

BEHAVIORAL DIFFICULTIES IN YOUTH WITH INFLAMMATORY BOWEL DISEASE:
PERCEIVED BARRIERS AS MEDIATOR OF MEDICATION ADHERENCE

by

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(Under the Direction of Ronald L. Blount)

ABSTRACT

Objectives are to examine the relationship between behavioral functioning specific to attention and conduct problems and prescription medication adherence in youth with Inflammatory Bowel Disease (IBD) and to examine the potential mediational role of perceived barriers to medication adherence. Low rates of medication adherence are a documented problem for youth with IBD with the potential for negative health consequences. There is a need to identify potentially malleable factors associated with poor adherence such as behavioral functioning and barriers so that treatment interventions can be developed. *Methods:* Eighty-five adolescents with IBD and their parents completed measures of adherence, attention and conduct problems, and barriers to adherence while attending a regularly scheduled clinic appointment. To examine the proposed mediation models, the traditional Baron & Kenny (1986) approach in combination with formally testing the indirect effect using procedures outlined by Preacher & Hayes (2004) was used. *Results:* Attention and conduct problems were negatively associated with adherence. Analyses supported the mediational role of perceived barriers in the relationship between behavioral problems and adherence. *Conclusions:* Results indicate that attention and

conduct problems are risk factors for lower adherence in youth with IBD and that barriers may account for the relationship.

INDEX WORDS: Adherence, Inflammatory Bowel Disease, Attention Problems, Conduct Problems

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DEDICATION

This work is dedicated to youth with Inflammatory Bowel Disease, their families, and their caregivers.

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TABLE OF CONTENTS

	Page
ACKNOWLEDGEMENTS	v
LIST OF TABLES	vii
LIST OF FIGURES	viii
CHAPTER	
1 INTRODUCTION	1
2 METHOD	8
3 RESULTS	14
4 DISCUSSION	29
REFERENCES	34

LIST OF TABLES

	Page
Table 1: Demographic and Disease Characteristics of the Sample	12
Table 2: Intercorrelations among Variables.....	21
Table 3: Means, Standard Deviations, and Ranges for Study Variables	22
Table 4: Individual Items on the PMBS and the Four Subscales	23

LIST OF FIGURES

	Page
Figure 1: Parent Reported Barriers to Adherence Mediate the Effect of Attention Problems on Parent Reported Adherence	24
Figure 2: Parent Reported Regimen Adaptation/Cognitive Issues Mediate the Relationship between Attention Problems and Parent Reported Adherence	25
Figure 3: Parent Reported Barriers to Adherence Mediate the Effect of Conduct Problems on Parent Reported Adherence	26
Figure 4: Parent Reported Regimen Adaptation/Cognitive Issues Mediate the Relationship between Conduct Problems and Parent Reported Adherence.....	27
Figure 5: Parent Reported Barriers to Adherence Mediate the Effect of Conduct Problems on Adolescent Reported Adherence.....	28

CHAPTER 1

INTRODUCTION

Crohn's Disease and ulcerative colitis, which are jointly referred to as Inflammatory Bowel Disease (IBD), are chronic, immune mediated diseases of the digestive tract that are often diagnosed in adolescence (Sandler & Eisen, 2000) and affect approximately 71 out of 100,000 youth below the age of 20 in the United States (Kappelman et al., 2007). Orally administered medications are fundamental for the successful treatment of IBD and include several classes of medications including anti-inflammatories, immunomodulators, corticosteroids, and antibiotics. Similar to youth with other chronic illnesses, adherence to medications is a significant concern for youth with IBD, particularly for adolescents who are among the least adherent of age groups (DiMatteo, 2004).

Past research assessing rates of adherence in youth with IBD has produced varying results ranging from 12% to 98% depending on the sample, the class of medications being assessed, and the assessment methodology utilized (Hommel, Davis, & Baldassano, 2009; Mackner & Crandall, 2005; Reed-Knight, Lewis, & Blount, 2011). Comparing self-report and objective measures, including metabolite bioassays and pill counts (Hommel, et al., 2009), pediatric patients with IBD were found to have adherence rates as low as 12% to 36% when using objective measures. Self-reported adherence was markedly higher, however, with rates of 90 to 98%. Mackner & Crandall (2005) found that only 48% of adolescents and 38% of parents reported the adolescent as "always adherent" to prescribed IBD medications. Within our lab, rates of adherence have varied across the class of medications assessed, with rates of adherence

for prescription medications being as high as 92.76% and 89.54% per parent and adolescent-reports, respectively, compared to their reports of adherence to medications prescribed by the gastroenterologist that are sold over-the-counter being much lower at 72.49% and 66.73% (Reed-Knight, et al., 2011).

The consequences of nonadherence can include decreased quality of life, additional and otherwise unnecessary prescriptions, drug interactions, drug resistance, and increased morbidity and mortality (Quittner, Modi, Lemanek, Ievers-Landis, & Rapoff, 2008). For patients with IBD, research cannot yet speak to the disease consequences of nonadherence for youth. For adults with ulcerative colitis, however, a recent study documented that those who were nonadherent were 5.5 times more likely to experience a relapse of disease symptoms compared to those who were adherent (Kane, Huo, Aikens, & Hanauer, 2003). Given the low documented rates of adherence for youth with IBD and the potential for negative outcomes, additional research is needed to examine adherence as well as potentially modifiable factors associated with poor adherence.

Using a risk and protective factors conceptual framework (Blount, Bunke, & Zaff, 2000), factors associated with adherence can be considered either fixed or malleable and potentially changeable through effective intervention. To date, a small body of research investigating malleable factors related to adherence in youth with IBD has developed (Hommel, Davis, & Baldassano, 2008; Mackner & Crandall, 2005; Reed-Knight, et al., 2011). Mackner & Crandall (2005) examined rates of adherence to prescribed medications and found adherence to be positively related to better family functioning and less use of maladaptive coping mechanisms. In our previous work, we have identified fixed factors associated with poorer adherence to prescription medications in youth with IBD including longer time since diagnosis in addition to

malleable factors including greater adolescent perceived disease severity and a lack of autonomous motivation to adhere (Reed-Knight, et al., 2011). Research on the relationship between adherence and quality of life in youth with IBD has shown mixed findings depending on the class of medication prescribed, with 6-MP/azathioprine adherence being related to better physical quality of life and 5-ASA adherence being related to poorer psychological quality of life (Hommel, Davis, et al., 2008). The authors speculate that the greater number of daily pills and doses required by a 5-ASA regimen compared to a 6-MP/azathioprine regimen may contribute to the poorer psychological quality of life.

In the pediatric literature, several studies have documented a relationship between potentially malleable emotional and behavioral difficulties in youth with chronic illnesses and poorer adherence. In pediatric patients with diabetes, adaptive coping has been associated with improved adherence over a 4-year period, suggesting that adjustment may predict adherence over the course of time (Hauser et al., 1990). In youth with end stage renal disease undergoing dialysis, low treatment adherence has been found to be associated with higher self-report ratings of anxiety and depression (Brownbridge & Fielding, 1994). In pediatric renal transplant recipients, nonadherence has been shown to be associated with the presence of a psychiatric diagnosis (i.e., major depression, adjustment disorders, oppositional defiant disorder, substance abuse, and psychological factors affecting a medical condition) (Shaw, Palmer, Blasey, & Sarwal, 2003). Further, the presence of a psychiatric diagnosis significantly predicted graft loss, highlighting the implications of failure to address nonadherence and associated factors. In a particularly applicable study to the current one, Gerson and colleagues (2004) examined the associations between adherence and modifiable psychosocial variables in kidney transplant recipients and found adherence to be positively related to better general child behavior and

negatively related to parent-reported attention problems on the Behavior Assessment System for Children (BASC) (Reynolds & Kamphaus, 2004).

In youth with IBD, research to date has primarily focused on documenting rates of internalizing disorders and emotional functioning (Mackner, Sisson, & Crandall, 2004), with less attention given to symptoms of externalizing disorders, attention difficulties, or behavioral problems (Hommel, Denson, Crandall, & Mackner, 2008). A recent study on the relationship between child behavioral functioning and family functioning in youth with IBD demonstrated that externalizing behavior problems accounted for the majority of the variance in family functioning, suggesting that externalizing behaviors may have greater impact on youth with IBD than previously thought (Odell, Sander, Denson, Baldassano, & Hommel, 2011). Results of studies conducted with several pediatric disease groups suggest that emotional and behavioral difficulties including both internalizing and externalizing and attention symptoms may be risk factors for poor adherence in youth with chronic illnesses. However, the relationship between externalizing behaviors and attention problems and adherence has not been examined in youth with IBD to date. Completion of such research is necessary to guide the development of interventions aimed at improving adherence.

In addition to researchers not having yet examined the association between externalizing behaviors and attention problems and adherence in youth with IBD, the mechanisms by which a child's everyday behavioral functioning might be related to adherence have not yet been examined in pediatric samples. Perceived barriers to medication adherence, which are specific behaviors or attitudes that occur close in time to medication taking such as forgetting, refusal/defiance, poor organization, and side effects, are one potential mechanism. Externalizing behaviors or attention problems may increase the number of barriers that adolescents and their

parents perceive as getting in the way of taking medication as prescribed. Primarily guided by the Health Belief Model (Bush & Iannotti, 1990), barriers have consistently been found to be associated with poorer rates of adherence in adults and youth (Bond, Aiken, & Somerville, 1992; Harrison, Mullen, & Green, 1992; Simons & Blount, 2007; Simons, McCormick, Devine, & Blount, 2010; Zelikovsky, Schast, Palmer, & Meyers, 2008). Research on barriers to medication adherence has identified several types and classes of barriers ranging from forgetfulness (Modi & Quittner, 2006) to disease factors including disease severity and regimen complexity (Modi & Quittner, 2006; Reed-Knight, et al., 2011) to emotional and cognitive factors including embarrassment or perceptions that the regimen is ineffective (La Greca & Mackey, 2009; Modi & Quittner, 2006). Modi & Quittner (2006) examined barriers to treatment adherence in youth with cystic fibrosis and asthma and identified oppositional behaviors specific to the medical regimen as some of the most frequently reported barriers by children and parents to pulmonary adherence tasks common to both diseases as well as disease-specific tasks. Further research is needed to examine the potential that oppositionality specific to required medical tasks may be a manifestation of general externalizing behavior problems in youth.

In youth with IBD, researchers have recently begun examining barriers to medication adherence with similar findings to other chronic illness groups (Greenley, Stephens, Doughty, Raboin, & Kugathasan, 2010; Ingerski, Baldassano, Denson, & Hommel, 2010). Ingerski and colleagues (2010) examined adolescent and caregiver reported barriers using 12 commonly reported barriers on the Medication Adherence Measure (Zelikovsky & Schast, 2008) and found that the most commonly endorsed barriers were forgetting, being away from home, interference with an activity, refusal/defiance, ran out/didn't fill the prescription, not feeling well, and belief that medication is not necessary. Similarly to Modi & Quittner (2006), this study identified

oppositonality as a frequently endorsed barrier, though neither study was designed to identify symptoms of general behavioral disorders that might also be related to adherence and the presence of the reported defiance related to adherence. Greenley and colleagues (2010) also recently examined barriers to adherence in youth with IBD and their parents, though their methodology was limited in that respondents were only provided with six possible barriers that could be endorsed. Despite this limitation, results indicated that the most commonly reported barriers by adolescents included a lack of time to take medication, followed by currently feeling well and therefore discontinuing medication, as well as medication side effects and a belief that the medication is ineffective. For parents, the most frequently reported barrier was also the belief that their child lacks the time, followed by the belief that their child perceives too many side effects. The overall number of barriers endorsed was related to adherence, with more barriers related to imperfect adherence (Greenley, et al., 2010).

In sum, a body of research in the pediatric literature has developed indicating that perceived barriers including oppositionality and defiance specific to adherence are associated with poorer medication adherence (Ingerski, et al., 2010; Modi & Quittner, 2006). In addition, research has found that potentially modifiable emotional and behavioral difficulties such as attention and behavioral problems are associated with less adherence (Gerson, et al., 2004; Shaw, et al., 2003). To date, however, research has not examined the potential relationship between children's and adolescents' general behavioral problems, reported barriers to medication taking, and medication adherence. The first aim of the current study was to examine the relationship between both symptoms of attention problems and conduct problems and prescription medication adherence in youth with IBD. Completion of this aim will build upon past work demonstrating a relationship between behavioral problems and poorer adherence in pediatric

transplant recipients to determine if similar relationships exist in youth with IBD (Gerson, et al., 2004). The target sample was youth with IBD presenting for outpatient gastrointestinal care as opposed to a clinical sample of youth with diagnosed attention and conduct problems so that results would be most applicable to the majority of youth with IBD. Second, we examined the relationship between perceived barriers and medication adherence for both adolescents and parents. Third, the current study aimed to examine the potential mediational role of perceived barriers in the hypothesized relationship between attention and conduct problems and medication adherence (Figure 1). I hypothesized the following: a) parent report of adolescents' problems with attention and conduct would be negatively related to both parent and adolescent report of prescription medication adherence, b) parent and adolescent report of barriers to medication adherence will be negatively related to parent and adolescent report of prescription medication adherence, c) parent report of adolescents' problems with attention and conduct will be positively related to both parent and adolescent report of barriers to medication adherence, and d) barriers to medication adherence will mediate the relationship between attention and conduct problems and prescription medication adherence. Although there are limitations to using only parent report of behavioral functioning, research has supported the validity of parent reported behavioral problems by demonstrating better parent-adolescent agreement for externalizing behaviors compared to internalizing behaviors (Rey, Schrader, & Morris-Yates, 1992).

CHAPTER 2

METHOD

Participants

Participants were 85 adolescents ages 11-18 years ($M = 14.76$, $SD = 2.27$) with a diagnosis of IBD and one of their primary caregivers. Parent respondents self-identified as the adolescent's mother (80%), father (19%), or grandmother (1%). Participants of the current study were part of a larger study examining adherence in youth with IBD. Demographic characteristics of the sample can be seen in Table 1. Participants were recruited from a large pediatric gastroenterology practice in the Southeast United States. Inclusion criteria included: (a) diagnosis of Crohn's disease, ulcerative colitis, or indeterminate colitis, (b) 11-18 years of age, (c) prescribed oral medications for the treatment of IBD, and (e) English fluency. Exclusion criteria included: (a) parent-reported or chart recorded developmental delay that would prevent the adolescent from being able to understand or complete the measures. No potential participants were excluded for this reason. Eight parent-child dyads were not included in the current analyses due to incomplete data that precluded planned analyses. Throughout recruitment for the current study, 109 parent-adolescent dyads were consecutively approached for participation, with the 93 consenting representing an 85% participation rate. Reasons for declining to participate included lack of time ($n = 5$), lack of interest ($n = 6$), adolescent felt too ill ($n = 3$), and chose not to indicate ($n = 2$).

Measures

A brief demographics questionnaire assessed the participant's age, gender, ethnicity, family income, diagnosis (CD, UC, or indeterminate colitis), date of diagnosis, and parental highest education levels. Chart reviews of the participants' medical charts at the pediatric gastroenterology clinic were conducted to obtain their currently prescribed medication regimen including the name, dosage frequency, dosage amount, and purpose of each medication.

Medical Adherence Measure (MAM). The Medication Module of the MAM (Zelikovsky & Schast, 2008) is a semi-structured interview to assess medication adherence to prescribed medications over the past 7 days. The MAM was administered separately to parents and adolescents to assess adherence to prescription medications. To quantify adherence, the number of prescribed doses minus the number of missed doses is divided by the number of prescribed doses, and multiplied by 100. In a recent study with renal transplant recipients, percent of missed doses identified on the MAM was associated with the number of documented acute rejection episodes by year two post-transplant ($r = .62, p < .001$), providing evidence as to adequate predictive validity of the MAM with established measures of adherence (Zelikovsky, et al., 2008).

Adolescent Medication Barriers Scale (AMBS). The AMBS (Simons & Blount, 2007) is a 17-item measure that assesses adolescent reported barriers to taking medications on a daily schedule. Respondents are asked to rate on a five point, Likert-like scale from "Strongly Disagree" to "Strongly Agree" how much they perceive each item to be a barrier to medication taking. A total score is calculated by summing items endorsed. In addition to a total score, the AMBS measures barriers along three subscales consisting of items measuring Disease Frustration/Adolescent Issues, Ingestion Issues, and Regimen Adaptation/Cognitive Issues. The AMBS demonstrated adequate internal consistency with a Cronbach's α of .86 for the total scale,

$\alpha = .77$ for Disease Frustration/Adolescent Issues, $\alpha = .73$ for Ingestion Issues, and $\alpha = .54$ for Regimen Adaptation/Cognitive Issues.

Parent Medication Barriers Scale (PMBS). The PMBS (Simons & Blount, 2007) is a 16-item measure that assesses parent reported barriers to their adolescents' medication taking on a daily schedule. Respondents are asked to rate on a five point, Likert-like scale from "Strongly Disagree" to "Strongly Agree" how much they perceive each item to be a barrier to medication taking. A total score is calculated by summing items endorsed. In addition to a total score, the PMBS measures barriers along four subscales consisting of items measuring Disease Frustration/Adolescent Issues, Ingestion Issues, Regimen Adaptation/Cognitive Issues, and the need for a Parent Reminder. The PMBS has demonstrated adequate internal consistency with a Cronbach's α of .83 for the total scale and $\alpha = .69$ for Disease Frustration/Adolescent Issues, $\alpha = .66$ for Ingestion Issues, and $\alpha = .77$ for Regimen Adaptation/Cognitive Issues.

Behavior Assessment System for Children-2nd Edition (BASC-II), Parent Form (Reynolds & Kamphaus, 2004). The BASC-II is a behavior assessment questionnaire. Parents are asked to rate how frequently behaviors occur from "Never" to "Almost Always." For scoring, items are grouped into clinical or maladaptive scales and are scored using *T*-scores that compare respondents' answers to those of parents from same gender and aged children. The BASC-II parent report consists of nine clinical scales, 5 adaptive scales, and three composite scales. For the current study, the two externalizing clinical scales measuring Attention Problems and Conduct Problems were examined. For the clinical scales, *T*-Scores between 41 and 59 fall in the average range, *T*-Scores between 60 and 69 fall in the "at risk" range, and *T*-Scores above 70 indicate clinically significant levels of maladaptive behavior

Procedure

All procedures were in accordance with Institutional Review Board approval. After obtaining the names and appointment times of potential participants from collaborating pediatric gastroenterologists and staff, research assistants contacted potential participants in clinic and invited them to participate in the study. Those who enrolled completed informed written consent and assent, whereas those who declined enrollment were asked to complete an anonymous demographics screener in order to compare participants to non-participants. Adolescent and parent participants independently self-reported on all measures, excluding the MAM, which was administered as a semi-structured interview separately to adolescents and their parents by the first author or trained research assistants. Prior to completion of the MAM, charts were reviewed to obtain the currently prescribed medication regimen. All interviews occurred in an exam room immediately before or after the medical appointment. Both parent and child participants were compensated for their time with a \$20 gift certificate to a local retail store.

Table 1. *Demographic and Disease Characteristics of the Sample*

<i>Variable</i>	<i>N</i>	<i>%</i>
Child's Gender		
Male	47	55
Female	38	45
Child's IBD Diagnosis		
Crohn's Disease	64	75
Ulcerative Colitis	21	25
Race		
White	67	79
African American	10	12
Asian	1	1
Hispanic	4	5
Other	3	4
Annual Family Income		
Under \$10,000	1	1
\$10,000-24,999	3	4
\$25,000-49,999	11	13
\$50,000-74,999	19	22
\$75,000-99,999	15	18
\$100,000 and above	34	40
Did not report	2	2
Maternal Education Level		
Some High School	1	1
High School Diploma/GED	14	17
Some College	17	20
College Degree	33	39

Professional Degree	20	24
Paternal Education Level		
Some High School	2	2
High School Diploma/GED	15	18
Some College	13	15
College Degree	36	42
Professional Degree	18	21
Missing	1	1

CHAPTER 3

RESULTS

Descriptive Analyses

One-way ANOVA and χ^2 tests found no significant differences between participants and those who declined participation and completed an anonymous demographics form based on adolescent's age, gender, IBD diagnosis, race, family income, or parental education level. The relationships between adolescents' attention and conduct problems, barriers to adherence, and medication adherence were analyzed using two-tailed Pearson product correlation coefficients (Table 2). Parent report of attention problems was positively associated with parent report of conduct problems and parent and adolescent report of barriers to medication adherence and negatively associated with parent report of adherence. Parent report of conduct problems was positively associated with parent report of barriers to medication adherence and negatively associated with parent and adolescent report of adherence. Parent report of barriers was positively associated with adolescent report of barriers and negatively associated with both parent and adolescent report of adherence. Finally, parent and adolescent report of adherence were positively associated. Means, standard deviations, and ranges for all study variables appear in Table 3. Although a clinical sample was not recruited, descriptive analyses revealed that two adolescents were rated as "at risk" for clinically significant attention difficulties on the BASC-II, and one adolescent was rated in the clinically significant range. All participants were rated as experiencing average levels of conduct problems.

Mediation Analyses

In order to examine the proposed mediation analyses, a combination of approaches that are best supported by the current literature were utilized. Specifically, the indirect effect was formally tested using procedures outlined by Preacher & Hayes (2004) in addition to the more traditional analyses outlined by Baron & Kenny (1986). Within the Baron & Kenny approach, mediation is established through a series of steps: (1) the independent variable (behavioral functioning) is significantly associated with the dependent variable (medication adherence), (2) the independent variable (behavioral functioning) is significantly associated with the mediator variable (perceived barriers to adherence), (3) the mediator variable (perceived barriers to adherence) is significantly associated with the dependent variable (medication adherence), and (4) the effect of the independent variable (behavioral functioning) on the dependent variable (medication adherence) decreases significantly when the mediator variable (perceived barriers to adherence) is included in the model. Prior to conducting the regression analyses described by Baron and Kenny, assumptions of the general linear model were examined. Also, given that the proposed study will use cross-sectional data, the proposed mediational analyses do not support determining causal relationships and are exploratory in nature.

In addition to examining the results from the Baron & Kenny (1986) approach described above, the indirect effect of the model were tested using an SPSS macro described by Preacher & Hayes (2004) and available at <http://www.comm.ohio-state.edu/ahayes/sobel.htm>. The indirect effect of the model was examined due to shortcomings of the traditional Baron and Kenny criteria including susceptibility to Type I error, serving as an indirect method of testing for mediation, and low statistical power, especially in small sample sizes (MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002; Preacher & Hayes, 2004). As a result of these limitations, the Preacher and Hayes (2004) macro which tests the significance of the indirect effect of the model

while also examining the model using the traditional Baron and Kenny procedures was utilized. The indirect effect of the model is formally tested by producing a bootstrapped estimation of the indirect effect and a 95% confidence interval for this estimate. In the event that zero does not lie within the 95% confidence interval for the bootstrapped results for indirect effects, we can conclude that the indirect effect is significantly different from zero and that mediation is demonstrated (Preacher & Hayes, 2004). Especially with small sample sizes, recent research supports the use of the bootstrapped samples and associated confidence interval to determine significance as opposed to sole use of the Sobel test compared to the normal distribution (Preacher & Hayes, 2004).

Do Barriers Account for the Relationship between Attention Problems and Adherence?

We tested whether parent reported barriers to adherence using the PMBS Total score mediated the effect between attention problems and parent reported adherence (Figure 1). The total effect of attention problems on adherence was significant ($B = -.0038, p < .05$) as was the effect of attention problems on barriers ($B = .4838, p < .001$) and the effect of barriers on adherence ($B = -.0049, p < .01$). The effect of attention problems on adherence became nonsignificant when barriers were included in the model ($B = -.0015, p = .40$), therefore providing evidence as to mediation according to the traditional Baron & Kenny procedures. The Sobel test of the indirect effect, which directly assesses whether the total effect of attention problems on adherence is reduced by the addition of barriers to the model, was significant, again suggesting mediation ($z = -.0024, p = .01$). Using 5000 bootstrapped samples, the estimate of the indirect effect again suggested mediation with a point estimate of $-.0024$ ($SE = .0009$; 95% CI = $-.0043$ to $-.0007$).

Given that the PMBS Total score served as a mediator of the relationship between attention problems and adherence, we sought to determine if specific subscales of the PMBS served as mediators by using a multiple mediator model. Determining if specific subscales serve as mediators in addition to the total score may help to inform treatment intervention. We tested a model in which the four subscales of the PMBS (i.e., Disease Frustration/Adolescent Issues, Ingestion Issues, Regimen Adaptation/Cognitive Issues, and the need for a Parent Reminder) served as mediators for the relationship between attention problems and parent reported adherence (Figure 2). As would be expected based on analyses using the total score, the total indirect effect of the four barriers subscales mediated the effect. At the subscale level, however, only the Regimen Adaptation/Cognitive Issues subscale served as a significant mediator, with a point estimate of $-.0025$ ($SE = .0014$; 95% CI = $-.0061$ to $-.0004$).

Due to the lack of a relationship between attention problems and adolescent reported adherence, mediation cannot exist.

Do Barriers Account for the Relationship between Conduct Problems and Adherence?

We tested whether parent reported barriers to adherence using the PMBS Total score mediated the effect between conduct problems and parent reported adherence (Figure 3). The total effect of conduct problems on adherence was significant ($B = -.0077$, $p < .01$) as was the effect of conduct problems on barriers ($B = .6540$, $p < .001$) and the effect of barriers on adherence ($B = -.0044$, $p < .01$). The effect of conduct problems on adherence became marginally significant when barriers were included in the model ($B = -.0048$, $p = .06$), therefore suggesting mediation according to the traditional Baron & Kenny procedures. The Sobel test of the indirect effect was significant, suggesting mediation ($z = -.0028$, $p < .05$). Using 5000

bootstrapped samples, the estimate of the indirect effect again suggested mediation with a point estimate of $-.0028$ ($SE = .0012$; 95% CI = $-.0054$ to $-.0008$).

Similar to analyses with parent reported attention problems, we tested a model in which the four subscales of the PMBS (i.e., Disease Frustration/Adolescent Issues, Ingestion Issues, Regimen Adaptation/Cognitive Issues, and the need for a Parent Reminder) served as mediators for the relationship between conduct problems and parent reported adherence (Figure 4). As would be expected based on analyses using the total score, the total indirect effect of the four barriers subscales mediated the effect between conduct problems and adherence. At the subscale level, however, only the Regimen Adaptation/Cognitive Issues subscale served as a significant mediator, with a point estimate of $-.0046$ ($SE = .0022$; 95% CI = $-.0099$ to $-.0012$).

We sought to cross-replicate to our findings by examining whether parent reported barriers using the PMBS Total score mediated the relationship between conduct problems and adolescent reported adherence (Figure 5). The total effect of conduct problems on adherence was significant ($B = -.0073$, $p < .01$) as was the effect of conduct problems on barriers ($B = .6515$, $p < .001$) and the effect of barriers on adolescent reported adherence ($B = -.0033$, $p < .05$). The effect of conduct problems on adherence became nonsignificant when barriers were included in the model ($B = -.0051$, $p > .05$), therefore suggesting mediation according to the traditional Baron & Kenny procedures. The Sobel test of the indirect effect was marginally significant when using a normal distribution ($z = -.0021$, $p = .09$). Using 5000 bootstrapped samples, however, the estimate of the indirect effect suggested mediation with a point estimate of $-.0021$ ($SE = .0013$; 95% CI = $-.0050$ to $-.0002$). Only the total score served as a mediator and no individual subscales served as mediators.

Due to the lack of a correlational relationship between adolescent reported barriers and parent or adolescent reported adherence, mediation cannot exist and was therefore not modeled.

Would the Interaction between Barriers and Attention/Conduct Problems Better Account for Adherence?

Given the cross-sectional nature of the data, causal relationships cannot be inferred from the previously described mediation analyses. The inability to infer causality raises the question of whether a moderated model would better explain the relationship between adherence, barriers, and attention and conduct problems. To answer this question, three exploratory, moderated models corresponding to the three mediation models described above were tested using mean centered variables. In all three models, parent report of the adolescent's behavioral functioning (attention problems or conduct problems) served as the moderator, with adherence as the outcome variable and parent reported barriers as the predictor. Therefore, the moderated models tested whether adolescents' attention or conduct problems moderated the relationship between barriers and adherence.

In the first model, parent reported adherence was regressed on the interaction between parent reported barriers and attention problems. This model did not support a moderated relationship, as evidenced by a non-significant interaction term, $t(81) = -1.47, p = .15$. Similarly, the second model regressed parent reported adherence on the interaction between parent reported barriers and conduct problem. This model also failed to support a moderated relationship, with a non-significant interaction term, $t(81) = -1.01, p = .32$. Finally, adolescent reported adherence was regressed on the interaction between parent reported barriers and conduct problems, and support for a significant interaction was not found, $t(81) = -.69, p = .49$. In sum, support was not

found for adolescents' attention or conduct problems moderating the relationship between barriers and adherence.

Table 2. *Intercorrelations among Variables*

Variables	1	2	3	4	5	6	7	8	9	10
1. BASC-II Attention Problems	--	.41**	.41**	.35**	.32**	.36**	.26*	.30**	-.24*	-.12
2. BASC-II Conduct Problems		--	.37**	.24*	.40**	.20	.32**	.19	-.33**	-.28**
3. Barriers to Adherence Total: Parent Report			--	.85**	.83**	.81**	.55**	.49**	-.40**	-.30**
4. Disease Frustration/Adolescent Issues: Parent Report				--	.50**	.85**	.31**	.56**	-.24*	-.25*
5. Regimen Adaptation/Cognitive Issues: Parent Report					--	.41**	.61**	.29**	-.51**	-.34**
6. Ingestion Issues: Parent Report						--	.18	.52**	-.11	-.12
7. Parent Reminder: Parent Report							--	.24*	-.34**	-.29**
8. Barriers to Adherence Total: Adolescent Report								--	-.09	-.16
9. Adherence: Parent Report									--	.74**
10. Adherence: Adolescent Report										--

Note. * $p \leq .05$, ** $p \leq .01$

Table 3. *Means, Standard Deviations, and Ranges for Study Variables*

Variable	<i>M</i>	<i>SD</i>	Observed Range
Adolescent Report			
Adherence: Prescription Medications	89.62%	14.44%	25-100%
Barriers to Adherence Total	41.99	11.65	18.00-68.00
Parent Report			
Adherence: Prescription Medications	92.83%	13.12%	21-100%
BASC-II Attention Problems ^a	48.91	8.32	35-72
BASC-II Conduct Problems ^a	45.12	5.57	38-62
Barriers to Adherence Total	39.08	9.90	18.00-65.00
Disease Frustration/Adolescent Issues	18.39	4.82	7.00-30.00
Regimen Adaptation/Cognitive Issues	11.73	4.15	5.00-22.00
Ingestion Issues	17.73	4.82	7.00-29.00
Parent Reminder	2.61	1.34	1.00-5.00

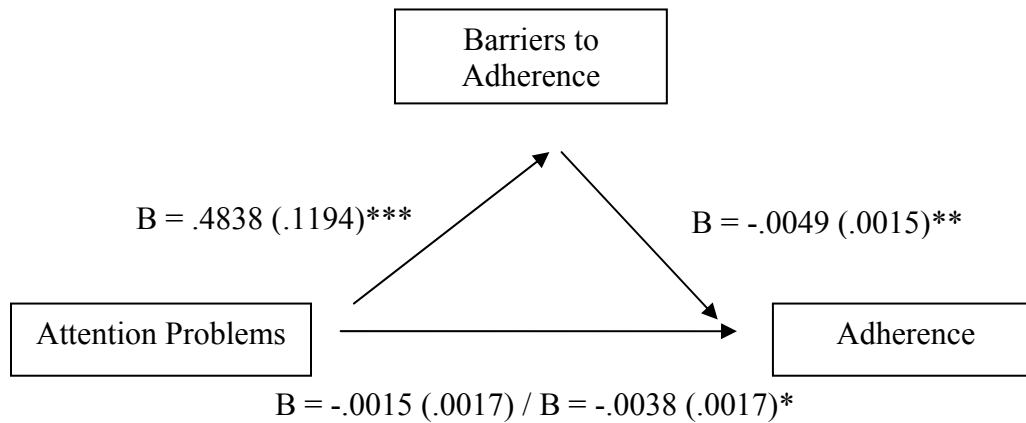
Note. ^a Scores are scaled to a *T*-score metric based on the normative sample in the BASC-II

manual, such that the mean for the normative samples is 50, and the standard deviation is 10.

Table 4. *Individual Items on the PMBS and the Four Subscales*

Items Listed Below each Factor of the PMBS	
Disease Frustration/Adolescent Issues	
1.	My child feels that it gets in the way of his/her activities
2.	My child does not want other people to notice him/her taking the medication
3.	My child sometimes feels sick and can't take the medication
4.	My child doesn't like what the medication does to his/her appearance
5.	My child is tired of taking medicine
6.	My child is tired of living with a medical condition
7.	My child believes the medicine has too many side effects
Regimen Adaptation/Cognitive Issues	
8.	My child is forgetful and doesn't remember to take his/her medication every time
9.	My child is not very organized about when and how he/she takes his/her medication
10.	My child is very busy with other things that get in the way of taking medication.
11.	My child finds it hard to stick to a fixed medication schedule
12.	I am not always there to remind my child to take his/her medication
Ingestion Issues	
13.	My child has a hard time swallowing the medicine
14.	My child has too many pills to take
15.	My child does not like how the medicine tastes
Parent Reminder	
16.	My child relies on me to remind him/her when to take his/her medication

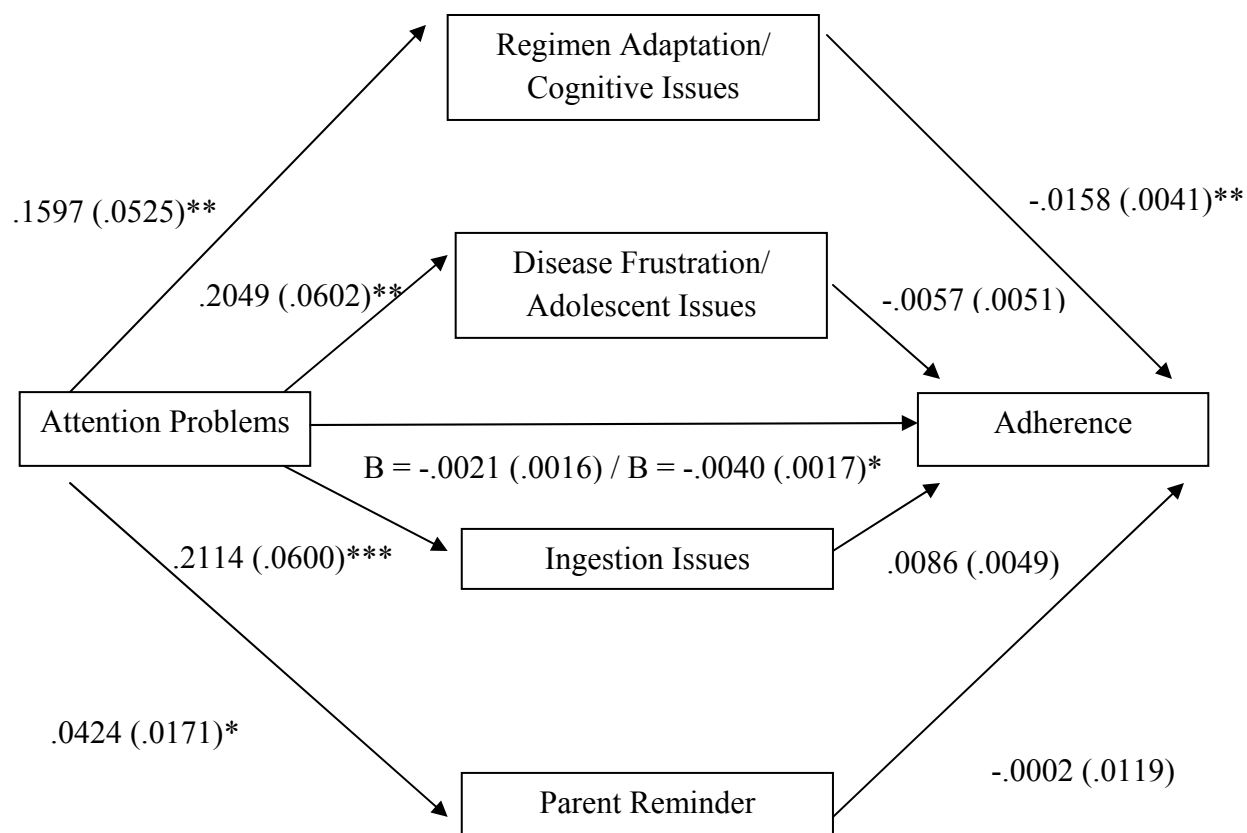
Figure 1. Parent Reported Barriers to Adherence Mediate the Effect of Attention Problems on Parent Reported Adherence



Note. Path values represent unstandardized regression coefficients. Standard errors are in parentheses. Values before the slash represent the direct effect of attention problems on adherence with the inclusion of the mediating variable. Values after the slash represent the total effect of attention problems on adherence without the inclusion of the mediator. $*p < .05$;

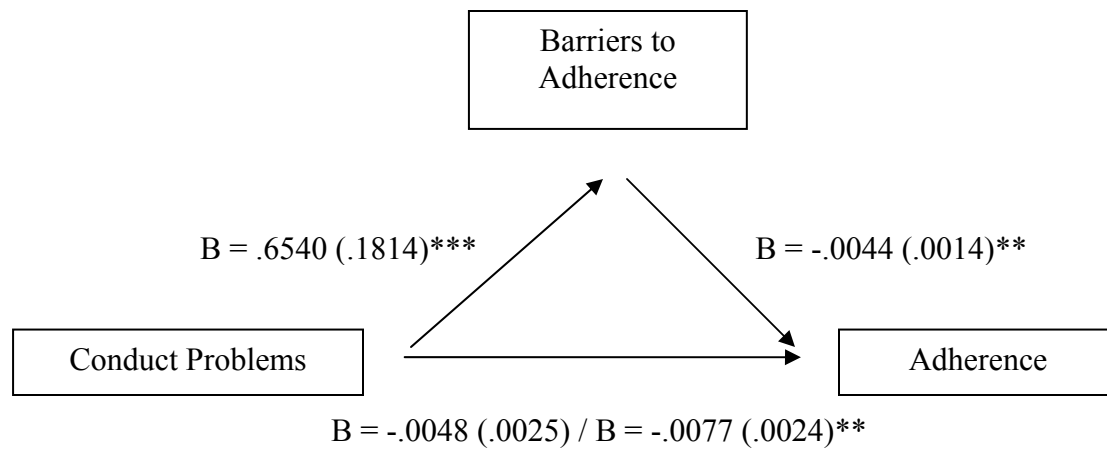
$**p < .01$; $***p < .001$

Figure 2. Parent Reported Regimen Adaptation/Cognitive Issues Mediate the Relationship between Attention Problems and Parent Reported Adherence



Note. Path values represent unstandardized regression coefficients. Standard errors are in parentheses. Values before the slash represent the direct effect of attention problems on adherence with the inclusion of the mediating variables. Values after the slash represent the total effect of attention problems on adherence without the inclusion of the mediator. $*p < .05$; $**p < .01$; $***p < .001$

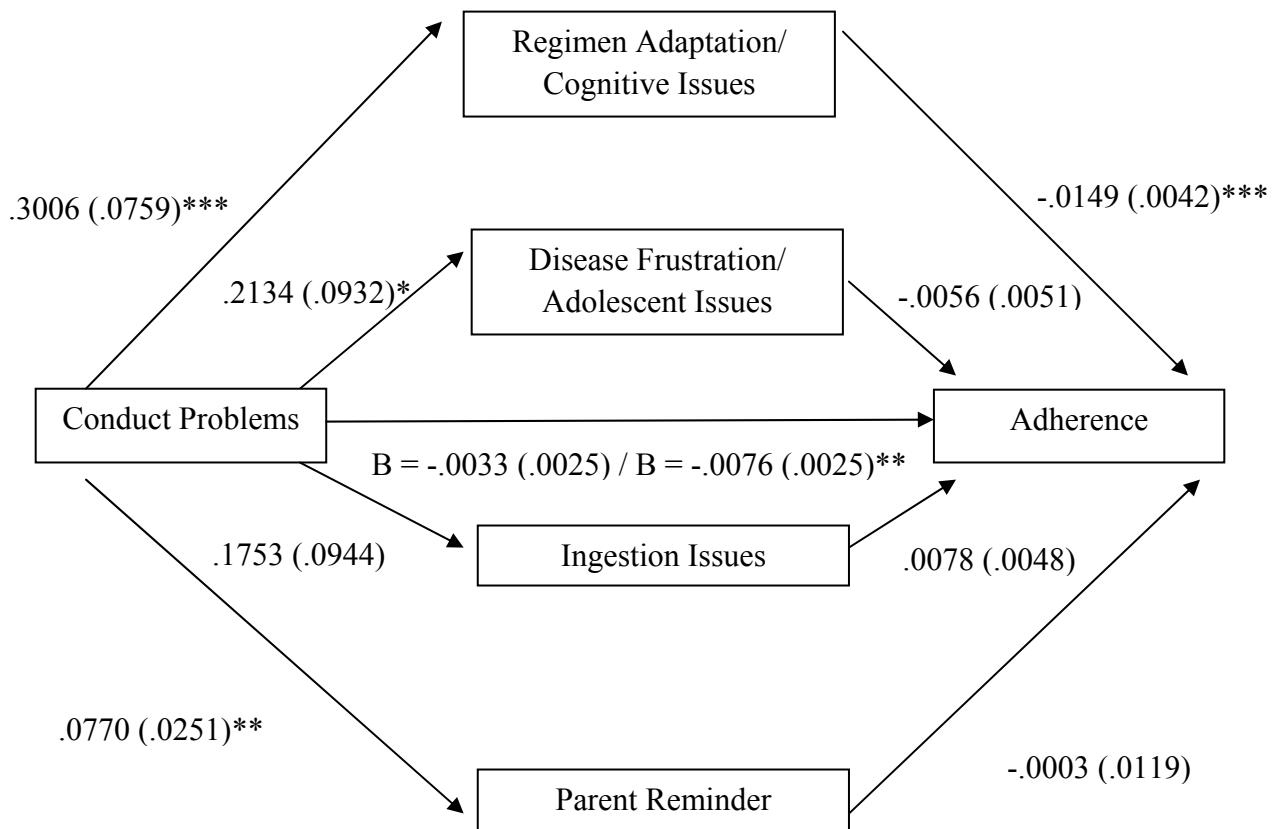
Figure 3. Parent Reported Barriers to Adherence Mediate the Effect of Conduct Problems on Parent Reported Adherence



Note. Path values represent unstandardized regression coefficients. Standard errors are in parentheses. Values before the slash represent the direct effect of conduct problems on adherence with the inclusion of the mediating variable. Values after the slash represent the total effect of conduct problems on adherence without the inclusion of the mediator. $*p < .05$;

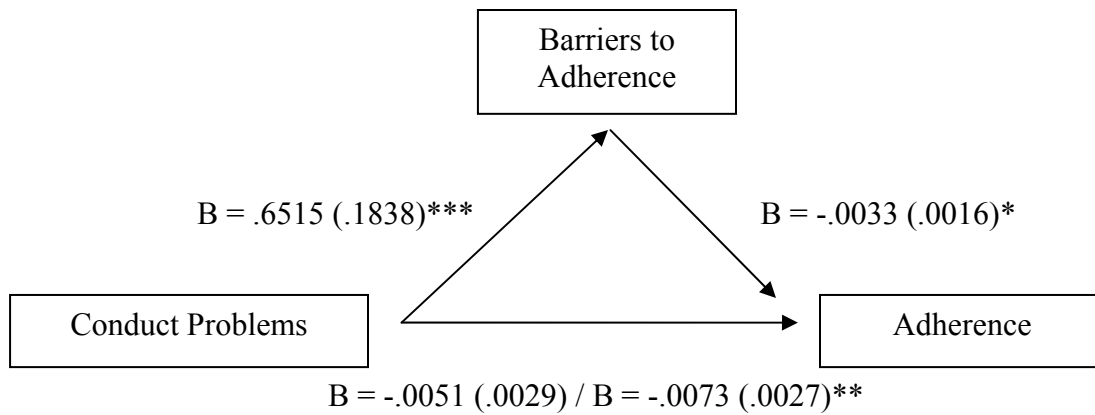
$**p < .01$; $***p < .001$

Figure 4. Parent Reported Regimen Adaptation/Cognitive Issues Mediate the Relationship between Conduct Problems and Parent Reported Adherence



Note. Path values represent unstandardized regression coefficients. Standard errors are in parentheses. Values before the slash represent the direct effect of attention problems on adherence with the inclusion of the mediating variables. Values after the slash represent the total effect of conduct problems on adherence without the inclusion of the mediator. * $p < .05$; ** $p < .01$; *** $p < .001$

Figure 5. Parent Reported Barriers to Adherence Mediate the Effect of Conduct Problems on Adolescent Reported Adherence



Note. Path values represent unstandardized regression coefficients. Standard errors are in parentheses. Values before the slash represent the direct effect of conduct problems on adherence with the inclusion of the mediating variable. Values after the slash represent the total effect of conduct problems on adherence without the inclusion of the mediator. $*p < .05$;

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

CHAPTER 4

DISCUSSION

Given the potential for negative consequences associated with nonadherence in youth with IBD, the present study sought to examine the associations between potentially modifiable symptoms of attention and conduct problems and medication adherence, with specific interest in the potential mediational role of barriers to adherence. At the bivariate level, attention and conduct symptoms were found to be related to both parent and adolescent reported adherence which builds upon past work with adolescent kidney transplant recipients demonstrating a relationship between child behavior and attention problems and lower adherence (Gerson, et al., 2004). In the current study, adolescent attention problems were negatively related to parent report of adherence and positively related to both parent and adolescent report of barriers to medication adherence. Conduct problems (e.g., rule breaking, lying, getting into trouble) were negatively related to both parent and adolescent report of adherence and positively related to parent report of barriers.

To better understand the mechanism by which higher levels of attention and conduct problems were associated with adherence, mediational analyses were conducted. When attention problems were examined, parent reported barriers mediated the relationship with parent reported, but not adolescent reported, adherence. Parent reported barriers mediated the relationship between conduct problems and both parent and adolescent reported adherence, however. Results suggest that an increase in the experience of barriers explains the relationship between attention and conduct problems and adherence in the current sample. Support for the mediational

relationship with parent reported conduct problems and barriers and adolescent reported adherence supports the validity of the findings and suggests that common reporter variance cannot be assumed to be responsible for the body of findings.

After documenting that the total scale score of the PMBS mediated the relationship between attention and conduct problems and adherence, we sought to add specificity to our findings by investigating whether subscales of the PMBS would also serve as mediators. Interestingly, one subscale, Regimen Adaptation/Cognitive Issues, emerged as significant in the two models predicting parent reported adherence. Examination of the specific items on the Regimen Adaptation/Cognitive Issues subscale (Table 4) reveals that these items measure constructs including forgetfulness, poor organizational strategies, and poor planning ahead. These barriers are face valid as to the types of barriers that we would expect youth with higher levels of conduct and, especially, attention symptoms to experience when attempting to manage a complicated medication regimen. These same adolescents may also experience difficulty managing schoolwork, chores, and multi-step commands, though the consequences of such difficulties may be less dire. Although all subscales of the PMBS except for Ingestion Issues were related to parent and adolescent-report of adherence at the bivariate level, only the Regimen Adaptation/Cognitive Issues subscale was a significant mediator in the relationship between attention and conduct problems and adherence. Results suggest that although other barriers are related to adherence, barriers loading on the Regimen Adaptation/Cognitive Issues subscale such as forgetfulness and poor organization with regards to the medical regimen account for the most variance in adherence and are an important area for research and intervention.

Similar to previously published research, we found a relationship between parent reported barriers and medication adherence (Greenley, et al., 2010; Ingerski, et al., 2010). Unexpectedly,

however, we did not find a relationship between adolescent reported barriers and adherence. It may be that parents were more adept at recognizing barriers that their adolescents experience or that adolescents were less willing to acknowledge barriers. Our hypotheses regarding a significant relationship between parent report of more barriers and poorer adherence were supported, and suggest that identification of barriers may be a point of intervention for youth experiencing higher levels of attention or conduct problems also experiencing medication nonadherence. For example, an adolescent with symptoms of attention problems might experience most difficulty with forgetting doses or planning ahead for a sleepover by packing extra doses. Assessment with an adolescent with symptoms of conduct problems might reveal defiance related to the medical regimen, medication refusal, or simply not being at home for doses. Results of the current study suggest that targeted interventions that successfully address barriers may be an effective treatment option for treating nonadherence in youth with IBD. The current study utilized a non-clinical sample experiencing average levels of attention and conduct symptoms for the most part. However, results can likely inform interventions for youth experiencing greater numbers of symptoms as well. To address Regimen Adaptation/Cognitive barriers, practitioners may help patients increase structure within the home such as a daily medication schedule or the use of a physical reminder such as a pillbox. Patients may also benefit from automatic, prescription medication refill reminders from the pharmacy. Technology also offers several solutions to difficulties with forgetting or poor organization including automatic text message reminders for cell phones. Further intervention work is needed, however, to test the development and implementation of such interventions.

Given the significant associations found with parent reported barriers, adolescents may benefit most when both parent and adolescent report of barriers to adherence are obtained.

Reliance on the adolescent's report alone may not be sufficient for identifying and addressing barriers that youth with higher levels of attention and conduct problems experience. When both parent and adolescent report are obtained, results can be used to guide collaborative discussion with parent and child on barriers that can be addressed and the most effective ways to do so at a family systems level.

Interpretation of these data must be done in light of study limitations. The use of mediational analyses should not be used to infer causation. The current study utilized cross-sectional data that prevents the inference of directionality. Longitudinal research is needed to test causal relationships between behavioral problems, barriers, and adherence. Second, the sample was primarily middle to high income, Caucasian, and limited to adolescents, which limits generalizability to youth with IBD from different ethnicities, income levels, and ages. The current sample is demographically similar in terms of ethnicity and income, however, to previous research on adolescents with IBD and is likely influenced by the fact that Caucasians are disproportionately diagnosed with IBD (Hommel, et al., 2009). Third, only self- and parent reports of adherence were utilized, which research using more objective measures of adherence suggests may be artificially elevated (Hommel, et al., 2009). Finally, mediation models examined yielded small effect sizes. Given our past research demonstrating relationships between adherence and more traditionally studied disease, family, and individual factors (Reed-Knight, et al., 2011), however, we sought to examine the contribution of less often studied factors including symptoms of attention and conduct problems and barriers. Although the demonstrated effect sizes are quantitatively small, results are meaningful in terms of suggesting risk factors for nonadherence and potential points of intervention.

Despite the acknowledged limitations, the results of the current study are an important addition to the growing body of literature on adherence in youth with IBD. Risk factors for nonadherence including attention and conduct problems and barriers were identified. More specifically, analyses demonstrated that parent reported barriers explained the relationship between attention problems and parent reported adherence as well as conduct problems and parent and adolescent reported adherence. To target barriers to adherence there are likely multiple points of intervention such as individualized problem solving, planning ahead, and communication skills. Clinically, results suggest that adolescents with IBD and comorbid attention or conduct problems may be at risk for nonadherence and may benefit from individualized assessment and treatment to target barriers.

REFERENCES

- Baron, R., & Kenny, D. (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology*, 51(6), 1173-1182. doi: 10.1037/0022-3514.51.6.1173
- Blount, R., Bunke, V., & Zaff, J. (2000). Bridging the gap between explicative and treatment research: A model and practical implications. *Journal of Clinical Psychology in Medical Settings*, 7(1), 79-90. doi: 10.1023/A:1009501604652
- Bond, G., Aiken, L., & Somerville, S. (1992). The health belief model and adolescents with insulin-dependent diabetes mellitus. *Health Psychology*, 11(3), 190-198. doi: 10.1037/0278-6133.11.3.190
- Brownbridge, G., & Fielding, D. M. (1994). Psychosocial adjustment and adherence to dialysis treatment regimes. *Pediatric Nephrology*, 8(6), 744-749. doi: 10.1007/BF00869109
- Bush, P., & Iannotti, R. (1990). A children's health belief model. *Medical Care*, 28(1), 69-86. doi: 10.1097/00005650-199001000-00008
- DiMatteo, M. (2004). Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Medical Care*, 42(3), 200-209.
- Gerson, A., Furth, S., Neu, A., & Fivush, B. (2004). Assessing associations between medication adherence and potentially modifiable psychosocial variables in pediatric kidney transplant recipients and their families. *Pediatric Transplantation*, 8(6), 543-550. doi: 10.1111/j.1399-3046.2004.00215.x

- Greenley, R., Stephens, M., Doughty, A., Raboin, T., & Kugathasan, S. (2010). Barriers to adherence among adolescents with inflammatory bowel disease. *Inflammatory Bowel Diseases*, 16(1), 36-41. doi: 10.1002/ibd.20988
- Harrison, J., Mullen, P., & Green, L. (1992). A meta-analysis of studies of the health belief model with adults. *Health Education Research*, 7(1), 107-116. doi: 10.1093/her/7.1.107
- Hauser, S., Jacobson, A., Lavori, P., Wolfsdorf, J., Herskowitz, R., Milley, J., . . . Stein, J. (1990). Adherence among children and adolescents with insulin-dependent diabetes mellitus over a four-year longitudinal follow-up: II. Immediate and long-term linkages with the family milieu. *Journal of Pediatric Psychology*, 15(4), 527-542. doi: 10.1093/jpepsy/15.4.527
- Hommel, K. A., Davis, C. M., & Baldassano, R. N. (2008). Medication adherence and quality of life in pediatric inflammatory bowel disease. *Journal of Pediatric Psychology*, 33(8), 867-874. doi: 10.1093/jpepsy/jsn022
- Hommel, K. A., Davis, C. M., & Baldassano, R. N. (2009). Objective versus subjective assessment of oral medication adherence in pediatric inflammatory bowel disease. *Inflammatory Bowel Diseases*, 15(4), 589-593. doi: 10.1002/ibd.20798
- Hommel, K. A., Denson, L. A., Crandall, W. V., & Mackner, L. M. (2008). Behavioral functioning and treatment adherence in pediatric inflammatory bowel disease: Review and recommendations for practice. *Gastroenterology & Hepatology*, 4(11), 785-791.
- Ingerski, L., Baldassano, R., Denson, L., & Hommel, K. (2010). Barriers to oral medication adherence for adolescents with inflammatory bowel disease. *Journal of Pediatric Psychology*, 35(6), 683-691. doi: 10.1093/jpepsy/jsp085

- Kane, S., Huo, D., Aikens, J., & Hanauer, S. (2003). Medication nonadherence and the outcomes of patients with quiescent ulcerative colitis. *The American Journal of Medicine*, 114(1), 39-43. doi: 10.1016/S0002-9343(02)01383-9
- Kappelman, M. D., Rifas-Shiman, S. L., Kleinman, K., Ollendorf, D., Bousvaros, A., Grand, R. J., & Finkelstein, J. A. (2007). The prevalence and geographic distribution of Crohn's disease and ulcerative colitis in the United States. *Clinical Gastroenterology and Hepatology*, 5(12), 1424-1429. doi: 10.1016/j.cgh.2007.07.012
- La Greca, A. M., & Mackey, E. R. (2009). Adherence to pediatric treatment regimens. In M. C. Roberts & R. G. Steele (Eds.), *Handbook of Pediatric Psychology* (4th ed., pp. 130-152). New York: The Guilford Press.
- MacKinnon, D., Lockwood, C., Hoffman, J., West, S., & Sheets, V. (2002). A comparison of methods to test mediation and other intervening variable effects. *Psychological Methods*, 7(1), 83-104. doi: 10.1037/1082-989X.7.1.83
- Mackner, L. M., & Crandall, W. V. (2005). Oral medication adherence in pediatric inflammatory bowel disease. *Inflammatory Bowel Diseases*, 11(11), 1006-1012. doi: 10.1097/01.MIB.0000186409.15392.54
- Mackner, L. M., Sisson, D. P., & Crandall, W. V. (2004). Review: Psychosocial issues in pediatric inflammatory bowel disease. *Journal of Pediatric Psychology*, 29(4), 243-257. doi: 10.1093/jpepsy/jsh027
- Modi, A., & Quittner, A. (2006). Barriers to treatment adherence for children with cystic fibrosis and asthma: What gets in the way? *Journal of Pediatric Psychology*, 31(8), 846-858. doi: 10.1093/jpepsy/jsj096

- Odell, S., Sander, E., Denson, L. A., Baldassano, R. N., & Hommel, K. A. (2011). The contributions of child behavioral functioning and parent distress to family functioning in pediatric Inflammatory Bowel Disease. *Journal of Clinical Psychology in Medical settings, 18*(1), 39-45. doi: 10.1007/s10880-011-9228-5
- Preacher, K., & Hayes, A. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behavior Research Methods, Instruments, & Computers, 36*(4), 717-731.
- Quittner, A. L., Modi, A. C., Lemanek, K. L., Ievers-Landis, C. E., & Rapoff, M. A. (2008). Evidence-based Assessment of Adherence to Medical Treatments in Pediatric Psychology. *Journal of Pediatric Psychology, 33*(9), 916-936.
- Reed-Knight, B., Lewis, J., & Blount, R. (2011). Association of disease, adolescent, and family factors with medication adherence in pediatric Inflammatory Bowel Disease. *Journal of Pediatric Psychology, 36*(3), 308-317. doi: 10.1093/jpepsy/jsq076
- Rey, J., Schrader, E., & Morris-Yates, A. (1992). Parent-child agreement on children's behaviours reported by the Child Behaviour Checklist (CBCL). *Journal of Adolescence, 15*(3), 219-230. doi: 10.1016/0140-1971(92)90026-2
- Reynolds, C., & Kamphaus, R. (2004). *Behavior Assessment System for Children Second Edition Manual*. Circle Pines MN: AGS Publishing.
- Sandler, R. S., & Eisen, G. M. (2000). Epidemiology of inflammatory bowel disease. In J. B. Kirsner (Ed.), *Inflammatory Bowel Disease* (pp. 89-112). Philadelphia: Saunders.
- Shaw, R., Palmer, L., Blasey, C., & Sarwal, M. (2003). A typology of non adherence in pediatric renal transplant recipients. *Pediatric Transplantation, 7*(6), 489-493. doi: 10.1046/j.1397-3142.2003.00117.x

- Simons, L. E., & Blount, R. L. (2007). Identifying barriers to medication adherence in adolescent transplant recipients. *Journal of Pediatric Psychology*, 32(7), 831-844. doi: 10.1093/jpepsy/jsm030
- Simons, L. E., McCormick, M. L., Devine, K., & Blount, R. L. (2010). Medication barriers predict adolescent transplant recipients' adherence and clinical outcomes at 18-month follow-up. *Journal of Pediatric Psychology*, 35(9), 1038-1048. doi: 10.1093/jpepsy/jsq025
- Zelikovsky, N., & Schast, A. (2008). Eliciting accurate reports of adherence in a clinical interview: Development of the Medical Adherence Measure. *Pediatric Nursing*, 34(2), 141-146.
- Zelikovsky, N., Schast, A., Palmer, J., & Meyers, K. (2008). Perceived barriers to adherence among adolescent renal transplant candidates. *Pediatric Transplantation*, 12(3), 300-308. doi: 10.1111/j.1399-3046.2007.00886.x