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The Prevalence and Epidemiology of Overweight and Obesity in Children with Inflammatory Bowel Disease

Millie D. Long, MD, MPH^{1,2}, Wallace V. Crandall, MD³, Ian H. Leibowitz, MD⁴, Lynn Duffy, MD⁴, Fernando del Rosario, MD⁵, Sandra C. Kim, MD^{2,6}, Mark J. Integlia, MD⁷, James Berman, MD⁸, John Grunow, MD⁹, Richard B. Colletti, MD¹⁰, Bess T. Schoen, MD¹¹, Ashish S. Patel, MD¹², Howard Baron, MD¹³, Esther Israel, MD¹⁴, George Russell, MD¹⁴, Sabina Ali, MD¹⁵, Hans H. Herfarth, MD^{1,2}, Christopher Martin, MSPH^{1,2}, Michael D. Kappelman, MD, MPH^{2,6}, and on behalf of the ImproveCareNow Collaborative for Pediatric IBD

¹ University of North Carolina at Chapel Hill, Department of Medicine, Division of Gastroenterology and Hepatology

² Center for Gastrointestinal Biology and Disease, Chapel Hill, NC

³ Division of Gastroenterology, Nationwide Children's Hospital, Columbus, Ohio

⁴ Inova Pediatric Digestive Disease Center, Fairfax, VA

⁵ Nemours Children's Clinic, Florida and Delaware

⁶ University of North Carolina at Chapel Hill, Department of Pediatrics, Division of Gastroenterology and Hepatology

⁷ The Barbara Bush Children's Hospital, Portland, ME

⁸ Department of Pediatrics, Loyola University, Chicago, IL

⁹ Department of Pediatrics, University of Oklahoma, Oklahoma City, OK

¹⁰ Department of Pediatrics, University of Vermont, Burlington, VT

¹¹ Department of Pediatrics, Emory University, Atlanta, GA

¹² Division of Pediatric Gastroenterology, UT Southwestern Medical Center and Children's Medical Center, Dallas, TX

¹³ Pediatric Gastroenterology Nutrition Associates, Las Vegas, NV

¹⁴ Department of Pediatrics, Massachusetts General Hospital, Boston, MA

¹⁵ Division of Gastroenterology, Children's Hospital and Research Center, Oakland, CA

Abstract

Background—Obesity is a significant public health threat to children in the United States.

Aims—1) Determine the prevalence of obesity in a multi-center cohort of children with IBD; 2) Evaluate whether overweight and obese status is associated with patient demographics or disease characteristics.

Methods—We used data from the ImproveCareNow Collaborative for pediatric IBD, a multi-center registry of children with IBD, collected between April 2007 and December 2009. Children

ages 2-18 years were classified into BMI percentiles. Bivariate analyses and multivariate logistic regression were used to compare demographic and disease characteristics by overweight (BMI>85%) and obese (BMI>95%) status.

Results—The population consisted of 1598 children with IBD. The prevalence of overweight/obese status in pediatric IBD is 23.6%, (20.0% for Crohn's disease (CD) and 30.1% for ulcerative colitis (UC) and indeterminate colitis (IC)). African American race (OR 1.64, 95% CI 1.10-2.48) and Medicaid insurance (OR 1.67, 95% CI 1.19-2.34) were positively associated with overweight/obese status. Prior IBD related surgery (OR 1.73, 95% CI 1.07-2.82) was also associated with overweight and obese status in children with CD. Other disease characteristics were not associated with overweight and obesity in children with IBD.

Conclusions—Approximately 1/5 of children with CD and 1/3 with UC are overweight or obese. Rates of obesity in UC are comparable to the general population. Obese IBD patients may have a more severe disease course, as indicated by increased need for surgery. Sociodemographic risk factors for obesity in the IBD population are similar to those in the general population.

Introduction

Across the United States, the prevalence of overweight and obese children has dramatically increased over the past decade.¹⁻² For the general population of United States children ages 2-19 during 2007-2008, 11.9% (95% CI 9.8%-13.9%) were at or above the 97th percentile, 16.9% (95% CI 14.1%-19.6%) were at or above the 95th percentile and 31.7% (95% CI 29.2%-34.1%) were at or above the 85th percentile of the BMI-for-age growth charts.³ With this increase in obesity, serious comorbid conditions such as diabetes and hypertension have also increased.⁴⁻⁶ Obese children are at increased risk for staying overweight or obese throughout adulthood.⁵⁻⁷ In addition to the general risks associated with overweight and obese status, obesity may have disease-specific risks in children with IBD. Prior studies in adults with IBD have shown increased morbidity, increased disease activity and more frequent perianal complications associated with obesity.⁸ Furthermore, obesity-related comorbidities may also contribute to long-term IBD morbidity and mortality as well as contribute to polypharmacy and possible medication interactions. Little is known about the prevalence and role of overweight and obesity among the sub-population of children with inflammatory bowel diseases (IBD).

Traditionally, children with IBD have been described as malnourished and underweight. In a previous study of body mass index (BMI) among those with juvenile onset IBD in Great Britain from 1968-1983, BMI was found to be lower than that of the general population.⁹ However, in a more recent study of North American children with newly diagnosed IBD from 2001-2005, approximately 10% of children with Crohn's disease and 20-30% of children with ulcerative colitis had a BMI consistent with overweight or at risk for overweight status at the time of IBD diagnosis.¹⁰ Rates of obesity in the treated pediatric IBD population remain unknown. Furthermore, rates of obesity within the general population have changed since this time, and such secular trends may similarly affect children with IBD.

We therefore aimed to determine the prevalence of obesity among a multi-center cohort of children with IBD and to evaluate whether overweight and obese status is associated with patient demographics or disease characteristics.

Methods

Study design

We performed a cross-sectional study of children with IBD enrolled in the ImproveCareNow collaborative for pediatric IBD. The collaborative has enrolled and prospectively followed children with previously and newly diagnosed IBD since April 2007. Demographic information was collected at the enrollment visit, and disease characteristics including weight and height, disease phenotype, medications, surgeries, presence of perirectal disease, and physician's global assessment of current disease were recorded at all visits. In this analysis, we included all patients, between the ages of 2 and 18 years of age, who were enrolled at actively participating centers (see appendix A) and had at least 2 documented visits between April 1, 2007 and December 31, 2009 in which height, weight and disease specific factors were measured and recorded. Patients were excluded if there was >10% reduction in height or >20% change in BMI at follow up visit, as this was felt to represent measurement error.

Determination of Outcome of Overweight and Obesity

Excess weight in children ages 2-19 is defined by BMI in relation to the 2000 Centers for Disease Control and Prevention (CDC) sex-specific BMI-for-age growth charts.¹¹ The most recent expert committee guidelines on childhood obesity have labeled children aged 2 through 19 years with a >95th BMI percentile as obese and children between the 85th and 95th BMI percentiles as overweight.¹² Therefore, for this study, we adapted BMI-for-age-percentiles for girls and boys ages 2-18 from the CDC percentile data values. Overweight status and obesity were defined by 3 levels: at or above the 85th percentile for BMI-for-age (overweight), at or above the 95th percentile (obese), or at or above the 97th percentile (severe obesity). These cut points have been used previously in the literature and coincide with expert guidelines.³ BMI cut points were analyzed by sub-category and also in a dichotomous fashion: overweight or obese ($\geq 85^{\text{th}}$ percentile) versus non-overweight or obese ($\leq 85^{\text{th}}$ percentile). For all children with results >97th percentile or <3rd percentile, individual sites were contacted to manually confirm height and weight measurements and units. Of the 131 records selected for auditing, only 4 errors (3%) were identified and corrected. Two charts could not be located. For each child, the most recent visit with height and weight data was used to calculate the BMI-for-age percentile.

Determination of Exposures

For each participant, demographic characteristics such as age, self-reported race, and insurance status were recorded. We additionally asked information on self-perceived ethnicity. Clinical characteristics of IBD were also obtained, including disease type [Crohn's disease (CD), Ulcerative colitis (UC) or indeterminate colitis (IC)], disease duration (defined as years from onset of disease to most current visit), disease phenotype (for CD), prior IBD related surgeries, presence of perianal disease on physical exam, and physician global assessment of disease status (inactive, mild, moderate or severe). Diagnosis of CD, UC or IC was made based on all available radiologic, pathologic and endoscopic information. Disease assessment was performed at each visit, and a diagnosis could be revised to another IBD subtype at subsequent visits. Physician global assessment has been shown to correlate with both the Pediatric Crohn's Disease Activity Index (PCDAI) and the short PCDAI in the data from this collaborative.¹³ Immunosuppressive medication use and corticosteroid use was also recorded from the most recent clinic visit where height and weight was assessed, in order to determine the effects of particular medications on BMI percentiles.

Statistical Analysis

Bivariate analyses were used to compare patient demographic characteristics and disease factors between overweight and obese children and non-overweight and obese children with both Crohn's disease (CD) and ulcerative colitis (UC) or indeterminate colitis (IC). Prevalence of various categories of BMI-for-age percentiles, including underweight, normal and overweight ranges of percentiles, in the IBD population by disease subtype were then compared. Multivariable logistic regression modeling was used to identify the independent effects of demographic and disease characteristics on overweight and obese status among children with IBD and by CD or UC/IC subtype. Variables were selected for the models a priori based on the prior literature.

For all analyses, p-values were two-sided, and a p-value of 0.05 or less was considered statistically significant. All statistical analyses were performed using STATA Version 9.0 (College Station, TX). The study protocol was approved by all sites participating in the collaborative, and informed consent was obtained if required by institutional review boards.

Results

The initial database contained data on 2042 children aged 2-18 years with IBD from actively enrolling sites. Of these, we excluded 417 children due to the lack of at least 2 separate measurements of height and weight and 46 children with >10% reduction in height, or >20% change in BMI between subsequent visits. One additional child was excluded, as there was no initial diagnosis of CD, UC or IC. Only 45 patients (2.8% of population) changed IBD subtype at subsequent visit. The final study population included 1598 children.

Table 1 demonstrates the demographic and clinical characteristics of children with CD by overweight or obese status. Those children who were overweight or obese were more likely to be of a non-Caucasian race and to have Medicaid insurance (as a marker for socioeconomic status). Younger age was also statistically associated with overweight and obese status, although the absolute magnitude of this difference was small (median 14 years versus 15 years). Table 2 shows similar characteristics among children with UC or IC. The only significant differences in this group were that overweight or obese children with UC or IC were more likely to have Medicaid insurance or to use methotrexate. There was also a non-significant increase in prednisone and infliximab use among obese or overweight children with UC/IC.

Overall, the prevalence of overweight or obesity among children with CD was 20.0%. This rate was higher (30.1%) among children with UC or IC. In the overall IBD population, the prevalence was 23.6%. Table 3 shows further breakdown of BMI-percentiles in children with CD or UC/IC. Children with UC/IC had greater rates of overweight, obese and severely obese than patients with CD. The rate of overweight and obesity in children with UC/IC more closely mirrored the reported rate in the general population. Patients with CD had relatively greater percentages of underweight children when compared to patients with UC/IC (Table 3).

Additional analyses were performed, limiting the population to only those children who were enrolled in the collaborative within 90 days of their initial IBD diagnosis (n=426, 277 with CD, 149 with UC/IC). The prevalence of overweight and obesity in this group was essentially unchanged from the entire study population, 20.9% among patients with newly diagnosed CD and 34.9% among patients newly diagnosed with UC/IC. We then investigated the population of patients who reported Hispanic ethnicity, as this is a risk factor for overweight and obesity in the general population. The prevalence of overweight and obesity for the Hispanic population with IBD was 35.2% as compared to 23.1% among

the non-Hispanic IBD population ($p=0.02$). By disease sub-type, the prevalence of overweight and obesity was 30.6% for CD and 40.0% for UC/IC in the Hispanic population. We finally performed a subanalysis further investigating any corticosteroid use. We defined any corticosteroid use as use at either the enrollment or most recent visit, in order to account for prior corticosteroid use. Among patients with CD, there was no difference in the rate of overweight and obesity (20.5% for those with any use of corticosteroids at prior or current visit, and 19.7% for non-users, $p=0.8$). A significant difference was found among patients with UC, with a rate of overweight and obesity of 35.0% for those with any use of corticosteroids at prior or current visit, as compared to 27.1% for non-users ($p=0.05$).

The independent effects via multivariate analysis of demographic and disease characteristics on overweight and obese status in children with IBD, presented overall and stratified by CD or UC/IC, are shown in table 4. On adjusted analyses for patients with IBD and among the CD population, African American race and having Medicaid insurance, rather than commercial insurance, were significantly associated with overweight and obese status. Among UC patients, the association between African American race and Medicaid insurance and overweight/obese status did not reach statistical significance. Among patients with CD, prior surgery was significantly associated with overweight and obesity (adjusted OR 1.73 95% CI 1.07-2.82). In patients with CD, thiopurine use was inversely associated with overweight and obese status (adjusted OR 0.68 95% CI 0.48-0.98). No other clinical disease characteristics were associated with overweight and obesity in children with IBD. Analyses were repeated with BMI-percentile as a continuous variable, and the independent effects of predictors were found to be similar (data not shown).

Discussion

Childhood obesity has become an epidemic in the United States, with an estimated 31.7% meeting the definition of overweight or obese.³ The results of this study indicate that a substantial proportion of children with IBD, particularly UC or IC, are also either overweight or obese. This is important, as obesity may be associated with increased complications of disease and also with long-term cardiovascular and metabolic complications. In the adult IBD population, obesity has been associated with shorter time to development of perianal complications, more active disease, and more frequent hospitalizations.⁸ Furthermore, obesity-related comorbidities may indirectly affect IBD-related morbidity and mortality, as well as increase the potential for polypharmacy and medication interactions. The pathophysiology of obesity supports the association with increased severity of disease. Obesity can be considered a chronic low-grade state of inflammation. In obesity, adipose tissue can undergo a transformation and become infiltrated by macrophages.¹⁴ In addition, many pro-inflammatory markers linked to obesity and adipose tissue (including leptin, adiponectin, resistin and ghrelin) have also been linked to IBD.¹⁵ 16 These markers may become upregulated, contributing to disease activity.

The results of this study are consistent with the results of a previously published study of newly diagnosed (untreated) CD and UC from two separate North American cohorts initiated in 2000. Kugathasan *et al* found that most children with CD or UC had a BMI percentile in the normative range. However, 10% of children with CD and 20-30% of children with UC were overweight or at risk for overweight (with new consensus definition, this would represent overweight or obese).¹⁰ In the present study of treated IBD, we found even greater rates of overweight and obesity. Similar to Kugathasan *et al*, we also found higher rates of overweight and obesity among children with UC/IC as compared to CD, although CD patients still had a 20% prevalence of overweight or obesity.

Similar to adult IBD populations,⁸ the results of this study also indicate that pediatric patients with CD who are either overweight or obese have had higher rates of IBD related surgery. In UC/IC, this trend did not reach statistical significance. These pediatric data, in combination with prior adult data, suggest that obesity in IBD may be an independent predictor of a more complicated disease course.

The early literature on pediatric IBD found associations between weight and growth retardation and juvenile onset of IBD, especially CD.⁹ Malnutrition is even a component of the most commonly used disease severity indices in CD, the Crohn's Disease Activity Index (CDAI) and the Pediatric Crohn's Disease Activity Index (PCDAI). Since the earliest descriptions of IBD, a greater number of medications have become available for treatment and both CD and UC may be recognized earlier in the course of the disease. For these reasons, malnourishment may no longer be a common manifestation of treated pediatric IBD. Rather, children with IBD may now be following the course of the rest of the population, with a greater percentage overweight or obese than ever before.

The factors we found to be associated with overweight and obesity, including non-Caucasian race and Medicaid insurance status (a proxy for lower socioeconomic status), have also been shown to be associated with overweight and obesity in the general pediatric population.³ We also found thiopurine use to be inversely associated with overweight and obesity in patients with CD. We speculate that current thiopurine use may be a marker for prior disease severity associated with malabsorption. Environmental factors such as excess energy consumption and decreased physical activity can exacerbate the tendency towards obesity in all children,⁴ regardless of chronic disease status. Appropriate lifestyle interventions for obesity, including dietary modifications and increased physical activity, are important for all overweight or obese children, including those with IBD.

Surprisingly, we found few associations between current medication use and overweight and obese status. Current prednisone use was not associated with overweight and obese status in CD, although a non-significant trend was observed in UC. Perhaps, this reflects the fact that prednisone use was reserved for the treatment of more severe disease, the population of patients which might have had the lowest BMI prior to corticosteroid initiation. Alternatively, it may only be prior use of corticosteroids that is associated with overweight and obese status, as the weight gain occurs over time. We did account for prior corticosteroid use in subanalyses (corticosteroid use at the time of enrollment or subsequent visit). We were unable to account for all prior corticosteroid use, as we only had information on current use at the time of visit. This may have contributed to the lack of association in patients with CD. We did find a significant increase in the prevalence of overweight and obesity in patients with UC/IC on prior or current corticosteroids. Of note, we also found a small and non-significant association between current infliximab use and overweight and obese status, an observation often noted in clinical practice.

There are several strengths to this multi-center study. We were able to study a large number of children with IBD, allowing for more precise estimates of BMI percentiles. The centers included in the Improve Care Now collaborative represent a mixture of private, not-for-profit, and academic centers of various sizes and from all regions of the United States, increasing the generalizability of these results. The database also contained extensive data on clinical disease characteristics, including duration of disease, phenotype, assessment of severity, and prescribed medications. Therefore, we were able to control for many potential confounders of the relationship between IBD and overweight and obese status.

There are several limitations to this study. The cross-sectional design of this analysis precludes definitive causal inferences regarding associations between BMI and specific

disease characteristics or medication utilization. In addition, confirmation of clinical variables in the database, other than anthropometrics, was beyond the scope of this study. However, we did ask sites to confirm outlying height and weight measurements, and found these to be remarkably accurate with very few errors (<3%). Also, the proportion of overweight and obesity in any given population will vary according to where the continuous variable for BMI is dichotomized. We did perform additional analyses using BMI-percentile as a continuous variable and found similar results. A priori, we chose to use standard definitions of overweight and obesity consistent with the CDC BMI-for-age growth charts. Use of other standards might result in other proportions, but would be unlikely to significantly change the independent effects of demographic and disease characteristics seen in our model.

In summary, overweight and obesity are common in pediatric IBD. Little is still known about how childhood obesity will affect the adult outcomes of patients with IBD. The results of this study have important implications for the care of children with IBD. It is important for providers to recognize that CD and UC/IC can exist in overweight and obese patients, and that the traditional description of malnourishment in pediatric IBD may no longer represent the majority of cases. Because gastroenterologists have unique expertise in nutrition and improved access to dietitians and other multidisciplinary resources, screening, counseling, and treatment for overweight and obesity should be the standard of care for the patient with IBD. Lifestyle modifications, including dietary modification and physical activity, are important for all overweight and obese children, including those with IBD. Further studies on the relationship between obesity and inflammation in the pediatric population are warranted.

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Table 1
 Characteristics of the Population of Children with Crohn's Disease by Overweight/Obesity

Characteristic	Not Overweight/Obese		Overweight/Obese		p value
	n	Median (IQR) or %	n	Median (IQR) or %	
Age (years)	822	15 (13-17)	205	14 (12-16)	<0.01
Gender (% female)	366	44.5	89	43.4	0.78
Race					
Caucasian	631	76.8	131	63.9	<0.01
African American	67	8.1	33	16.1	
Other [^]	124	15.1	41	20.0	
Insurance status					
Medicaid	97	11.8	45	22.2	<0.01
Commercial	701	85.5	151	74.4	
None/don't know	22	2.7	7	3.4	
Disease duration (years)	822	2.9 (1.4-4.9)	205	2.7 (1.3-4.8)	0.31
Perianal disease (% yes)	103	12.5	32	15.6	0.24
Prior surgery ^{**} (% yes)	87	10.6	30	14.6	0.10
Prior tube feeds (% yes)	21	2.6	5	2.4	0.93
Medications ⁺					
Prednisone (% yes)	92	11.2	25	12.2	0.69
Infliximab (% yes)	216	26.3	60	29.3	0.39
Methotrexate (% yes)	49	6.0	9	4.4	0.38
6MP/Azathioprine (%yes)	395	48.1	86	42.0	0.12
Physician Global Assessment					
Inactive	536	66.1	138	67.3	0.48
Mild	210	25.9	54	26.3	
Moderate	62	7.6	11	5.4	
Severe	3	0.4	2	1.0	
Disease phenotype					
Inflammatory	604	85.4	147	83.0	0.69
Penetrating	69	9.8	21	11.9	

Characteristic	Not Overweight/Obese		Overweight/Obese		p value
	n	Median (IQR) or %	n	Median (IQR) or %	
Obstructive	34	4.8	9	5.1	

*P value by Wilcoxon rank sum for continuous variables and by Pearson's chi squared test statistic for categorical variables

^ "Other" defined as Asian, American Indian, Alaskan Native, Native Hawaiian, Pacific Islander, more than 1 race, other or don't know

** Defined as any IBD-related surgery

+ Medications as recorded at subject's most recent visit, during which BMI was measured.

Table 2
 Characteristics of the Population of Children with Ulcerative Colitis or Indeterminate Colitis by Overweight/Obesity

Characteristic	Not Overweight/Obese		Overweight/Obese		p value
	n	Median (IQR) or %	n	Median (IQR) or %	
Age (years)	399	15 (11-16)	172	14 (11-16)	0.34
Gender (% female)	211	52.9	100	58.1	0.25
Race					
Caucasian	288	72.2	115	66.9	0.20
African American	29	7.3	20	11.6	
Other [^]	82	20.5	37	21.5	
Insurance status					
Medicaid	51	12.8	33	19.5	0.05
Commercial	336	84.4	128	75.7	
None/don't know	11	2.8	8	4.7	
Disease duration (years)	399	2.6(1.1-4.8)	172	2.2(1.0-4.4)	0.16
Perianal disease (% yes)	9	2.3	3	1.7	0.70
Prior surgery ^{**} (% yes)	18	4.5	6	3.5	0.58
Prior tube feeds (% yes)	1	0.25	2	1.2	0.17
Medications ⁺					
Prednisone (% yes)	63	15.8	35	20.4	0.19
Infliximab (% yes)	42	10.5	26	15.1	0.12
Methotrexate (% yes)	5	1.3	8	4.7	0.01
6MP/Azathioprine (% yes)	119	70.2	118	68.6	0.71
Physician Global Assessment					
Inactive	267	67.8	110	66.7	0.60
Mild	91	23.1	41	24.9	
Moderate	32	8.1	14	8.5	
Severe	4	1.0	0	0	

*P value by Wilcoxon rank sum for continuous variables and by Pearson's chi squared test statistic for categorical variables

[^] "Other" defined as Asian, American Indian, Alaskan Native, Native Hawaiian, Pacific Islander, more than 1 race, other or don't know

^{**} Defined as any IBD-related surgery

[†] Medications as recorded at subject's most recent visit, during which BMI was measured.

Table 3

BMI percentile for age in Children with IBD, stratified by Crohn's disease (CD) or Ulcerative Colitis/Indeterminate Colitis

BMI-percentile categories	Children with CD		Children with UC or IC		Total IBD, %
	n	%	n	%	
<5th	32	3.1	14	2.5	2.9
5 th -25 th	165	16.1	80	14.0	15.3
>25 th -50 th	221	21.5	104	18.2	20.3
>50 th -85 th	404	39.3	201	35.2	37.9
>85 th -95 th	131	12.8	95	16.6	14.1
>95 th -97 th	32	3.1	30	5.2	3.9
>97 th	42	4.1	47	8.2	5.6

Table 4
Independent effects of demographic and disease characteristics on overweight and obese status in children with IBD

	IBD		CD		UC/IC	
	OR*	95% CI	OR*	95% CI	OR*	95% CI
Age (years)**	0.96	0.93-1.0	0.93	0.89-0.99	0.99	0.95-1.05
Race						
White	1.0		1.0		1.0	
African American	1.64	1.10-2.48	1.74	1.07-2.95	1.66	0.84-3.29
Other	1.38	0.99-1.91	1.65	1.06-2.55	0.88	0.63-1.72
Insurance						
Commercial	1.0		1.0		1.0	
Medicaid	1.67	1.19-2.34	1.98	1.28-3.06	1.37	0.79-2.38
None/Don't know	1.40	0.71-2.78	0.85	0.31-2.39	2.30	0.83-6.41
Prior surgery%						
None	1.0		1.0		1.0	
At least 1	1.31	0.85-2.02	1.73	1.07-2.82	1.25	0.41-3.82
Disease duration (years)**	0.99	0.94-1.04	1.00	0.94-1.08	0.97	0.89-1.05
Disease severity [^]						
Inactive/mild	1.0		1.0		1.0	
Moderate/severe	0.83	0.58-1.19	0.94	0.59-1.51	0.70	0.40-1.23
Thiopurine use [#]						
No	1.0		1.0		1.0	
Yes	0.77	0.59-1.00	0.68	0.48-0.96	1.06	0.69-1.64
Infliximab use [#]						
No	1.0		1.0		1.0	
Yes	1.17	0.86-1.58	1.10	0.76-1.59	1.60	0.89-2.87
Prednisone use [#]						
No	1.0		1.0		1.0	
Yes	1.17	0.82-1.67	0.89	0.53-1.51	1.36	0.82-2.28

* Multivariate logistic regression model adjusted for age, race, insurance status, prior surgery, disease duration, disease severity, methotrexate use, thiopurine use, infliximab use and prednisone use

** Continuous, in 1 year increments

% Defined as any IBD-related surgery

^ As defined by physician global assessment

Medication use classified as no current use or use of this medication at the time of measurement of height and weight

Appendix A

Actively Enrolling Sites in the ImproveCareNow Pediatric IBD Collaborative

1. Nationwide Children's Hospital, Columbus, OH
2. Inova Pediatric Digestive Disease Center, Fairfax, VA
3. Nemours Children's Clinic
4. University of North Carolina at Chapel Hill, Chapel Hill, NC
5. The Barbara Bush Children's Hospital, Portland, ME
6. Loyola University, Chicago, IL
7. University of Oklahoma, Oklahoma City, OK
8. University of Vermont, Burlington, VT
9. Emory University, Atlanta, GA
10. Children's Medical Center of Dallas, Dallas, TX
11. Pediatric Gastroenterology & Nutrition Associates, Las Vegas, NV
12. Massachusetts General Hospital, Boston, MA
13. Oakland Children's Hospital, Oakland, CA