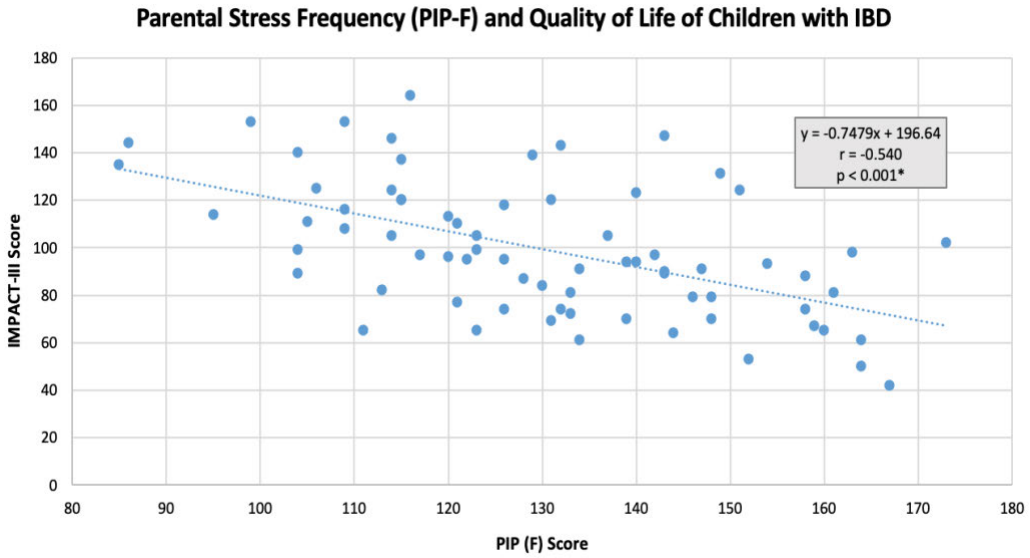

Figure 7. Parental Stress Frequency and Child Quality of Life in Pediatric IBD. A correlational analysis between PIP-F scores for parental stress frequency and the IMPACT-III scores for child quality of life. Data shows a significant, negative, moderate correlation ($r = -0.540$; $p < 0.001$).

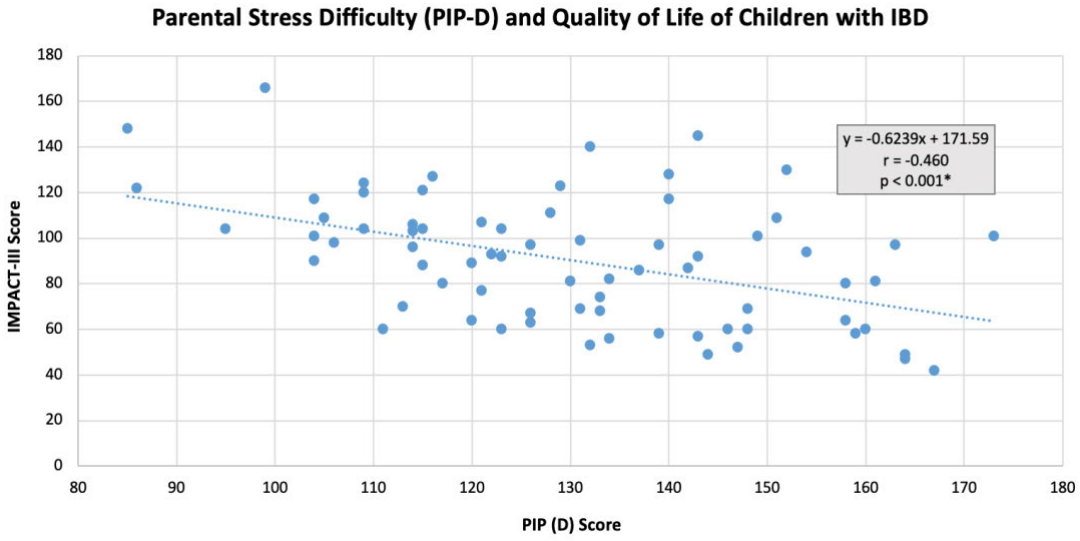

Figure 8. Parental Stress Difficulty and Child Quality of Life in Pediatric IBD. A correlational analysis between PIP-D scores for parental stress difficulty and the IMPACT-III scores for child quality of life. Data shows a significant, negative, moderate correlation ($r = -0.460$; $p < 0.001$).

We next investigated the relationship between parental stress and parental anxiety and depression. We compared the mean PIP-F and PIP-D scores in parents that had (HADS-A score > 8) or did not have anxiety (HADS-A score < 8). Using an independent t-test, anxious parents experienced greater parental stress frequency (113.46) and parental stress difficulty (104.64) than parents without anxiety (89.98 and 81.07, respectively), significant with a p-value less than 0.001, as seen in Table 13.

Table 13. Parental Stress and Anxiety in Pediatric IBD. A comparison of mean PIP scores in parents with and without anxiety using independent t-test analysis. HADS-A score > 8 was used as the cut-off for parental anxiety.

PIP Questionnaire	Parental Anxiety (n=28)	No Parental Anxiety (n=44)	p-value
Mean PIP-Frequency	113.46	89.98	< 0.001*
Mean PIP-Difficulty	104.64	81.07	< 0.001*

**p < 0.05 is significant*

Similar results were observed regarding comparisons of parental stress and depression. As described in Table 14, parents with depression (HADS-D score > 8) reported greater parental stress frequency (119.0) and parental stress difficulty (108.29) scores than parents without depression (96.97 and 88.29, respectively). This difference was significant, with p = 0.031 for PIP-F and p = 0.026 for PIP-D.

Table 14. Parental Stress and Depression in Pediatric IBD. Mean PIP scores in parents with depression versus parents without depression were compared using independent t-test analysis. HADS-D score > 8 was used as the cut-off for parental depression.

PIP Questionnaire	Parental Depression (n=7)	No Parental Depression (n=65)	p-value
Mean PIP-Frequency	119.90	96.97	0.031*
Mean PIP-Difficulty	108.29	88.29	0.026*

**p < 0.05 is significant*

We next studied the relationship between parental and child anxiety and depression. This was done using the Fisher's Exact Test. As described in Table 15, out of 81 children, 20% of children with anxiety had parents with anxiety. The other 11% of children with anxiety did not have parents with anxiety. This result is significant, with a p-value of 0.007. 48% of participants had neither anxiety nor anxious parents. On the other hand, Tables 16 and 17 depict parental depression and child depression scores. In this study, we utilized two different questionnaires to screen for child depression, the CDI and PHQ-9. As seen in Table 16, none of the 3.7% of children screening positive for depression (CDI score > 20) had parents with depression. Of the 12.3% of parents with depression (HADS-D > 8), none of their children had depression. Using the Fisher's Exact Test, this result was insignificant, with a p-value of 0.999. In contrast, as seen in Table 17, 13.5% of children screened positive for depression using the PHQ-9. 4.9% of the children who screened positive for depression also had parents with depression, while

the other 8.6% of children with depression had parents that did not have depression. This was significant, with a p-value of 0.026 (Table 17).

Table 15. Parental Anxiety and Child Anxiety in Pediatric IBD. 81 pairs of children and their parents with the percentages of those with and without anxiety. Child anxiety was determined with a SCARED score > 25 and parental anxiety was determined with a HADS-A score > 8.

	Child Anxiety	**No Child Anxiety**	**p-value**
Parental Anxiety	20% (16)	21% (17)	0.007*
No Parental Anxiety	11% (9)	48% (39)	

**p < 0.05 is significant*

Table 16. Parental Depression and Child Depression (CDI Questionnaire) in Pediatric IBD. 81 pairs of children and their parents with the percentages of those with and without depression. Child depression was determined with a CDI score > 20 and parental depression was determined with a HADS-D score > 8.

	Child Depression	**No Child Depression**	**p-value**
Parental Depression	0% (0)	12.3% (10)	0.999
No Parental Depression	3.7% (3)	84% (68)	

**p < 0.05 is significant*

Table 17. Parental Depression and Child Depression (PHQ-9 Questionnaire) in Pediatric IBD. 81 pairs of children and their parents with the percentages of those with and without depression. Child depression was determined with a PHQ-9 score > 10 and parental depression was determined with a HADS-D score > 8.

	Child Depression	**No Child Depression**	**p-value**
Parental Depression	4.9% (4)	7.4% (6)	0.026*
No Parental Depression	8.6% (7)	79.1% (64)	

**p < 0.05 is significant*

Figures 9, 10, and 11 provide a more visual representation of these results using a correlational analysis between child anxiety/depression and parental anxiety/depression. We found a significant positive correlation between child anxiety (SCARED) and parental anxiety (HADS-A) scores ($r = 0.0359$; $p < 0.001$). There was a significant positive correlation between child anxiety (SCARED score) and parental anxiety (HADS-A) score ($r = 0.0359$; $p < 0.001$). This relationship is seen with parental depression and child depression only when using the PHQ-9 questionnaire for child depression, as seen in Figures 10 and 11. The data in Figure 10 show no significant correlation between parental and child depression when using the CDI questionnaire ($r = 0.064$; $p = 0.574$). However, there is still what appears to be a positive relationship, given the character of the trendline. When using the PHQ-9 questionnaire, as seen in Figure 11, there is a significant positive correlation between parental depression and child depression ($r = 0.219$; $p = 0.049$).

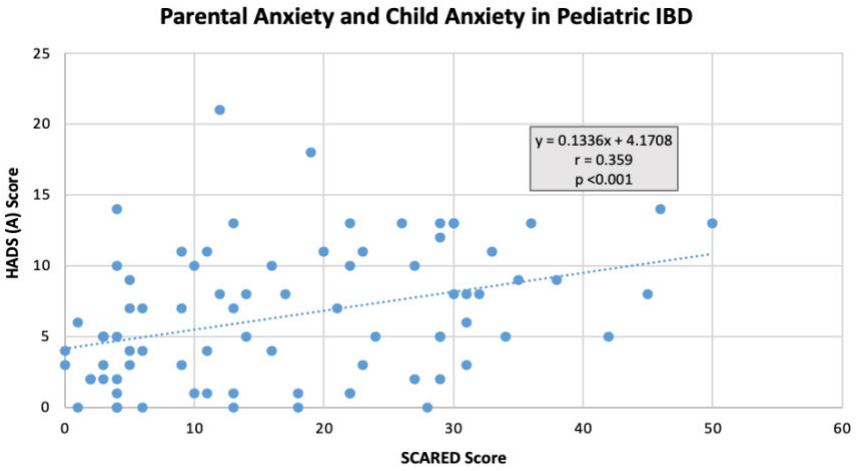

Figure 9. Parental Anxiety and Child Anxiety in Pediatric IBD. A correlational analysis between HADS-A scores for parental anxiety and SCARED scores for child anxiety. Data show a significant, positive, moderate correlation ($r = 0.359$; $p < 0.001$).

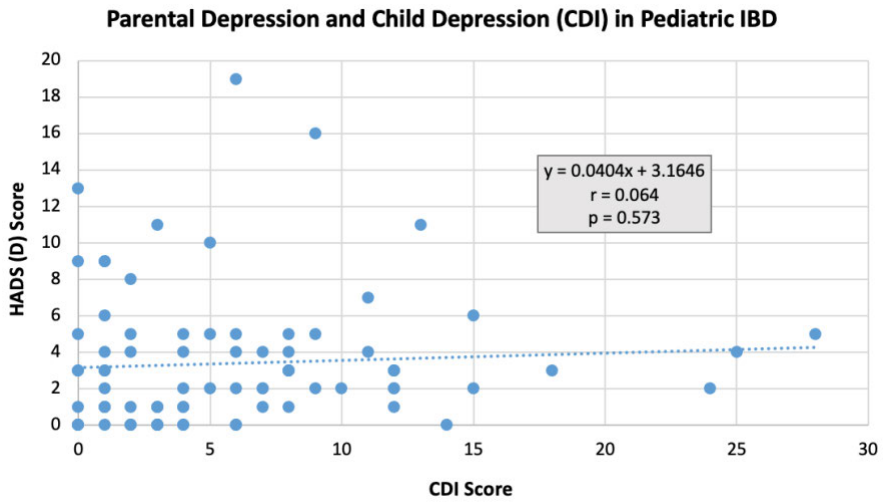

Figure 10. Parental Depression and Child Depression (CDI Questionnaire) in Pediatric IBD. A correlational analysis between HADS-D scores for parental depression and CDI scores for child anxiety. Data show a positive trend but no significant correlation (r = 0.064; p = 0.573).

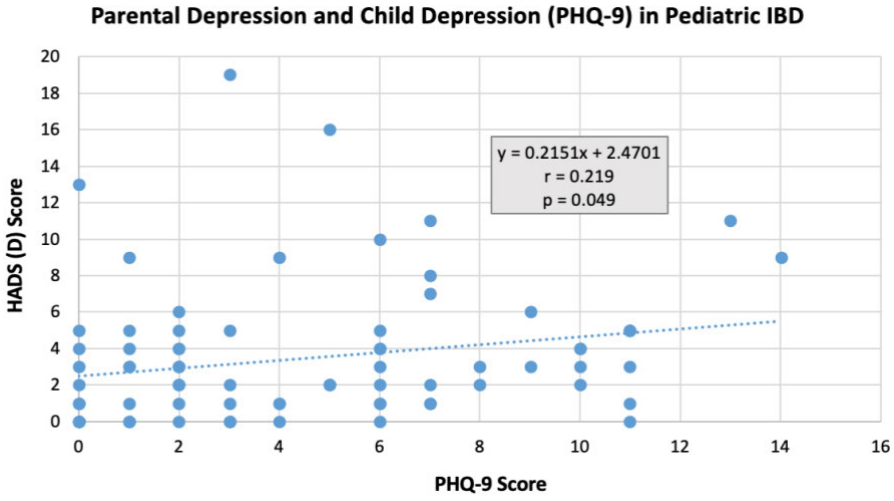

Figure 11. Parental Depression and Child Depression (PHQ-9 Questionnaire) in Pediatric IBD. A correlational analysis between HADS-D scores for parental depression and PHQ-9 scores for child anxiety. Data shows a significant, positive, weak correlation (r = 0.219; p = 0.049).

In addition, we investigated associations between the quality of life and anxiety or depression. In Table 18, there was a significant decrease in the mean IMPACT-III score in children with anxiety (123.42) compared to children without anxiety (133.33), with a p-value of 0.040. In comparing depressed children to those without depression, there are slightly different results when using the CDI questionnaire versus the PHQ-9 questionnaire. There is a decrease seen in the mean IMPACT-III score for children with depression compared to those without depression when using both the CDI and PHQ-9, and this difference only reaches statistical significance when using data collected in the PHQ-9 questionnaire. For children with depression using the CDI questionnaire, the mean IMPACT-III score was 111.00, compared to 131.16 for those without depression ($p = 0.087$). For children with depression using the PHQ-9 questionnaire, the mean IMPACT-III score was 117.36, compared to 132.41 for those without depression ($p = 0.019$). Three children screened for depression using the CDI, whereas 11 screened for depression using the PHQ-9. Nevertheless, there was a decrease in the quality of life (IMPACT-III score) when children scored higher on the SCARED, CDI, or PHQ-9 questionnaires.

Table 18. Child Anxiety & Depression and Their Quality of Life in Pediatric IBD. Mean IMPACT-III scores for children with or without anxiety and depression. Significant differences were seen in the mean IMPACT-III scores with the SCARED questionnaire for child anxiety and the PHQ-9 questionnaire for child depression. The cutoffs for anxiety and depression were 25 (SCARED), 20 (CDI), and 10 (PHQ-9).

Questionnaire	Child Coping	Mean IMPACT-III Score	p-value
SCARED	Anxiety (n=24)	123.42	0.040*
	No Anxiety (n=58)	133.33	
CDI	Depression (n=3)	111.00	0.087
	No Depression (n=79)	131.16	
PHQ-9	Depression (n=11)	117.36	0.019*
	No Depression (n=71)	132.41	

**p < 0.05 is significant*

Disease Severity

Disease severity was measured using PUCAI and PCDAI scores abstracted from the Boston Children's Hospital's Electronic Medical Records. Figure 12 illustrates the relationship between Crohn's Disease severity (PCDAI score) and child anxiety (SCARED). Though no correlation was significant, we observed increased SCARED scores ($r = 0.247$; $p = 0.069$) in the context of rising PCDAI scores. A similar positive relationship is seen in PUCAI scores and scores for anxiety in children with ulcerative colitis. As described in Figure 13, while a positive relationship exists between disease severity and anxiety score, it is not significant ($r = 0.064$, $p = 0.765$). There were 55 patients with PCDAI scores and 24 with PUCAI scores used for these analyses.

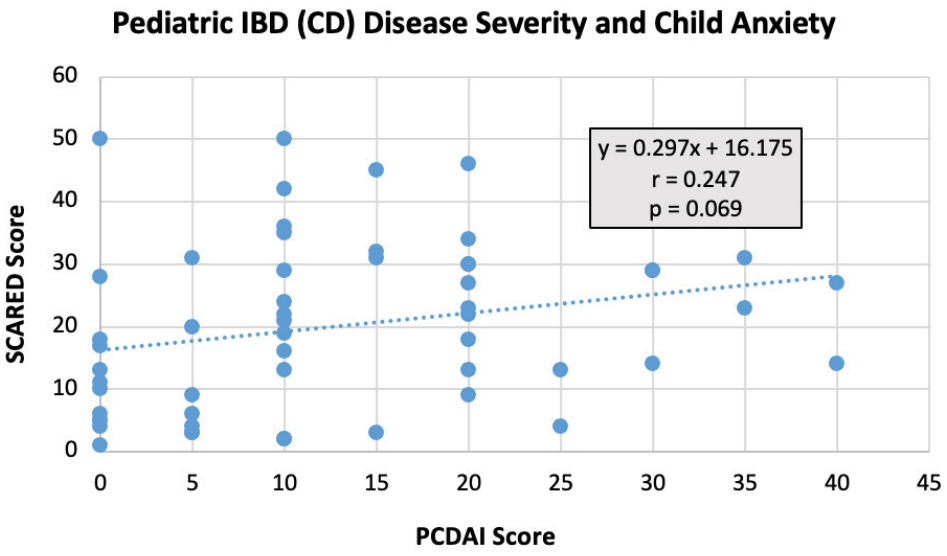

Figure 12. Child Anxiety and Disease Severity in Pediatric Crohn's Disease. A correlational analysis between SCARED scores for child anxiety and PCDAI scores for disease severity. Data shows a moderately positive trend but no significant correlation (r = 0.247; p = 0.069).

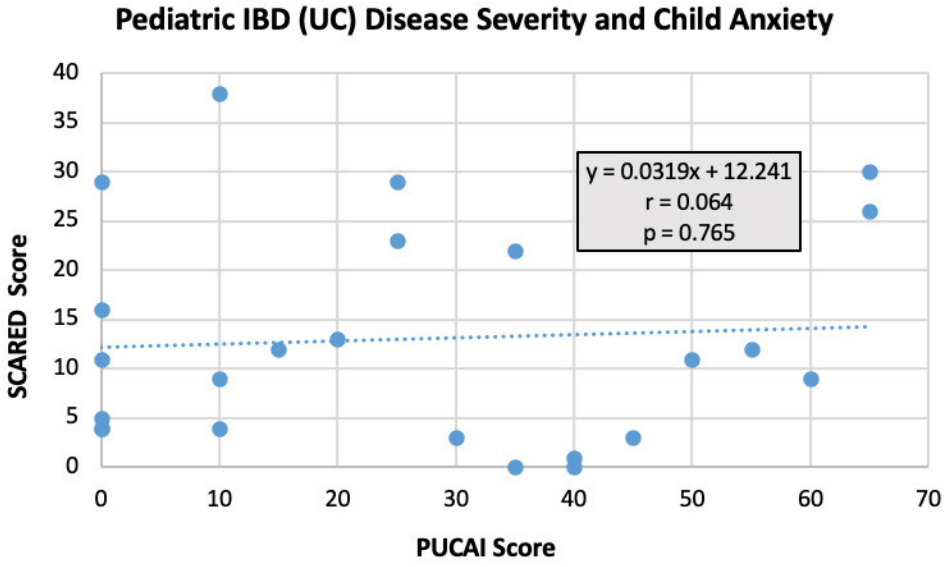

Figure 13. Child Anxiety and Disease Severity in Pediatric Ulcerative Colitis. A correlational analysis between SCARED scores for child anxiety and PUCAI scores for disease severity. Data shows a weakly positive trend but no significant correlation (r = 0.064; p = 0.765).

Figures 14 and 15 illustrate the relationship between disease severity of Crohn's disease and depression (CDI and PHQ-9, respectively) in children with Crohn's disease. A significant positive correlation can be seen in Figure 14, with an increase in the PCDAI score corresponding with an increase in the CDI score for child depression ($r = 0.375$; $p = 0.005$). While a positive trend between child depression and Crohn's disease severity is also seen in Figure 15, which uses PHQ-9 to screen for child depression, the correlation between the PHQ-9 score and PCDAI score was not found to be statistically significant ($r = 0.167$; $p = 0.224$).

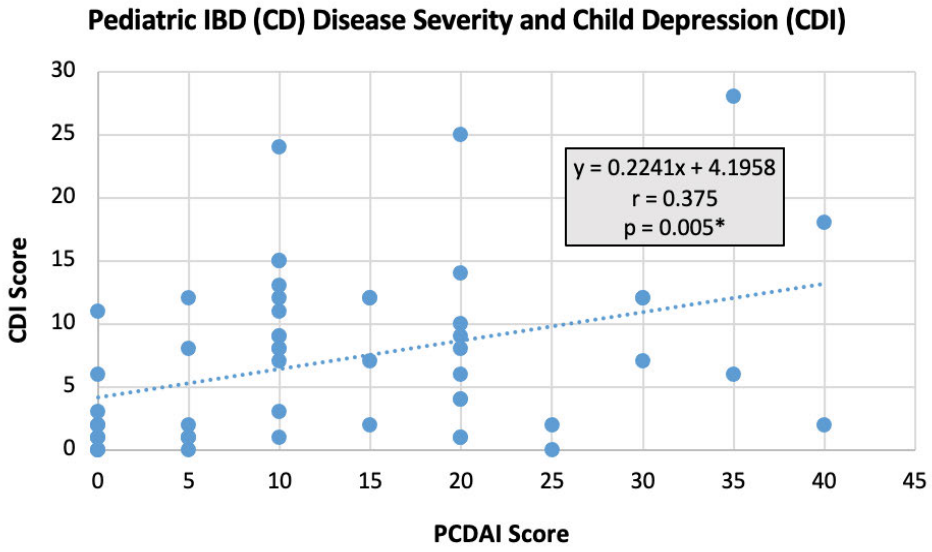

Figure 14. Child Depression (CDI Questionnaire) and Disease Severity in Pediatric Crohn's Disease. A correlational analysis between CDI scores for child depression and PCDAI scores for disease severity. Data shows a significant, moderate, positive correlation ($r = 0.375$; $p = 0.005$).

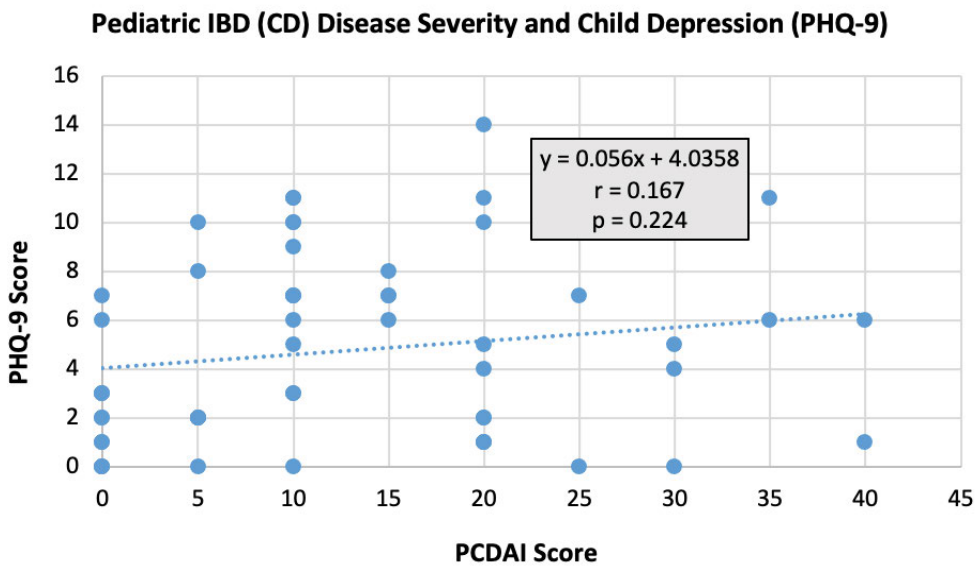

Figure 15. Child Depression (PHQ-9 Questionnaire) and Disease Severity in Pediatric Crohn's Disease. A correlational analysis between PHQ-9 scores for child depression and PCDAI scores for disease severity. Data shows a positive trend but no significant correlation ($r = 0.167$; $p = 0.224$).

No significant associations were seen with respect to disease severity and depression in children with ulcerative colitis. Similarly, as illustrated in Figure 16, there is no significant correlation between CDI scores for child depression and PUCAI scores for disease severity ($r = 0.454$; $p = 0.160$). While there was a positive trend between PHQ-9 scores for child depression and PUCAI scores ($r = 0.105$; $p = 0.626$), this did not reach statistical significance.

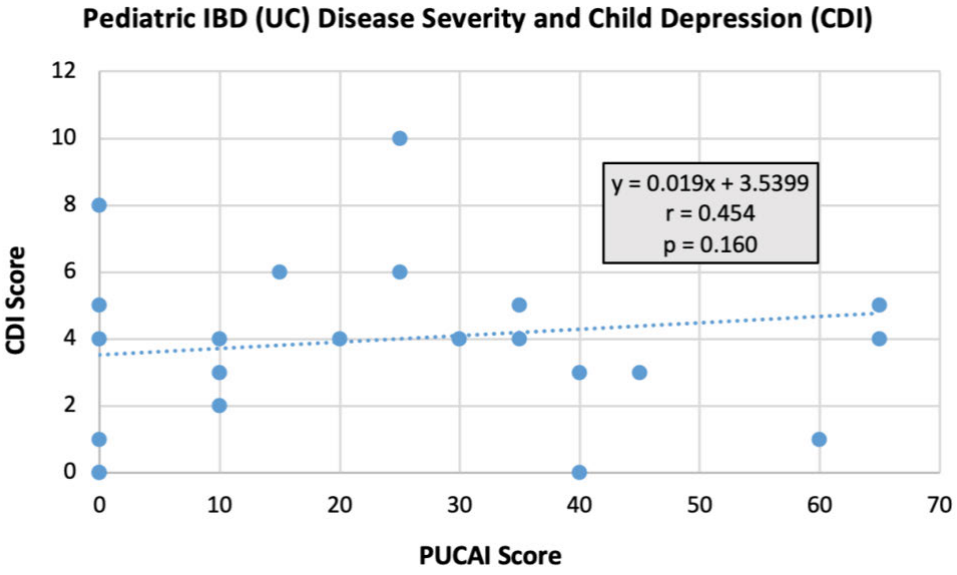

Figure 16. Child Depression (CDI Questionnaire) and Disease Severity in Pediatric Ulcerative Colitis. A correlational analysis between CDI scores for child depression and PUCAI scores for disease severity. Data shows a positive trend but no significant correlation (r = 0.454; p = 0.160).

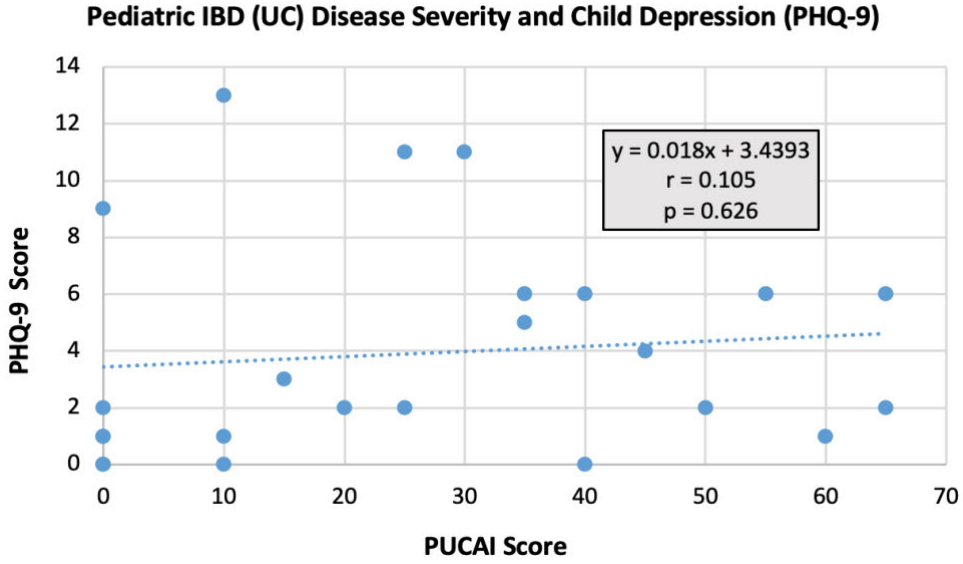

Figure 17. Child Depression (PHQ-9 Questionnaire) and Disease Severity in Pediatric Ulcerative Colitis. A correlational analysis between PHQ-9 scores for child depression and PUCAI scores for disease severity. Data shows a positive trend but no significant correlation (r = 0.105; p = 0.626).

We analyzed how the quality of life of a child with IBD may change with disease severity. A one-way ANOVA stratified disease severity into three groups: inactive, mild, and moderate-severe. The score cut-offs for each activity group and the corresponding mean IMPACT-III score can be seen in Tables 19 and 20. In particular, the data in Table 19 shows a significant decrease in the mean IMPACT-III score as the disease severity for Crohn's Disease rises significantly (p-value of 0.036) in patients with inactive (136.09), mild (126.95), and moderate-severe (115.60) disease activity. A similar inverse correlation is observed between disease activity and quality of life in patients with ulcerative colitis in Table 20. The mean IMPACT scores are 134.40 (inactive), 105.20 (mild), and 123.55 (moderate-severe), with a p-value of 0.051.

Table 19. Pediatric Quality of Life and Crohn's Disease Severity. Mean IMPACT-III scores for children with inactive (score less than 10), mild (score between 11-30), or moderate-severe (score greater than 30) Crohn's Disease. A one-way ANOVA analysis was done using a total of 59 PCDAI scores.

Disease Severity	**n**	**Mean IMPACT-III Score**	**p-value**
Inactive (<10)	34	136.09	p = 0.036*
Mild (11-30)	20	126.95	
Moderate-Severe (>30)	5	115.60	

**p < 0.05 is significant*

Table 20. Pediatric Quality of Life and Ulcerative Colitis Severity. Mean IMPACT-III scores for children with inactive (score less than 10), mild (score between 11-30), or moderate-severe (score greater than 30) Ulcerative Colitis. A one-way ANOVA analysis was done using a total of 24 PUCAI scores.

Disease Severity	**n**	**Mean IMPACT-III Score**	**p-value**
Inactive (<10)	10	134.40	p = 0.051*
Mild (11-30)	5	105.20	
Moderate-Severe (>30)	9	123.55	

**p < 0.05 is significant*

We next assessed the correlation between disease severity and parental anxiety and depression. Figure 18 depicts how the severity of the PCDAI scores for Crohn's disease change with the HADS scores for parental anxiety and depression. While a positive trend is seen for both parental anxiety ($r = 0.127$; $p = 0.342$) and parental depression ($r = 0.015$; $p = 0.912$), the correlation is not significant. In contrast, the data in Figure 19 suggest a negative correlation between PUCAI scores and parental anxiety ($r = -0.351$; $p = 0.085$) and parental depression ($r = -0.128$; $p = 0.542$).

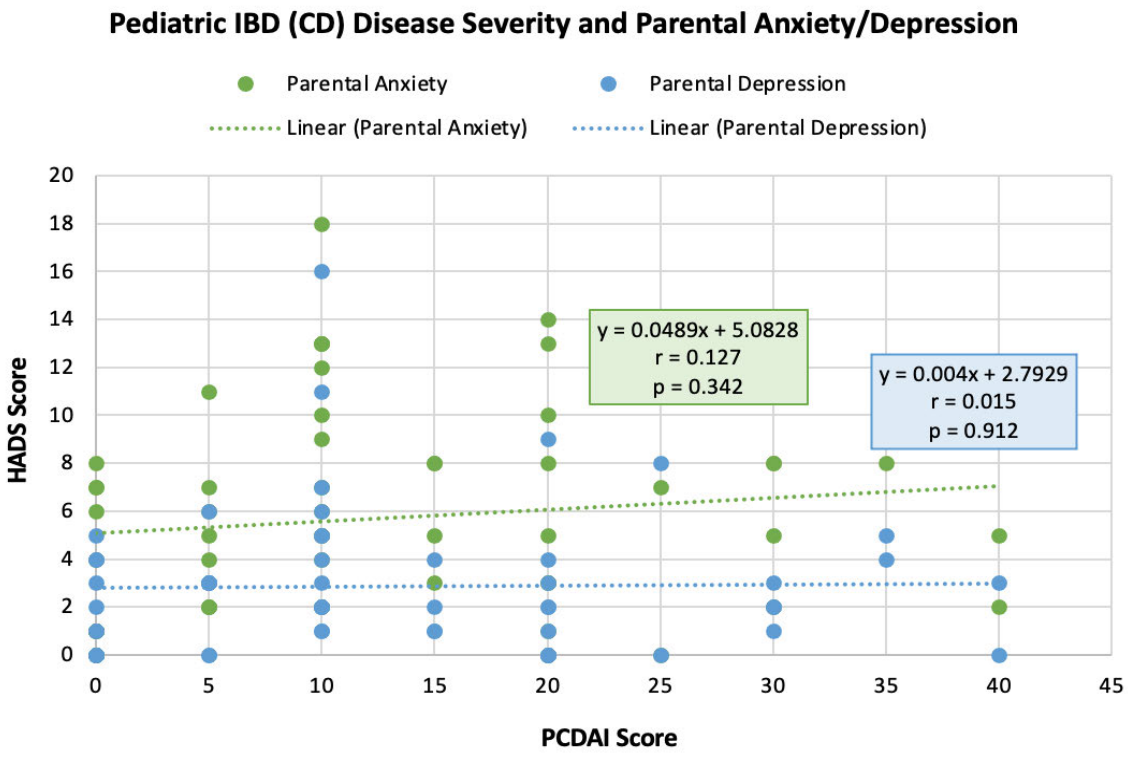

Figure 18. Parental Anxiety/Depression and Disease Severity in Pediatric Crohn's Disease. A correlational analysis between HADS scores for parental anxiety and depression and PCDAI scores for disease severity. Data shows a positive trend but no significant correlation for both parental anxiety ($r = 0.127$; $p = 0.342$) and parental depression ($r = 0.015$; $p = 0.912$).

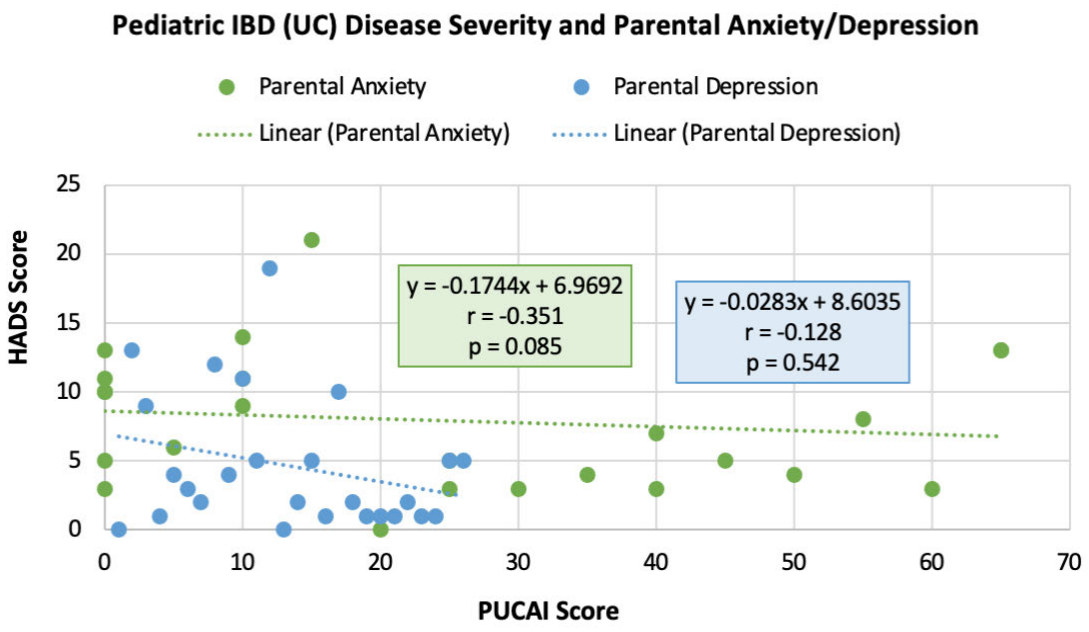

Figure 19. Parental Anxiety/Depression and Disease Severity in Pediatric Ulcerative Colitis. A correlational analysis between HADS scores for parental anxiety and depression and PUCAI scores for disease severity. Data shows a negative trend but no significant correlation for both parental anxiety ($r = -0.351$; $p = 0.085$) and parental depression ($r = -0.128$; $p = 0.542$).

Healthcare Utilization

We assessed the relationship between parental anxiety/depression and healthcare utilization. This was done by assessing the correlation between HADS scores and the data abstracted from the healthcare utilization survey. The data in Figure 20 illustrates a significant positive correlation between HADS-A and healthcare utilization, indicating greater healthcare utilization in more anxious parents ($r = 0.269$; $p = 0.017$). Similarly, in Figure 21, a significant positive correlation is also observed between HADS-D scores for parental depression and healthcare utilization scores ($r = 0.327$; $p = 0.004$).

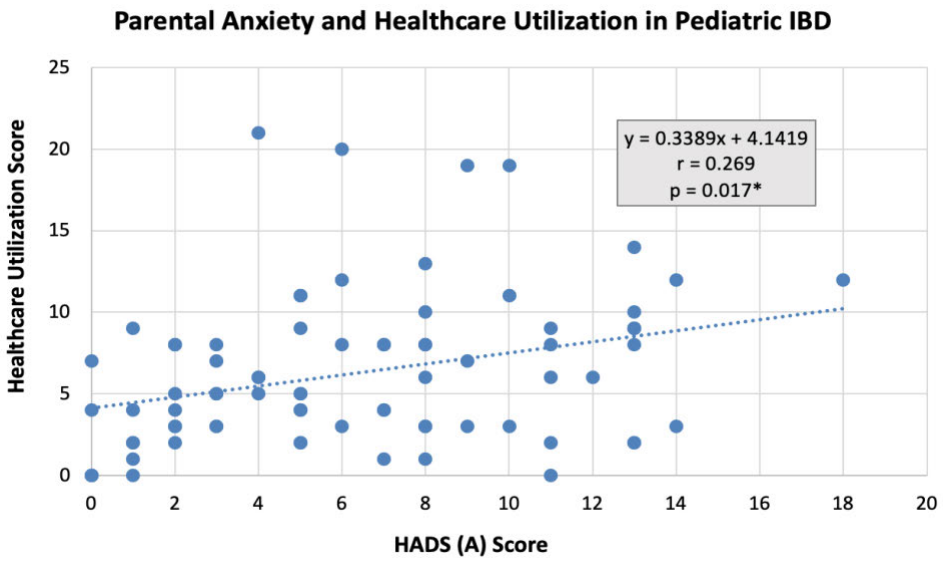

Figure 20. Parental Anxiety and Healthcare Utilization in Pediatric IBD. A correlational analysis between HADS-A scores for parental anxiety and healthcare utilization scores from the Healthcare Utilization Survey (HUS). Data shows a significant, moderate, positive correlation between parental anxiety and healthcare utilization ($r = 0.269$; $p = 0.017$).

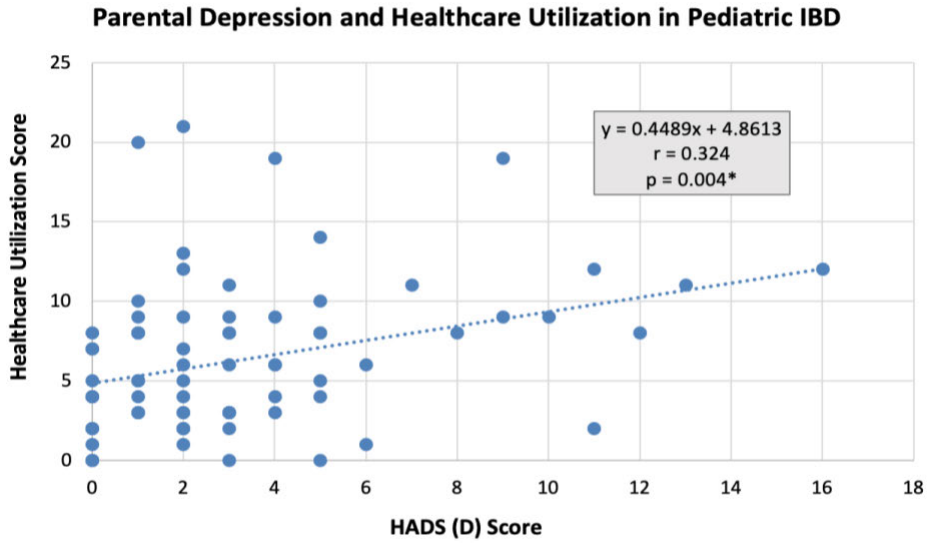

Figure 21. Parental Depression and Healthcare Utilization in Pediatric IBD. A correlational analysis between HADS-D scores for parental depression and healthcare utilization scores from the Healthcare Utilization Survey (HUS). Data shows a significant, moderate, positive correlation between parental depression and healthcare utilization ($r = 0.324$; $p = 0.004$).

One-Year Follow-Up

We next used a paired t-test to conduct a preliminary analysis to assess how child and parental scores changed over a year since their child had been initially diagnosed with IBD. As seen in Figure 22, despite a perceived decrease in the mean HADS scores, no significant difference was seen in parental anxiety or depression over time ($p = 0.676$ and $p = 0.550$, respectively).

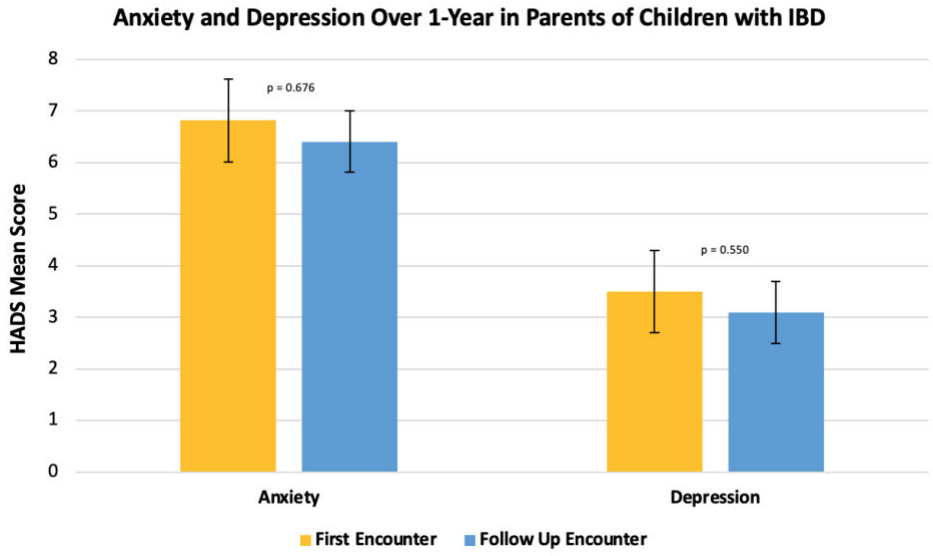

Figure 22. Parental Anxiety and Depression Over 1-Year in Pediatric IBD. Mean HADS-A and HADS-D scores at the first encounter versus at the follow-up encounter (after one year). A paired t-test was conducted with an n = 22. The mean HADS-A score at the first encounter is 6.82, while at the follow-up encounter it is 6.41 ($p = 0.676$). The mean HADS-D score at the first encounter is 3.50, while at the follow-up encounter it is 3.09 ($p = 0.550$).

We investigated the change in parental stress scores over the one-year study period by analyzing the change in PIP scores. Paired t-test analysis demonstrated a significant decrease in both parental stress frequency (PIP-F) and difficulty (PIP-D)

scores over time ($p < 0.001$). In Figure 23, PIP-F decreases from a mean score of 115.81 to 75.86 over time, while PIP-D decreases from a mean score of 96.71 to 74.62 over the same interval.

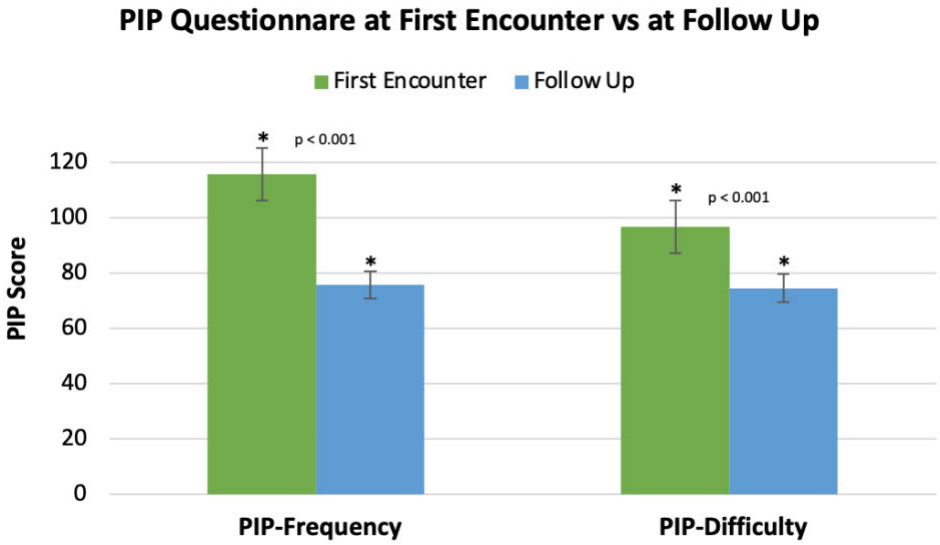

Figure 23. Parental Stress Over 1-Year in Pediatric IBD. Mean PIP-F and PIP-D scores at the first encounter versus at the follow-up encounter (after one year). A paired t-test was conducted with an $n = 21$. The mean PIP-F score at the first encounter is 115.81, while at the follow-up encounter it is 75.86 ($p < 0.001$). The mean PIP-D score at the first encounter is 96.71, while at the follow-up encounter it is 74.62 ($p < 0.001$).

We next analyzed the change in the quality of life in children with newly diagnosed IBD over one year. The data illustrated in Figure 24 demonstrates a significant improvement in a child's quality of life from the first encounter (mean IMPACT-III score of 122.42) to the follow-up encounter (mean IMPACT-III score of 142.50) with a p-value of <0.001.

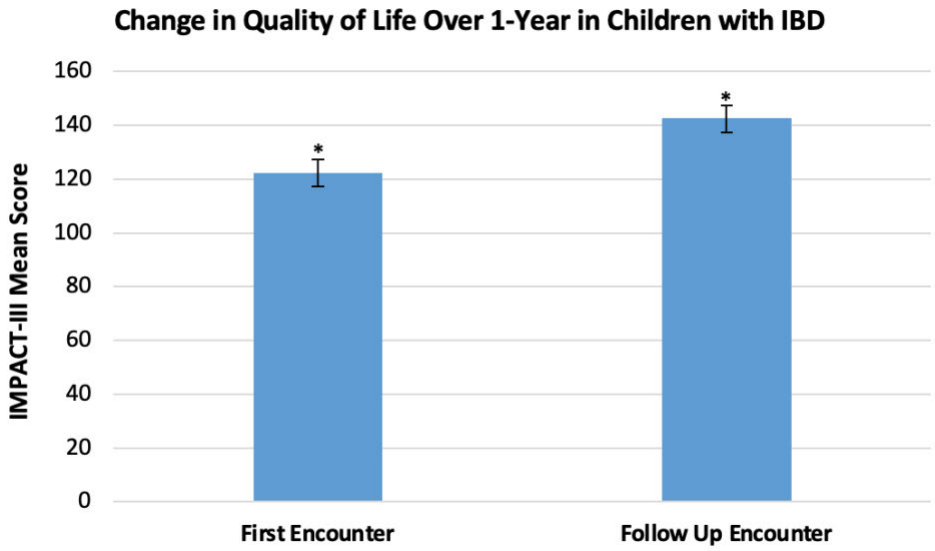

Figure 24. Quality of Life Over 1-Year in Pediatric IBD. Mean IMPACT-III scores at the first encounter versus at the follow-up encounter (after one year). A paired t-test was conducted with an n = 24. The mean IMPACT-III score at the first encounter is 122.42, while at the follow-up encounter it is 142.50 ($p < 0.001$).

A change in healthcare utilization was also seen from the first encounter to the follow-up encounter. The data in Figure 25 demonstrates a significant decrease in healthcare utilization by parents of children with newly diagnosed IBD, from a mean of 7.58 at the first encounter to 1.95 at the follow-up encounter ($p < 0.001$). The maximum healthcare utilization score at the first encounter is 21, while at the follow-up, the maximum is 6. The minimum healthcare utilization score at the first encounter is 2, while at the follow-up, the minimum is 0.

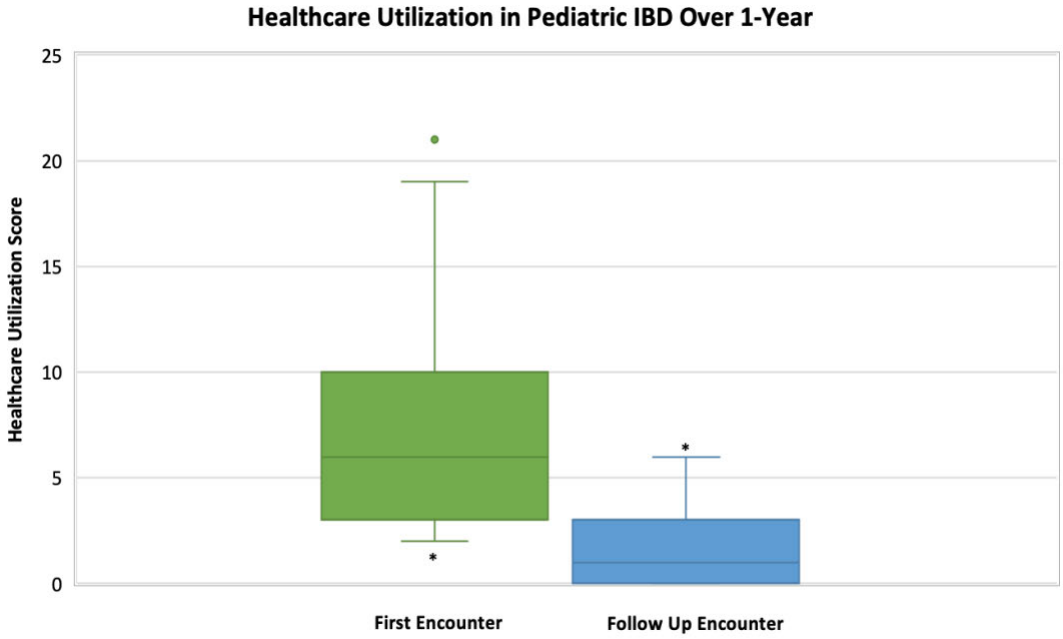

Figure 25. Healthcare Utilization Over 1-Year in Pediatric IBD. Range of healthcare utilization at the first encounter versus at the follow-up encounter (after one year). A paired t-test was conducted with an n = 19. The mean healthcare utilization score at the first encounter is 7.58, while at the follow-up encounter it is 1.95 ($p < 0.001$).

Table 21 displays the change in child anxiety and depression scores over the one-year study period. A significant decrease is seen in child anxiety over a year, with a mean SCARED score of 22.14 at the first encounter and a mean score of 18.68 at the follow-up encounter, with a p-value of 0.048. No significant changes were seen for child depression using the CDI or the PHQ-9 questionnaires, with p-values of 0.112 and 0.445, respectively.

Table 21. Child Anxiety and Depression Over One-Year Period. Mean SCARED, CDI, and PHQ-9 scores at the first encounter versus at the follow-up encounter (after one year). A paired t-test analysis showed a significant decrease in SCARED score from the first encounter (22.14) to the follow-up (18.68) at p = 0.048. No significant difference was observed for child depression over one year.

Questionnaire	**First Encounter**	**Follow-Up Encounter**	**p-value**
SCARED (n = 22)	22.14	18.68	0.048*
CDI (n = 23)	8.22	6.17	0.112
PHQ-9 (n = 20)	5.10	4.40	0.445

**p < 0.05 is significant*

DISCUSSION

The increased prevalence of IBD, particularly in children, mandates research that will enable us to best support those suffering from it. Affected children are not the only victims of IBD; the lives of parents/caregivers and siblings are impacted tremendously. Current literature suggests a complex interplay between psychosocial and biological factors in the onset, progression, and treatment of IBD. Some previous studies have found that negative coping behaviors in parents, such as being overly protective and anxious, predicted worse disease outcomes in their children with IBD[19,22]. However, the validity of this impact is still unclear, as some studies find no associations at all[21]. Several studies have also suggested a possible interaction between parent and child coping behaviors, which suggest the possibility of a positive or negative impact on disease management[19,21]. Many of these studies have not been as rigorous, which may explain the conflicting conclusions that have been reported where some studies find an interaction while others have not. The absence of consistent and/or comprehensive research findings has made it difficult for academic clinicians to standardize medical and behavioral recommendations to improve the quality of care for their pediatric patients with IBD.

Thus, the current study further investigated the associations between parental coping, child coping, and other psychosocial and clinical factors to gain a better understanding of how we can best identify and support the most vulnerable children and families. In particular, our study evaluated how the quality of life of a child with newly diagnosed IBD may or may not be related to parental anxiety, depression, and stress, as well as child anxiety and depression. Moreover, we also investigated how these factors

may be associated with disease severity and healthcare utilization. Finally, given the longitudinal nature of this study, we investigated how these various factors changed over the period of one-year.

Demographics

Previous studies have reported gender-based differences in the incidence and prevalence of IBD[31,32,33]. Herzog et al. (2014) noted a 2:1 ratio of males to females in pediatric patients with IBD, while Rustgi et al. (2020) found a 1.5:1 ratio of males to females with IBD (including adolescents and adults)[31,32]. Of the 86 children in our study, 59.3% were male and 40.7% were female (ratio of 1.4:1), which is consistent with current literature that indicates a greater prevalence of IBD in males. Furthermore, Gupta et al. (2007) found that female children reported worse disease severity and quality of life than male children[33]. This finding was not observed in our study. As described in Table 10, we found no significant difference (p-value of 0.213) in the mean IMPACT-III (quality of life) scores between males (132.61) and females (127.06).

In addition to gender, age is also a factor that may play a role in the clinical and behavioral course of IBD. Most studies compare pediatric patients with IBD to their adult counterparts[34, 35]. However, we investigated the quality of life scores within the pediatric IBD group by comparing data collected from younger children (below 12) and older children (above 12). Interestingly, we found a significant difference in IMPACT-III quality of life scores measured in older children (126.55) when compared to younger children (137.67) (Table 9). One explanation for this could be that older children

experienced a longer lag time between the onset of clinical symptoms and a diagnosis of IBD. As such, they had been suffering from the clinical and psychosocial impacts of the disease for longer before receiving any treatment. If this hypothesis is correct, efforts to better inform clinicians about recognizing the signs and symptoms of IBD could have a large impact.

Behavioral Factors and Outcomes

We next investigated how parental and child coping may predict a child's quality of life when dealing with IBD. While studies like Bramuzzo et al. 2020 found no interaction between parental anxiety/depression and outcomes in children with IBD, several other studies found that maladaptive parental coping, like anxiety and depression, may predict a worse clinical course for their children with IBD[19, 20, 21, 22].

In our study, we found a significant association between increased parental anxiety/depression and worse quality of life in children with newly diagnosed IBD (Figures 3, 4). This significant, negative correlation was observed when comparing parental anxiety (measured by HADS-A, $p < 0.001$) and parental depression (measured by HADS-D, $p < 0.010$) scores with a child's IMPACT-III score. Interestingly, when stratifying by anxious (HADS-A score > 8) vs. non-anxious parents (HADS-A score < 8) and depressed (HADS-D score > 8) vs. non-depressed parents (HADS-D score < 8), a significant decrease in the mean IMPACT-III score for quality of life was only observed for parental anxiety (Table 6, Figures 5 and 6). It is likely that we observed a significant correlation between HADS-D scores for depression and IMPACT-III scores in Figure 4,

but no significant difference when comparing the mean IMPACT-III score between groups of depressed parents with non-depressed parents because only 12.6% of parents (10 of 79) screened positive for depression on the HADS questionnaire. In addition to the small sample size, the HADS questionnaire is a screen for mood disorders and does not make an actual diagnosis, indicating that the scale is more fluid[30, 36]. While it is not possible to make any causal inferences when looking at the significant correlations in Figures 3 and 4, we can nonetheless appreciate the apparent link between greater anxiety and depressive behaviors in parents and worse quality of life in children with newly diagnosed IBD.

Moreover, published studies have reported a correlation between greater parental stress and poorer psychological adjustment in parents of children with chronic illnesses. Therefore, we analyzed the PIP questionnaire results for parental stress[19]. First, we found that greater parental stress frequency (PIP-F) and stress difficulty (PIP-D) were significantly associated with parental anxiety and depression (Tables 13 and 14). This further supports a link between stress and maladaptive coping behavior. Upon further analyzing the PIP questionnaire results, we also found that greater parental stress frequency and difficulty were significantly associated with a worse quality of life in their child ($p < 0.0001$, Figures 7 and 8). However, it remains unclear if the child's symptoms and quality of life may lead to poorer coping behavior in parents or vice versa. Nevertheless, it is evident that all of these factors are closely intertwined and may perpetuate one another. Thus, proper care and support must target both the child and their caregiver(s).

We next analyzed how parental coping may impact child coping. We found that 31% (25 of 81) of the children in our study had anxiety (SCARED score > 25), and 64% (16 of 25) of anxious children also had parents with anxiety (Table 15). We did not find a similar association between child and parental depression (Tables 16 and 17). However, the number of children who screened positive for child depression was quite low, resulting in a small sample size for comparison. Additionally, there were some discrepancies in the results obtained using the two different questionnaires used in this study to screen for child depression, the CDI and PHQ-9. 11 children (13.6%) screened positive for depression using the PHQ-9, and only three children (3.7) screened positive for depression using the CDI (Tables 16 and 17). This may have contributed to the differences observed in the analyses displayed in Figures 10 and 11, in which a significant correlation was seen between childhood depression and parental depression scores only when using the PHQ-9. The PHQ-9 is a more widely used questionnaire, can be used for both adolescents and adults, and has a sensitivity between 70-89%[28]. On the other hand, the CDI is more specific to younger children and has a sensitivity of 44-76%[37]. Additional research is needed on whether these are the best metrics to screen for child depression, especially given their disparate sensitivities. Nevertheless, despite differences in these metrics, the data presented in Figures 10 and 11 show an upward trend with greater child depression scores and parental depression scores. In future studies, a larger sample size would be beneficial in parsing out any differences and increasing confidence regarding these associations.

We further investigated how maladaptive childhood anxiety and depression may impact behavioral and clinical outcomes of IBD. There is considerable data supporting the existence of psychiatric comorbidity in children with IBD. However, it is unclear how much disease progression may be associated with anxiety and depression[6,7,13,15,16]. We found that children with anxiety reported significantly worse quality of life (123.42) than children without anxiety (133.33) (Table 18). Regarding child depression, a significant reduction in the mean IMPACT-III score was only seen in children that screened positive for depression using the PHQ-9 questionnaire (Table 18). These results support the prevalence of psychiatric comorbidities seen in the current literature. However, it is difficult to determine which factors may be the primary influence. In a study done by Pollard et al. (2018), researchers investigated how pediatric abdominal pain disorders and associated behavioral factors progressed throughout different seasons[38]. They found that children reported significantly less anxiety and abdominal pain during the summer months[38]. Similar to our study, it is unclear whether anxiety is the cause or the effect of the improvement in pain symptoms over the summer months. Nonetheless, there is certainly an important association with anxiety, which is also seen in our results.

Clinical Outcomes

While a significant difference is seen in the quality of life of children with IBD when they have anxiety or depression, we did not observe any significant association between disease severity and child coping. Specifically, no significant correlations were

observed in comparisons of PUCAI and PCDAI scores with SCARED scores for child anxiety and PHQ-9 scores for child depression (Figures 12, 13, 15, 17). A significant correlation was observed when comparing PCDAI scores with the CDI scores for child depression but not when comparing the PUCAI scores with the CDI scores (Figures 14 and 16). Given the discrepancies mentioned above between the CDI and PHQ-9 questionnaires, it is unclear whether this may be an anomaly, or it suggests a degree of association between disease activity and child coping[39]. Further analyses between these two questionnaires would be needed to support any claims regarding the relationship between disease severity and child depression.

Furthermore, we found that worse disease severity was significantly associated with a worse quality of life (Tables 19 and 20). This is an interesting finding, as previously, we found significant associations between quality of life and child coping but not disease severity and child coping. This could suggest a stronger relationship between behavioral and psychosocial outcomes and child coping behaviors, rather than clinical outcomes. However, future studies incorporating additional clinical outcomes are needed for further comparison, as PUCAI and PCDAI scores can vary between scorers and clinicians, and this may confound our results relating to disease severity[40,41].

Healthcare utilization is also an important factor in the epidemiology of disease progression and management. Recent literature shows that an increase in anxiety and depression may indicate greater healthcare utilization in patients with adult-onset IBD[42]. Given the role of parents and caregivers in pediatric IBD, we analyzed how parental anxiety and depression predict healthcare utilization for their children. Our results show a

significant correlation between parental anxiety/depression and healthcare utilization, indicating greater levels of healthcare utilization when parents were more anxious or depressed (Figures 20 and 21).

One-Year Follow-Up

Another unique aspect of our study was the longitudinal nature in which we followed participants over a one-year period. We found that children's quality of life significantly improved over a year, underscoring the importance of effective IBD treatment and intervention (Figure 24). We also found that parental stress and child anxiety decreased over a year period (Figure 23 and Table 21). However, we did not observe a similar improvement in parental anxiety, parental depression, or child depression (Figure 22 and Table 21). These results are still limited, as we only have data from 27 participants thus far. By increasing the power of this study with respect to long-term data, significant differences may also be observed in other measures.

Coping in Pediatric IBD

The strengths of this study lie in the comprehensive and validated metrics used, as well as the reduction in biases by having both parents and children report on these measures. Nevertheless, improvements in sample size and diversity, further analyses between the child depression screenings, and additional clinical measures are all needed to inform healthcare providers on how parental and child coping affects the clinical and psychological outcomes in pediatric IBD.

While the ability to draw causal inferences is limited, our results support an association between parental coping, child coping, and a child's experience with IBD. Given the impact of parental anxiety, depression, and stress on a child's quality of life, it is evident that support is needed for both children and their caregivers. This sort of holistic approach to clinical care would help break a maladaptive feedback loop in which parental or child coping, along with other clinical or behavioral symptoms of the child, may be perpetuating one another. Future research aiming to further investigate the long-term impacts and the extent to which all of these factors interact would help us to further deepen our understanding and provide better care for those who are vulnerable.

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