ALEXITHYMIA IN ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE

APPROVED BY SUPERVISORY COMMITTEE

Crista Wetherington, Ph.D. _____

Ashish Patel, M.D. _____

Gabriela Reed, Ph.D. _____

Stephen Robertson, Ph.D. _____

Sunita Stewart, Ph.D. _____

DEDICATION

To the woman who tackled a master's thesis with three young children giggling beneath her desk and somehow managed to merrily join in their play, while devoting to each her unconditional love.

Mommy, you never cease to inspire me.

ALEXITHYMIA IN ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE

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JAIME DORIAN CROWLEY

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ALEXITHYMIA IN ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE

JAIME DORIAN CROWLEY, B.A.

The University of Texas Southwestern Medical Center at Dallas, 2012

CRISTA WETHERINGTON, Ph.D.

Adolescents with inflammatory bowel disease exhibit increased psychosocial problems, such as higher rates of depressive symptoms; however, the relationship between psychological factors and health outcomes remains relatively unstudied in this pediatric population. Both depression and stress have been linked to health outcomes in adults with inflammatory bowel disease. Alexithymia, defined as a personality trait and affective deficit disorder, may represent another psychological variable influencing health outcomes in inflammatory bowel disease populations. While no prior studies have investigated alexithymia in adolescents with inflammatory bowel disease, higher rates of alexithymia have been documented and associated with poorer quality of

life in adults with inflammatory bowel disease. This study investigated the prevalence of alexithymia in adolescents with inflammatory bowel disease and examined the relationship between alexithymia and other psychological variables (i.e., depressive symptoms and perceived stress). An additional aim was to determine whether these psychological variables predicted adolescent inflammatory bowel disease patients' health outcomes. An investigation of 63 participants with inflammatory bowel disease between the ages of 13 to 17 years revealed a significant prevalence of alexithymia compared to a previously reported rate in a normal adolescent population. Higher alexithymia scores were associated with greater depressive symptoms, perceived stress of major life events, perceived stress of daily hassles, and perceived recent stress. None of the psychological variables were significantly related to illness course, and only perceived stress of major life events was significantly correlated with disease severity. In contrast, all of the psychological variables showed significant inverse correlations with disease-specific quality of life. Notably, alexithymia emerged as the strongest predictor of disease-specific quality of life and consistently accounted for more unique variance than depressive symptoms and perceived stress. Taken together, the present results implicate alexithymia as a risk factor for poor illness perception and adjustment in adolescents with inflammatory bowel disease. The potential lifelong repercussions of alexithymia make it an

important topic for health outcome research, which may guide the development of psychological interventions for this pediatric chronic illness population.

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Inflammatory Bowel Disease (IBD) – A category of chronic autoimmune diseases of the digestive tract characterized by a relapsing and remitting course of uncontrolled intestinal inflammation.

Crohn's Disease (CD) – One of two subtypes of IBD characterized by intestinal inflammation occurring anywhere within the gastrointestinal tract and pervading the thickness of the intestinal lining.

Ulcerative Colitis (UC) – One of two subtypes of IBD characterized by inflammation that is regionally restricted to the deepest stratum of the intestinal wall in the colon or large intestine.

Alexithymia – A normally distributed personality trait and an affective deficit disorder that is defined as an impairment or inability to identify, understand, and modulate emotions using the cognitive processes of imagination, fantasy, and reflective introspection.

Secondary Alexithymia – Developing alexithymic tendencies as a state reaction to stress, often accompanied by depressive symptoms.

Health Outcomes – Encompasses illness course, disease severity, and disease-specific QOL.

Illness Course – An objective measure of the trajectory of disease over time. For the purposes of the current study, Illness Course is calculated by summing the number of outpatient clinic visits, number of hospital admissions, length of

steroid exposure in months, and number of IBD medication increases over the past 12 months prior to the baseline clinic visit.

Disease Severity – An objective measure of disease activity at a given time point. For the purposes of the current study, disease severity is calculated by a physician-rated objective index of disease activity.

Disease-Specific Quality of Life (QOL) – Subjective health outcome measure that reflects an individuals' physical, emotional, and social attitudes as they relate to health status and affect daily living.

CHAPTER ONE
Introduction

Inflammatory bowel disease (IBD), comprised of ulcerative colitis and Crohn's disease, is a chronic, relapsing and remitting illness characterized by inflammation in the gastrointestinal tract. Approximately 1.4 million Americans and 2.2 million Europeans suffer from IBD (Abraham & Cho, 2009), with rates on the rise in previously low-incidence areas, such as southern Europe, Asia, and much of the developing world (Loftus, 2004). Roughly 25% of all IBD patients are children and adolescents (Hanauer, 2006). In fact, most pediatric IBD cases are diagnosed in adolescence, with incidence rates peaking between ages 15 and 25 years (Crohn's and Colitis Foundation of America [CCFA], 2010a). These adolescents face a lifelong disease for which there is no cure. Since adolescence represents a critical developmental period, identifying the specific characteristics of adolescent IBD patients is important for understanding their treatment needs.

Adolescents with IBD must cope with the common and troublesome symptoms of the disease, including abdominal pain, frequent diarrhea, and malnutrition. In addition to the disease's physical effects, IBD can be detrimental to a child's emotional and social functioning (Calsbeek, Rijiken, Bekkers, Dekker, & van Berge Henegouwen, 2006; Greenley et al., 2010; Mackner & Crandall, 2006, 2007; Mackner, Crandall, & Szigethy, 2006; Mackner, Sisson, & Crandall, 2004; Moody, Eaden, & Mayberry, 1999). Higher rates of depression and anxiety

have been found in pediatric IBD populations (Burke, Kocoshis, Chandra, Whiteway, & Sauer, 1990; Burke et al., 1989; Burke, Neigut, Kocoshis, Chandra, & Sauer, 1994; Engström, 1992; Szigethy et al., 2004) as well as significantly lower quality of life (QOL) (Akobeng et al., 1999; Cunningham, Drotar, Palermo, McGowan, & Arendt, 2007; De Boer, Grootenhuis, Derkx, & Last, 2005; Haapamäki, Roine, Sintonen, & Kolho, 2011; Lix et al., 2008; Loonen, Grootenhuis, Last, Koopman, & Derkx, 2002; Otley et al., 2006; Rabbett et al., 1996; Sawyer et al., 2004).

As no cure exists, understanding the factors affecting health outcomes (i.e., illness course, disease severity, and disease-specific QOL) has become an important area for research. However, studies on health outcomes in general are severely lacking in the pediatric IBD literature (Mackner et al., 2004; Szigethy, McLafferty, & Goyal, 2010). Among adult IBD populations, both depression and stress have been implicated in health outcomes (Cámara, Ziegler, Begré, Schoepfer, & von Känel, 2009; Drossman, 2000; Ghia et al., 2009; Graff, Walker, & Bernstein, 2009; Singh, Graff, & Bernstein, 2009). To our knowledge, no prior studies have explicitly looked at the relationship between these particular psychological variables (i.e., stress and depression) and health outcomes in pediatric IBD populations.

In addition to stress and depression, alexithymia, defined as both a personality trait and an affective deficit disorder (Zackheim, 2007), may represent

another psychological variable influencing health outcomes in IBD patients. Directly translated as "lacking words for feelings," alexithymia is an impairment or inability to identify, understand, and modulate emotions using the cognitive processes of imagination, fantasy, and reflective introspection (Nemiah, Freyberger, & Sifneos, 1976; Taylor, Bagby, & Parker, 1997; Wolff, 1977). Among chronic illness populations, prior research supports a relationship between alexithymia and maladaptive illness behaviors (Lumley, Stettner, & Wehmer, 1996), emotional dysregulation (Taylor, 2000; Taylor et al., 1997), and poor health outcomes (Porcelli et al., 2003).

Adult IBD populations show significant rates of alexithymia (Porcelli, Leoci, Guerra, Taylor, & Bagby, 1996; Porcelli, Taylor, Bagby, & De Carne, 1999; Porcelli, Zaka, Leoci, Centone, & Taylor, 1995). Moreover, higher rates of alexithymia have been associated with poorer QOL in adult IBD patients (Verissimo, Mota-Cardosa, & Taylor, 1998). While studies have documented the prevalence of alexithymia among adults with IBD (Nakagawa, Sugita, Nakai, & Ikemi, 1979; Porcelli et al., 1996; Porcelli et al., 1999; Porcelli et al., 1995; Taylor, Doody, & Newman, 1981), none have extended their investigation of the trait's occurrence to include adolescents in this chronic illness population. In fact, research on adolescent alexithymia in general is in its early stages, and thus, is somewhat limited. Still, preliminary evidence links higher rates of alexithymia in adolescents with poorer health and well-being (Burba et al., 2006).

Adolescence provides a unique opportunity for examining alexithymia because it is a developmental period marked by major physical, cognitive, and emotional change. Alexithymia is thought to arise from a disruption in emotional development (Lumley, Mader, Gramzow, & Papineau, 1996; Taylor et al., 1997), and adolescence represents a critical stage in the process of emotional development (Saarni, 1999, 2000). In recognizing the theoretical parallel between adolescence and alexithymia, the investigation of alexithymia in an adolescent IBD population becomes particularly relevant for understanding both the emergence of alexithymia and its potential consequences for an individual's functioning in the context of chronic illness.

Adolescents with IBD may already have emotional deficits or may be at risk for developing alexithymia as a result of their chronic illness. When managing the stress related to a chronic illness, adolescents with alexithymia may be at a disadvantage due to their deficits in emotional regulation. Examining alexithymia in adolescent medical populations may provide an opportunity for early identification of emotional skill deficits and subsequently early intervention, thereby reducing the development of major problems (Ciarocchi, Heaven, & Supavadeeprasit, 2008).

The current study was the first to examine the prevalence of alexithymia in adolescent patients with IBD. This project was also the first to examine alexithymia, depressive symptoms, and perceived stress in relation to health

outcomes in an adolescent IBD population. As such, this project represents a step towards identifying those influential psychological factors that contribute to adolescent patients' physical and emotional responses to IBD and its treatment, with potential implications for future interventions.

CHAPTER TWO
Review of the Literature

Inflammatory bowel disease (IBD) refers to a category of chronic autoimmune diseases of the digestive tract characterized by a relapsing and remitting course of uncontrolled intestinal inflammation. Alexithymia, which is defined as both an affective deficit disorder and a personality trait, has been shown to occur at higher rates in numerous chronic illness populations, including in adults with IBD. The following sections provide an overview of general and adolescent IBD, its impact on adolescents' psychosocial functioning, and potential risk factors for socio-emotional problems in teens with IBD before moving onto introducing alexithymia as one such risk factor.

INFLAMMATORY BOWEL DISEASE

Crohn's disease (CD) and ulcerative colitis (UC) represent the two related but distinct subtypes of IBD, affecting 1.4 million Americans (Abraham & Cho, 2009). Considered separate entities, UC and CD differ primarily in anatomical site, character of inflammation, and their hypothesized causative mechanism. In CD, the intestinal inflammation can arise anywhere within the gastrointestinal tract and pervade the thickness of the intestinal lining. In UC, inflammation is

regionally restricted to the deepest stratum of the intestinal wall in the colon or large intestine. Endoscopy is used as the primary method of diagnosis while non-invasive procedures aid diagnosis and provide interval assessments of disease severity. These assessments entail a study of certain biochemical markers of intestinal inflammation, such as erythrocyte sedimentation rate, C-reactive protein, and serum albumin (Rufo & Bousvaros, 2006).

Although the cause(s) of IBD remain unknown, it is widely believed that a large of number of IBD cases can be attributed to a genetic predisposition (Cuffari, 2010) in which an environmental trigger (e.g., medication, smoking, infection) causes an overactive immune response to bacteria in the gastrointestinal tract (Achkar & Duerr, 2008; Calkins, 1989; Mathew & Lewis, 2004; Shih, Targan, & McGovern, 2008). Childhood-onset of CD shows a strong hereditary link, with 30% of those diagnosed before age 20 having a positive family history in comparison to 18% after age 20 and 13% after age 40 (Sauer & Kugathasan, 2009; Van Limbergen et al., 2008; Vernier-Massouille, Balde, & Salleron, 2008).

ADOLESCENT INFLAMMATORY BOWEL DISEASE

Approximately 25% of the new cases of IBD diagnosed annually are children and adolescents (Griffiths, 2004), making IBD a significant pediatric chronic illness. Since the peak age of onset is between the ages of 15 and 25

years (CCFA, 2010a), most cases of pediatric IBD are adolescents and young adults (Sandler & Eisen, 2000). With the incidence of IBD seemingly on the rise over the past 50 years, the number of children afflicted may be as high as 7 in 100,000 (Turunen et al., 2006).

Youth with IBD must cope with the lifelong trial of managing a chronic illness and its irritating symptoms. The predominant symptoms of IBD in adolescents include frequent diarrhea, bloody stools, abdominal pain, and malnutrition (Griffiths, 2004; King, 2003; Mamula, Markowitz, & Baldassano, 2003; Rufo & Bousvaros, 2006; Sauer & Kugathasan, 2009; Szigethy et al., 2010). Other problems often occurring in conjunction with pediatric IBD include decreased appetite, fever, fatigue, perianal disease, arthritis, weight loss, delayed puberty, stunted growth, and negative medication side effects. Compared to adult-onset IBD, pediatric IBD is often more extensive when first diagnosed (Langholz, Munkholm, Krasilnikoff, & Binder, 1997), with the most intense disease progression occurring 5 to 7 years post diagnosis (Szigethy et al., 2010). The illness course of pediatric IBD is so significant that over one third of individuals with childhood-onset IBD require surgery in the 20 years following their diagnosis (Langholz et al., 1997).

Treatment

Treating IBD is a complex process due to the variable nature of the disease and the wide range of treatment options. Generally, the primary goal of treatment is mucosal healing through a regimen of medical, surgical, and nutritional interventions intended to prevent disease progression, reduce complications, promote nutrition, and enhance QOL (Rufo & Bousvaros, 2006; Szigethy et al., 2010). Treatment focuses on managing inflammation and illness symptoms, primarily through the use of oral medications, but the most severe cases of IBD require non-curative surgery. Common medications used in treating adolescent IBD include anti-inflammatories, immunomodulators, corticosteroids, and antibiotics as well as multivitamins and mineral supplements (CCFA, 2010b; Reed-Knight, Lewis, & Blount, 2010).

A patient's illness severity, illness duration, presenting symptoms, and type of IBD shape individual treatment needs, making it a challenge to find the appropriate medication regimen and adjust it according to fluctuations in an individual's illness course. Medication treatment usually begins with an induction phase targeting disease remission, followed by maintenance therapy, the goal of which is to prevent relapse. A list of primary induction and maintenance therapies used for treating various disease severities of pediatric IBD can be found in Appendix C (p.134). More aggressive treatments (e.g., infusions, special diet, hospitalizations, and surgery) are needed for severe cases of IBD and for disease flare-ups. Surgery is used only when other treatments are ineffective. Since

surgery is not curative in patients with CD and has a high potential for relapse, it is only recommended when a CD patient has severe complications, such as abscess, perforation, stricture, or fistulizing disease (Schwartz & Cohen, 2008; Rutgeerts, Vermeire, & Van Assche, 2009). In severe or refractory cases of UC, a colectomy is the standard of care and can be curative (Rufo & Bousvaros, 2006). Even though a colectomy may improve a patient's QOL, it too is only considered when absolutely necessary because it requires the temporary or permanent use of an ostomy (Rutgeerts et al., 2009; Schwartz & Cohen, 2008).

Developmental Considerations in Treating Adolescents with IBD

Treating adolescents with IBD is complex and requires consideration of the relationship between treatment needs and development. Several developmental, psychosocial, and physiologic factors of adolescents distinguish their treatment needs from those of adult IBD patients. These include differences in medication and dosage, the possibility of sustaining disease-related disruptions of puberty and linear growth, and changes in the child's emotional, social, and cognitive development (Rufo & Bousvaros, 2006; Szigethy et al., 2010). Furthermore, adolescents with IBD are at risk for developing micronutrient deficiencies either from the disease or medication side effects; thus, their nutrition must be carefully monitored (Ruemmele, Roy, Levy, & Seidman, 2000). Treatment must be specialized not only to target the clinical manifestations of the

disease but also to optimize growth and development through pharmacologic interventions, nutritional therapies (e.g., special diets), psychological support, and surgery when deemed necessary (Ruemmele et al., 2000; Rufo & Bousvaros, 2006; Smith, 2008; Szigethy, 2005; Zachos, Tondeur, & Griffiths, 2007). While much is known about how to tailor to treatment to the needs of adolescents, little is known about the effect of IBD on adolescent developmental outcomes (Mackner & Crandall, 2007).

Impact on Psychosocial Functioning

Psychological Adjustment

IBD presents specific obstacles for adolescents who are already navigating typical developmental changes (Drossman, 2000). For example, receiving a diagnosis of IBD has been described as initiating a grieving process (Szigethy et al., 2010) about an illness that children do not wish to discuss (Akobeng et al., 1999). With persistent questioning, youth will endorse feelings of anger and frustration about the diagnosis (Akobeng et al., 1999). Specifically, children must adjust to the trauma of invasive medical procedures, which often leads to reactions of anger, anxiety, dissociation, and emotional blunting (Szigethy et al., 2010).

The nature of the disease, its clinical presentation, and its treatment all hold various implications for an adolescent's adjustment to IBD. First, the gastrointestinal symptoms may prove embarrassing and difficult for adolescents to discuss (Mamula et al., 2003). Second, two potential side effects of corticosteroids used in treating IBD, emotional lability and alterations in physical appearance, may cause teens to feel physically different from their peers (Greenley et al., 2010; Mackner & Crandall, 2007; Mackner et al., 2006; Mackner et al., 2004). Lastly, dietary restrictions, another aspect of treatment, can prove frustrating and challenging for adolescents to maintain due to their increasing independence from parents and desire to eat the same foods as their friends (Calsbeek et al., 2006).

IBD may interfere in a teen's ability to engage in normal, developmentally appropriate adolescent behaviors, such as forming his or her identity, dating, socializing with peers, and establishing autonomy (Mackner & Crandall, 2007; Mackner et al., 2006; Mackner et al., 2004). The inconveniences of the illness (e.g., frequent bathroom trips, severe abdominal pain, numerous doctor visits) can limit teens' participation in school and social activities (Moody et al., 1999), potentially isolating them from peers and impacting their social functioning. In fact, IBD patients diagnosed in adolescence exhibit worse social competence than patients diagnosed in childhood (Mackner & Crandall, 2007).

Interestingly, it appears that older teenagers diagnosed with IBD have a more difficult adjustment to IBD than those diagnosed earlier in childhood (Szigethy et al., 2010). Multiple explanations exist for this discrepancy between children diagnosed with IBD at younger and older ages. One potential explanation is that IBD-related puberty delays may interfere in an adolescent's development of the higher cognitive functions normally achieved during adolescence (Holmbeck & Shapera, 1999; Mackner et al., 2004). Other explanations highlight the fact that adolescents have "a more flexible sense of self-identity, cognitive maturation, or differences in the grieving process or processing of illness experience" (Szigethy et al., 2010, p. 306). These varying hypotheses highlight the complexity of adolescence as a developmental stage.

Behavioral and Emotional Symptoms

Compared to healthy adolescents, the physical symptoms and treatment of IBD have been associated with adolescents' emotional and behavioral functioning (Mackner & Crandall, 2007; Mackner et al., 2006; Mackner et al., 2004). Apart from one study (Mackner & Crandall, 2005a), researchers have repeatedly found pediatric IBD patients to exhibit greater behavioral and emotional symptoms relative to their healthy, same aged peers (Bennett, 1994; De Boer et al., 2005; Engström, 1992, 1999; Engström & Lindquist, 1991; Raymer, Weininger, & Hamilton, 1984; Szajnberg et al., 1993; Wood et al., 1987). However, they

demonstrate similar symptom rates to other pediatric chronic illness populations, namely cystic fibrosis (Burke et al., 1989) and diabetes (Engström, 1992). On the other hand, youth with IBD experience fewer behavioral and emotional symptoms than those with Functional Gastrointestinal Disorders (FGID) (Gold, Issenman, Roberts, & Watt, 2000), likely as a result of the psychosomatic nature of FGID versus the organic disease status of IBD (Scharff, 1997).

In pediatric IBD patients, the most common emotional symptoms fall in the categories of depression and anxiety (Engström, 1991a, 1991b, 1992, 1999; Engström & Lindquist, 1991; Wood et al., 1987). While it remains unclear whether the symptoms endorsed meet full criteria for a psychiatric disorder (Greenley et al., 2010; Mackner & Crandall 2007), depressive and anxiety symptoms have demonstrated a negative impact on the relationship between barriers to adherence and adherence among adolescents with IBD (Gray, Denson, Baldassano, & Hommel, 2012).

Szigethy et al.'s (2004) study revealed important distinctions between their adolescent IBD population and other studies' younger aged IBD participants. In contrast to younger children with IBD, adolescent participants actually displayed higher rates of depression (approximately 25%) compared to adolescents with other chronic illnesses (e.g., approximately 4% in cystic fibrosis and 5% in diabetes) (Burke et al., 1990; Burke et al., 1989; Engström, 1992, Raymer et al., 1984). Therefore, adolescents may be at an increased risk for

depression as well as other impairments in their psychological functioning (Szigethy et al., 2004).

Pediatric patients with moderate and severe IBD disease activity may experience greater depressive symptoms compared to patients in remission (Szigethy et al., 2004). This finding supports an association between behavioral or emotional symptoms and IBD illness severity, but the relationship is limited to certain measures of disease activity and particular symptoms of depression (Burke et al., 1989; Ondersma, Lumley, Corlis, Tojek, & Tolia, 1997; Szigethy et al., 2004; Wood et al., 1987). Burke et al.'s (1989) study discovered that emotional symptoms were associated with subjective reports of greater disease severity but not objective laboratory findings of greater disease activity (Burke et al., 1989). From these findings, one might infer that adolescents with IBD whose emotional functioning is more limited may report increased somatic complaints, and these somatic symptoms are not supported by findings on medical examinations or biological evidence.

Stress and Coping

Although the literature on stress and coping in pediatric IBD remains relatively limited (Mackner & Crandall, 2007; Mackner et al., 2004), children with IBD report less perceived stress than healthy children (Gitlin et al., 1991; Reinhart, 1982). To explain this finding, researchers hypothesize that these

children may struggle with identifying and reporting stressors and/or may use denial defenses to cope with stress (Gitlin et al., 1991; Reinhart, 1982). In particular, adolescents with IBD often use avoidance or emotion-focused coping strategies, which represent two less effective coping styles that are more rigid and passive (Calsbeek et al., 2006; Gitlin et al., 1991; Van der Zaag-Loonen, Grootenhuis, Last, & Derkx, 2004). This passive depressive coping style has been linked to poorer QOL in adolescents with IBD in comparison to those using a more positive, active means of coping (Van der Zaag-Loonen et al., 2004). Additionally, adolescents with IBD are more likely to have an external locus of control (Engström, 1991a). In one study, worse disease severity was associated with a greater external locus of control, which suggests that adolescent IBD patients may interpret a severe illness course as beyond their control (Engström, 1991a).

Quality of Life

In the QOL literature, health-related quality of life (HRQOL) describes physical, emotional, and social attitudes as they relate to health status and affect daily living (Drotar et al., 1998). Compared to healthy children, youth with IBD show poorer HRQOL (Cunningham et al., 2007; De Boer et al., 2005; Haapamäki et al., 2011; Loonen, Grootenhuis, Last, Koopman et al., 2002). Both childhood and adolescent onset of IBD have been linked to worse HRQOL in young adults

with IBD compared to healthy age-matched controls (Turunen et al., 2009). However, age differences with the pediatric IBD population are evident. As children enter adolescence, their HRQOL appears to decrease (Haapamäki et al., 2011; Otley et al., 2006). Compared to children and adult IBD patients, adolescent IBD patients show worse impairments in their HRQOL as disease severity increases (Haapamäki et al., 2011; Loonen, Grootenhuis, Last, Koopman et al., 2002; Otley et al., 2006; Taft, Keefer, Leonhard, & Nealon-Woods, 2009).

Psychological Interventions

Research on psychological interventions for IBD patients has focused on Cognitive Behavioral Therapy (Szigethy, 2005) and support groups (Shepanski et al., 2005). Cognitive Behavioral Therapy has shown positive results for depressed adolescents with IBD (Szigethy, 2005; Szigethy et al., 2007; Szigethy et al., 2009). Skill-based psychological interventions have demonstrated efficacy in improving adolescent IBD patients' somatic symptoms and adaptive coping, as well as improving parental cognitive-behavioral reactions to their child's physical symptoms (McCormick, Reed-Knight, Lewis, Gold, & Blount, 2010). However, other promising psychological interventions, such as narrative therapy and hypnosis (Shaoul, Sukhotnik, & Mogilner, 2009), have not been extensively evaluated in adolescent IBD populations (Szigethy et al., 2010).

Risk Factors Affecting Psychosocial Functioning

Biological Risk Factors

Biological risk factors affecting psychosocial functioning stem from IBD-related organic processes as well as IBD treatments. One specific biological explanation for depressive symptoms in IBD may be the physiologic effects of inflammatory proteins (i.e., cytokines) on the brain. Szigethy and colleagues (2004) observed a positive correlation between three specific symptoms of depression (i.e., anhedonia, decreased appetite, and fatigue) and disease severity. Interestingly, these symptoms can all manifest with the release of cytokines, which are proteins involved in the inflammatory process characteristic of IBD (Maier & Watkins, 1998; Reichenberg et al., 2001). Extended treatment by exogenous steroids can also lead to impairments in mood as well as to short-term memory and executive functioning problems (Mackner & Crandall, 2005b; Mrakotsky, Bousvaros, & Chriki, 2005).

Environmental Risk Factors

Family dysfunction has been linked to increased disease severity, more frequent bowel movements, greater pain and fatigue, and higher reports of behavioral and emotional symptoms in pediatric IBD (Burke et al., 1990; Tojek, Lumley, Corlis, Ondersma, & Tolia, 2002; Wood et al., 1989). Maternal

depression and stressful life events have also been observed as risk factors for worsened emotional and behavioral functioning in children with IBD (Burke et al., 1994; Szigethy et al., 2004).

Clinical Risk Factors

Research has not consistently identified specific clinical risk factors for pediatric IBD (Mackner et al., 2006; Mackner et al., 2004). Several studies have not been able to demonstrate a relationship between illness factors and emotional/behavioral function (Ondersma et al., 1997; Steinhausen & Kies, 1982; Wood et al., 1987). Further, the existing literature has not adequately investigated what factors place some adolescents with IBD at greater risk for negative psychosocial and behavioral/emotional functioning (Mackner et al., 2004). Other unidentified psychosocial variables, such as alexithymia, may explain why a subset of youth with IBD seems at risk for psychological problems, lower HRQOL, or poor illness responses (Mackner & Crandall, 2005a).

ALEXITHYMIA

Alexithymia may represent one risk factor for poor psychosocial functioning and health outcomes not yet explored in adolescent IBD populations.

Defined as a "distinct personality construct, characterized by a specific disturbance in the cognitive appraisal of emotions" (Zackheim, 2007, p. 345), alexithymia presents as a reduction in emotional awareness and an externally oriented or operational style of thinking, termed *pensée opératoire* (Marty & de M'Uzan, 1963; Verissimo, Taylor, & Bagby, 2000). The construct of alexithymia arose from psychoanalysts' clinical observations of patients with classical psychosomatic disease displaying difficulties identifying and discussing their feelings. The term *alexithymia* was coined to capture the distinguishing feature of the construct – the absence of words for feelings (Nemiah et al., 1976). Alexithymia is currently regarded as both a normally distributed personality trait and an affective deficit disorder (Martínez-Sánchez, Ato-Garcia, & Ortiz-Soria, 2003) as opposed to a psychosomatic disorder or defensive coping strategy (Lundh, Johnsson, Sundqvist, & Olsson, 2002; Taylor, Bagby, & Parker, 1991).

A multidimensional construct, alexithymia encompasses the following four distinct but related features:

> (i) Difficulty identifying and distinguishing between feelings and the bodily sensations of emotional arousal; (ii) difficulty describing feelings to other people; (iii) constricted imaginal processes, as evidenced by a paucity of fantasies; and (iv) a stimulus-bound, externally oriented cognitive style (Taylor et al., 1997, p. 29).

Unable to form mental associations between their particular affective state and their visual images, fantasies, or cognitions, individuals with alexithymia focus instead on the somatic component of emotional arousal, experiencing emotions as

amplified cognitive states of feeling (Lundh et al., 2002; Nemiah et al., 1976; Taylor & Bagby, 1988; Taylor et al., 1997; Wolff, 1977). These characteristics have been hypothesized to explain the heightened propensity of an individual with alexithymia to experience somatic symptoms, psychiatric disorders, and medical illness (Bach & Bach, 1996; Posse & Hällström, 1998; Taylor, 1984; Taylor et al., 1997).

The emotional deficits in alexithymia have both intrapersonal and interpersonal consequences. Intrapersonally, individuals with alexithymia appear emotionally inhibited and show a limited capacity for self-reflection (Paez, Basabe, Valdoseda, Velasco, & Iraurgi, 1995). In addition to having limited self-awareness of their own emotions, individuals with alexithymia struggle to understand and relate to others emotionally, thereby demonstrating a deficient capacity for empathy (Taylor, 1984). Since they struggle with identifying and expressing their own subjective feeling states, individuals with alexithymia cannot verbally communicate their distress to others, which limits the available social support system needed to aid and comfort them. Indeed, alexithymia has been associated with less perceived social support, fewer close relationships, and poor social skills (Lumley, Ovies, Stettner, Wehmer, & Lakey, 1996; Spitzer, Siebel-Jurges, Barnow, Grabe, & Freyberger, 2005).

Associated Traits

Associations with other personality factors, coping styles, and negative affect states lead some theorists to doubt alexithymia as an independent trait (Ahrens & Deffner, 1986; Bonanno & Singer, 1990; Hogan, 1995; Knapp, 1981); however, alexithymia emerges repeatedly as a separate construct (Picardi, Toni, & Caroppo, 2005; Lipsanen, Saarijärvi, & Lauerma, 2004; Luminet, 2010; Taylor et al., 1991; Tolmunen et al., 2010). Both equal and unique to other personality traits, alexithymia is in fact represented through a cluster of traits across the five-factor model of personality (Luminet, 2010; Luminet, Bagby, Wagner, Taylor, & Parker, 1999; Wise, Mann, & Shay, 1992). As such, alexithymia stands as a separate but related personality trait, one which continues to prove itself as an independent construct capable of withstanding mood fluctuations, external stressors, and time.

Individuals with alexithymia demonstrate a more external locus of control, and both alexithymia and external locus of control have been associated with maladaptive, immature coping styles (Horton, Gewirtz, & Kreutter, 1992; Martin, Pihl, Young, Ervin, & Tourjman, 1986; Paez et al., 1995; Parker, Taylor, & Bagby, 1998; Verissimo et al., 2000). Still, alexithymia cannot be explained as a defensive style alone, but rather a complex construct (Luminet, Rokbani, Ogez, & Jadoulle, 2007) that is characterized by employing less effective and more

immature strategies when faced with psychological distress (Horton et al., 1992; Martin et al., 1986).

Furthermore, alexithymia has been shown to correlate with disorders of negative affect, such as anxiety and depression (Di Schiena, Luminet, & Philippot, 2011; Karukivi et al., 2010); however, while anxiety and depressive symptoms may come and go, alexithymia remains stable (Marchesi, Bertoni, Cantoni, Maggini, 2008; Marchesi, Brusamont, & Maggini, 2000). Research indicates some overlap between dimensions of alexithymia and anxiety (Burba et al., 2006; Karukivi et al., 2010; Marchesi et al., 2000), but alexithymia continues to demonstrate its independence from anxiety (Tolmunen et al., 2010). Alexithymia has also been associated with depression in both normal and clinical populations (Di Schiena et al., 2011; Fukunishi, Miguchi, & Nishihara, 1996). Yet, studies on depression and alexithymia show that these psychological constructs never share more than approximately one third of the common variance in predicting outcomes (Bagby, Taylor, & Ryan, 1986; Lipsanen et al., 2004; Luminet, 2010). In addition, factor analyses support the distinction between the constructs because of the lack of item overlap on alexithymia and depression measures (Müller, Bühner, & Ellgring, 2003).

In contrast to depression measures (Prenoveau et al., 2011), alexithymia shows relative stability over time (Honkalampi, Hintikka, Saarinen, Lehtonen, & Viinamaki, 2000; Luminet et al., 2007). Given its association with depression and

its relative stability, alexithymia has drawn attention as a potential risk factor for depression. Although this vulnerability hypothesis has received some initial support (Di Schiena et al., 2011; Kojima et al., 2007), the mechanisms underlying the association between alexithymia and depression need further clarification through prospective studies (Luminet et al., 2007).

Stability

The association between alexithymia and negative affectivity has fueled investigations of alexithymia as a stable personality trait (e.g., Honkalampi et al., 2000). Research on the stability of alexithymia has focused on relative and absolute stability. *Absolute stability* "refers to the extent to which personality scores change over time, whereas *relative stability* [emphasis added] indicates the extent to which relative differences among individuals remain the same over time" (Luminet, Bagby, & Taylor, 2001, p. 642). Absolute stability is rarely achieved because it requires that every score stay exactly the same across time and situations (Mikolajczak & Luminet, 2006). Indeed, alexithymia has demonstrated poor absolute stability (Luminet et al., 2001; Luminet et al., 2007; Mikolajczako & Luminet, 2006). However, alexithymia continues to demonstrate high relative stability, even in the face of acute increases in distress, thereby establishing itself as a stable personality trait (De Gucht, 2003; Luminet et al.,

2001; Luminet et al., 2007; Martínez-Sánchez et al., 2003; Mikolajczako & Luminet, 2006; Picardi et al., 2005).

ALEXITHYMIA AND ILLNESS

Alexithymia has been observed in a wide range of medical and psychiatric illness populations including somatoform pain disorders (Lumley, Asselin, & Norman, 1997; Waller & Scheidt, 2004), somatic disorders (Jula, Salminen, & Saarijärvi, 1999; Porcelli et al., 1999), substance abuse disorders (Loas, Otmani, Lecercle, & Jouvent, 2000), eating disorders (Karukivi et al., 2010), depressive disorders (Di Schiena et al., 2011; Fukunishi et al., 1996), posttraumatic stress disorder (Zlotnick, Mattia, & Zimmerman, 2001), and panic disorder (Parker, Taylor, Bagby, & Acklin, 1993). Patients with somatic disorders have higher rates of alexithymia compared to normal controls (Fernandez, Siram, Rajkumar, & Chadrasekar, 1989; Porcelli et al., 1995; Waller & Scheidt, 2004), and a positive correlation exists between alexithymia and physical symptoms as well as between alexithymia and subjective reports of ill health (De Gucht, Fischler, & Heiser, 2003; De Gucht & Heiser, 2003; Lumley, Stettner, et al., 1996).

Despite advances in alexithymia research, it remains unclear whether alexithymia is a risk factor for physical illness or if it is a corollary of the disease (Lumley, Stettner, et al., 1996; Porcelli et al., 1996). Lumley, Stettner, et al.

(1996) reviewed and critiqued the empirical literature on alexithymia and physical illness by adopting a perspective of physical illness as it pertained to both organic disease and illness behavior. They determined that the two most commonly researched pathways were that "(a) alexithymia leads to organic disease through physiological or behavioral mechanisms; and (b) alexithymia leads to illness behavior (physical symptoms, disability, excessive health care use) through cognitive or social mechanisms" (Lumley, Stettner, et al., 1996, p. 505). Theorized relationships between alexithymia, organic disease, and illness behavior are described below (see Figure 1).

Pathways

Alexithymia Leads to Organic Disease

Organic disease can be identified through laboratory tests or clinical observations, and includes an etiology, progression, exacerbation, and remission of tissue pathology (Lumley, Stettner, et al., 1996). The deficiency in psychological affect regulation strategies characteristic of alexithymia may be a pathway to organic disease (Horton et al., 1992). Instead of using cognitive strategies to modulate their emotional states, individuals with alexithymia are more prone to use compulsive or impulsive behaviors, such as binge drinking (Loas et al., 2000) and eating (Karukivi et al., 2010) as well as distraction or

avoidant activities, all of which are avoidant styles of coping (Horton et al., 1992; Parker et al., 1998). Whether these alexithymia-associated unhealthy behaviors lead to organic disease is not yet known.

Without the psychological and cognitive abilities to regulate affect, physiological arousal remains heightened in an individual with alexithymia, potentially disturbing hormonal stress-response and/or immune systems, leading to tissue pathology (Lumley, Stettner, et al., 1996). In one study, individuals with a peptic ulcer had higher rates of alexithymia and a higher number of stressful life events relative to a control group (Banerjee & Vyas, 1992). Indeed, alexithymia may lead to extended exposure to stressors, which stimulates the somatovisceral response, thereby heightening the risk for peptic ulcers (Banerjee & Vyas, 1992).

Alexithymia Leads to Illness Behavior

Illness behavior refers to the patient's subjective reports of physical symptoms, pain and disability expressed through behaviors, and seeking of medical care (Lumley, Stettner, et al., 1996). Alexithymia has also been shown to contribute to somatic symptoms by influencing illness behaviors through cognitive and social pathways (Lumley, Stettner, et al., 1996), such as somatosensory amplifications leading to excessive symptom reporting (Wise & Mann, 1994) and poor social skills leading to less social support (Fukunishi, Kaji, Hosaka, Berger, & Rahe, 1997). In their literature review, Lumley, Stettner, et al.

(1996) found evidence relating alexithymia to various illness behaviors, including the experience and self-report of somatic complaints (De Gucht et al., 2003) as well as an increased tendency to seek medical care in those with chronic health conditions (Fitzgibbon, Stolley, & Kirschenbaum, 1993). They hypothesize that these relationships result from a variety of factors overlapping with the alexithymia construct, including neuroticism, somatosensory amplification, discordance between physiological arousal and subjective reports, and beliefs favoring treatment seeking (Wise et al., 1992; Lumley, Stettner, et al., 1996).

The neurotic tendencies of individuals with alexithymia may help explain the link between alexithymia and excessive symptom reporting. Alexithymia has been associated with neuroticism, which refers to the tendency to notice and complain about emotional and physical distress (Wise et al., 1992). While alexithymic and neurotic individuals have similar sensitizing styles, the two personality constructs have distinct differences. For example, alexithymia's external cognitive orientation and diminished fantasy life distinguish it from neuroticism (Taylor et al., 1997). These deficiencies in cognitive processes and emotional regulation specific to alexithymia may steer an individual with alexithymia towards particular illness behaviors, such as complaints of symptoms or treatment-seeking tendencies, as opposed to actually causing true organic disease (Lumley, Stettner, et al., 1996).

Alexithymia and Inflammatory Bowel Disease

Rates of alexithymia are significantly higher in the adult IBD population (35.7%) than in the general population (4.5%), but are lower than in individuals with FGID (66%) (Porcelli et al., 1996; Porcelli et al., 1999; Porcelli et al., 1995). The relationship between alexithymia and adult IBD has been examined specifically in regards to QOL. One study found that adult IBD patients with higher alexithymia scores reported more bowel symptoms, systemic symptoms, and worse emotional functioning than patients with low levels of alexithymia; however, alexithymia did not impair occupational, social, or academic functioning (Verissimo et al., 1998). Although two later studies failed to replicate Verissimo et al.'s (1998) finding, both of the studies used less standardized measures of alexithymia (Boye, Jahnsen et al., 2008; Boye, Lundin et al., 2008; Weinryb, Gustavsson, & Barber, 1997; Weinryb, Gustavsson, & Barber, 2003; Weinryb, Gustavsson, Liljeqvist, Poppen, & Rössel, 1997), making findings difficult to generalize. Given the potential relationship between alexithymia and QOL in adult patients with IBD (Verissimo et al., 1998) as well as the significant moderate association between alexithymia and IBD (Porcelli et al., 1996; Porcelli et al., 1999; Porcelli et al., 1995), further studies are needed to understand the development of alexithymia and its effect within the subgroup of IBD patients showing alexithymic features (Taylor et al., 1997).

ADOLESCENT ALEXITHYMIA

In comparison to the prolific study of alexithymia in various adult populations, research on adolescent alexithymia in general is limited. The overall rate of alexithymia in a normal adolescent population (ages 13 to 18 years; *n* = 7087) is 7.3% (Honkalampi et al., 2009); however, the limited number of studies prevents researchers from making firm conclusions on gender and age effects (Joukamaa et al., 2007; Säkkinen, Kaltiala-Heino, Ranta, Haataja, & Joukamaa, 2007). In all adolescent age groups, the prevalence differed between sexes, with higher rates of alexithymia in girls (approximately 10%) than in boys (7%) (Joukamaa et al., 2007). These findings are inconsistent with rates found in a general adult population (*n* = 5454), which showed men (11.9%) as more frequently alexithymic than women (8.1%), with an overall prevalence of 9.9% (Mattila et al., 2008; Mattila, Salminen, Nummi, & Joukamaa, 2006).

In Honkalampi and colleague's (2009) study, alexithymia was higher among the younger adolescents (i.e., 8.4% for 13-year-olds and 9.6% for 15-year-olds) and was lowest among the 18-year-olds (5.1%). This finding suggests that older adolescents judge themselves as better able to identify and express their feelings (Honkalampi et al., 2009). In contrast, rates of alexithymia in adults increase with age, a finding that may be due to generational factors or age-related

cognitive and neurobiological-emotional processing alterations (Lane, Sechrest, & Riedel, 1998; Mattila et al., 2006). Despite the discrepancies in age and gender patterns between adults and adolescents, the overall prevalence of alexithymia among normal adolescent populations appears similar to the approximate 10% rate observed in population studies on adults (Honkalampi et al., 2009; Joukamaa et al., 2007; Mattila et al., 2008; Mattila et al., 2006).

In the few studies on alexithymia among adolescents, alexithymia has been linked to poor socio-emotional and physical outcomes such as obesity (Baldaro et al., 2003), the experience of post-traumatic responses following medical treatments (Fukunishi, Tsuruta, Hirabayashi, & Asukai, 2001), greater dissociative tendencies (Sayar, Kose, Grabe, & Topbas, 2005; Tolmunen et al., 2010), and greater somatic complaints (Ebeling, Moilane, Linna, & Räsänen, 2001; Jellesma, Rieffe, Terwogt, & Westenberg, 2009; Rieffe et al., 2007; Rieffe, Oosterveld, & Terwogt, 2006). Empirical evidence also suggests higher rates of alexithymia among adolescents with the following problems: eating disorders such as anorexia nervosa (Zonnevylle-Bender, van Goozen, Cohen-Kettenis, van Elburg, & van Engeland, 2004), somatoform pain disorders (Burba et al., 2006), borderline personality disorder (Loas, Speranza, Pham-Scottez, Perez-Diaz, Corcos, 2012), FGID (Rieffe et al., 2007), depressive symptoms (Chinet, Bolognini, Plancherel, Stéphan, & Halfon, 1998; Honkalampi et al., 2009), anxiety symptoms (Karukivi et al., 2010), academic difficulties (Ebeling et al.,

2001; Parker, Austin, Hogan, Wood, & Bond, 2005), social problems (Ebeling et al., 2001; Honkalampi et al., 2009), and behavioral problems such as delinquency (Zimmermann, 2006).

Developmental Theories of Alexithymia

Normal Emotional Development

When one considers normal models of emotional development, alexithymia emerges as an especially relevant and important construct to investigate within adolescence. The stage-like progression of emotional competence begins with children first developing awareness of their emotional experiences between 12 to 28 months (Saarni, 1999). As young as 2½ to 5 years of age, preschoolers begin to develop the ability to communicate with others about emotions and emotion-related events. In middle school, children begin to understand that they can experience multiple and even contradictory emotions toward the same person. Lastly, by adolescence, teens become cognizant of their personal emotional cycles (e.g., embarrassment about being fearful).

Emotional awareness and identification is a precursor to emotional regulation. Larsen's (2000) two-stage model of emotional regulation asserts that an individual must first be able to properly identify an adverse affective state in order to elicit the appropriate emotional regulation processes. Individuals who

struggle identifying affective states are more likely to have problems with regulating distressing emotions through cognitive and behavioral mechanisms. For example, research shows that adolescents who score higher on alexithymia measures are able to identify emotions in basic terms (Ciarrochi et al., 2008); however, they are more inclined to use less sophisticated means of coping, such active behavioral strategies (e.g., bicycle riding, sexual activities), rather than higher-level psychological solacing strategies (e.g., accessing social support, memories) (Horton et al., 1992). These action-oriented coping strategies may prove less adaptive and may even lead to unhealthy behavior (e.g., substance abuse, binge eating) when attempting to regulate distressing affect (Karukivi et al., 2010; Loas et al., 2000). Larsen's (2000) theory may also be used to explain somatization as a developmental deficit, where lower levels of emotional awareness lead to poor emotional differentiation and heightened focus on bodily sensations (Waller & Scheidt, 2006).

Disruptions in Development

During normal periods of emotional and cognitive development, any arrests in the acquisition of emotional vocabulary and adaptive scripts for emotional expression are believed to result in increased levels of alexithymia later in life (Krystal, 1978; Lemche, Klann-Delius, Koch, & Joraschky, 2004). Indeed, problems with affect processing have been correlated with impaired verbal

abilities and pragmatic language skills in both children (Bajgar, Ciarrochi, Lane, & Deane, 2005) and adults (Kokkonen et al., 2003). Low emotion identification skills have been shown to relate to low social support and poor emotional well-being in teens (Ciarrochi et al., 2008; Heaven et al., 2010).

Alexithymia as a Developmental Phenomenon

One major criticism of adolescent alexithymia research is that displaying lower emotional identification and awareness in adolescence may represent a normal state of development rather than a true affective disorder, as it may in adulthood (Parker et al., 2010). Support for this argument stems from replicated findings of significant age group differences in mean scores of TAS-20, with adolescents scoring higher on the TAS-20 than young adults (Parker et al., 2010; Säkkimen et al., 2007; Zimmerman, Quartier, Bernard, Salamin, & Maggiori, 2007). Older adolescents also exhibit more variability in responses than younger teens that is not systematically related to the readability of items (Parker et al., 2010). These findings depict alexithymia as a developmental phenomenon, which decreases with age as it correlates with natural increases in emotional awareness (Lane & Garfield, 2005; Lane & Schwartz, 1987; Taylor et al., 1997).

On the other hand, preliminary research indicates that alexithymia emerges in early adolescence as a relatively stable trait and continues into adulthood (Ciarrochi et al., 2008; Taylor et al., 1997). In a longitudinal one year

study, emotional experiences and social support did not influence alexithymia scores, whereas alexithymia scores did impact socio-emotional experiences (Ciarrochi et al., 2008). Although adolescents may continue to advance their emotional skills as they transition into adulthood, those teens who already display low emotion identification skills may be at risk for developing a fixed affective deficit disorder (Ciarrochi et al., 2008). The relationship between the low emotion identification skills and poor socio-emotional functioning (Ciarrochi et al., 2008) makes it especially important to identify adolescents who exhibit emotional skill deficits before significant problems develop.

Adolescent Alexithymia Measures

The paucity of research on adolescent alexithymia may be attributed to limitations in available measures. Since no well-validated adolescent alexithymia measure has been published to date, the few studies on alexithymia in adolescents have relied on measures similar to or the same as those used with adults. For instance, the most widely used measure, the Toronto Alexithymia Scale (TAS-20), has been validated in numerous studies with various adult populations (Bagby, Parker, & Taylor, 1994; Bagby, Taylor, & Parker, 1994); however, it has yet to be validated with or normed on adolescents.

When used with adolescents, concerns with TAS-20 include problems with factor structure and non-validated clinical cutoff scores (Parker, Eastabrook, Keefer, & Wood, 2010). Other research suggests that in the absence of validated measures of alexithymia for adolescents, the TAS-20 can be used, provided that clinicians and researchers consider incorporating certain recommendations stemming from recent investigations into the psychometric properties of the TAS-20 for use with adolescents (Parker et al., 2010).

Challenges with the TAS-20

The TAS-20 is a 20-item self-report measure comprised of three subscales: difficulty identifying feelings (DIF), difficulty describing feelings (DDF), and externally-oriented thinking (EOT) (Bagby, Parker, et al., 1994; Bagby, Taylor, et al., 1994). In one study, the three-factor model of the TAS-20 and the quality of the self-report assessment declined at young ages, with the youngest adolescent age group (13- to 14-year-olds) showing the worst fit with the data (e.g., a "borderline" standardized root-mean-square residual (SRMR) value of .08, with criteria for good fit defined as SRMR $\leq$ .08) (Parker et al., 2010). Since the clinical cutoffs (i.e., TAS-20 total scores of $\geq$ 61) were developed on adults and have yet to be validated with adolescents, researchers should be cautious when applying the cutoff score to define adolescent alexithymia cases (Bagby, Parker, et al., 1994; Bagby, Taylor, et al., 1994; Parker

et al., 2010). The use of adult scoring norms with a lack of consideration of adolescent individual differences (e.g., reading level), might lead to a systematic overidentification of alexithymia in adolescent populations (Parker et al., 2010). Of the individual subscales on the TAS-20, the EOT subscale showed the least reliability across the three adolescent groups (Cronbach's alpha = .49 to .68), failing to elicit reliable responses and revealing significant deviations from the adult measurement structure on five of its items (Parker et al., 2010).

Support for the TAS-20

Despite psychometric concerns, the theoretical three-factor model was still recognizable in all of the adolescent age groups (Parker et al., 2010). For example, the three-factor model of the TAS-20 demonstrated adequate psychometric properties for ages 13 to 18 years (e.g., root-mean-square error approximation (RMSEA) values from .023 to .056, with criteria for acceptable fit defined as RMSEA $\leq$ .08). In contrast to the EOT subscale, the DDF subscale displayed stable item structure for all ages and high internal consistency for every age group with the exception of the 13-year-olds (Parker et al., 2010). Rieffe et al. (2006) examined alexithymia in children with an average age of 12 years and found that both the DIF and DDF scales of the TAS-20 could be reliably assessed in this age group. Only two items on the DIF subscale revealed significant deviations from the adult measure; i.e., "I have physical sensations that even

doctors don't understand" (Item 3) and "I am often puzzled by sensations in my body" (Item 7) (Bagby, Parker et al., 1994; Bagby, Taylor et al., 1994; Parker et al., 2010). Parker et al. (2010) hypothesize that this finding may be attributed to developmental factors of emotional awareness and/or puberty-related biological and hormonal changes.

Based on the findings of differences on the measure in adolescents, researchers have suggested how the TAS-20 can be used in this age group. One recommendation is to omit the EOT subscale due to its weak psychometric properties in adolescent populations (Parker et al., 2010; Säkinen et al., 2007). More recent studies that have followed this recommendation show promising findings (Ciarrochi et al., 2008; Heaven, Ciarrochi, & Hurell, 2010). Heaven et al.'s (2010) study found that alexithymia could be reliably and validly measured in adolescents with a modal age of 13 years using an abbreviated version of the TAS-20 that contained 12 of the original 20 items. Furthermore, the brief TAS-20 was able to distinguish adolescent alexithymia from other measures of self-evaluative constructs, such as self-esteem (Heaven et al., 2010). Taken together, these studies support the use of a modified version of the TAS-20, excluding the EOT subscale for use with adolescent populations. Researchers advise cautious interpretation of findings while waiting for the development and publication of a well-validated adolescent alexithymia instrument.

HEALTH OUTCOMES IN IBD

The term *health outcomes* broadly encompasses the objective measure of physiological changes attributed to illness course and responsiveness to treatment as well as a person's subjective experience of the disease. In the present study, health outcomes were defined as illness course, disease severity, and disease-specific QOL. Both personality traits and emotional states have the potential to influence health outcomes of adolescent IBD patients by generating physiological effects on the intestines (Banerjee & Vyas, 1992; Ghia et al., 2009; Singh et al., 2009), influencing an IBD patient's experience and response to symptoms (Lumley, Stettner, et al., 1996), and steering the illness course and response to treatment (Porcelli et al., 2003; Verissimo et al., 1998).

Effects of Depression on Health Outcomes

Research in the area of health outcomes is particularly lacking for pediatric IBD populations. While depression and stress have been linked with poor health outcome in adult IBD populations (Cámara et al., 2009; Drossman, 2000; Ghia et al., 2009; Graff et al., 2009; Singh et al., 2009), these potential relationships have not been specifically studied in adolescents with IBD (Mackner et al., 2004; Szigethy et al., 2010). Empirical evidence suggests a correlation

between depression and IBD symptom flare-ups in adults (Ghia et al., 2009; Graff et al., 2009). For instance, one study found that adult IBD patients suffering from depression showed a worse illness course than non-depressed patients (Graff et al., 2009). Another study involving a colitis animal model showed that inducing a depressive episode in mice led to a reactivation of colitic inflammation (Ghia et al., 2009), suggesting a physiological link between depression and inflammation.

Effects of Stress on Health Outcomes

While research on stress in general is limited for the pediatric IBD population, an abundance of adult IBD literature exists supporting an association between stress and flares of IBD (Brantley & Jones, 1993; Kuroki et al., 2007; Langhorst et al., 2007; Levenstein et al., 2000; Maunder, 2000; Pellissier, Dantzer, Canini, Mathieu, & Bonaz, 2010; von Wietersheim, Köhler, & Feiereis, 1992). Recent research with rodents demonstrated that exposure to chronic/repeated psychosocial stressors resulted in spontaneous colits, thereby depicting a relationship between stress and gastrointestinal dysfunction similar to the presentation of IBD in humans (Reber, 2012). Furthermore, observational human studies discovered that psychological stress caused marked ultrastructural changes of the mitochondria in adults with IBD compared to healthy controls, and an empirical review supported perturbed mitochondrial function in the entrocyte

or metabolic stress as a contributing factor to the onset of inflammation and relapses in IBD (Shoultz, Söderholm, & McKay, 2011). Controversy ensues over which form of stress exerts more influence on IBD symptom exacerbation, major life events and/or daily hassles (Duffy et al., 1991; Duffy et al., 1992; Garrett, Brantley, Jones, & McKnight, 1991; Greene, Blanchard, & Wan, 1994; Keefer, Keshavarzian, & Mutlu, 2008; Mawdsley & Rampton, 2006; Traue & Kosarz, 1999). *Daily hassles*, which refer to the minor stressors involved in day-to-day living, differ both qualitatively and quantitatively with *major life events*, which are dramatic or traumatic events that potentially exert long-term effects (Cámara et al., 2009). Yet, recent research emphasizes the importance of perceived stress levels when examining the link between stress and IBD health outcomes over and above stressful life events and daily hassles (Cámera et al., 2009; Singh et al., 2009).

Effects of Alexithymia on Health Outcomes

Another potential predictor of health outcomes not yet explored among either adults or adolescents with IBD is alexithymia. As a personality trait linked to both illness behaviors and emotional dysregulation (Taylor, 2000; Taylor et al., 1997), alexithymia may also prove to be a powerful predictor of health outcomes (Verissimo et al., 1998).

In patients with FGID, alexithymia was found to be a stable and reliable predictor of treatment outcomes and its predictive power proved stronger than depression and anxiety (Porcelli et al., 2003; Porcelli, De Carne, & Todarello, 2004). Similar to FGID, IBD has long been considered to have some psychosomatic overlay, as stress and negative affect tend to exacerbate symptoms (Bruce, 1986). Even in remission, adolescents with IBD are likely to report acute gastrointestinal symptoms analogous to IBS functional presentations (Faure & Giguère, 2008), and these patients show an impaired HRQOL that resembles those IBD patients in the active phase of their disease (Anarsi et al., 2008). Alexithymia could serve as an underlying mechanism explaining the occurrence of functional gastrointestinal symptoms among some pediatric IBD patients, and thereby act as a mediator or moderator in the relationship between risk factors and poor psychosocial adjustment (Mackner & Crandall, 2007). Alternatively, alexithymia could stand as a psychosocial risk factor by its own accord. Either way, both explanations lend support for an investigation into alexithymia's related role as a potential risk factor for adolescents with IBD.

Although no prior studies have explored alexithymia and its potential impact on IBD health outcomes, studies have examined causality in the other direction. A six-month longitudinal study on adult IBD patients revealed that alexithymia was unaffected by disease activity or duration of illness in contrast to symptoms of depression and anxiety (Porcelli et al., 1996), which not only

supports the relative stability of alexithymia in IBD patients (Porcelli et al., 1996), but also suggests that alexithymia plays a predictive rather than reactive role in disease severity and illness course (Searle & Bennett, 2001). Further longitudinal research is needed in order to clarify the predictive properties of alexithymia in IBD (Searle & Bennett, 2001). If alexithymia proves both powerful and stable in predicting health outcomes, the trait could be a potential target for future interventions.

CONCLUSION

Adolescence marks a particularly challenging developmental stage due to the significant biological, emotional, and social changes occurring. Adolescents with limited skills in emotional identification and awareness may experience even greater challenges when attempting to navigate this developmental period. When alexithymia and adolescence merge within an individual with a chronic illness, such as IBD, that adolescent may encounter further difficulties. However, the research on alexithymia in adolescence is particularly lacking when it comes to pediatric chronic illness populations. A better understanding of alexithymia in adolescents with chronic illnesses could inform interventions, potentially obviating problems from continuing into adulthood. Therefore, it is critical to study the extent and impact of alexithymia not only in adolescents in general, an

age group at-risk for the development of emotion-related vulnerabilities, but also in adolescents with IBD, who face the added challenges of a lifelong chronic illness.

As the first study to investigate the prevalence of alexithymia and its potential influence on health outcomes in adolescents with IBD, the current study signifies a new direction for research in this pediatric population – one that moves toward examining developmentally-relevant psychological factors in relation to health outcomes. In doing so, it is hoped the study can identify those risk factors associated with poor health outcomes to inform future interventions for these adolescents.

PURPOSE OF STUDY AND HYPOTHESES

Purpose of Study

The purpose of the present study was to examine the prevalence of alexithymia in an adolescent IBD population as well as to investigate whether alexithymia might be a predictor for health outcomes in these patients. An additional goal was to observe the relationship between alexithymia and other psychological variables, namely depressive symptoms and perceived stress, in

adolescents with IBD. Furthermore, the study investigated the impact of these other psychological variables on health outcomes, comparing them to the predictive power of alexithymia. It is hoped that the findings from the current study will add important knowledge to the literature base about the psychological factors that place adolescents with IBD at increased risk for poor health outcomes.

Aims and Hypotheses

Specific Aim 1

The first aim of the present study was to investigate the prevalence of alexithymia in an adolescent IBD population.

Hypothesis 1: The incidence of alexithymia in a sample of adolescents with IBD would be significantly higher than the rate observed in a normal adolescent population (7.3%) (Honkalampi et al., 2009).

Rationale 1: High rates of alexithymia have been documented in adults with IBD (Nakagawa et al., 1979; Porcelli et al., 1996; Porcelli et al., 1999; Porcelli et al., 1995; Taylor et al., 1981); however, no prior studies have examined the trait's occurrence within adolescent IBD populations. Given the significant prevalence of alexithymia in adult IBD populations (Porcelli et al., 1996; Porcelli et al., 1995) as well as the similar trends in alexithymia between normal

populations of adults and adolescents (Honkalampi et al., 2009; Joukamaa et al., 2008; Mattila et al., 2008; Mattila et al., 2006), we expected to observe elevated rates of alexithymia in adolescents with IBD.

Specific Aim 2

The second aim of the present study was to understand the relationship between alexithymia and other psychological variables.

Hypothesis 2A: There would be a significant positive correlation between alexithymia and depressive symptoms, with higher alexithymia scores associated with higher depressive symptoms.

Hypothesis 2B: There would be a significant positive correlation between alexithymia and perceived stress, with higher alexithymia scores associated with higher perceived stress scores.

Rationale 2: Alexithymia has been shown to correlate with anxiety and depression (e.g., Burba et al., 2006; Di Schiena et al., 2011); however, research has demonstrated that despite the overlap, alexithymia remains a distinct trait (Tolmunen et al., 2010; Luminet, 2010). Given the overlap between alexithymia and negative affect disorders, it is important to investigate the relationship between alexithymia, depressive symptoms, and perceived stress within the adolescent IBD population. Understanding the quality and intensity of these

relationships was necessary for interpreting how these psychological variables relate to health outcomes and other clinical factors.

Specific Aim 3

The final aim of the present study was to elucidate the relationship between alexithymia and health outcomes. For the purposes of this study, *health outcomes* referred to illness course, disease severity, and disease-specific QOL. Illness course and disease severity constituted objective health outcomes, while disease-specific QOL represented a self-report measure of subjective health outcomes.

Hypothesis 3A: There would be a significant inverse correlation between alexithymia and health outcomes such that high alexithymia scores would be associated with worse health outcomes in adolescents with IBD.

Hypothesis 3B: There would be a significant inverse correlation between depressive symptoms and health outcomes such that high depressive symptom scores would be associated with worse health outcomes in adolescents with IBD.

Hypothesis 3C: There would be a significant inverse correlation between perceived stress and health outcomes such that high perceived stress would be associated with worse health outcomes in adolescents with IBD.

Hypothesis 3D: Alexithymia would significantly predict health outcomes in adolescents with IBD.

Hypothesis 3E: The variance in health outcomes would not be better accounted for by depressive symptoms or perceived stress.

Rationale 3: Alexithymia has been demonstrated to have significant associations with health outcomes in other gastrointestinal populations (Porcelli et al., 2003); therefore, we anticipated that alexithymia would be the strongest and most reliable predictor of illness course, disease severity, and disease-specific QOL in adolescents with IBD. The factors that put a particular subgroup of adolescents with IBD at risk for worse health outcomes remain largely unknown (Mackner & Crandall, 2005a). Depressive symptoms and perceived stress have been considered in adult IBD populations; however, alexithymia has not been previously explored in an adolescent IBD population. Thus, it would be useful to understand how much unique variance alexithymia adds to commonly considered variables, such as depressive symptoms and perceived stress. Obtaining a deeper understanding of the psychological factors influencing adolescent IBD patients' health outcomes could potentially offer future directions for research and treatment.

CHAPTER THREE
Methodology

PARTICIPANTS

The current study was based on a single group, single measure, within subject design. The study included 63 adolescents between the ages of 13 years, 0 months and 17 years, 11 months who had been diagnosed with and were currently receiving treatment for IBD (i.e., either CD or UC). Participants were recruited from the department of Gastroenterology (GI) at Children's Medical Center Dallas (CMCD), in accordance with the guidelines of UT Southwestern Medical School's (UTSW) Institutional Review Board that oversees research at both UTSW and CMCD.

Inclusion Criteria

1. Histopathologically diagnosed with one of the two subtypes of IBD, either CD or UC
2. Currently being treated for IBD in the GI clinic at CMCD
3. Proficiency in English

4. Absence of any developmental or serious mental health disorder (per parent/legal guardian report) that would interfere with the ability to complete measures
5. No history of any traumatic brain injury, stroke, neurological disorder, or other major medical condition unrelated to IBD

MEASURES

Clinician Completed Forms

Comprehensive Medical Chart Review Form

Medical records were reviewed to obtain demographic and clinical information related to illness course and disease severity. In addition to demographic data such as gender, date of birth, and payor status, researchers collected medical information, such as diagnosis, date of diagnosis, surgical history, concurrent medications and therapies related to IBD, and Physician's Global Assessment (PGA) from each GI clinic visit in the previous 12 months prior to and including baseline (i.e., remission, mild, moderate, severe).

Illness course was measured by examining data from the patient's medical chart as far as twelve months back from the patient's baseline study visit. To calculate illness course, researchers collected the following data: number of

outpatient clinic visits, number of hospital admissions, length of steroid exposure in months, and number of IBD medication increases (Szigethy et al., 2004; Wahed, Corser, Goodhand, & Rampton, 2010). All of these variables were summed to quantify illness course over the last 12 months.

Individual Disease Severity Review Form

Disease severity was measured by a physician-rated objective index of disease activity, i.e., either the Pediatric Crohn's Disease Activity Index (PCDAI; Hyams et al., 1991) or the Pediatric Ulcerative Colitis Activity Index (PUCAI; Turner et al., 2007). The PCDAI and the PUCDAI have demonstrated good test-retest reliability and responsiveness to disease change as well as positive correlations with PGA (Blank & Switzer, 2006; Griffiths et al., 2005; Turner et al., 2009). Both of these well-validated scales (Griffiths et al., 2005; Turner et al., 2009) use continuous scores and ranked categories of disease severity ratings. The PCDAI (Hyams et al., 1991) is made up of both subjective (i.e., patient-reported assessments of abdominal pain, general well-being, and stool pattern) and objective data (i.e., physical exam findings and laboratory test data). The PCDAI defines evidence of improvement as a decrease of 12.5 points or more on the total score, with the following cutoff scores for categories of disease activity: less than 10 for inactive disease, 10 to 27.5 for mild disease, 30 to 37.5 for moderate disease, and 40 to 100 for severe disease (Turner et al., 2010).

More recently developed, the PUCAI (Turner et al., 2007) is a 6-item disease activity index for pediatric ulcerative colitis. Physicians score items related to pediatric patients' abdominal pain, rectal bleeding, number of stools per 24-hours, nocturnal stools, and activity level. In contrast to the PCDAI, the PUCAI defines clinically significant responses as a point change of 20 or more, with the following cutoff scores defining categories of disease activity: less than 10 points for inactive disease, 10 to 34 for mild disease, 35 to 64 for moderate disease, and 65 to 85 for severe disease. Furthermore, the PUCAI does not include physical findings and laboratory values like the PCDAI, because laboratory tests have demonstrated poor reliability and validity in the correspondence to disease activity in UC (Mack et al., 2007).

Caregiver Completed Measures

Baseline Caregiver Form

Parents or legal guardians completed a six-page demographic and clinical history questionnaire for the adolescent during his or her baseline assessment visit which detailed the patient's psychological, educational, and medical history. Information was also obtained regarding the patient's home environment, family's educational history, and current parental employment.

Participant Completed Measures

Adolescent Minor Stress Inventory

The Adolescent Minor Stress Inventory (AMSI; Ames et al., 2005) consists of 72 self-report items that are intended to assess an adolescent's perceived stress of daily hassles. The questionnaire is appropriate for ages 13 to 17 years, with a reading grade level of 3.9. There are six subscales assessing minor stressors associated with performance (20 items), relationship (10 items), education (6 items), financial (6 items), family (6 items), and other stress (24 items). In the present study, the 24 items pertaining to "other stress" were not included. Since those 24 questions represented items that did not load on any factor, one prior study eliminated those 24 items, opting for an abbreviated version of the questionnaire (Salafia & Lemer, 2012). For the five remaining subscales (48 items), the study found an internal reliability (Cronbach's alpha) ranging from .79 to .93.

Examples of items on the measure include the following: "I had too many responsibilities" (performance), "My friends left me out of an activity" (relationship), "I had trouble writing" (education), "I did not have nice clothes to wear" (financial), and "I argued with my parents or guardian" (family). Adolescents endorse the occurrence of a daily hassle in the last two weeks and indicate their level of perceived stress by responding to each item on a 6-point

Likert scale ordered as follows: "0 = *did not happen*," "1 = *happened but was not stressful*," "2 = *happened and was a little stressful*," "3 = *happened and was somewhat stressful*," "4 = *happened and was very stressful*," "5 = *happened and was extremely stressful*." Higher scores indicate higher levels of perceived stress from daily hassles.

Children's Depression Inventory

Children's Depression Inventory (CDI; Kovacs, 1981) is the most widely used self-report measure that assesses common cognitive, affective, and behavioral symptoms of depression in children ages 7 through 17 years. The present study used the CDI-2. The most recent edition of CDI, the CDI-2, includes new items targeting the essential features of childhood depression, revised scales with improved reliability and validity, and updated norms that represent the U.S. population (Kovacs, 2010). The CDI-2 requires a first grade reading level and takes approximately 5 to 15 minutes to complete. The 28-item, self-rated measure asks children to select one of the three responses that best describes them within the last two weeks. Each item is scored as a 0, 1, or 2, with higher scores reflecting more extreme endorsements of depressive symptoms. The total score, which reflects the overall severity of depressive symptoms, was used to measure depressive symptoms in the present study. The CDI has established reliability and validity with internal consistency coefficients from .71

to .89 and test-retest coefficients from .74 to .83. Additionally, it has been used in prior published studies on depressive symptoms among adolescent IBD populations (Szigethy et al., 2009; Szigethy et al., 2004).

IMPACT-III

The IMPACT-III (Otley et al., 2002) is a disease-specific measure of HRQOL designed for pediatric IBD patients ages 9 to 17 years (Griffiths et al., 1999). The 35-item, self-administered measure covers six domains: bowel symptoms, systemic symptoms, emotional functioning, social functioning, body image, and treatment/interventions. Patients respond on a 5-point Likert scale. Scores range from 35 to 185, with higher scores indicating better HRQOL. The measure takes approximately 15 minutes to complete. As a disease-specific questionnaire, the IMPACT-III is capable of measuring changes in HRQOL over time or with treatment (Szigethy et al., 2010). The IMPACT questionnaire shows a high internal reliability of .96 (Blank & Switzer, 2006; Griffiths et al., 2005; Otley et al., 2002) and good test-retest stability in clinically stable patients (Loonen, Grootenhuis, Last, de Haan et al., 2002). Additionally, the measure demonstrates good discriminate validity between symptom groups and illness course severity (Loonen, Grootenhuis, Last, de Haan et al., 2002).

Life Events Checklist for Adolescents

The Life Events Checklist (LEC; Johnson & McCutcheon, 1980) is a 46-item, self-report questionnaire assessing adolescents' major life changes. The current study used a revised version of the LEC (Jackson & Frick, 1998), modified for adolescents ages 13 to 17 years. The questionnaire asked participants about major life events over the last 12 months. Not only does the scale measure the frequency of major life events, but it also obtains the subjective appraisal of events in terms of their desirability and impact. For example, participants endorsed the occurrence of the event in the past year, their feelings about it (i.e., good or bad), and the degree to which the event impacted their lives (i.e., four-point Likert rating scale). The LEC shows adequate test-retest reliability with correlation coefficients ranging from .66 to .72 (Compas, 1987). Also, it has shown significant correlations with emotional adjustment, physical health, and personality variables, where correlation coefficients range from .21 to .36 (Compas, 1987).

Toronto Alexithymia Scale

The Toronto Alexithymia Scale (TAS-20; Bagby, Parker, et al., 1994; Bagby, Taylor, et al., 1994) is a 20-item self-report measure designed to measure alexithymia through three subscales: (1) difficulty identifying feelings (DIF); (2) difficulty describing feelings (DDF); and (3) externally-oriented thinking. Examples of items are "I have feelings that I can't quite identify" (DIF) and "It is

difficult for me to find the right words for my feelings" (DDF) as well as reversed scored items, such as "Being in touch with emotions is essential" (EOT) (Bagby, Parker, et al., 1994; Bagby, Taylor, et al., 1994). Participants respond to items using a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). TAS-20 total scores range from 20 to 100 and the test developers recommend the total TAS-20 cutoff point to be $\geq$ 61 to define alexithymia cases (Bagby, Parker, et al., 1994; Bagby, Taylor, et al., 1994). Among adults, the TAS-20 demonstrates good reliability, with an internal consistency of .81 and test-retest correlations of .77 (Bagby, Parker, et al., 1994). Furthermore, it has shown good convergent and discriminate validity as well as modest concurrent validity (Bagby, Taylor, et al., 1994).

Following recommendations from recent psychometric investigations (Heaven et al., 2010), the current study did not include the third scale (EOT) of the TAS-20 because it has demonstrated less-than-optimal reliability for use with adolescents (Parker et al., 2010; Rieffe et al., 2006). In Heaven et al.'s (2010) study, the abbreviated 12-item TAS showed that alexithymia was distinguishable from other self-evaluative traits in an adolescent sample. Heaven et al.'s (2010) study also demonstrated good internal consistency (Cronbach's alpha = .88) with the abbreviated format and provided evidence for overall reliability in assessing alexithymia among adolescents. Both the DIF and DDF factors require a reading level of Grade 5 or 6 (Parker et al., 2010).

Recent Stress Question

In addition to the other stress questionnaires, participants were asked to reflect on their experience of stress by answering the question, "In the last 12 months, how much stress have you experienced on a scale of 0 to 100?". Participants rated their recent stress level on a scale from 0 to 100, with 0 being "not stressed at all" and 100 being "extremely stressed."

PROCEDURES

Participant Recruitment

Before conducting the proposed study, approval was obtained from the IRB of UTSW. The names of the adolescent patients who had confirmed endoscopic and histologic evidence of disease were acquired through the GI patient schedules at CMCD using ICD-9 codes 555.0-556.9 (U.S. Department of Health and Human Services, 1980). Weekly reports identified those who met the study's age criteria and were scheduled for upcoming GI clinic visit. Recruitment and enrollment was ongoing. Parents or legal guardians of the identified adolescents were approached at their child's routine GI clinic visit. A description

of the study was provided and written, informed consent from the parent or legal guardian and assent of the minor child was given at this time.

To obtain consent and assent, the researcher supplied the parent(s) or guardian(s) and adolescent with a full description of the study based on how the study was described in the IRB-approved informed consent document. The researcher described the study's purpose, benefit, and potential risks to the patient and to the parent(s) or guardian(s). Parents/legal guardians and adolescents were informed that their participation was voluntary and that they could choose to withdraw from the study at any time. They were encouraged to ask questions pertaining to the study. If the parent/legal guardian and adolescent wished to participate, they provided informed, written consent. Also, the researcher verified that the adolescent participant understood his or her role in the study. Next, parents/guardians completed the Health Insurance Portability and Accountability Act (HIPAA) Release document, which authorized the use of the adolescent's protected health information for the purpose of the study. The parent(s) or guardian(s), CMCD Medical Records, and the GI department at CMCD were provided with signed copies of both the consent form and the HIPAA release form.

Data Collection

After consent and assent were obtained, participants were enrolled in the study and their participation in the study began that same day. The single measure design involved the collection of pre-baseline and baseline data for each participant. Data collection occurred during the participant's scheduled GI clinic visits, with participants completing the following self-report study measures at 0 months (baseline): (1) AMSI; (2) CDI-2; (3) IMPACT-III; (4) LEC; (5) TAS-20; and (6) the Recent Stress Question. The participant's parent(s) or legal guardian(s) completed the Baseline Caregiver Form at the same time. The researcher conducting the assessment visit was trained in the administration and scoring of the questionnaires.

After the baseline study visit, researchers completed a retrospective chart review to examine the participant's illness course and disease severity. Illness course was a cumulative measure of the designated items in the past 12 months. Disease severity represented either the PUCAI or the PCDAI score from the baseline clinic visit. The clinical information needed to calculate the PUCAI and PCDAI scores were documented by the physician or medical staff at the time of each GI clinic visit and made available in the medical chart as standard practice of the GI department at CMCD.

CHAPTER FOUR
Results

In the present study, *p* values of less than .05 were reported as significant. When *p* values fell between .05 and .10, they were classified as marginally significant. Values above .10 were deemed non-significant.

Preliminary Analysis

An a priori power analysis indicated that a total sample size of 62 was needed to detect a medium effect size ($f^2 = 0.15$) with a power of .85 (Numerator $df = 1$, Number of predictors = 5, $\alpha = .05$) (Faul, Erdfelder, Buchner, & Lang, 2009). Our goal was to recruit as many participants as possible to enhance the representativeness of our sample. We recruited 63 participants in an 8-month timeframe, which was sufficient to yield effect sizes reflecting clinically significant effects as indicated by the a priori power analysis test.

In a preliminary analysis, descriptive statistics were generated for the relevant demographic and clinical variables. These procedures allowed for examination of any violations of normality or other statistical assumptions. Preliminary analysis of normal P-P plots, skewness statistics, frequency histograms, and Kolmogorov-Smirnov test statistics were examined to check

continuous variables of interest for normality. Disease-specific QOL, alexithymia, depressive symptoms, and perceived recent stress scores were normally distributed. In contrast, disease severity, illness course, perceived stress of major life events, and perceived stress of daily hassles showed a moderate positive skew. These variables were transformed using a Log 10 command (Howell, 2007), and the following results are based on those transformations.

When multiple linear analyses were conducted, each analysis was preceded by preliminary analyses and bivariate correlations to check that assumptions of normality and linearity were met. Furthermore, all multiple linear regression models were examined for potential collinearity among the variables. These examinations yielded no evidence to suggest multicollinearity. The Durbin-Watson statistic was used to test for the presence of serial correlation among the residuals. No correlations were found among the residuals, as all the Durbin-Watson statistics fell within the acceptable range (1.50 - 2.50). Moreover, the standardized residuals for all our linear and multiple regressions also fell within the acceptable range of less than +/- 3.0, suggesting that there were no outliers affecting our analyses.

Characteristics of the Sample

A total of 63 participants comprised the final sample for data analysis. Demographic and clinical data were available for the full sample, including

psychological, educational, and medical history; however, only 62 participants had complete data for home environment, family education history, parental employment, and household income. Data on alexithymia, perceived stress, and disease-specific QOL were available for the full sample, whereas a reduced sample of 62 participants was used for analyses involving depressive symptoms due to one participant declining to complete the CDI-2. In terms of the retrospective chart review, cumulative illness course and baseline disease severity scores were calculated for the full sample.

A complete breakdown of descriptive demographic and clinical data can also be found in Tables 1-3, while Tables 4-5 display descriptive data for the main variables of interest.

Differences Between IBD subtypes. The two IBD subtypes of CD and UC were compared on demographic and clinical variables using independent *t* tests for continuous variables and chi-square tests for categorical variables. Tables 1-3 summarize these findings. An independent samples *t* test revealed a significant difference between the CD and UC groups in participants' age at diagnosis, $t(61) = -2.41$, $p = .02$, and marginally significant differences in illness duration, $t(61) = 1.95$, $p = .06$, and steroid exposure, $t(28.41) = 1.73$, $p = .09$. However, between the two IBD subtypes, there were no group differences in gender, race, ethnicity, participants' age at baseline, or grade level in school. Furthermore, no significant differences were found between UC and CD participants in terms of the five

psychological variables and three health outcomes measures. Given the predominantly non-significant findings indicating minimal differences between the two IBD subtypes, the UC and CD groups were combined for the remainder of the analyses.

Differences in Alexithymia Scores. When comparing participants with alexithymia (TAS-12 scores $\geq$ 37) to those without alexithymia (TAS-12 scores $\leq$ 36), significant differences were found for age at diagnosis, $t(45.58) = -3.12$, $p = .003$, and illness duration, $t(36.05) = 3.26$, $p = .002$, such that adolescents in the alexithymia group were older at the time of their IBD diagnosis and had a shorter illness duration than adolescents in the non-alexithymia group. However, Pearson correlations revealed that the full range of alexithymia scores were unrelated to age at baseline, $r(61) = -.05$, $p = .29$, age at diagnosis, $r(61) = .13$, $p = .29$, illness duration, $r(61) = -.17$, $p = .17$, and grade level in school, $r(61) = -.08$, $p = .52$. There were no significant differences in race, gender, ethnicity, household income, mental health history as reported by parents, or academic performance between adolescents with alexithymia and those without.

Age-Related Differences in Alexithymia Scores at Baseline. Using an analysis of variance (ANOVA), we assessed for age-related differences on the TAS. Table 6 displays the results from the ANOVA assessing for age-related differences in alexithymia scores between groups of adolescents by age. Five age groups were compared (i.e., 13, 14, 15, 16, and 17 year olds). The analysis found

no significant age-related differences for the TAS-20, its three subscales, or the adjusted TAS-12.

Illness Duration and Age at Diagnosis. In addition to examining the relationship between alexithymia, illness duration, and age at diagnosis, we examined these two illness-related variables in association with the other variables of interest. A series of Pearson correlations revealed significant relationships between illness duration and perceived stress of major life events, $r(61) = -.31$, $p = .02$, illness course, $r(61) = -.26$, $p = .04$, and disease-specific QOL, $r(61) = .29$, $p = .02$,. A marginally significant relationship was found between illness duration and perceived stress of daily hassles, $r(61) = -.22$, $p = .09$. No significant relationships were found between illness duration and perceived recent stress, $r(61) = -.19$, $p = .13$, depressive symptoms, $r(60) = -.06$, $p = .63$, or disease severity, $r(61) = .05$, $p = .67$. Age at diagnosis demonstrated significant relationships with perceived stress of daily hassles, $r(61) = 29$, $p = .02$, and disease-specific QOL, $r(61) = -.28$, $p = .03$, but not with perceived stress of major life events, $r(61) = 17$, $p = .19$, perceived recent stress $r(61) = .20$, $p = .11$, depressive symptoms $r(60) = -.07$, $p = .59$, illness course $r(61) = .20$, $p = .11$, or disease severity, $r(61) = -.11$, $p = .38$.

Steroid Effects. Lastly, since oral steroids can negatively affect mood and physical appearance, we examined steroid exposure in relation to the five psychological variables using a series of Pearson correlations. Steroid exposure

did not significantly correlate with alexithymia, $r(61) = .19$, $p = .15$, depressive symptoms, $r(60) = .05$, $p = .71$, perceived stress of major life events, $r(61) = .19$, $p = .15$, or perceived stress of daily hassles, $r(61) = .18$, $p = .15$. However, a marginally significant correlation was found between steroid exposure and perceived recent stress, $r(61) = .25$, $p = .051$. Aside from this one marginally significant finding, these findings suggest that the participants' reported psychological distress cannot be better accounted for by potential side effects related to their steroid treatment. A significant inverse correlation was, however, found between steroid exposure and disease-specific QOL, $r(61) = -.28$, $p = .03$. Participants with greater steroid exposure likely perceive medication side effects or inconveniences from their treatment regimen as associated with their chronic illness.

Hypothesis Testing

Aim 1

The first aim of the current study was to investigate the prevalence of alexithymia in adolescents with IBD. We hypothesized that alexithymia would occur at a percentage higher than 7.3% (Honkalampi et al., 2009) in an adolescent IBD sample. Two one-sample proportion tests were conducted to compare the frequency of alexithymia in our adolescent IBD sample relative to the normal

adolescent population (.073). Since our comparison group (Honkalampi et al., 2009) based their findings on the TAS-20, we generated our first one-sample proportion test using the full-scale alexithymia score. On the TAS-20, we used the empirically derived cutoff score of $\geq$ 61 as recommended by the test publishers to define alexithymia cases (Bagby, Parker, et al., 1994; Bagby, Taylor, et al., 1994).

We calculated the second one-sample proportion test using the abbreviated TAS-12, which did not include the EOT subscale as recommended by recent research to address the TAS-20's validity concerns for use with adolescents (Heaven et al., 2010). To define alexithymia cases on the TAS-12, we calculated an adjusted cutoff score of $\geq$ 37 by extrapolating from the TAS-20's empirically derived cutoff score. It should be noted that this adjusted cutoff score has yet to be validated, as the recommendation to use an abbreviated TAS with adolescents is fairly recent (Heaven et al., 2010). Yet, descriptive statistics comparing the TAS-12 and the TAS-20 indicated that participants' scores on the two versions of the scale did not differ significantly with regard to gender, age at baseline, grade level in school, race, ethnicity, age at diagnosis, illness duration, household income, mental health history, or academic performance.

Our first comparison, using the full alexithymia questionnaire (TAS-20), revealed that the observed proportion of .16 significantly differed from the hypothesized value of .073, one-tailed $p = .02$. The second comparison, which

used the abbreviated alexithymia score (TAS-12), had an observed proportion of .21 that also significantly differed from .073, one-tailed $p = .001$. Thus, on both versions of the TAS, adolescents with IBD had a higher rate of alexithymia than did a normal adolescent population.

Using a one-sample proportion test, we also compared the rate of alexithymia in our adolescent IBD sample to the rates previously reported in an adult IBD population (38%) (Porcelli et al., 1999). Both the TAS-20 (.16) and the TAS-12 (.21) observed proportions were found to significantly differ from the hypothesized value of .38, one-tailed $p < .001$, indicating that the rate of alexithymia in our adolescent IBD sample was significantly lower than the rate documented in an adult IBD population.

Since differences were not detected between the two forms, and the shorter version has been recommended for adolescents (Heaven et al., 2010), the remaining results describe findings for the TAS-12 only.

Aim 2

The second aim sought to understand the relationship between alexithymia and other psychological variables. We expected to find a significant positive correlation between alexithymia and depressive symptoms as well as between alexithymia and perceived stress. A series of Pearson correlations were conducted to assess the relationship between alexithymia and the other four

psychological variables: depressive symptoms, perceived stress of major life events, perceived stress of daily hassles, and perceived recent stress. Table 7 displays these correlational findings. Alexithymia was significantly associated with all three stress measures (i.e., perceived stress of major life events, perceived stress of daily hassles, and perceived recent stress). Of all the psychological variables, alexithymia demonstrated the strongest relationship with depressive symptoms.

Aim 3

The third aim of the current study sought to elucidate the relationship between alexithymia and health outcomes. We predicted that alexithymia would be inversely correlated with health outcomes, such that higher alexithymia scores would be associated with worse health outcomes. We also expected to observe a similar relationship between the other psychological variables (i.e., depressive symptoms and perceived stress) and health outcomes. A series of Pearson correlations were computed to assess the relationship between baseline scores on the psychological questionnaires and: (a) illness course, (b) baseline disease severity, and (c) baseline disease-specific QOL. Illness course represented a cumulative measure of the entire 12 months prior to and including the baseline visit.

Table 8 displays the results of the Pearson correlational analyses among the psychological and health outcomes measures. Contrary to our predictions, none of the psychological variables were significantly correlated with illness course. Only one of the psychological variables, perceived stress of major life events, was significantly related to disease severity, $r(61) = .27$, $p = .03$. In contrast to illness course and disease severity, disease-specific QOL was significantly and negatively correlated with all five of the psychological variables. These correlation coefficients were all of at least moderate size.

Since all the psychological variables were significantly correlated with disease-specific QOL, the next set of analyses was designed to determine which ones added unique variance to our outcome. We hypothesized that alexithymia would significantly predict disease-specific QOL in adolescents with IBD. In the first multiple linear regression analysis, we entered all five psychological measures into the model at the same time. The independent variables were alexithymia, perceived stress of major life events, perceived stress of daily hassles, perceived recent stress, and depressive symptoms. The dependent variable was disease-specific QOL. As shown in Table 9, this model revealed that the linear combination of the five psychological variables was significantly related to disease-specific QOL, $R^2 = .49$, $F(5, 56) = 10.60$, $p < .001$. Forty-nine percent of the variance of disease-specific QOL in the sample was accounted for by the linear combination of the five psychological variables. Most importantly,

alexithymia was the only variable that significantly contributed independent variance in disease-specific QOL, although perceived stress of major life events was a marginally significant independent predictor.

Next, a hierarchical linear regression analysis was conducted to determine how much variance alexithymia added to disease-specific QOL, over and above the depressive symptoms and perceived stress. First, we entered perceived stress of major life events, perceived stress of daily hassles, perceived recent stress, and depressive symptom scores as a single block (Step 1), followed by a second block containing only alexithymia scores (Step 2). The resulting hierarchical linear regression model is displayed in Table 10. The combination of all the psychological variables minus alexithymia accounted for 43% of the variance in disease-specific QOL. Of the four psychological variables included in this block, only depressive symptoms proved a significant independent predictor of disease-specific QOL. After accounting for these variables, alexithymia contributed an additional 6% to the variance in disease-specific QOL.

Lastly, we conducted an automatic stepwise linear regression analysis to determine the combination of psychological variables that predicted non-overlapping variance in the dependent variable. Table 11 displays the results of this follow-up analysis. All five psychological variables were entered into an automatic stepwise regression analysis. The most parsimonious regression model consisted of two variables, alexithymia and perceived stress of major life events,

which together accounted for 44.5% of the variance in disease-specific QOL scores. In the automatic stepwise linear regression, the first variable selected was alexithymia, which alone accounted for 34.3% of the variance in disease-specific QOL. The second variable was perceived stress of major life events, which only contributed an additional 10.2% to the variance. Taken together, this follow-up analysis supports alexithymia as the strongest predictor of disease-specific QOL, as alexithymia accounted for the majority of the variance.

Exploratory Analysis

Somatic Items as Potential Confounds

Both the alexithymia and depressive symptom questionnaires included items that target somatic or physical symptoms associated with these two psychological constructs. IBD and its related treatment (e.g., oral steroids) can cause neurovegetative symptoms that can mimic the somatic symptoms of alexithymia and depression. Hence, the current study's adolescent IBD sample may have been more inclined to endorse somatic or physical symptom items than the normative populations due to the nature of their chronic illness and its treatment. To determine whether the somatic items on the alexithymia and depressive symptom questionnaires were responsible for our findings, we re-ran

aims 1 through 3 excluding the somatic items from our total alexithymia and depressive symptom scores.

On the TAS-20, item 3 (i.e., "I have physical sensations that even doctors don't understand") and item 7 (i.e., "I am often puzzled by sensations in my body") were removed from our alexithymia score calculations (Bagby, Parker, et al., 1994; Bagby, Taylor, et al., 1994). As stated previously, these are the only two TAS questions on which adolescent responses have significantly deviated from adult responses (Parker et al., 2010). We sought to examine if the rates of alexithymia cases decreased when the somatic items were not included in our alexithymia score calculations. We examined both the total alexithymia score minus the two somatic items (TAS-18) and the abbreviated alexithymia score minus the two somatic items (TAS-10). On the TAS-18, we calculated an adjusted cutoff score of $\geq$ 55 to define alexithymia cases by extrapolating from the TAS-20's empirically derived cutoff score. The same procedure was used to calculate an adjusted cutoff score of $\geq$31 for the TAS-10.

The sample mean for alexithymia scores was 46.02 (*SD* = 10.20) on the TAS-18 and 24.17 (*SD* = 8.71) on the TAS-10. The proportion of alexithymia cases based on the TAS-18 was .16, which identical to the proportion of alexithymia cases found for the TAS-20. The second proportion of alexithymia cases based on the TAS-10 was .25, which was higher than the proportion of .21 found for the TAS-12. Thus, compared to a healthy adolescent population,

alexithymia occurred at significantly greater rates in an adolescent IBD sample even when accounting for the influence of physical complaints on overall alexithymia scores.

We next sought to differentiate between true depressive symptoms and neurovegetative depressive symptoms attributable to IBD. Although controversy ensues regarding the best strategy for doing so, we based our approach on Szigethy et al's (2004) findings that demonstrated specific items on the CDI (i.e., anhedonia, fatigue, and decreased appetite) as positively correlated with disease severity. These neurovegetative depressive symptoms have also been associated with the release of inflammatory proteins, cytokines, during IBD flare-ups (Maier & Watkins, 1998; Reichenberg et al., 2001). To clarify the relationship between depression and IBD, we recalculated depressive symptom scores leaving out the following questions pertaining to neurovegetative depressive symptoms: item 4 (e.g., "I have fun in many things"), item 15 (e.g., "I have trouble sleeping every night"), item 16 (e.g., "I am tired once in a while"), item 17 (e.g., "Most days I do not feel like eating"), item 18 (e.g., "I do not worry about aches and pains"), item 20 (e.g., "I never have fun at school"), and item 26 (e.g., "I fall asleep during the day all the time"). The sample mean for depressive symptom scores minus these items was 48.21 (SD = 9.10).

A series of Pearson correlations were conducted to examine the relationship between the revised alexithymia scores, revised depressive symptom

scores, and disease-specific QOL. Paralleling our previous findings, the revised alexithymia variable, which excluded the somatic symptom items, was found to positively correlate with the revised depressive symptom variable, which excluded the neurovegetative items, $r(60) = .58$, $p < .001$. Both revised psychological variables were found to significantly and inversely correlate with disease-specific QOL, with the revised alexithymia variable maintaining the strongest correlation with disease-specific QOL, $r(61) = -.57$, $p < .001$, followed by the revised depressive symptom score, $r(60) = -.50$, $p < .001$. Therefore, the correlations between alexithymia, depressive symptoms, and disease-specific QOL were not better explained by somatic and neurovegetative symptoms shared by all three variables.

Controlling for Illness Course and Disease Severity

Conceptually, disease-specific QOL as a subjective health outcome measure is likely to be heavily influenced by objective health outcomes, such as illness course and disease severity. Therefore, we re-ran the analyses outlined in aim 3 controlling for disease-severity and illness course. First, we conducted a hierarchical linear analysis in which illness course and disease severity were entered first as predictor variables (Step 1). The five psychological variables were selected one at a time and entered as a single predictor into the 2nd block (Step 2). A separate hierarchical analysis was conducted for each psychological

variable, with disease-specific QOL consistently serving as the dependent variable. As shown in Table 12, the results changed minimally, with all significant relationships remaining at comparable levels.

A second hierarchical linear regression sought to determine which of the five psychological variables remained significant predictors of disease-specific QOL after controlling for illness course and disease severity. In this analysis, illness course and disease severity were again entered into the first block (Step 1), followed by a block comprised of alexithymia, perceived stress of major life events, perceived stress of daily hassles, perceived recent stress, and depressive symptoms (Step 2). Table 13 displays the results of this analysis. When the psychological variables were added to the model, they significantly increased the variance by 42%. Furthermore, alexithymia remained the only significant independent contributor; however, disease severity emerged as a marginally significant independent predictor. Thus, even when controlling for disease severity and illness course, the linear combination of our five psychological variables significantly contributed to the variance in disease-specific QOL.

Lastly, we repeated the same block entry described above, but ran an automatic stepwise regression analysis (Table 14). Consistent with our initial analysis, alexithymia prevailed as the strongest predictor, accounting for 32% of the variance in disease-specific QOL. Just as before, the next variable selected was perceived stress of major life events, which contributed an additional 6% to

the variance. Together, these exploratory analyses indicated that controlling for illness course and disease severity did not impact our previous findings regarding the predictive power of psychological variables on disease-specific QOL.

Controlling for Illness Duration

Since illness duration was correlated with disease-specific QOL, we investigated whether controlling for illness duration altered alexithymia as a predictor of disease-specific QOL. We conducted a hierarchical linear regression, in which illness duration was entered in the first block (Step 1), followed by a block containing the five psychological variables (Step 2). Illness duration was a significant predictor of disease-specific QOL, $\beta = .29$, $p = .02$. The linear combination of illness duration plus the five psychological variables was found to significantly contribute to the variance in disease-specific QOL, $R^2 = .49$, $F(6, 55) = 9.21$, $p < .001$. Most importantly, even after controlling for illness duration, alexithymia emerged as the most significant independent predictor of disease-specific QOL, $\beta = -.29$, $p = .03$, compared to the other four psychological variables.

Comprehensive Model for Predicting Disease-Specific QOL

Disease-specific QOL is an important overall outcome measure in chronic illness populations. As such, it was necessary to understand how psychological

and disease-related variables impacted adolescent IBD patients' QOL. The present study provided the opportunity to determine whether psychological variables, objective health indices, or both were most predictive of disease-specific QOL. We sought to create a comprehensive model for calculating disease-specific QOL that combined both psychological variables and objective health indices as predictors.

First, we computed Pearson correlations to assess the relationship between our objective health outcome measures (i.e., illness course and disease severity) and disease-specific QOL. Disease-specific QOL was significantly related to disease severity, $r(61) = -.32$, $p = .01$, but not to illness course, $r(61) = -.18$, $p = .16$. The results of these bivariate correlations justified our continued investigation of disease severity as an independent predictor variable of disease-specific QOL.

Next, a multiple linear regression analysis was conducted to determine which of the significant predictors independently contributed to the variance in disease-specific QOL. Our previous analyses revealed that of the psychological variables, only alexithymia and perceived stress of major life events added unique variance to disease-specific QOL (see Table 11). In terms of objective health indices, only disease severity showed a significant bivariate relationship with disease-specific QOL. Therefore, our comprehensive multiple linear regression model only included alexithymia, perceived stress of major life events, and

disease severity as predictor variables. Disease-specific QOL remained our dependent variable. This analysis found that the linear combination of psychological and objective health variables was significantly related to disease-specific QOL, $R^2 = .49$, $F(3, 59) = 18.87$, $p < .001$. Together, these variables accounted for 49% percent of the variance in disease-specific QOL. When controlling for the other predictor variables, alexithymia, perceived stress of major life events, and disease severity all prevailed as significant and unique predictors of disease-specific QOL. Alexithymia accounted for the most independent variance in disease-specific QOL, $\beta = -.49$, $t(59) = -4.98$, $p < .001$, followed by perceived stress of major life events, $\beta = -.28$, $t(59) = -2.73$, $p = .008$, and then disease severity, $\beta = -.22$, $t(59) = -2.26$, $p = .03$.

Lastly, we conducted a hierarchical linear regression analysis to determine how much variance disease severity adds to disease-specific QOL, over and above alexithymia and perceived stress of major life events. First, we entered alexithymia and perceived stress of major life events (Step 1), followed by a second block containing only disease severity (Step 2). The combination of the two psychological variables accounted for 45% of the variance in disease-specific QOL, $R^2 = .45$, $F(2, 60) = 24.10$, $p < .001$. Adding disease severity significantly increased the variance in disease-specific QOL by an additional 4%, $F(3, 59) = 18.87$, $p = .03$. These exploratory analyses indicate that psychological variables, specifically alexithymia and perceived stress of major life events, explained more

of the unique variance in disease-specific QOL than the objective measure of disease severity (see Figure 2).

Perceived Stress of Major Life Events as a Mediator of the Relationship Between Disease Severity and Disease-Specific QOL

When controlling for alexithymia and perceived stress of major life events, the amount of variance explained by disease severity was reduced. Furthermore, worse disease severity was related to higher perceived stress of major life events but not to alexithymia. These results suggested a potential inter-relationship between perceived stress of major life events and disease severity in predicting disease-specific QOL. Given the abundance of literature supporting a link between biological disease markers and perceived stress in adults with IBD (Reber, 2012; Schoultz et al., 2011), we sought to investigate whether the effects of disease severity on disease-specific QOL may be mediated by perceived stress of major life events. To establish mediation, the following four relationships must be demonstrated: (1) predictor is correlated with the outcome, (2) predictor is correlated with the mediator, (3) mediator influences the outcome, independent of the predictor, and (4) the relationship between the predictor and outcome is weakened when controlling for the mediator (Baron & Kenny, 1986). By definition, a variable is a mediator if it accounts for the effect of the independent variable on the dependent variable. Full mediation occurs when the effect of the

independent variable on the dependent variable controlling for the mediator is zero (Step 4), whereas partial mediation occurs if the presence of the mediator results in a significant reduction in the variance explained by the independent variable.

To test for mediation, we used the bootstrapping technique developed by Preacher & Hayes (2004). As a non-parametric test, the bootstrap method does not require assumptions of normality to be met and is recommended for small sample sizes. The bootstrap analysis functions by randomly drawing multiple samples from the larger dataset and generating statistics on each of those selections to provide a statistical distribution across the random samples. Basing our estimates on 5,000 bootstrap samples, we conducted a bootstrapping mediational analysis to determine if disease severity was indirectly linked to disease-specific QOL through perceived stress of major life events (Preacher & Hayes, 2008). Disease severity was the independent variable, while perceived stress of major life events was entered as the mediator. Disease-specific QOL served as the dependent variable. Significant mediation is assumed if the confidence interval for the indirect effect (i.e., independent variable to dependent variable, controlling for the mediator) does not cross zero.

The results of the bootstrapping mediational analysis suggested that perceived stress of major life events indirectly influenced the relationship between disease severity and disease-specific QOL (Table 15). Follow-up regression

analyses found that the relationship between disease severity and disease-specific QOL was, in fact, fully mediated by perceived stress of major life events (see Figure 3).

Depressive Symptoms

Given that alexithymia is a variable that has not been previously explored in adolescents with IBD, comparing our results on alexithymia to previous findings in this population was not possible. In contrast, depressive symptoms have commonly been considered an important variable in adolescents with IBD; therefore, we were able to compare the occurrence of depressive symptoms in our study's sample with a prior study's findings.

Using a one-sample proportion test, we compared the prevalence of significant depressive symptoms in our sample of adolescents with IBD to the rate previously published (25%, with significant depression indicated by a CDI Raw Score $\geq$12) (Szigethy et al., 2004). Following the procedures outlined by the CDI-2 test publishers (Kovacs, 2010), we converted the CDI cutoff score used by Szigethy et al., 2004 to obtain a CDI-2 cutoff raw score ($\geq$15). The observed proportion of .16 in our study was only marginally less than the reported value of .25, one-tailed $p = .07$. Our results suggested that our adolescent IBD sample showed a comparable rate of depression to what has previously been published in

research on this pediatric chronic illness population (M = 14.7, SD = 1.9) (Szigethy et al., 2004).

When alexithymia was not included as a predictor variable, depressive symptoms were the only significant predictor of disease specific-QOL of all the psychological variables examined (Table 10). This interesting finding led us to examine the relationship between depressive symptoms and the other unique predictors of QOL. Depressive symptoms were significantly correlated with both perceived stress of major life events, $r(60) = .51$, $p < .001$, and with alexithymia, $r(60) = .61$, $p < .001$. However, as expected from previous analyses, when depressive symptoms, alexithymia, and perceived stress of major life events were all included as predictors, only alexithymia and perceived stress of major life events offered unique prediction to QOL (Table 11).

Perceived Stress of Major Life Events as a Mediator of the Relationship between Depressive Symptoms and Disease-Specific QOL

We further explored how these three psychological variables might inter-relate in predicting disease-specific QOL. We considered the relationship between perceived stress of major life events and depressive symptoms and sought to determine whether the effect of depressive symptoms on disease-specific QOL may be mediated by perceived stress of major life events. Using the Cognitive Behavior Therapy model of the effect of mood on cognitions,

individuals with greater depressive symptoms may experience major life events as being more stressful. It would be the perceived stress of major life events rather than depressive symptoms per se that relate to disease-specific QOL. In statistical terms, we would expect bivariate relationships between each pair of the three variables, but in a multivariate analysis, only perceived stress of major life events would predict disease-specific QOL.

The relationship between depressive symptoms and disease-specific QOL was examined with perceived stress of major life events as the mediator. The bootstrapping method outlined above was repeated with depressive symptoms as the independent variable, perceived stress of major life events as the mediator, and disease-specific QOL as the dependent variable. Results suggested that perceived stress of major life events indirectly influenced the relationship between depressive symptoms and disease-specific QOL (Table 16). Follow-up regression analyses found that perceived stress of major life events only partially mediated the relationship between depressive symptoms and disease-specific QOL (Figure 4).

Depressive Symptoms as a Mediator of the Relationship between Alexithymia and Disease-Specific QOL

When considered together as predictors, alexithymia and depressive symptoms were independent predictors of disease-specific QOL, both adding

unique variance to the outcome (Table 17). Alexithymia is conceptualized as a personality trait that is independent of mood state (Marchesi et al., 2000). Given that alexithymia represents a relatively stable trait and that depressive symptoms are state-dependent, depressive symptoms should not influence the development of alexithymic tendencies. Conceptually, the effect of alexithymia could be mediated by depressive symptoms, but not vice versa. Consistent with this conceptualization, depressive symptoms did not fit criteria for a mediator of the relationship between alexithymia and disease-specific QOL. Specifically, when alexithymia and depressive symptoms were the only independent variables entered into multiple linear regression analysis predicting disease-specific QOL, both variables predicted unique variance in the outcome (Table 17).

Psychological Model for Predicting Disease-Specific QOL

As shown in Table 17, when depressive symptoms and perceived stress of major life events were entered as the only predictor variables in a multiple linear regression analysis, both significantly contributed unique variance to disease-specific QOL. However, the effect of the depressive symptoms on disease-specific QOL was reduced when controlling for perceived stress of major life events, implicating perceived stress of major life events as a partial mediator of the relationship between depressive symptoms and disease-specific QOL (see Figure 4).

Of note, when the third variable, alexithymia was added to depressive symptoms and perceived stress of major life events as predictors of disease-specific QOL, the depressive symptoms' contribution was no longer unique. When tested in pairs, there was non-overlapping variance in the prediction by depressive symptoms and each of the two other unique predictors tested (i.e., alexithymia and perceived stress of major life events). However, when all three were in the equation, the previously unique variance from depressive symptoms was absorbed by the other two variables. These findings suggest a relationship among alexithymia, perceived stress of major life events, and depressive symptoms consistent with Figure 5.

CHAPTER FIVE
Discussion

Overview

The goals of the present study were to examine alexithymia in adolescents with IBD and to evaluate this personality trait in relation to other psychological variables (i.e., depressive symptoms, perceived stress of major life events, perceived stress of daily hassles, and perceived recent stress) previously proposed in the pediatric IBD literature as potential risk factors for poor health outcomes. The current study also sought to determine if these psychological variables significantly predicted health outcomes (i.e., disease-specific QOL, illness course, and disease severity) in adolescents with IBD and whether alexithymia was the strongest predictor of these health outcomes. Our findings on alexithymia in adolescents with IBD paralleled adult IBD literature in two primary ways. First, alexithymia was significantly more prevalent (Porcelli et al., 1995) in our adolescent IBD sample relative to the healthy adolescent population (Honkalampi et al., 2009). Second, alexithymia was associated with greater emotional distress (Porcelli et al., 1996) and was significantly correlated with worse disease-specific QOL (Verissimo et al., 2000). Additionally, while depressive symptoms and perceived stress were also significantly related to disease-specific QOL,

alexithymia proved the strongest independent predictor of this subjective health outcome variable. Taken together, the present study supports alexithymia as an important risk factor in adolescents with IBD – one that negatively influences these patients' perceptions of their health and makes them vulnerable to impairments in physical, social, and emotional functioning.

Aim 1

The first aim of the present study was to investigate the prevalence of alexithymia in an adolescent IBD population. The current study reports, for the first time, a high prevalence of alexithymia in a sample of adolescents with IBD (21%) compared to a population of healthy adolescents (7.3%) reported by Honkalampi et al. (2009). This finding was consistent with previous research, which has documented significantly higher rates of alexithymia in adults with IBD (38%) compared to a healthy control group (4.5%) (Porcelli et al., 1999). It is important to note that, while higher than the rate reported in the healthy adolescent population (Honkalampi et al., 2009), the rate of alexithymia in our adolescent IBD sample was significantly lower than the reported rate in the adult IBD population (Porcelli et al., 1999). While this finding may be attributed to unknown demographic or illness-related differences between our adolescent IBD sample and the adult IBD population, it may also be interpreted as support for

using the TAS scale to measure adolescent alexithymia. In prior studies, one concern regarding the use of the TAS-20 with adolescents has been that it may over-identify alexithymia in this age group (Parker et al., 2010) because of adolescents' still-developing levels of emotional, cognitive, and social skills (Larsen, 2000; Saarni, 1999). This concern stems from previous research documenting higher scores on the TAS-20 in younger adolescents compared to older adolescents or adults (Parker et al., 2010; Säkkimen et al., 2007; Zimmerman et al., 2007). In contrast to these previous findings, the present study's results are inconsistent with the developmental concerns for measuring adolescent alexithymia using the TAS. Rather, the study supports continued empirical investigations of alexithymia in adolescent populations using this measure.

While we did not find that alexithymia was related to participants' age at baseline, we discovered some evidence to suggest a relationship between alexithymia, age at diagnosis, and illness duration. Specifically, when adolescents met the cutoff score for alexithymia, they were significantly older at the time of their IBD diagnosis and had been more recently diagnosed than those who did not meet criteria for alexithymia. These findings are similar to prior research that indicates those adolescents diagnosed with IBD at an older age are more at risk for emotional problems, such as greater depressive symptoms (Szigethy et al., 2004), compared to pediatric IBD patients diagnosed at a younger age. However,

in the current study, alexithymia was not significantly correlated with age at diagnosis or illness duration.

Developmental mechanisms might be hypothesized to explain the relationship between alexithymia and age at diagnosis; however, it should be noted that the current study did not examine such developmental pathways. One widely accepted conceptualization of alexithymia posits that the trait emerges from a disruption in one's emotional development (Krystal, 1978; Lemche et al., 2004). Emotional awareness becomes more sophisticated in adolescence with the development of advanced emotional processes (Saarni, 1999). Given that IBD is most commonly diagnosed between the ages of 15 and 25 (CCFA, 2010a), our study allowed for a better examination of the trait's occurrence nearer to disease onset than offered in adult IBD populations. From the results of our present study, we may begin to speculate that a diagnosis of IBD in adolescence may serve as a potential disruption to later stages of emotional development, thereby making adolescents with IBD more vulnerable to developing alexithymic tendencies. Again, these inferences remain speculative especially since they are based on correlational and cross-sectional analyses.

Aim 2

The second aim of the present study was to understand the relationship between alexithymia and other psychological variables. Alexithymia was found to significantly correlate with all of the psychological variables (i.e., depressive symptoms, perceived stress of major life events, perceived stress of daily hassles, and perceived recent stress).

Alexithymia and Depressive Symptoms

We found a significant positive correlation between alexithymia and depressive symptoms, such that individuals with higher alexithymia scores endorsed more depressive symptoms. Our findings are consistent with prior research documenting a strong relationship between alexithymia and depression in both normal and clinical adult populations (Di Schiena et al., 2011; Fukunishi et al., 1996; Marchesi et al., 2008). Despite the high correlation between these variables in our study and in other studies, prior research contends that alexithymia and depressive symptoms are two separate constructs (Bagby, Taylor, & Parker, 1986; Lipsanen et al., 2004; Luminet, 2010; Müller et al., 2003; Taylor et al., 1991).

Competing theories put forth to explain the overlap between alexithymia and depressive symptoms include the following: (1) alexithymia is a state reaction to stress ("secondary alexithymia") that is accompanied by depressive symptoms (Parker, Bagby, & Taylor, 1991); (2) alexithymia signifies a defensive coping

strategy for the purpose of mitigating painful affects or physiological arousal in patients with psychiatric and somatic illness (Marchesi et al., 2008); (3) alexithymia is a personality trait that predisposes people to depression and other mental health disorders (Kojima et al., 2007; Di Schiena et al., 2011); and (4) the alexithymia questionnaire, particularly its dimension assessing awareness of feelings, may be an alternate measure of depression (Parker et al., 1991). Future longitudinal research is needed to understand better the pathways between alexithymia and depression.

In general, the correlation between alexithymia and depressive symptoms observed in the present study (.61) was greater than previously reported in adolescent alexithymia research, with correlation coefficients ranging from .39 to .48, $p < .001$ (Di Schiena et al., 2011; Honkalampi et al., 2009). One exception is Bagby et al.'s (1986) study of alexithymia in a sample of undergraduate university students, in which the correlation between alexithymia and depressive symptoms, $r = 60$, $n = 81$, $p < .001$, was comparable to the present study's findings. While this variability in the research might be attributed to methodological or sample differences between studies, it may also been driven by the different mechanisms hypothesized to explain the relationship between alexithymia and depression. However, the present study's cross-sectional design prevented us from measuring potential mechanisms underlying the robust

correlation between alexithymia and depressive symptoms observed in our adolescent IBD sample.

Deficits in emotion-processing and emotion-regulation may make alexithymia a risk factor for medical and psychiatric disorders associated with affect dysregulation (Taylor et al., 1997; Waller & Scheidt, 2006), such as depression. A recent study discovered that youth with IBD demonstrated exaggerated initial pupil response to negative emotional stimuli relative to a healthy control group. This pupillary response style was not associated with depression, IBD inflammation, and steroid exposure (Jones et al., 2011). From these findings, the authors inferred that youth with IBD may encounter difficulties with regulating negative emotional information and managing stress, and these difficulties cannot be fully explained by depression or the effects of corticosteroids (Jones et al., 2011). Since the alexithymia construct is marked by similar deficits in emotional regulation, it could underlie this pupillary response finding in youth with IBD. Youth with IBD may be at risk for not only depression but also impairments in their abilities to emotionally process stressful information.

Alexithymia and Perceived Stress

Alexithymia was also correlated with all three measures of perceived stress, suggesting that alexithymia may be a reaction to stress, a state-dependent

phenomenon, or a trait that predisposes individuals to experience greater stress. Consistent with the secondary alexithymia hypothesis, those individuals with higher alexithymia tended to experience greater perceived stress along with greater depressive symptoms. Also in support of the secondary alexithymia explanation, perceived stress of major life events was significantly correlated with illness duration, such those that were diagnosed with IBD more recently were more likely to experience greater perceived stress of major life events and to meet criteria for alexithymia. However, the current study's cross-sectional design prevented us from ruling out whether these emotional symptoms resulted from their more recent diagnosis or their age at diagnosis.

How alexithymia manifests within an individual can help explain its relationship to perceived stress. To manage distress and cope with stressors effectively, individuals must be equipped with adequate emotional regulation skills. Horton et al. (1992) found that compared to matched controls, adolescents with alexithymia reported using less psychological, self-solacing coping strategies (e.g., memories) and preferred external (e.g., other people) or avoidant (e.g., watching TV) strategies. Alexithymia has also been associated with maladaptive and immature defense styles, such as avoidance and inhibition, in adults (Horton et al., 1992; Martin et al., 1986; Paez et al., 1995; Parker et al., 1998). These less sophisticated forms of coping may make it difficult for individuals with alexithymia to manage stressors adequately (Martin et al., 1986). Similar to the

coping style characteristic of individuals with alexithymia, adolescent IBD patients have a greater tendency to use avoidant coping styles (Calsbeek et al., 2006; Gitlin et al., 1991; van der Zaag-Loonen et al., 2004) and possess an external locus of control (Engström, 1991) compared to healthy adolescents. Since an external locus of control (Marty & de M'Uzan, 1963; Verissimo et al., 2000) and an avoidant coping style are key features of the alexithymia construct (Horton et al., 1992; Parker et al., 1998), alexithymia may contribute to deficient coping resources in some adolescents with IBD, making them more susceptible to stress.

Aim 3

The third aim of the current study was to elucidate the relationship between alexithymia and health outcomes. This study is the first to examine alexithymia as a potential predictor of health outcomes in adolescents with IBD. The health outcomes targeted in the study were illness course over a 12 month period, disease severity at baseline, and disease-specific QOL at baseline. Illness course and disease severity were objective indicators of IBD; disease-specific QOL, however, was a subjective health outcome because it reflected self-reported illness perceptions.

Objective Health Outcomes

Illness course did not correlate significantly with alexithymia, depressive symptoms, or measures of perceived stress (i.e., perceived stress of daily hassles, perceived recent stress, and perceived stress of major life events). Disease severity also did not correlate with alexithymia, depressive symptoms, perceived stress of daily hassles, or perceived recent stress. In contrast to previous research identifying alexithymia as a predictor of disease severity (Fukunishi et al., 1997) and treatment outcomes (Porcelli et al., 2003) in adult gastrointestinal illness populations, our study found no such relationship between alexithymia and objective health outcomes. Prior research also suggests a potential physiological link between depression and inflammation (Ghia et al., 2009); however, the present study found no evidence to support any such relationship between depressive symptoms and objective disease activity in an adolescent IBD sample.

Of all the correlations between objective health outcomes and psychological variables, the only significant relationship was between disease severity and perceived stress of major life events. Consistent with this finding, adult IBD research depicts an important association between perceived life stress and IBD (Kuroki et al., 2007; Langhorst et al., 2007; Levenstein et al., 2000; Maunder, 2000; Pellissier et al., 2010), with chronic psychosocial stress repeatedly observed as a risk factor for IBD (Reber, 2012; Schoultz, 2011). These observations are supported by animal models that demonstrate chronic and

psychosocial stressors as the type of stressors that result in the colitis-promoting effect of decreased glucocorticoid signaling (Reber, 2012). Although perceived stress of major life events did indeed relate to disease severity in the current study, we cannot assume a causal relationship because of our cross-sectional design.

Several possibilities may explain the lack of significant findings related to illness course and disease severity. First, our sample may represent an uncharacteristically healthy IBD population, whose disease is well-controlled. Our participants were all recruited from the same pediatric GI outpatient clinic and all received the same standard of care. Hence, we must be cautious when generalizing our results to the adolescent IBD population at large. A second possibility is that by only measuring a brief snapshot of these patients' disease activity, we failed to capture a true and comprehensive portrayal of their illness. Since IBD is characterized by a relapsing and remitting illness course, our measure of IBD disease severity may be a less accurate representation of these patients' illness courses over their lifetimes. Yet, even when we calculated the cumulative average of disease severity over the 12 months preceding baseline, we obtained the same results.

Subjective Health Outcomes

In contrast to the non-significant findings concerning the objective health outcome measures, the subjective health outcome measure of disease-specific QOL proved to be significantly related to all five psychological variables. Most notably, alexithymia emerged as having the strongest correlation with disease-specific QOL and was also the most robust independent predictor of disease-specific QOL, even after controlling for disease severity, illness course, and illness duration. Extending upon previous adult IBD research (Verissimo et al., 1998), our adolescent IBD participants who had higher alexithymia scores (i.e., demonstrated more symptoms of alexithymia) were more likely to report a poorer subjective experience of their disease. Although it accounted for less variance than the combination of depressive symptoms and the three perceived stress variables, alexithymia significantly increased the overall predictive power of our model. Alexithymia's unique predictive power was also evidenced by its primary ranking in the automatic stepwise regression.

The most parsimonious model for predicting disease-specific QOL in adolescents with IBD consisted of alexithymia and perceived stress of major life events. Perceived stress of major life events proved to be a significant predictor of disease-specific QOL, albeit slightly less powerful than alexithymia. Adult IBD research is inconclusive as to whether major life events or daily hassles more strongly influence health outcomes (Keefer et al., 2008; Mawdsley & Rampton, 2006). In the present study, we focused on perceived stress because of the recent

empirical emphasis on the subjective experience of stress as the common denominator between various types of stress and IBD (Cámera et al., 2009; Singh et al., 2009). The perceived stress of major life events questionnaire enabled us to compare the number of major life events to the perceived stress from these reported events. While both the number of negative life events and perceived stress of major life events were significantly correlated with disease-specific QOL, the correlation between perceived stress of major life events and disease-specific QOL was stronger (i.e., -.49 versus -.42). Unlike perceived stress of major life events, the number of negative life events was not significantly related to baseline disease severity or the cumulative average of disease severity. This finding makes a case for subjective experience of life stress as being a more important correlate of health outcomes in adolescents with IBD, compared to a frequency count of stressful events.

Theories explaining the association between stress, alexithymia, and illness perception are based upon the defining features of the alexithymia construct, specifically, deficits in emotional regulation and an externally oriented cognitive style (Paez et al., 1995). These traits result in a communication style marked by limited verbal expression of feeling states and fantasy, with increased focus on external experiences and bodily symptoms (Lundh et al., 2002). Theorists hypothesize that the combination of this communication style and poor emotional regulation skills causes individuals with alexithymia to report somatic

symptoms and to be at an increased risk for medical illness and psychiatric disorders (Taylor, 1984; Taylor et al., 1997). For instance, individuals with alexithymia may experience negative affect more intensely overall, but especially in response to and following stressors (Connelley & Denney, 2007). An exaggerated somatic response to environmental demands is characteristic of alexithymia and represents one possible mechanism connecting affect regulation deficits to ill health.

Secondary alexithymia has also been conceptualized as a response to the overall changes in QOL that commonly follow stressful events, such as onset of illness (Parker et al., 1991). For instance, investigations of alexithymia in patients with physical illness support this view, as alexithymic characteristics sometimes decline following recovery from acute illness (Haviland, MacMurray, & Cummings, 1988). Yet, in illnesses that remain chronically debilitating, such as IBD, secondary alexithymia may become permanent and indistinguishable from primary or trait alexithymia (Parker et al., 1991). In the context of our findings on alexithymia and disease-specific QOL, if adolescent IBD patients do not have adequate resources to communicate or manage emotional responses to stressors, they are more likely to respond negatively to the variable nature of IBD and to feel overwhelmed by their chronic illness.

Differences Between Objective and Subjective Health Outcomes

An important finding in the current study is the observed difference between objective health outcomes and subjective health outcomes. In general, psychological variables were not associated with objective health outcomes in adolescents with IBD, with the exception of the relationship between disease severity and perceived stress of major life events. Conversely, psychological variables consistently and significantly predicted subjective health outcomes. Our findings are similar to those of Burke et al. (1989), who found that emotional symptoms were related to adolescent IBD patients' subjective reports of greater disease severity, yet not to biological measures of disease. The present study expanded this knowledge by including the construct of alexithymia. Hence, in our present study, those participants with higher alexithymia scores perceived their IBD as worse and more disruptive, and these subjective reports did not necessarily match up with the objective or biological indicators of their disease.

One possible explanation for these findings may be that adolescent IBD patients who demonstrate alexithymic tendencies are less effective in regulating their emotional distress, and therefore, more prone to somatization (Ringel & Drossman, 1999; Taylor, 2000; Taylor et al., 1997) as well as poorer psychological functioning (Burke et al., 1989; Waller & Scheidt, 2006). In chronic illness populations in particular, the tendency to focus selectively on the somatic manifestations of emotional distress may make individuals with alexithymia more prone to seek medical treatment for physical complaints

associated with psychological changes. There is little consensus about the relationship between alexithymia and the decision to seek treatment in acute physical illness research (Kenyon, Ketterer, Gheorghiade, & Goldstein, 1991; Kirmayer & Robbins, 1993). Studies on alexithymia in chronic illness populations, by contrast, generally indicate that alexithymia is associated with illness behaviors, including increased symptom reporting and treatment seeking (Lumley, Stettner, et al., 1996). The symptom chronicity inherent in a diagnosis of IBD may cause a patient with alexithymia to attend to and potentially amplify responses to somatic sensations that accompany states of emotional arousal and other normal bodily reactions. Consequently, adolescent IBD patients with alexithymia may be vulnerable to developing distorted perceptions of their illness. In turn, these experiences of poor subjective health may lead to maladaptive illness behaviors, such as excessive clinic visits and hospitalizations, that can ultimately impact healthcare expenditures and paradoxically impact perceptions of health.

Exploratory Findings

Comprehensive Model

In our exploratory analyses, we sought to design a comprehensive, biopsychosocial model for predicting disease-specific QOL that combined both

psychological variables and objective disease markers as predictors. In these analyses, disease-specific QOL appeared driven primarily by psychological variables, specifically alexithymia and perceived of major life events, rather than by objective variation in disease. However, perceived stress of major life events was found to fully mediate the relationship between disease severity and disease-specific QOL. This finding depicts a pathway in which disease severity affected our sample of adolescent IBD patients' perception of life stress, and their perceived stress then shaped their subjective experience of their illness (i.e., disease-related QOL). Increased disease severity may influence disease-specific QOL in adolescents with IBD because of the nature of the disease (e.g., disruptive GI symptoms) and its related treatment (e.g., corticosteroids, surgery). Adolescents with IBD are also likely to experience increased emotional distress (i.e., perceived stress of major life events) due the disruptive and unpredictable nature of their disease, especially during symptom flare-ups (i.e., disease severity) when their disease is more likely to impair their daily functioning (i.e., QOL). It can be inferred from our findings that greater emotional distress then leads to further decline in their disease-specific QOL.

Similar to our mediational model, Gray et al. (2011) discovered that internalizing (i.e., anxiety and depressive) symptoms partially mediated the relationship between disease severity and health-related QOL in adolescents with IBD. Therefore, in addition to targeting disease severity, our findings suggest the

importance of targeting symptoms of emotional dysfunction in order to improve QOL in adolescents with IBD. However, all of our exploratory mediational analyses should be interpreted with caution, as they were based on cross-sectional data. Thus, they may not accurately reflect longitudinal mediational effects and cannot imply causality.

Psychological Model

Perceived stress of major life events also partially mediated the relationship between depressive symptoms and disease-specific QOL. This model fits with a cognitive-behavioral conceptualization of mood as it affects cognition. That is, greater symptoms of depression in adolescents with IBD appear to exacerbate their perception of stressful life events. This mediational relationship is important to consider when designing interventions aimed at improving adolescent IBD patients' QOL. While therapeutic interventions cannot change or prevent major life events from occurring, the Cognitive Behavioral model posits that individuals can modify their perception of stressful life events. In adolescents with IBD, learning techniques for cognitively reframing major life events may subsequently improve their perceptions of their illness. In keeping with this idea, Cognitive Behavioral interventions have shown positive results in reducing depressive symptoms, improving perceptions of health and physical

functioning, as well as enhancing resources for coping with pain and somatic symptoms (McCormick et al., 2010; Szigethy, 2005).

In line with prior research, alexithymia and depressive symptoms contributed significant non-overlapping variance of disease-specific QOL (Luminet, 2010); however, when perceived stress of major life events was added to the model containing alexithymia and depressive symptoms, depressive symptoms no longer uniquely contributed to the variance in disease-specific QOL. Given the significant correlation between depressive symptoms and alexithymia, it is likely that these two variables share a small amount of the variance in disease-specific QOL. The overlap between depressive symptoms and alexithymia may be attributed to an unidentified, underlying mechanism responsible for the association between these two psychological variables.

The different characteristics of alexithymia, depressive symptoms, and perceived stress of major life events may help to distinguish their roles in predicting disease-specific QOL. For instance, alexithymia exerted a direct influence on disease-specific QOL, while depressive symptoms and perceived stress of major life events indirectly affected this subjective health outcome. One difference between these psychological variables is their stability over time. Whereas depressive symptoms and perceived stress of major life events are considered state-dependent (Prenoveau et al., 2011), alexithymia is conceptualized as a stable construct that remains relatively unchanged despite

fluctuations in mood, stress, or disease activity (Honkalampi et al., 2000; Luminet et al., 2007). Although investigating the stability of alexithymia in an adolescent IBD population was beyond the scope of the current study, alexithymia's constancy as a trait would boost its value as a predictor variable and make it an important factor to consider when treating adolescents with IBD. Prior research suggests that individuals with alexithymia do not respond as well to traditional psychotherapeutic interventions compared to individuals without alexithymia (McCallum, Piper, Ogrodniczuk, & Joyce, 2003). By integrating this literature with the current study's findings, alexithymia may likely be a key factor to consider when developing novel interventions for adolescents with IBD.

Methodological Considerations

When interpreting the findings of the present study, several methodological considerations should be taken into account. First, although the number of participants was large enough for the majority of our analyses as indicated by the a priori power analysis, the statistical power of some of the analyses, particularly the mediational analysis, could be increased with a larger sample size. The mediational and multiple linear regression analysis were further limited by the cross-sectional design of our study. As such, we were only able to characterize relationships between objective health outcomes and psychological

factors and were restricted from measuring the trajectories of these relationships over time.

Our cross-sectional data on disease severity and illness course were almost entirely limited to retrospective medical chart reviews collected during routine clinic visits. Moreover, disease-specific QOL and psychological factors were obtained through subjective self-reports at one measurement time point only. Thus, method variance could potentially be confounding our results. Without longitudinal and prospective data, we are unable to examine the processes or mechanisms by which these health outcome trajectories occur.

Another important limitation in the current study is the absence of a well-validated adolescent alexithymia measure. In an effort to increase the validity and developmental appropriateness of our adolescent alexithymia measure, the present study used an adjusted alexithymia scale as recommended by prior researchers to account for possible age-related differences (Parker et al., 2010; Säkkinen et al., 2007). Since using an adjusted TAS-12 score to measure adolescent alexithymia represents a fairly recent recommendation (Parker et al., 2010; Säkkinen et al., 2007), the adjusted TAS-12 scale has limited research supporting its validity for use with adolescents, and its accuracy for detecting alexithymia has not been extensively investigated (Ciarrochi et al., 2008; Heaven et al., 2010). In support of the use of the measure, we found no evidence of age-related differences in

alexithymia scores between older and younger adolescents. Moreover, rates of alexithymia did not differ by IBD subtype, gender, or race.

The current study was also limited by the absence of a healthy age-matched control group. Since we did not have a control group, we used a population proportion taken from a previous study of alexithymia in a normal adolescent population (Honkalampi et al., 2009). One limitation related to the lack of a control group was generalizability. Specifically, the population proportion used for our prevalence comparisons was based on the prevalence of alexithymia in a normal adolescent sample in Finland (Honkalampi et al., 2009). Therefore, cultural differences between our current sample and the normal adolescent population may influence our findings. Additionally, our adolescent IBD sample was all recruited from a single site and generally appeared to have well-controlled IBD. Data was obtained almost exclusively at outpatient clinic visits. Therefore, our study may consist of a healthier adolescent IBD sample compared to those collected during inpatient hospitalizations. Multi-site studies that reflect more variability in IBD treatment and disease severity would expand the current findings and increase overall generalizability.

While our findings should be interpreted with these limitations in mind, the current study represents the first attempt to explore alexithymia and its relationship to health outcomes in adolescents with IBD. These initial findings

call for longitudinal and prospective investigations of alexithymia and its influence on health outcomes in adolescents with IBD.

Clinical Implications

Despite the limitations of the present study, several significant findings surfaced that may bear important implications for future research and clinical interventions. Consistent with prior pediatric IBD research, our findings indicate that adolescents with IBD appear particularly at risk for emotional difficulties and poor self-reported QOL. Most notably, our study is the first to report a significant prevalence of alexithymia in adolescents with IBD.

The alexithymia construct shows promise for deepening our knowledge of how and why some adolescents with IBD manifest socio-emotional problems while others emerge from adolescence unscathed. Adolescence, in general, signals a time of significant social-emotional change (Holmbeck & Shapera, 1999). Emotional awareness and identification, which fully evolve in adolescence, represent a precursor to emotional experience and social support (Ciarrochi et al., 2008); therefore, disruptions in normal emotional development may result in socio-emotional problems. Alexithymia is thought to arise from disruptions in emotional development; however, whether an IBD diagnosis is disruptive enough to result in affective deficits remains unknown.

Although alexithymia has been observed in a number of illness populations, including IBD, questions about its link to illness remain unanswered (Jula et al., 1999; Lumley, Stettner, et al., 1996; Zackheim, 2007). For instance, alexithymia may be a risk factor for developing chronic illness or the consequence of disease (Lumley, Stettner, et al., 1996). Continued investigations of alexithymia in pediatric IBD populations may allow for a better examination of the trait's emergence nearer to disease onset than that offered in adult IBD samples. These studies would also provide important information on the stability of alexithymia and changes in alexithymia secondary to stress. Prospective and longitudinal designs should be utilized in future projects to understand better the development of alexithymia in adolescent patients with IBD, its enduring pattern, and its potential effects on health outcomes (Porcelli et al., 1996; Searle & Bennett, 2001).

The combination of alexithymia and IBD may predispose adolescents to a lifelong illness course marked by poor QOL and psychosocial problems. In addition to identifying appropriate medical interventions, it is important to understand the developmental and psychosocial factors potentially influencing adolescent patients' responses to treatment (Greenley et al., 2010). Future research can further elucidate alexithymia's role in predicting disease-specific QOL in adolescents with IBD and facilitate the identification of critical periods of vulnerability for this pediatric illness population. From both prognostic and

therapeutic standpoints, the presence of the alexithymia trait in adolescents with IBD may determine the suitability, efficacy, and long-term responsiveness of interventions aimed at improving QOL in this pediatric population. From a developmental perspective, understanding alexithymia in adolescents with IBD can inform interventions to promote illness adjustment and ensure a smoother transition into adulthood.

APPENDIX A
Figures

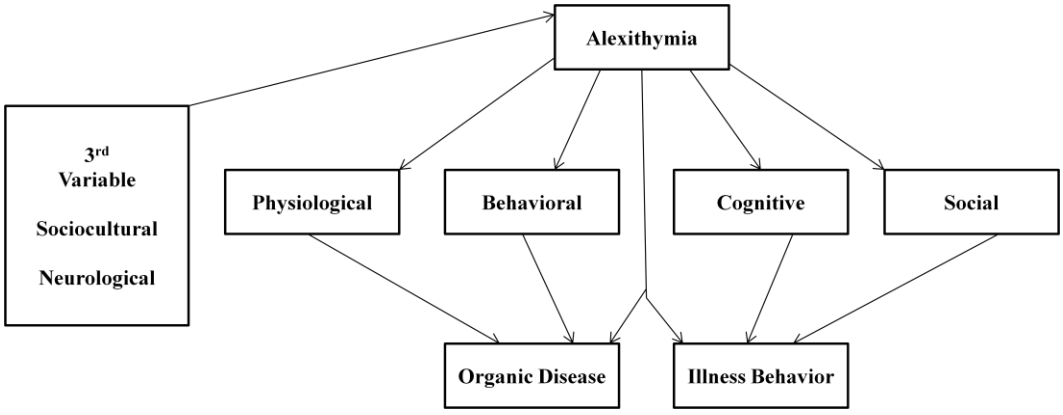

Figure 1. Overview of various pathways linking alexithymia and physical illness. The absence of arrows between parts of the model (e.g., from Organic Disease to Illness Behavior) does not imply a lack of relationship. Adapted from "How Are Alexithymia and Physical Illness Linked? A Review and Critique of Pathways," by M. A. Lumley, L. Stettner, and F. Wehmer, 1996, *Journal of Psychosomatic Research, 41*(6), p. 506.

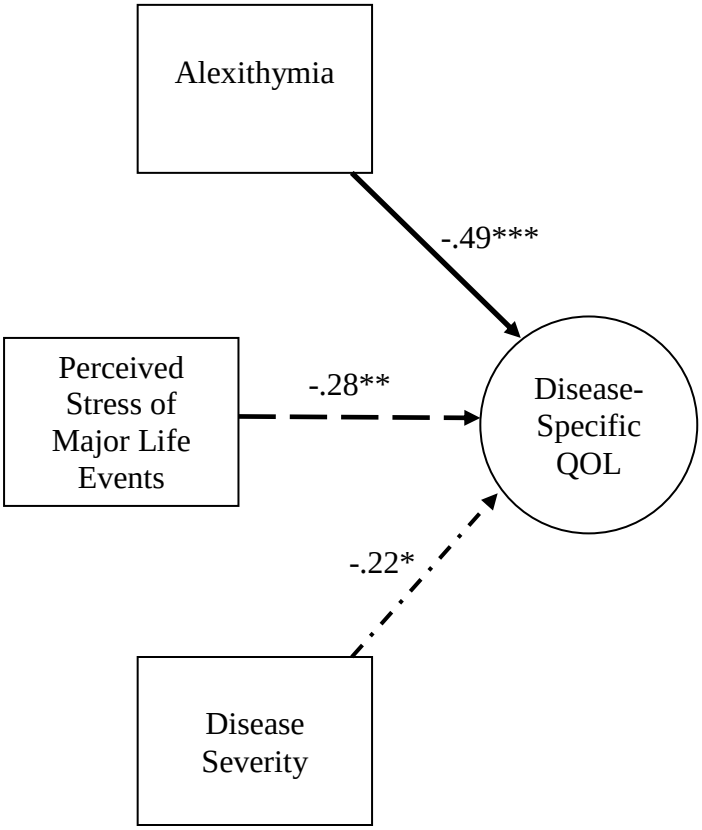

Figure 2. The comprehensive model for predicting disease-specific QOL with standard regression coefficients for alexithymia, perceived stress of major life events, and disease severity.
* $p < .05$. ** $p < .01$. *** $p < .001$.

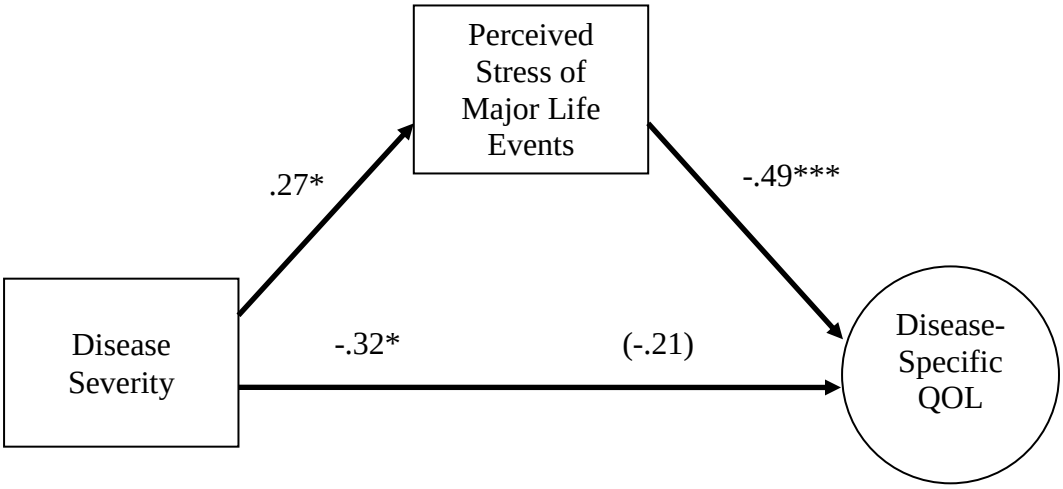

Figure 3. Standard regression coefficients for the relationship between disease severity and disease-specific QOL as mediated by perceived stress of major life events. The standard regression coefficient between disease severity and disease-specific QOL controlling for perceived stress of major life events is in parentheses.
* $p < .05$. *** $p < .001$.

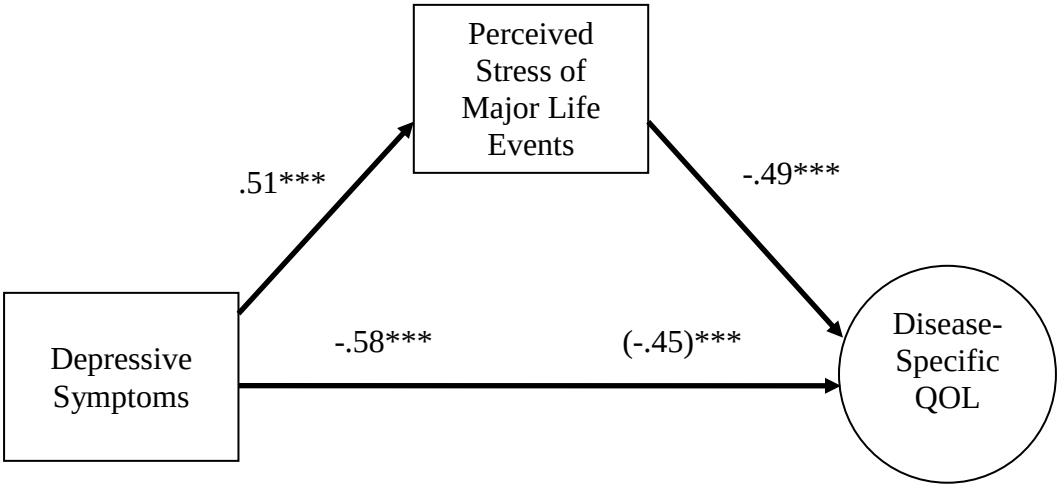

Figure 4. Standard regression coefficients for the relationship between depressive symptoms and disease-specific QOL as mediated by perceived stress of major life events. The standard regression coefficient between depressive symptoms and disease-specific QOL controlling for perceived stress of major life events is in parentheses.
*** $p < .001$.

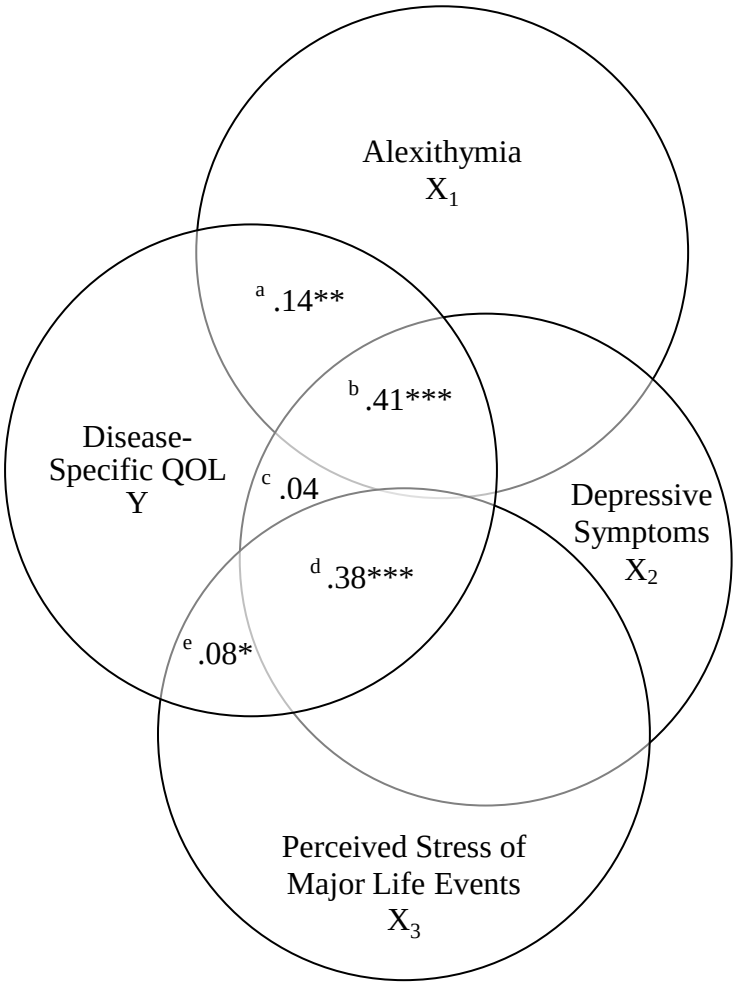

Figure 5. Venn diagram of the psychological model. Y = disease-specific QOL; X_1 = alexithymia; X_2 = depressive symptoms; X_3 = perceived stress of major life events. The variance overlap for the psychological model is as follows: (a) proportion of Y uniquely predicted by X_1; (b) proportion of the variance in Y accounted for by X_1 and X_2; (c) proportion of Y uniquely predicted by X_2; (d) proportion of the variance in Y accounted for by X_2 and X_3; and (e) proportion of Y uniquely predicted by X_3.
*$p < .05$. ** $p < .01$. *** $p < .001$.

APPENDIX B
Result Tables

Table 1

Descriptive Demographic Data With Summary Statistics for Independent t and χ^2 Tests by IBD Subtype

	Total	CD	UC		
Variable	*M* (*SD*) or *N* (%)	*M* (*SD*) or *n* (%)	*M* (*SD*) or *n* (%)	*t*, df	χ^2, df
Age at Baseline	15.62 (1.34)	15.50 (1.44)	15.84 (1.12)	-0.97, 61	
Grade Level in School	9.78 (1.62)	9.54 (1.70)	10.23 (1.38)	-1.63, 61	
Gender (%)					.36, 1
Female	29 (46.03)	20 (48.78)	9 (40.90)		
Male	34 (53.97)	21 (51.22)	13 (59.09)		
Race (%)					1.37, 3
African American	13 (20.63)	7 (17.07)	6 (27.27)		
Asian	3 (4.76)	2 (4.88)	1 (4.55)		
Caucasian	46 (73.02)	31 (75.60)	15 (68.18)		
Mixed Race	1 (1.59)	1 (2.44)	0 (0)		
Ethnicity (%)					.01, 1
Hispanic/Latino	11 (17.46)	7 (17.07)	4 (18.18)		
Not Hispanic/Latino	52 (82.54)	34 (82.93)	18 (81.81)		

Note. None of the results reported in this table were significant. For total $N = 63$, CD $n = 41$, and UC $n = 22$.

Table 2
Descriptive IBD-Specific Medical Data With Summary Statistics for Independent t and χ^2 Tests by IBD Subtype

Variable	Total	CD	UC		
	M (*SD*) or *N* (%)	*M* (*SD*) or *n* (%)	*M* (*SD*) or *n* (%)	*t*, df	χ^2, df
Age at Diagnosis	12.85 (2.45)	12.32 (2.51)	13.83 (2.04)	2.41, 61*	
Illness Duration (in mos)	33.21 (27.57)	38.07 (28.71)	24.15 (23.20)	1.95, 61†	
Colectomy %	6 (9.52)	5 (12.20)	1 (4.55)		.97,1
Med. Increases in last 12 mos	2.79 (2.95)	2.73 (2.89)	2.91 (3.23)	0.23, 61	
Steroid Exposure (in mos)	1.42 (2.37)	0.99 (1.76)	2.23 (3.10)	1.73, 28.41†	
Outpt. Visits in last 12 mos	3.84 (2.55)	3.68 (2.70)	4.14 (2.30)	0.67, 61	
Hospital Adm. in last 12 mos	.78 (1.13)	0.88 (1.25)	0.59 (0.85)	.96, 61	

Note. For total $N = 63$, CD $n = 41$, and UC, $n = 22$.
* $p < .05$. † $p < .10$.

Table 3
Variables of Interest With Summary Statistics for Independent t tests by IBD Subtype

Measure	CD	UC	
	M (*SD*)	*M* (*SD*)	*t*, *df*
Alexithymia	27.29 (9.56)	28.68 (11.09)	-0.52, 61
Perceived Stress Score of Major Life Events	0.62 (0.46)	0.65 (0.39)	-0.28, 61
Perceived Stress of Daily Hassles	1.32 (0.48)	1.28 (0.59)	0.18, 61
Perceived Recent Stress	47.24 (28.89)	52.864 (27.26)	-0.75, 61
Depressive Symptoms +	50.43 (13.21)	50.50 (12.61)	-0.02, 60
Disease-Specific QOL	137.05 (20.71)	129.32 (24.50)	1.32, 61
Illness Course	0.75 (0.40)	0.84 (0.39)	-0.82, 61
Disease Severity	0.74 (0.58)	0.59 (0.63)	1.00, 61

Note. None of the reported results in this table were significant. For total $N = 63$, CD $n = 41$, and UC $n = 22$. For those otherwise noted, + Total $N = 62$, CD $n = 40$, and UC $n = 22$.

Table 4
Psychological Variables

Variable	Instrument Used	Cutoff Score	Normative *M* (*SD*)	Sample *M* (*SD*)	Sample Range
Total Alexithymia Score	Toronto Alexithymia Scale (TAS-20)[a]	$\geq$ 61 = high alexithymia[a]	46.65 (9.25)[f]	49.62 (11.44)	29 – 87
Alexithymia	Abbreviated Toronto Alexithymia Scale (TAS-12)[b]	$\geq$ 37 = high alexithymia	31.50 (8.64)[g]	27.78 (10.05)	12 – 55
Perceived Stress of Major Life Events	Life Events Checklist (LEC)[c]		13.7 (9.6)[h]	5.78 (6.58)	0 – 29
Perceived Stress of Daily Hassles	Adolescent Minor Stress Inventory (AMSI)[d]		85.3 (51.89)[i]	33.10 (37.89)	0 – 188
Perceived Recent Stress	Recent Stress Question (RSQ)	0 = no stress 100 = extremely stressed		49.21 (28.24)	0 – 100
Depressive Symptoms	Children's Depressive Index-2 (CDI-2)[e]	$\geq$ 65 = elevated[b]	53.59 (13.58)[e]	50.45 (12.74)	3 – 90

Note. In the above table, non-transformed means and standard deviations were reported for perceived stress of major life events and perceived stress of daily hassles for the purpose of making comparisons with the normative population. For the transformed variables, perceived stress of major had $M = 0.63$, $SD = 0.43$, and perceived stress of daily hassles had $M = 1.30$, $SD = 0.50$. [d]Ames et al., 2005; [a]Bagby, Parker, et al., 1994; [h]Brand & Johnson, 1982; [b]Heaven et al., 2010; [f]Honkalampi et al., 2009; [c]Johnson & McCutcheon, 1980; [e]Kovacs, 2010; [g]Parker et al., 2010; [i]Salafia & Lemer, 2012.

Table 5
Health Outcome Measures

Variable	Instrument Used	Definition of Variable	Normative *M* (*SD*)	Sample *M* (*SD*)	Sample Range
Disease-Specific QOL	IMPACT-III[a]		153 (32.33)[a]	134.35 (22.22)	69 – 174
Illness Course	Retrospective Illness Course Review	Cumulative measure of prior12 months: # outpatient clinic visits + # hospital admissions + steroid exposure in months + # IBD medication increases		8.84 (7.56)	1 – 33.79
Disease Severity	Baseline Pediatric Crohn's Disease Activity Index (PCDAI)[b] Baseline Pediatric Ulcerative Colitis Activity Index (PUCAI)[c]	Inactive: <10 Mild: 10-27.5 (PCDAI); 10- 34 (PUCAI) Moderate: 30-37.5 (PCDAI) 25-64 (PUCAI) Severe: 40-100 (PCDAI); 65-85 (PUCAI)		9.72 (12.58)	0 – 65

Note. In the above table, non-transformed means and standard deviations were reported for disease severity and illness course. For the transformed variables, disease severity had $M = 0.69$, $SD = 0.60$, and illness course had $M = 0.79$, $SD = 0.39$. [b]Hyams et al., 1991; [a]Otley et al., 2002; [c]Turner et al., 2007.

Table 6
ANOVA Analysis of Alexithymia by Age

Score	*13yo* *M* (*SD*)	*14yo* *M* (*SD*)	*15yo* *M* (*SD*)	*16yo* *M* (*SD*)	*17yo* *M* (*SD*)	*F*	η^2
Total TAS-20 Score	51.50 (13.31)	49.54 (15.31)	47.50 (8.31)	51.59 (9.94)	48.00 (11.81)	0.34	0.02
Adjusted TAS-12 Score	29.13 (11.58)	26.69 (12.00)	27.50 (8.85)	29.12 (9.89)	26.36 (9.66)	0.20	0.01
DIF Subscale	16.63 (7.07)	14.15 (6.85)	13.93 (5.85)	15.06 (6.28)	14.00 (4.73)	0.32	0.02
DDF Subscale	12.50 (5.43)	12.54 (6.02)	13.57 (3.61)	14.06 (4.47)	12.36 (5.61)	0.32	0.02
EOT Subscale	22.38 (4.31)	22.85 (4.54)	20.00 (4.62)	22.47 (3.78)	21.64 (3.91)	0.98	0.06

Note. None of the reported results in this table were significant. For 13 yo, $n = 8$. For 14 yo, $n = 13$. For 15 yo, $n = 14$. For 16 yo, $n = 17$. For 17 yo, $n = 11$.

Table 7
Correlations Between Alexithymia and Psychological Variables

Variable	Alexithymia
Perceived Stress of Major Life Events	.31**
Perceived Stress of Daily Hassles	.36**
Perceived Recent Stress	.52***
Depressive Symptoms +	.61***

Note. All of the variables included $N = 63$ with the exception of those otherwise noted. + $N = 62$
** $p < .01$. ***$p < .001$.

Table 8
Correlations Between Psychological Variables and Health Outcome Measures

Variable	Illness Course	Disease Severity	Disease-Specific QOL
Alexithymia	.004	.06	-.59***
Perceived Stress of Major Life Events	.05	.27*	-.49***
Perceived Stress of Daily Hassles	.09	.17	-.47***
Perceived Recent Stress	.10	.13	-.50***
Depressive Symptoms +	.001	.14	-.58***

Note. All of the variables included $N = 63$ with the exception of those otherwise noted. + $N = 62$.
* $p < .05$. *** $p < .001$.

Table 9

Multiple Linear Regression Analysis for Variables Predicting Disease-Specific QOL (N = 62)

	Disease-Specific QOL		
Variable	*B*	*SE B*	*β*
Alexithymia	-0.71	0.28	-.32*
Perceived Stress of Major Life Events	-10.53	6.19	-.20†
Perceived Stress of Daily Hassles	-4.49	5.72	-.10
Perceived Recent Stress	-0.09	0.10	-.12
Depressive Symptoms	-0.31	0.24	-.18
R^2 = .49			
$F(5, 56) = 10.60$***			

* $p < .05$. *** $p < .001$. † $p < .10$.

Table 10

Hierarchical Linear Regression Analysis Predicting Disease-Specific QOL (N = 62)

Variable	Disease-Specific QOL		
	B	*SE B*	*β*
Step 1			
Perceived Stress of Major Life Events	-9.61	6.45	-.19
Perceived Stress of Daily Hassles	-4.39	5.98	-.10
Perceived Recent Stress	-0.16	0.11	-.20
Depressive Symptoms	-0.60	0.22	-.34**
R^2 =.43			
$F(4, 57) = 10.69$***			
Step 2			
Alexithymia	-0.70	0.28	-.32*
$\Delta R^2 = .06$			
$F(5, 56) = 10.60$***			

* $p < .05$. ** $p < .01$. *** $p < .001$.

Table 11

Automatic Stepwise Regression Analysis for Disease-Specific QOL (N = 62)

Variable	Disease-Specific QOL		
	B	*SE B*	*β*
Step 1			
Alexithymia	-1.29	0.23	-.58***
R^2 = .34			
$F(1, 60) = 30.25$***			
Step 2			
Alexithymia	-1.07	0.23	-.48***
Perceived Stress of Major Life Events	-17.41	5.28	-.34**
ΔR^2 = .10			
$F(2, 59) = 23.60$***			

** $p < .01$. *** $p < .001$.

Table 12

Summary of Five Separate Linear Regression Analyses for Predicting Disease-Specific QOL While Controlling for Illness Course and Disease Severity

	Disease-Specific QOL		
Variable	ΔR^2	$F(3, 59)$	β
Alexithymia	.32	15.80***	-.57***
Perceived Stress of Major Life Events	.17	8.13***	-.43***
Perceived Stress of Daily Hassles	.17	8.02***	-.41***
Perceived Recent Stress	.20	9.48***	-.46***
Depressive Symptoms +	.30	13.86***	-.55***

Note. All of the separate linear analyses included $N = 63$ with the exception of those otherwise noted. + $N = 62$. The ΔR^2 in the table above is the additional R^2 after accounting for the control variables (i.e., illness course and disease severity). Illness course and disease severity were entered into the first step, $R^2 = .12$, $F(2, 60) = 4.17$, $p = .02$. For illness course, $\beta = -.14$, $p = .25$. For disease severity, $\beta = -.30$, $p = .02$.

*** $p < .001$.

Table 13

Hierarchical Linear Regression Analysis for Psychological Variables Predicting Disease-Specific QOL While Controlling for Illness Course and Disease Severity (N = 62)

	Disease-Specific QOL		
Variable	*B*	*SE B*	*β*
Step 1			
Illness Course	-9.79	7.23	-.17
Disease Severity	-10.47	4.63	-.28*
R^2 =.12			
$F(2, 59) = 4.12$*			
Step 2			
Illness Course	-7.43	5.56	-.13
Disease Severity	-7.13	3.61	-.19†
Alexithymia	-0.74	0.27	-.33**
Perceived Stress of Major Life Events	-7.75	6.05	-.15
Perceived Stress of Daily Hassles	-3.96	5.50	-.09
Perceived Recent Stress	-0.07	0.10	-.09
Depressive Symptoms	-0.33	0.23	-.19
ΔR^2 =.42			
$F(7, 54) = 9.16$***			

* $p < .05$. ** $p < .01$. *** $p < .001$. † $p < .10$.

Table 14

Automatic Stepwise Linear Regression Analysis for Psychological Variables Predicting Disease-Specific QOL While Controlling for Illness Course and Disease Severity (N =62)

	Disease-Specific QOL		
Variable	*B*	*SE B*	*β*
Step 1			
Illness Course	-9.79	7.23	-.17
Disease Severity	-10.47	4.63	-.28*
R^2 =.12			
$F(2, 59) = 4.12$*			
Step 2			
Alexithymia	-1.25	.22	-.56***
ΔR^2 =.32			
$F(3, 58) = 15.12$***			
Step 3			
Perceived Stress of Major Life Events	-14.08	5.23	-.27**
ΔR^2 =.06			
$F(4, 57) = 14.38$***			

Note. The ΔR^2 in the table above is the additional R^2 after accounting for the control variables (i.e., illness course and disease severity).

* $p < .05$. ** $p < .01$. *** $p < .001$.

Table 15

Bootstrap Analysis for Perceived Stress of Major Life Events as a Mediator for the Relationship Between Disease Severity and Disease-Specific QOL (N = 62)

Independent Variables	Mediating Variable	Dependent Variable	Effect of IV on M	Effect of M on DV	Direct Effect of IV on DV	Total Effects	Indirect Effect IV on DV through M
(IV)	(M)	(DV)	(a)	(b)	(c′)	(c)	95% CI†
Disease Severity	Perceived Stress MLE	Disease-Specific QOL	.19*	-22.17 ***	-7.62	-11.91**	-10.21 to -.46

Note. Perceived Stress MLE = perceived stress of major life events. Unstandardized regression coefficients (*B)* are presented above.

†Mediation is concluded if the confidence interval (CI) does not cross zero [Bootstrap samples = 5000].

*p<.05. ** p<.01. *** p < .001.

Table 16

Bootstrap Analysis for Perceived Stress of Major Life Events as a Mediator for the Relationship Between Depressive Symptoms and Disease-Specific QOL (N = 62)

Independent Variables	Mediating Variable	Dependent Variable	Effect of IV on M	Effect of M on DV	Direct Effect of IV on DV	Total Effects	Indirect Effect IV on DV through M
(IV)	(M)	(DV)	(a)	(b)	(c′)	(c)	95% CI†
Depressive Symptoms	Perceived Stress MLE	Disease-Specific QOL	.02***	-12.94*	-.79***	-1.01***	-.55 to -.02

Note. Perceived Stress MLE = perceived stress of major life events. Unstandardized regression coefficients (*B)* are presented above.

†Mediation is concluded if the confidence interval (CI) does not cross zero [Bootstrap samples = 5000].

*p<.05. *** p < .001.

Table 17

Follow-up Regression Analyses for Psychological Variables Predicting Disease-Specific QOL (N = 62)

	Disease-Specific QOL		
Variable	*B*	*SE B*	*β*
Block 1			
Depressive Symptoms	-0.79	0.21	-.45*
Perceived Stress of Major Life Events	-12.94	6.16	-.25***
R^2 =.38			
$F(2, 59) = 17.95$***			
Block 2			
Depressive Symptoms	-0.81	0.28	-.36**
Alexithymia	-0.62	0.22	-.35**
R^2 =.41			
$F(2, 59) = 20.81$***			
Block 3			
Depressive Symptoms	-13.36	5.77	-.26
Perceived Stress of Major Life Events	-0.38	0.24	-.22*
Alexithymia	-0.82	0.27	-.37**
R^2 =.46			
$F(3, 58) = 16.69$***			

Note. Each block represents a separate multiple linear regression analysis.

* $p < .05$. ** $p < .01$. *** $p < .001$.

APPENDIX C
Common Medications for Pediatric IBD

Primary Induction Drugs

Pediatric Ulcerative Colitis

	Mild Disease	***Moderate Disease***	***Severe Disease***
Drug Class	**Aminosalicylates**	**Corticosteroids**	**Immunomodulators**
	Sulfasalazine	Prednisone	Cyclosporine A
	Mesalamine	Methylprednisolone	Tacrolimus
	Olsalzine	Hydrocortisone	Methotrxate
	Balsalzide	Budesonide	

Pediatric Crohn's Disease

	Mild Disease	***Moderate Disease***	***Corticosteroid-resistant or Fistualizing Disease***
Drug Class	**Aminosalicylates**	**Corticosteroids**	**Biologic Therapy**
	Sulfasalazine	Prednisone	Infliximab
	Mesalamine	Methylprednisolone	Cimzia pegol
	Olsalzine	Hydrocortisone	Adalimumab
	Balsalzide	Budesonide	

Drug Class	**Antibiotics**	**Nutritional Therapies**
	Metronidazole	Enteral Nutrition
	Ciprofloxacin	Gastrostomy Tube
		Total Parenteral Butrition

Maintenance Therapies

Pediatric Ulcerative Colitis

Drug Class	**Aminosalicylates**	**Immunomodulators**
	(see above)	*(see above)*
		Azathioprine and 6-mercaptopurine

Pediatric Crohn's Disease

Drug Class	**Aminosalicylates**	**Immunomodulators**	**Biologic Therapies**
	(see above)	(*see above)*	*(see above)*
		Azathioprine and 6-mercaptopurine	

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