Treatment Adherence in Adolescents With Inflammatory Bowel Disease: The Collective Impact of Barriers to Adherence and Anxiety/Depressive Symptoms

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Objective Knowledge of factors impacting adolescents’ ability to adhere to their inflammatory bowel disease (IBD) regimen is limited. The current study examines the collective impact of barriers to adherence and anxiety/depressive symptoms on adolescent adherence to the IBD regimen. Methods Adolescents (n = 79) completed measures of barriers to adherence, adherence, and anxiety/depressive symptoms at one of two specialty pediatric IBD clinics. Results Most adolescents reported barriers to adherence and 1 in 8 reported borderline or clinically elevated levels of anxiety/depressive symptoms. Anxiety/depressive symptoms moderated the relationship between barriers to adherence and adherence. Post hoc probing revealed a significant, additive effect of higher anxiety/depressive symptoms in the barriers–adherence relationship, with adherence significantly lower among adolescents with higher barriers and higher anxiety/depressive symptoms. Conclusions In order to optimize adherence in adolescents, interventions should target not only barriers to adherence but also any anxiety/depressive symptoms that may negatively impact efforts to adhere to recommended treatment.

Key words adherence; adolescent; anxiety; barriers; depression.

Introduction

Crohn’s disease and ulcerative colitis (collectively known as inflammatory bowel disease [IBD]) are chronic conditions characterized by gastrointestinal inflammation and unpredictable periods of disease activity and remission (Dubinsky, 2008). Occurring at an incidence rate of 71 cases per 100,000 in youth below 17 years of age, common symptoms of IBD include abdominal pain, diarrhea, delayed growth/puberty, and weight loss (Auvin et al., 2005). Management of IBD symptoms may involve a complex, potentially burdensome, treatment regimen consisting of multiple medication doses per day, dietary modifications, and in some cases, surgery (Kappelman et al., 2007). Although dietary modifications are individually tailored, youth may be asked to abstain from foods that commonly cause gastrointestinal discomfort such high fiber...
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ship between increased barriers to adherence and de-
social demands all have the potential to negatively impact
from parent to adolescent, and increased academic and
independence, the transition of treatment responsibility
mental factors such as adolescents’ increased
ating course. These challenges, combined with develop-
absence of IBD symptoms due to its unpredictable, fluctu-
undesirable social implications or when they occur in the
also impact adherence, particularly when those side-effects
commonly reported barrier (Greenley et al., 2010), may
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treatment, and the developmental period of adolescence
further exacerbates disease activity. Research among
play a role in the development of IBD (for a review, see Micocka-Walus et
behavioral symptoms (Mackner, Sisson, & Crandall, 2004). They have a 4.6 times greater
odds of having clinically significant symptoms of anxiety/
depression than healthy peers (Mackner & Crandall, 2006)
and 20% of youth report clinically elevated emotional and
behavioral symptoms (Mackner & Crandall, 2005a). On
the Children’s Depression Inventory, 18.5–24.5% of
youth exceed the clinical cut-off for depression (Hommel,
Davis, et al., 2008; Szegethy et al., 2004).

The lack of prospective, well-controlled research has
led to significant controversy regarding the interplay be-
tween anxiety/depressive symptoms and the onset and
clinical course of IBD (for a review, see Micocka-Walus et al., 2007). There is no evidence that emotional problems
play a role in the development of IBD, but they have
been observed as an associated outcome of the disease
that further exacerbates disease activity. Research among
other pediatric populations suggests that illness-associated
physical, academic and social impairments, and feelings of
helplessness, dependency, and self-consciousness, com-
bined with difficulties managing demanding lifelong
treatment regimens may play a role in the development
of adjustment problems (Bennett, 1994). Moreover,
IBD-specific factors such as difficulties coping with the
unpredictable waxing and waning course of IBD symptoms
and medication-related side-effects may also contribute to
psycho-emotional vulnerability. Collectively, these symp-
toms may have direct implications for youth’s ability to
adhere to their treatment regimen.

Characteristics unique to the clinical course of IBD, its
treatment, and the developmental period of adolescence
are likely to increase the challenge of being adherent.
Many adolescents struggle with managing a complex oral
medication regimen and dietary modifications and cite the
time consuming nature of IBD treatment as a major barrier
to adherence (Greenley, Stephens, Doughty, Raboin, &
Kugathasan, 2010; Ingerski, Baldassano, Denson, &
Hommel, 2010). Medication-related side effects, another
commonly reported barrier (Greenley et al., 2010), may
also impact adherence, particularly when those side-effects
(e.g., weight gain, facial swelling, emotional lability) have
undesirable social implications or when they occur in the
absence of IBD symptoms due to its unpredictable, fluctu-
ating course. These challenges, combined with develop-
mental factors such as adolescents’ increased
independence, the transition of treatment responsibility
from parent to adolescent, and increased academic and
social demands all have the potential to negatively impact
adherence in adolescents with IBD. Indeed, the relation-
ship between increased barriers to adherence and de-
creased adherence has been well-documented in other
pediatric populations (Logan, Zelikovsky, Labay, &
Spergel, 2003; Modi & Quitter, 2006; Simons,
McCormick, Devine, & Blount, 2010; Zelikovsky, Schast,
Palmer, & Meyers, 2008) as well as among adolescents
with IBD (Greenley et al., 2010; Ingerski et al., 2010).

In addition to having problems with treatment adher-
ence, adolescents with IBD are also at an increased risk for
problems in emotional functioning (Mackner & Crandall,
2006; Mackner, Crandall, & Szegethy, 2006; Mackner,
Sisson, & Crandall, 2004). They have a 4.6 times greater
odds of having clinically significant symptoms of anxiety/
depression than healthy peers (Mackner & Crandall, 2006)
and 20% of youth report clinically elevated emotional and
behavioral symptoms (Mackner & Crandall, 2005a). On
the Children’s Depression Inventory, 18.5–24.5% of
youth exceed the clinical cut-off for depression (Hommel,
Davis, et al., 2008; Szegethy et al., 2004).

Although a link between nonadherence and health
outcome has not been firmly established in adolescents
with IBD, research from the adult literature suggests that
consequences of nonadherence to the IBD regimen can be
severe. Adults who are nonadherent are up to 5.5 times
more likely to experience a relapse in symptoms (Kane,
Huo, Aikens, & Hanauer, 2003) and generate 12.5% great-
er annual health care costs than adherent patients (Higgins,
Rubin, Kaulback, Schoenfeld, & Kane, 2009). Considering
these consequences, and that many lifelong positive and
negative health management behaviors become established
during adolescence (Holmbeck, 2002a), understanding fac-
tors which impact adolescents’ ability to adhere to their
IBD regimen can play a critical role in the design of inter-
ventions to improve lifelong IBD management.

Research from other pediatric illness populations,
such as asthma, HIV, and diabetes (Bender, 2006;
Gonzalez et al., 2008; Murphy et al., 2005; Williams et
al., 2006), suggests a link between poorer adolescent emo-
tional functioning and suboptimal adherence. However,
the relationship between emotional functioning and adher-
ence has not been thoroughly examined in pediatric IBD.
In the one known study that examined this relationship,
emotional functioning (as measured by the Total Problems
score on the Child Behavior Checklist) approached, but did
not reach, a significant association with self-reported ad-
herence in a sample of 50 adolescents with IBD (Mackner
& Crandall, 2005b). The unestablished link between emo-
tional functioning and adherence in IBD may be due to
The current study moves the IBD literature forward by examining the relationship between barriers to adherence, anxiety/depressive symptoms, and adherence in a multi-site sample of adolescents with IBD. Anxiety/depressive symptoms were hypothesized to moderate the relationship between barriers to adherence and medication adherence such that the relationship between these two variables would be strongest among youth with greater anxiety/depressive symptoms.

Methods

Participants and Procedures

The current study is a part of a larger two-site project examining treatment adherence and health outcome in adolescents with IBD. Institutional review board approval was obtained at each study site. Participants were 79 adolescents (ages 13–17 years) receiving treatment for either Crohn’s disease or ulcerative colitis at one of two hospital-based specialty IBD clinics located in the Midwest (n = 34) and Northeastern (n = 45) United States, and their accompanying legal guardian. Study eligibility included: (a) adolescent between ages of 13 and 17 years, (b) diagnosis of IBD, and (c) current prescription of oral 5-aminosalicylic acid (5-ASA) and/or 6-mercaptopurine (6-MP)/azathioprine medication (the two most commonly prescribed medications in pediatric IBD). Presence of a neurocognitive disorder (e.g., mental retardation, autism), other chronic illness, limited English literacy, or corticosteroid treatment prescribed at greater than 1 mg/kg/day precluded study participation. This latter criterion was established due to higher risk of treatment-associated behavioral and psychiatric side-effects (Kayani & Shannon, 2002; Soliday, Grey, & Lande, 1999).

Eligible participants were recruited by a member of the research team while in private patient rooms during a regularly scheduled medical appointment or via telephone following their appointment. Consent and assent were obtained prior to data collection and each family was compensated $25 for completion of the study measures. With the exception of the adherence interview, all measures were paper-based and independently completed by the adolescent or their parent. Of 109 adolescent–parent pairs approached by study personnel, 21 declined study participation, citing either lack of time, lack of interest, or not wanting a blood draw for disease severity assessment as primary reasons for refusal. Participants with incomplete behavioral data (n = 9) were excluded from the study, resulting in a final sample of 79.

Measures

Demographic Questionnaire

Parents completed a brief questionnaire designed for this study to obtain information regarding family annual income, caregiver marital status, and child age, race, and gender.

Child Behavior Checklist Youth Self-Report

Adolescents completed the Youth Self-Report (YSR) version of the Child Behavior Checklist (Achenbach, 1988). This well-validated measure assesses behavioral and emotional functioning in adolescents by asking them to rate the frequency with which they have experienced various problem behaviors/symptoms over the past six months. Participant responses are then scored and compared to age and gender-normed data to produce t-scores. T-scores below 65 are classified as “normal,” 65–69 are considered “Borderline” elevated, and scores above 69 indicate “Clinical” levels of symptoms. The YSR yields eight subscale scores of emotional/behavioral functioning and two broad measures of functioning: Internalizing and Externalizing symptoms. The anxiety/depression subscale was used in the current study. This subscale was purposefully chosen over the more global Internalizing syndrome scale which, being partly comprised of the Somatic Complaints scale, may inappropriately produce elevated scores for youth with chronic health conditions (Perrin, Stein, & Drotar, 1991). The anxiety/depression scale of YSR has good test-retest reliability (r = .74) and internal consistency (α = .84) and significantly discriminates between referred and nonreferred youth (Achenbach & Rescorla, 2001).

Medical Adherence Measure

Adolescent barriers to adherence and adherence to prescribed oral medications were assessed using the Medication Adherence Measure (MAM) (Zelikovsky & Schast, 2008). Designed to be administered during
standard clinical care, the MAM is a semi-structured interview conducted jointly with the adolescent and their parent to assess knowledge of their medical regimen, adherence, organization, and barriers to adherence. The MAM contains multiple self-contained modules that can be administered individually or collectively based on the aims of the clinician, clinical population, or purpose of research. For the current study, global assessments of barriers to adherence and adherence were used as this approach is most similar to what is typically done in a clinical setting (La Greca & Bearman, 2003; Rapoff, 2010). Specifically, barriers to adherence were assessed with the question “What are some reasons you miss taking your medications?” After recording spontaneously reported barriers, the interviewer provides the opportunity to endorse any additional barriers by reading the barriers listed in the MAM that were not previously identified. The number of barriers endorsed is summed to generate a barriers score, with higher scores indicating greater number of barriers to adherence. Adolescent self-report of adherence to their treatment regimen was assessed with the question “On a scale of 0 (hardly ever take my medications; usually miss) to 10 (always take my medications; rarely miss), how would you rate how well you take your medications, on average?” Research has shown that patient global report of self-management, such as the approach adopted in this current study, is a more accurate predictor of adherence behavior than more specific assessment methods such as adolescent report of number of pills missed over the past week (Greenley et al., in press). The MAM demonstrates adequate convergent validity (electronic monitoring $r = .40$, $p < .05$), test–retest reliability ($r = .89$, $p < .05$), and is predictive of long-term health outcome in other pediatric populations ($r = .62$, $p < .001$; Zelikovsky, 2007; Zelikovsky et al., 2008).

Disease Activity
Disease activity was collected for descriptive purposes using either the Pediatric Crohn’s Disease Activity Index (PCDAI; Hyams et al., 1991) for youth with Crohn’s disease or the Lichtiger Colitis Activity Index (LCAI; Lichtiger et al., 1994) for youth with ulcerative colitis. Both measures provide an objective rating of disease activity for their respective IBD subtypes using patient medical data. Each item response is associated with a numerical value and scores are summed to generate a disease activity score. Scores on the PCDAI range from 0 to 100. The PCDAI has strong convergent validity with other measures of disease activity (physician global assessment $r = .80$, $p < .001$; modified Harvey–Bradshaw index score $r = .81$, $p < .001$) and is able to discriminate between categories of disease activity (Hyams et al., 1991). Scores on the LCAI range from 0 to 21. The LCAI has been used extensively in clinical trials, is sensitive to changes in disease activity in response to treatment, and discriminates well between patients adequately responding to treatment and those requiring surgical intervention (Lichtiger et al., 1994). Reliability in the current sample for both the PCDAI ($\alpha = .83$) and the LCAI ($\alpha = .79$) was good.

Statistical Analyses
All analyses were conducted using SPSS 17.0 software (Chicago, IL, USA). Prior to combining samples, t-tests and chi-squared tests were conducted to ensure that participant demographic data (i.e., age, gender, ethnicity, family income, diagnosis) did not differ by recruitment site. All variables were used in their continuous form and were centered prior to analyses. Pearson product correlations between disease severity, barriers to adherence, anxiety/depressive symptoms, and adherence were calculated. Hypothesized moderating relationships and post-hoc probing of significant moderator effects were examined according to the guidelines proposed by Holmbeck (Holmbeck, 1997, 2002b). Per these guidelines, the interaction term (barriers to adherence $\times$ anxiety/depressive symptoms) was entered into a regression predicting the outcome variable (adherence) after controlling for the individual predictor variables (barriers to adherence and anxiety/depressive symptoms) and other variables of interest (disease severity). If the interaction term is significantly associated with the outcome variable, moderation is suggested. Although this initial analysis suggests that the association between the predictor and the outcome significantly varies across different levels of the moderator, it does not provide any information about the specific conditions in which this relationship significantly varies. Post hoc probing clarifies this situation through the use of post hoc regressions in which the simple slopes of conditional levels of the moderator (defined as 1 SD above or below the mean of anxiety/depressive symptoms) are computed and individually evaluated for statistical significance. Results of post hoc probing can then be visually depicted by substituting high (1 SD above the mean) and low (1 SD below the mean) values of the independent variable (barriers to adherence) into the post hoc regression equations to illustrate the conditions in which the relationship between the barriers to adherence and adherence vary by level of anxiety/depressive symptoms.
Results

Participant Characteristics
Independent samples t-tests and chi-square tests revealed no significant differences in demographic variables by recruitment site; thus, samples were combined for all analyses. Demographic data for the combined sample are presented in Table I. Of the 80% of adolescents diagnosed with Crohn’s disease, 58.7% had inactive disease (PCDAI score ≤ 10), 38.1% had mild disease activity (PCDAI = 11–29), and 3.2% had moderate-to-severe disease activity (PCDAI ≥ 30; Hyams et al., 2005). Among participants with ulcerative colitis, 50% had disease activity in the quiescent range (LCAI score ≤ 2), 43.8% were in the mild range and responding to therapy (LCAI = 3-9), and 6.3% had active disease that was not responding to therapy (LCAI ≥ 10; Fanjiang, Russell, & Katz, 2007).

Anxiety/Depressive Symptoms, Barriers to Adherence, and Adherence
Almost all patients (96.2%) endorsed one or more barriers to adherence (M = 2.33 barriers, SD = 1.47). Most commonly reported barriers included: forgetting (endorsed by 84.8% of sample), being away from home (43%), and medication interfered with an activity (34.2%; Table II). Out of a possible range from 0 (hardly ever take my medications; usually miss) to 10 (always take my medications; rarely miss), mean adolescent self-report of adherence was 8.63 out of 10 (SD = 1.32). Table III presents means, standard deviations, and intercorrelations between anxiety/depressive symptoms, barriers to adherence, and self-report of adherence. All relationships were statistically significant (p < .05) and of small to moderate magnitude. Most adolescents (87.3%) had an anxiety/depression t-score within the normal range. A smaller percentage reported anxiety/depression levels in the Borderline range (6.3%) or Clinical range (6.3%).

Table I. Participant Characteristics

<table>
<thead>
<tr>
<th>Percentage or M (SD)</th>
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<tbody>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Gender, female (%)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
</tr>
<tr>
<td>Caucasian</td>
</tr>
<tr>
<td>African American</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Caregiver relationship to adolescent, mothers (%)</td>
</tr>
<tr>
<td>Caregiver marital status, married (%)</td>
</tr>
<tr>
<td>Family income, median</td>
</tr>
</tbody>
</table>

Table II. MAM Endorsed Barriers to Adherence

<table>
<thead>
<tr>
<th>MAM Barrier</th>
<th>Adolescents endorsing (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Just forget</td>
<td>84.8</td>
</tr>
<tr>
<td>Wasn’t home</td>
<td>43.0</td>
</tr>
<tr>
<td>Interferes with activity</td>
<td>34.2</td>
</tr>
<tr>
<td>Ran out/didn’t fill</td>
<td>15.3</td>
</tr>
<tr>
<td>Hate the taste</td>
<td>12.7</td>
</tr>
<tr>
<td>Not feeling well</td>
<td>12.7</td>
</tr>
<tr>
<td>Refused to/defiant</td>
<td>11.4</td>
</tr>
<tr>
<td>Don’t think necessary</td>
<td>10.1</td>
</tr>
<tr>
<td>Hard to swallow pills</td>
<td>7.6</td>
</tr>
<tr>
<td>Don’t like the side effects</td>
<td>6.4</td>
</tr>
<tr>
<td>Can’t afford</td>
<td>0</td>
</tr>
<tr>
<td>Other reasons:</td>
<td></td>
</tr>
<tr>
<td>Fell asleep/was sleeping</td>
<td>3.9</td>
</tr>
<tr>
<td>Too busy</td>
<td>2.6</td>
</tr>
<tr>
<td>Tired</td>
<td>3.9</td>
</tr>
<tr>
<td>Pharmacy ran out of medicine</td>
<td>1.3</td>
</tr>
<tr>
<td>Did not fill pill box</td>
<td>1.3</td>
</tr>
<tr>
<td>Lazy</td>
<td>1.3</td>
</tr>
<tr>
<td>Lost medicine</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Table III. Intercorrelations Among Anxiety/Depressive Symptoms, Barriers to Adherence, and Adherence

<table>
<thead>
<tr>
<th>Variable</th>
<th>M (SD)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Disease severity</td>
<td>9.01 (9.13)</td>
<td>.19</td>
<td>.33**</td>
<td>.27</td>
<td></td>
</tr>
<tr>
<td>2. Anxiety/depressive symptoms</td>
<td>55.32 (6.98)</td>
<td>.29**</td>
<td>.29**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Barriers to adherence</td>
<td>2.33 (1.47)</td>
<td></td>
<td>.47***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Adherence</td>
<td>8.63 (1.32)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p < .05; **p < .01; ***p < .001.
Post hoc probing was conducted to examine the extent to which anxiety/depressive symptoms moderated this relationship. As seen in Figure 1, adherence generally declined as barriers increased. However, this relationship was only significant among youth who had higher levels of anxiety/depressive symptoms ($b = -0.43$, $p < .001$). By converting the scale of patient report into percentages (i.e., reported numeric value of adherence/10), findings illustrate that an increase in barriers results in an overall decrease of 2% in adherence among patients with lower levels of anxiety/depressive symptoms. However, among patients with higher levels of anxiety/depressive symptoms, adherence decreases by 12.6% as barriers increase. These results suggest that the presence of anxiety/depressive symptoms intensifies the negative impact of barriers to adherence on adolescent’s ability to adhere to their regimen.

**Discussion**

The current study is the first and only known report of the negative additive impact of anxiety/depressive symptoms on the relationship between barriers to adherence and adherence among adolescents with IBD. Although prior research has linked poorer adherence with increased barriers to adherence, our study is the first to demonstrate that the extent to which this relationship occurs is affected by the presence of anxiety/depressive symptoms. Thus, our findings suggest that anxiety/depressive symptoms may be a critical risk factor in adherence among youth with IBD. Improved understanding of this risk factor may play a vital role in the design of timely, effective adherence interventions. Ultimately, helping adolescents establish positive health management behaviors may help prevent nonadherence and its associated medical and financial consequences in adulthood.

Results indicate that barriers to adherence are normative, rather than the exception, among youth with IBD (barriers endorsed by 96.2% of sample). Additionally, the reasons why adolescents do not take their medication vary greatly. In our study sample, forgetting, being away from home, and treatment interfering with an activity were the most commonly reported barriers to adherence. These barriers in particular illustrate the many difficulties adolescents experience when attempting to manage their IBD treatment in the context of their busy everyday lives. However, when working with adolescents to reduce barriers to adherence, it is important not to assume a one-size-fits-all approach as the underlying causes of the most commonly endorsed barriers may vary greatly and thus require different intervention approaches. For example, when dealing with the barrier of “forgetting,” it is important to determine what factors cause the adolescent to forget to take their medicine. If poor planning and organization are the underlying cause, working with the adolescent to better integrate their medications into their normal routine may be helpful. Other adolescents, who forget to take their medicine when away from home, may benefit most from reminder tools (e.g., cell phone alarm, reminder text messages). However, either of these two approaches would likely be unsuccessful when working with an adolescent whose primary contributors to forgetting are a lack of parental support/monitoring or low motivation to adhere to treatment. In many cases, addressing barriers to adherence is not a straightforward process and in depth problem solving, planning, and support from family, friends, and medical providers is often needed to promote change. Thus, adolescent report of barriers should primarily be considered a starting point in an attempt to...
understand the complex manner in which barriers negatively impact adherence.

In order to overcome barriers to adherence, it is important to first recognize when problems with adherence occur. Although adolescents generally assume greater treatment responsibility over time, it is essential that parents continue to play an active role in their adolescent’s care by monitoring their adherence (Shaw, 2001). This can be done overtly (e.g., checking in with adolescent to see if dose was taken) or covertly (e.g., checking pill box, counting pills). Ideally, the method of monitoring should be a shared decision between the adolescent and their parent to minimize the potential for declines in adherence due to parent-teen conflict (Hauser et al., 1990).

Regardless of the method used, monitoring of adherence is essential in first identifying barriers to adherence, then taking steps to address them.

However, addressing barriers to adherence may be more challenging among adolescents with poorer emotional functioning. The current study is the first and only report of higher anxiety/depressive symptoms having an additive effect on the barriers–adherence relationship. Among adolescents with lower anxiety/depressive symptoms, increasing barriers did not significantly impact adherence. However, among those with high anxiety/depressive symptoms, adherence was significantly lower (12.6 percentage points) than those with fewer barriers, suggesting that the presence of anxiety/depressive symptoms amplifies the negative impact of barriers on adherence in youth with IBD.

Barriers to adherence and anxiety/depressive symptoms may combine to impact adherence in several ways. The presence of problematic emotional functioning may undermine adolescents’ ability to recognize declines in adherence, identify barriers, and actively take steps to overcome them. Adolescents with poorer emotional functioning may also struggle with soliciting needed support from family and friends to maintain good adherence. Additionally, those with emotional problems may mistakenly interpret the physiological symptoms of anxiety (e.g., nausea, abdominal distress) and depression (e.g., fatigue) as symptoms of IBD, erroneously concluding that treatment is not working (treatment efficacy barrier), and stop taking their medication. Such health beliefs have been consistently linked with poorer adherence (Brownlee-Duffeck et al., 1987; Bucks et al., 2009; Janz & Becker, 1984).

The detrimental combined impact of barriers to adherence and emotional functioning on symptoms among adolescents suggests that solely assessing for barriers to adherence among adolescents with IBD is inadequate. In order to optimize improvements in adherence, clinicians must routinely screen for barriers to adherence and symptoms of anxiety and depression. This can easily be done by administering brief, well-validated screeners of anxiety (e.g., Beck Anxiety Inventory [BAI]; Beck & Steer, 1990), depression (e.g., Center for Epidemiological Studies Depression for Children [CES-DC]; Weissman, Orvaschel, & Padian, 1980), and barriers to adherence (e.g., barriers module of Medication Adherence Measure; Zelikovsky & Schast, 2008) during clinic visits and using patient responses on these measures to guide discussion of factors impacting their health and their medical care. Adolescents endorsing clinically elevated levels of anxiety or depression should be referred to a psychologist or other mental health professional for additional care.

Findings from the current study should be considered in the context of its strengths and limitations. The current study moves the pediatric IBD literature forward in several ways. First, this is one of the few known studies to examine multiple factors impacting adherence through the use of predictive, rather than descriptive, statistical analyses. Another strength is the use of multi-site data collection, which allowed for the recruitment of a sample larger than typically included in pediatric IBD research. The use of a well-validated, norm-referenced measure of anxiety/depressive symptoms and the assessment of barriers to adherence and adherence as it is typically done in clinical practice are additional strengths. Limitations of the current study include the cross-sectional nature of data, a relatively homogeneous sample of youth with IBD, the use of self-report to assess adherence, and high self-report of adherence. Although our sample was relatively homogeneous, it is demographically similar to samples previously reported in pediatric IBD studies (Mackner & Crandall, 2007). Self-report, the most commonly used method to measure adherence, has a tendency to overestimate adherence compared to more objective measures such as pill counts, electronic monitoring, or blood assays (Hommel et al., 2009; La Greca, 1995). However, this approach was used for two reasons. Compared to these more objective approaches, which may not be feasible due to time and budgetary constraints, our assessment approach is consistent with what is typically done in clinical practice and is therefore more generalizable. Second, compared to our global assessment approach, objective approaches are less able to capture the multifaceted nature of adherence. Blood assay data, which were available for some participants, were not used for this reason as these data are easily influenced by recent adherence and, as they are medication-specific, do not capture overall adherence. Recent research suggests that adopting a more global approach to adherence assessment is more predictive of actual adherence behaviors than more specific
approaches such as asking patients to report the number of pills missed over the past week (Greenley et al., in press). High self-report of adherence is another limitation as this restriction of range may have deflated our correlation coefficients. Given this, it is possible that the combined impact of barriers to adherence and poorer emotional functioning on adherence has been underestimated in our study.

Additional adherence research is needed among adolescents with IBD. Specifically, prospective studies examining the dynamic, interactive relationship between barriers to adherence, emotional functioning, and adherence are needed. Such research would greatly inform the design of effective, well-timed interventions among youth with IBD and would aid in clinical decision making when problems with adherence or anxiety/depressive symptoms become known. Research examining the role of parental monitoring on adherence is also needed as there is little guidance on the optimal type or amount of parental involvement to protect against declines in adherence among adolescents with IBD. Additionally, adolescent beliefs regarding treatment efficacy and the benefits and consequences of nonadherence should be examined as improved understanding of the adolescent’s perspective can inform the approach clinicians and parents take to effectively engage the adolescent in a collaborative discussion of problems with adherence.

Although nonadherence is linked with poor health outcome and increased health expenditures among adults with IBD, little is known regarding the consequences of nonadherence to the IBD regimen among pediatric populations. Our cross-sectional data suggest a relationship between adherence and disease activity. However, longitudinal assessment is critically needed to determine the extent to which adherence affects health outcome. Due to our limited knowledge of this issue, it is currently unknown what constitutes a clinically significant increase in adherence or to what extent a minimum adherence threshold exists. Thus, it is difficult to determine the extent to which a 12.6% difference in adherence found among adolescents with high or low barriers to adherence and high anxiety/depressive symptoms corresponds to long term differences in health outcome. These are a critical gaps in the literature that need to be addressed as the pharmacokinetics of IBD medications in children may vary significantly from adults due to children’s continuous state of physiological development (Rylance, 1981).

Ultimately, the current study is an important first step toward our understanding of additional factors that negatively impact adherence among adolescents with IBD. Our findings suggest that anxiety/depressive symptoms play a critical role in whether or not barriers to adherence will impact adherence and findings may guide the development of risk profiles to help identify and preventatively intervene with patients at risk for problematic adherence. Continued research in this area would greatly move the pediatric IBD literature closer to providing optimal disease management support for adolescents with IBD.

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References
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