Disease Severity and Depressive Symptoms in Adolescents With Inflammatory Bowel Disease: The Mediating Role of Parent and Youth Illness Uncertainty

Marissa N. Baudino,1 MS, Kaitlyn L. Gamwell,1 MS, Caroline M. Roberts,1 MS, John E. Grunow,2 MD, Noel J. Jacobs,2 PhD, Stephen R. Gillaspy,2 PhD, Clayton S. Edwards,1 Larry L. Mullins,1 PhD, and John M. Chaney,1 PhD

1Oklahoma State University and 2University of Oklahoma Health Sciences Center

All correspondence concerning this article should be addressed to Marissa N. Baudino, MS, Oklahoma State University, Department of Psychology, 116 N. Murray, Stillwater, OK 74078, USA. E-mail: marissa.baudino@okstate.edu

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Abstract

Objective The objective of this study is to examine parent and youth appraisals of illness uncertainty as potential serial mediators in the relation between disease severity and youth depressive symptoms in adolescents with inflammatory bowel disease (IBD). Methods Participants were 85 adolescents 13–18 years of age (M.age = 15.75, SD = 1.51) with a confirmed diagnosis of IBD (Crohn’s disease, 59%; ulcerative colitis, 41%) and a primary caregiver. At a scheduled outpatient visit, caregivers completed a measure of illness uncertainty, while adolescents completed measures of illness uncertainty and depressive symptoms. Pediatric gastroenterologists provided global estimates of disease severity. Results Path analysis revealed several significant direct and indirect associations among the modeled variables. Importantly, results provided support for the hypothesized disease severity → parent illness uncertainty → youth illness uncertainty → youth depressive symptoms serial mediation path (95% confidence interval = 0.04 to 1.10). Conclusions Results indicate that increased disease activity may serve to magnify the unpredictable nature of IBD for parents, reflected in heightened perceptions of illness uncertainty. Our findings also suggest that increased parent illness uncertainty has a significant influence on youth illness uncertainty appraisals, which in turn translates into elevated depressive symptoms in adolescents with IBD. The clinical implications of our findings and suggestions for future studies are discussed.

Key words: chronic illness; inflammatory bowel disease; depression; gastroenterology; psychosocial functioning.

Introduction

Inflammatory bowel disease (IBD) is characterized by episodic, intermittent, and recurrent abdominal distress associated with inflammation of the digestive tract (Tamboli, 2007). The prevalence of pediatric onset IBD has increased in recent years (Day, Ledder, Leach, & Lemberg, 2012). Further, approximately 25% of patients are diagnosed before the age of 20, with the peak age of onset occurring in adolescence (Rosen, Dhawan, & Saeed, 2015). Symptoms can include frequent diarrhea, rectal bleeding, pubertal delay, and weight loss (Mamula, Markowitz, &
Baldassano, 2003). The goals of IBD management are aimed at reducing inflammation in the digestive tract to minimize symptoms. Although treatment regimens vary, they typically include dietary restrictions, multiple medications, and even surgical intervention (Tamboli, 2007).

Studies suggest that the difficult and embarrassing symptoms, as well as demanding treatment regimens, pose significant challenges for youth with IBD and can result in psychosocial adjustment difficulties, particularly depression and depressive symptomatology (Clark et al., 2014; Gamwell et al., 2018; Greenley et al., 2010; Guilfoyle, Gray, Herzer-Maddux, & Hommel, 2014; Mackner & Crandall, 2006; Schuman, Graef, Janicke, Gray, & Hommel, 2013). In addition, adolescents with IBD in particular may be at increased risk for experiencing adjustment problems (Mackner & Crandall, 2006; Szigethy et al., 2004), owing in part to the social and emotional sequelae of IBD symptoms that can be especially disruptive for adolescents during this critical developmental period (Karwowski, Keljo, & Szigethy, 2009; Mackner et al., 2013).

IBD symptom severity appears to have significant implications for adolescent adjustment and is associated with some psychosocial outcomes in this age group (i.e., school functioning, health-related quality of life, and depressive symptoms; Carreon, Bugno, Wojtowicz, & Greenley, 2018; Gray, Denson, Baldassano, & Hommel, 2011; Schuman et al., 2013). However, the link between objective estimates of IBD disease activity/severity and adolescent adjustment is inconclusive, suggesting that indices of IBD activity explain only a portion of the variance in youth outcomes (Reed-Knight, Lee, Greenley, Lewis, & Blount, 2016; Reed-Knight et al., 2017; Walter et al., 2016). Further, consistent with observations across a number of pediatric chronic illness populations, including IBD (Gamwell et al., 2018; Guilfoyle et al., 2014; Ramsey et al., 2014; Ryan et al., 2010; Wagner et al., 2003), these findings may also suggest that IBD impacts youth emotional functioning indirectly through subjective illness appraisals. In other words, the manner in which IBD symptom activity is personally perceived may create an increased vulnerability for youth adjustment difficulties. A better understanding of illness appraisals emanating from the clinical experience of IBD that are associated with depressive symptoms could ultimately inform prevention and/or clinical intervention efforts for youth with IBD.

Of particular interest to the present investigation is the highly variable nature of IBD, characterized by diagnostic delays, differential patterns of disease activity/severity, variable disease progression, and unanticipated disease flares (Hommel, Denson, & Baldassano, 2011; Lix et al., 2008; Mamula et al., 2003). Multiple discussions in the pediatric IBD literature highlight the challenges created by the unpredictable and uncertain nature of IBD (Greenley, Reed-Knight, Blount, & Wilson, 2013; Herzer, Denson, Baldassano, & Hommel, 2011; Reed-Knight et al., 2014; Schuman et al., 2013; Szigethy, McLafferty, & Goyal, 2010). One clear inference from these commentaries is that the clinical course and treatment of pediatric IBD embodies many of the key features of the illness uncertainty process that can ensue when important domains of illness are not easily discernible (e.g., diagnostic imprecision/delay, regimen ambiguity, prognostic uncertainty, and unpredictable disease flares; Stewart & Mishel, 2000). Indeed, the inherent uncertainty in IBD has been implicated as a likely contributor to youth adjustment outcomes (Loreaux, Gray, Denson, & Hommel, 2015). Gray and colleagues (2011) point specifically to the need to examine illness uncertainty as an important appraisal process associated with adjustment in youth with IBD. This appeal is supported by findings in the pediatric literature across a range of chronic illness conditions demonstrating reliable associations between youth perceptions of illness uncertainty and adjustment outcomes, including depressive symptoms (Carpentier, Mullins, Wagner, Wolfe-Christensen, & Chaney, 2007; Pai et al., 2006). However, no known studies have examined the contribution of illness uncertainty to adjustment outcomes in youth with IBD.

Importantly, a number of authors have noted that not only youth but parents may also struggle with the unpredictability that accompanies IBD (Gray, Graef, Schuman, Janicke, & Hommel, 2013; Guilfoyle, Denson, Baldassano, & Hommel, 2012). These observations may have direct implications for adolescent adjustment, particularly in light of findings indicating that the majority of parents continue to be involved in managing their adolescent child’s IBD and providing extensive oversight at a time normally characterized by increased youth independence (Fishman, Barendse, Hait, Burdick, & Arnold, 2010). Moreover, if parents experience their child’s IBD as unpredictable and uncertain, it may increase the likelihood for parents’ uncertainty appraisals to influence adolescent illness perceptions in a similar direction, resulting in increased depressive symptoms. Although the literature in this area is not extensive, existing studies in other pediatric chronic illness groups indicate that parents’ perceptions of illness uncertainty have significant effects on youth adjustment outcomes (e.g., depressive symptoms and quality of life; Chaney et al., 2016; Mullins et al., 2016), particularly among adolescents (Fedele et al., 2011). Notably, evidence suggests that the manner in which parent illness uncertainty impacts youth adjustment is indirect and operates through its influence on youth perceptions of illness uncertainty (Page et al., 2012).
Taken together, the existing pediatric IBD literature indicates that youth, and adolescents in particular, may be at risk for experiencing depressive symptoms. Further, the inconsistent evidence linking IBD symptom severity and youth adjustment outcomes points to the need to examine subjective illness appraisals to more fully understand the mechanisms by which IBD impacts youth emotional adjustment. Although no known studies have examined the impact of perceived illness uncertainty on adjustment in youth with IBD, findings in other pediatric chronic illness populations indicate that both parent and youth perceptions of illness uncertainty are reliably associated with youth adjustment outcomes, including depressive symptoms. Perhaps more importantly, evidence suggests that youth perceptions of illness uncertainty mediate the association between parent illness uncertainty and youth depressive symptoms.

The present study was designed to investigate illness uncertainty appraisals as potential intermediary variables linking IBD disease severity and youth depressive symptoms. Specifically, we examined parent and youth-perceived illness uncertainty as serial mediators in the relation between disease severity and depressive symptoms in adolescents with IBD. We tested a model in which increased IBD disease severity was hypothesized to engender heightened perceptions of parent illness uncertainty, which impact youth-perceived illness uncertainty, and in turn elevated levels of youth depressive symptoms. Although the primary aim of our study was to test the proposed disease severity—parent illness uncertainty—youth illness uncertainty—youth depressive symptoms serial mediation path, the direct and alternative indirect paths of the modeled variables were also examined.

**Methods**

**Participants and Procedure**

Participants included 85 caregiver–adolescent dyads. Adolescents (48.2% female) were between the ages of 13–18 years (M<sub>age</sub> = 15.75, SD = 1.51) and were diagnosed with IBD (Crohn’s disease [CD] 58.8% and ulcerative colitis [UC] 41.2%). Medication regimens consisted of anti-inflammatory (N = 28; 33%), steroid (N = 28; 33%), and immunosuppressant/biologic (N = 50; 59%) treatments. The average duration of illness was 2.96 years (SD = 2.90). The sample was largely Caucasian (74.1%), followed by African American (5.9%), Hispanic (4.7%), Native American (4.7%), Asian (1.2%), and other (9.4%). Eighty percent of caregiver participants were mothers, followed by fathers (18%), and grandmothers (2%). The mean age of caregivers was 43.9 years (SD = 6.7). Sixty-two caregivers (73%) reported they were married/remarried, 17 (20%) were divorced, and 6 (7%) were never married, widowed, or other.

Adolescents and a primary caregiver were recruited from a pediatric gastroenterology clinic at a large children’s hospital in the southwest United States. Institutional review board approvals were obtained before initiation of the study, and all procedures adhered to American Psychological Association standards. Inclusion criteria for the study were (1) youth participant had an IBD diagnosis confirmed by a pediatric gastroenterologist; (2) youth participant was between 13 and 18 years of age; (3) both youth and caregiver were English proficient; and (4) neither youth participant nor caregiver had existing documented cognitive deficits. Pediatric gastroenterologists identified families who met eligibility criteria. Of the 88 potential adolescent participants identified, three declined to participate because of time constraints/schedule conflicts. Complete data were collected on all 85 (97%) participants, resulting in a 100% completion rate. Members of the research team informed families of their eligibility via mail and recruited them during routine clinic visits. During the visit, informed consent was obtained and participants were administered self-report measures; physicians completed ratings of disease severity. After completing the measures, participants were compensated with $20.

**Measures**

A 24-item Background Information Questionnaire was administered to caregivers to obtain demographic information (e.g., child age, child gender, family income, and race/ethnicity). Medical chart reviews were also conducted to gather relevant disease information (e.g., illness duration and current medications).

**Physician’s Global Assessment**

The attending pediatric gastroenterologist completed the Physician’s Global Assessment (PGA), an index of disease activity/severity that is rated on a 0–3 scale (i.e., quiescent, mild, moderate, and severe), with higher scores indicating greater disease severity. The PGA has been shown to correlate highly with specific measures of CD and UC activity (e.g., Pediatric Crohn’s Disease Activity Index [PCDAI], Pediatric Ulcerative Colitis Activity Index [PUCAI]; Hyams et al., 2005; Turner et al., 2009).

**Parent Perceptions of Uncertainty Scale**

The Parent Perceptions of Uncertainty Scale (PPUS) is a 31-item, self-report measure to assess caregiver perceptions regarding the uncertainty of their child’s illness (Mishel, 1983). The PPUS assesses four components of illness uncertainty: unpredictability, lack of clarity, lack of information, and ambiguity. In the present study, parents indicated the extent to
which they agreed with each of the 31 items (e.g., My child’s symptoms continue to change unpredictably) on a five-point scale (e.g., Strongly Agree to Strongly Disagree). Items were summed to obtain total scores in which higher scores indicated increased perceived illness uncertainty. The PPUS has demonstrated good internal consistency in parents of youth with other chronic illnesses (Chaney et al., 2016; Fedele et al., 2011). Cronbach’s alpha for the current sample was .81.

Child Uncertainty in Illness Scale
The Child Uncertainty in Illness Scale (CUIS; Mullins & Hartman, 1995) is a 23-item, self-report measure adapted from the Mishel Uncertainty in Illness Scale—Community Form (Mishel, 1983) and is used to assess youth perceptions of uncertainty regarding the prognosis, course, and treatment of their illness. Similar to the PPUS, the CUIS assesses perceptions of illness uncertainty in youth across the following domains: unpredictability, lack of clarity, lack of information, and ambiguity. In the current sample, adolescents indicated the extent to which they agreed with each item (e.g., I never know how I will feel; I have good days and bad days) on a five-point scale (e.g., Very true to Very False). Total scores were obtained by summing all items with higher scores indicating higher perceived illness uncertainty. The CUIS has demonstrated good internal consistency across a range of pediatric chronic illness groups (Page et al., 2012; White et al., 2005). In the current sample, Cronbach’s alpha was .84.

Children’s Depression Inventory-2nd Edition
The children’s depression inventory-2nd Edition (CDI-2; Kovacs, 2011) is a 28-item self-report measure used to assess child and adolescent depressive symptoms during the previous 2-week period. Youth rated the severity of depression-related items on a scale from 0 to 2 (e.g., 0= I am sad once in a while, 1= I am sad many times, 2= I am sad all the time). Items on the CDI-2 assess functioning across five areas: negative mood/physical symptoms, interpersonal problems, functional problems, ineffectiveness, and negative self-esteem (Kovacs, 2011). Total scores used in the primary analyses were calculated by summing all 28 items; higher scores indicated more severe depressive symptoms. The original CDI has demonstrated good internal consistency in youth with IBD (Clark et al., 2014; Reed-Knight et al., 2014; Schuman et al., 2013). The CDI-2 has also demonstrated good internal reliability in previous studies of youth with IBD (Gamwell et al., 2018). In the present sample, Cronbach’s alpha was .88.

Results
Data Analytic Plan
Serial mediation was tested in the primary analyses using the structural equation software Mplus version 7.31 (Muthén & Muthén, 1998-2012). Consistent with current recommendations (Hayes, 2013), direct and indirect effects were assessed by evaluating the 95% confidence intervals yielded from 5,000 bootstrapped resampling draws with replacement. Mediation was specified for a serial mediation path with PGA predicting child depressive symptoms via sequential indirect effects through parent illness uncertainty and child illness uncertainty (i.e., PGA→PPUS→CUIS→CDI-2). In addition to testing the overall serial mediation model, we examined the direct effects and alternative indirect paths among modeled variables.

Preliminary Analyses
Relatively low levels of disease severity were observed on the PGA (M = .27, SD = .64, Range = 0.0–3.0); 82.4% (N = 70) of youth were rated on the PGA as having quiescent disease, 9.4% (N = 8) as mild, 7% (N = 6) as moderate, and 1.2% (N = 1) as severe. Parent mean scores on the PPUS were 65.9 (SD = 14.2, Range = 39.00–100.0); youth mean scores on the CUIS were 51.6 (SD = 13.4, Range = 27.0–87.0). Although mild levels of depressive symptoms were observed (M = 8.7, SD = 6.9, Range = 0.0–33.0), general scoring guidelines (raw scores ≥14; Kovacs, 2011) indicated that 26% (N = 22) of the sample endorsed clinically elevated levels of depressive symptoms.

Mean comparisons (t-tests) indicated that CDI-2 scores did not differ by ethnicity, IBD type (UC or CD), or medication type (anti-inflammatory, corticosteroid, immunosuppressant, and biologic agents; all p’s > .05). However, a significant gender difference in CDI-2 scores was found, with girls (M = 11.07) endorsing more depressive symptoms than boys (M = 6.57), t(83) = 3.158, p = .002. Further, bivariate correlations revealed that no potential demographic (i.e., age and income) or disease (i.e., duration) covariates were significantly correlated with CDI-2 depressive symptoms. Based on the preliminary analyses, gender was included as a covariate in the primary analyses.

Primary Analyses
Direct Effects
Path coefficients (see Table 1) revealed direct effects for PGA→PPUS (a₁), PPUS→CUIS (d₂₁), and CUIS→CDI-2 (b₂), indicating significant associations between disease severity and parent illness uncertainty, parent illness uncertainty and youth illness uncertainty, and between youth illness uncertainty and youth depressive symptoms. No significant direct effects were observed for PGA→CDI-2 (c), PGA→CUIS (a₂), or PPUS→CDI-2 (b₁) (all p’s > .05). Thus, no significant direct associations were observed.
between disease severity and either youth depressive symptoms or youth illness uncertainty, and parent illness uncertainty was not directly related to youth depressive symptoms. All variables in the model combined to account for significant variance in youth depressive symptoms ($R^2 = .28, p < .001$).

### Indirect Effects
Bias-corrected bootstrap confidence intervals revealed significant indirect paths for PGA → PPUS → CUIS ($a_1d_{21}$) and PPUS → CUIS → CDI-2 ($d_{21}b_2$) (see Figure 1), indicating that elevated disease severity indirectly influenced youth illness uncertainty through heightened parent illness uncertainty, and that greater parent illness uncertainty had an indirect effect on increased youth depressive symptoms via youth illness uncertainty. Importantly, mediation results also supported the hypothesized PGA → PPUS → CUIS → CDI-2 serial indirect path ($a_1d_{21}b_2$), suggesting that the effect from disease severity to youth depressive symptoms was conveyed indirectly through the influence of increased disease severity on heightened parent illness uncertainty, and the effect of parent illness uncertainty on greater youth illness uncertainty, eventuating in elevated youth depressive symptoms.

### Discussion
Studies indicate that adolescents with IBD are at increased risk for experiencing depressive symptoms, and that disease severity explains only a portion of the observed emotional challenges in this population. Based on speculation in the literature implicating the unpredictable nature of IBD in youth adjustment outcomes, the present study examined the role of parent and youth perceptions of illness uncertainty in the association between disease severity and depressive symptoms in adolescents with IBD. Specifically, we tested a serial mediation model in which increased IBD disease severity was hypothesized to predict youth depressive symptoms via sequential indirect effects through parent illness uncertainty and adolescent illness uncertainty. Results supported the hypothesized serial mediation model, indicating that disease severity was directly associated with increased parent illness uncertainty, which was indirectly related to elevated adolescent depressive symptoms via youth illness uncertainty. Although the CUIS and PPUS measures used in the present study were not designed to assess IBD-specific uncertainty, our results were consistent with studies across a number of pediatric chronic illness conditions (Fedele et al., 2011; Page et al., 2012; Pai et al., 2006; White et al., 2005) and highlight the role of parent and youth illness uncertainty appraisals in adjustment outcomes in adolescence with IBD. That parent-perceived illness uncertainty impacted adolescent depressive symptoms indirectly through youth illness uncertainty further underscores the transactional nature of adjustment observed in this population (Guilfoyle et al., 2014; Herzer et al., 2011).

Although the present results suggest that greater parent-perceived uncertainty contributes directly to youth perceptions of uncertainty and indirectly to elevated youth depressive symptoms during periods of increased disease activity, a number of authors in the IBD literature have pointed out that youth and their families likely experience some degree of ongoing uncertainty even during times of quiescent disease (Gray et al., 2013; Guilfoyle et al., 2012, Nicholas, Otley, Smith, & Avolio, 2007; Varni et al., 2017). In other words, the intermittent and often unpredictable nature of IBD provides multiple occasions for exposure to ambiguous disease-related situations (e.g., unanticipated disease flares, unreliable illness cues, and tentative responses to disease flares), which may sensitize both parents and youth to the uncertain prospects of future aversive disease events. Although prospective examinations would be needed to determine the

### Table I. Path Analysis Estimates of Direct and Indirect Effects

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<th>Direct paths</th>
<th>Indirect Paths</th>
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<tr>
<td>PGA → PPUS</td>
<td>PGA → PPUS → CUIS (a1d21)</td>
</tr>
<tr>
<td>PGA → CUIS</td>
<td>PPUS → CUIS → CDI-2 (d21b2)</td>
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<td>PPUS → CUIS</td>
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<td>PPUS → CDI-2</td>
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<td>CUIS → CDI-2</td>
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<td>PGA → CDI-2</td>
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**Note.** All analyses controlled for youth gender. CDI-2 = Children’s Depression Inventory-2nd Edition; CUIS = Child Uncertainty in Illness Scale; PGA = Physician’s Global Assessment; PPUS = Parent Perceptions of Uncertainty Scale.
temporal relation between disease course features, uncertainty, and adjustment outcomes, our findings suggest that when youth disease activity is elevated it is associated with heightened parent perceptions of uncertainty, which negatively impact youths’ uncertainty and, in turn, youth depressive symptoms.

Unfortunately, our data do not inform us of the precise manner in which parent uncertainty is conveyed to youth. However, studies in other pediatric chronic illness groups (e.g., diabetes, asthma, cystic fibrosis) suggest that it is probably a function of indirect and direct parent behaviors that communicate uncertainty regarding IBD management and/or the course of disease (Page et al., 2012). For example, as a function of their parents’ heightened illness uncertainty, adolescents may pick up on verbal and non-verbal cues that reveal parents’ confusion about/unmet needs for disease information, misgivings or self-doubt regarding specific strategies for handling day-to-day aspects of IBD, or their inability to forecast future disease flares. More directly, parents who are experiencing a great deal of uncertainty may be reticent or unable to answer youths’ illness-related questions, which could contribute to adolescents’ existing perceptions of uncertainty surrounding their IBD.

Although it is unclear the exact mechanism(s) by which parent uncertainty is transmitted to youth, the research literature is clear that uncertainty for aversive events has the effect of heightening expectations for future negative outcomes and increasing negative mood (Grüpe & Nitschke, 2011; Sarinopoulos et al., 2010). Given existing findings demonstrating a link between disease expectations and adjustment outcomes in adolescents with IBD (i.e., van der Zaag-Loonen, Grotenhuis, Last, & Derkx, 2004), it may be that youth who experience greater uncertainty associated with disease flares come to anticipate future aversive disease outcomes as inevitable, potentially resulting in ineffective coping strategies, feelings of despair, and an increased vulnerability for depressive symptoms.

Clinical Implications
Because illness uncertainty provides a potentially malleable target for clinical interventions, the current results have a number of important clinical implications for youth with IBD and their parents. Although some equivocal results have been reported (Stapersma et al., 2018), cognitive behavioral therapy (CBT) programs for youth have yielded positive treatment effects for perceptions of control, feelings of helplessness, and depressive symptoms in adolescents with IBD (e.g., Primary and Secondary Control Enhancement Training-Physical Illness [PACET-PI]; Szigethy et al., 2004, 2007). Significant elements of such treatment approaches focus on psychoeducation about IBD, identifying/modifying negative cognitive distortions about IBD, encouraging behavioral activation, and developing effective problem-solving skills and coping strategies. Illness uncertainty could be easily incorporated into CBT protocols as a specific target of intervention.

Similar randomized clinical trials designed to teach parents effective management of uncertainties associated with their child’s illness have likewise yielded positive results in parents of youth with chronic medical conditions (e.g., diabetes and cancer; Hoff et al., 2005; Mullins et al., 2012). Of particular relevance to the transactional parent–youth uncertainty associations observed in the present study, these studies demonstrated significant improvement in child adjustment outcomes, despite the fact that only parents were

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**Figure 1.** Serial mediation model and observed significant direct paths.

*Note.* All analyses controlled for youth gender. Indirect paths PGA—PPUS—CUIS (a1d1), PPUS—CUIS—CDI-2 (d1b2), and PGA—PPUS—CUIS—CDI-2 (a1d1b2) were statistically significant (p < .05). PGA = Physician’s Global Assessment; PPUS = Parent Perceptions of Uncertainty Scale; CUIS = Child Uncertainty in Illness Scale; CDI-2 = Children’s Depression Inventory-2nd Edition.
involved in treatment (Fedele et al., 2013). Evidence for such downstream effects could suggest that parent-focused interventions for the uncertainties surrounding IBD may have direct benefits for parents and indirectly facilitate better youth adjustment.

**Limitations**

Interpretation of the present findings is primarily limited by the cross-sectional design of our investigation. In addition to the potential for biased estimates in the associations among variables (compared with longitudinal data; see Maxwell & Cole, 2007), the cross-sectional nature of our data precludes definitive statements regarding the hypothesized sequential links between our modeled variables. Further, it should be noted that our hypothesized model is not intended to be inclusive of all potential variables that influence youth adjustment in IBD but suggests one potential route by which parent and youth cognitive appraisals negatively impact youth emotional outcomes. Indeed, several studies in the pediatric IBD literature have demonstrated that other parent and youth variables (e.g., parenting stress, parent depression, illness stigma, and social belongingness) are associated with youth adjustment outcomes (Gamwell et al., 2018; Guilfoyle et al., 2014; Loreaux et al., 2015). Finally, the majority of participants in our sample were Caucasian from middle to upper socioeconomic classes and were experiencing mild disease activity. These demographic and disease characteristics are similar to other samples in the pediatric IBD literature (Greenley et al., 2010; Reed-Knight et al., 2016). However, the relatively homogeneous nature of our sample limits the generalizability our findings to youth from more diverse ethnic and socioeconomic backgrounds, or youth experiencing more active disease.

**Summary and Future Directions**

To our knowledge, the present study is the first to empirically demonstrate the contribution of illness uncertainty to adjustment in youth with IBD. In general, our findings highlight the importance of examining disease-relevant parent and youth cognitive appraisals related to depressive symptoms in adolescents with IBD. Future studies that use longitudinal designs could allow for a better understanding of the temporal relations between illness uncertainty appraisals and youth adjustment outcomes. Further, although the pediatric IBD literature indicates that disease progression and clinical disease patterns (e.g., acute, chronic, and fluctuating) are not directly associated with youth outcomes (Szigelth et al., 2004; van der Zaag-Loonen et al., 2004), it is possible that disease patterns may indirectly relate to youth outcomes through their effect on IBD uncertainty. Thus, prospective studies could also provide insight into the potential impact of chronological disease patterns on illness appraisal variables like uncertainty and youth adjustment outcomes.

Although research in pediatric IBD has begun to examine a variety of potential determinants of depressive symptoms in youth with IBD (e.g., socioeconomic status, stigma, and parenting stress; Clark et al., 2014; Gamwell et al., 2018; Guilfoyle et al., 2014), investigations have yet to fully explore cognitive appraisals associated with the unique clinical features of IBD that may contribute to youth depressive symptoms. Because IBD often imposes significant lifestyle disruptions for adolescents and their parents (Gray et al., 2013; Guilfoyle et al., 2014), future research examining the impact of IBD intrusiveness, as well as other relevant illness appraisals, could further our understanding of the adjustment challenges faced by both youth with IBD and their parents. Inconsistent findings of clinical intervention studies in the pediatric IBD literature (Stapersma et al., 2018) may also point to the continued need for studies to identify resiliency variables that could inform treatment efforts aimed at reducing the impact of IBD on youth psychosocial adjustment.

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