

HEALTHCARE DISPARITIES AND NONCOMPLIANCE IN CHILDREN AND YOUNG
ADULT'S WITH CROHN'S DISEASE

A Masters Thesis Presented

By

Robert J. McLoughlin

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The signatures of the Master's Thesis Committee signify completion and approval as to style and
content of the Thesis

Robert Goldberg PhD, Chair of Committee

Catherine Dube PhD, Member of Committee

Karim Alavi MD MPH, Member of Committee

Jeremy Aidlen MD, Member of Committee

The signature of the Dean of the Graduate School of Biomedical Sciences signifies that the
student has met all master's degree graduation requirements of the school.

Mary Ann Lane
Dean of the Graduate School of Biomedical Sciences

Program
Master of Science in Clinical Investigation

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Abstract

Objective:

Treatment compliance in children with Crohn's disease is associated with higher levels of symptom remission. We hypothesized that the management, comorbidities, and complications for children with Crohn's disease would differ based on a diagnosis of noncompliance.

Methods:

Using the Kids' Inpatient Database for 2006-2012, we identified young patients (<21 years) with a diagnosis of Crohn's disease. Diagnoses and procedures were analyzed according to a recorded diagnosis of noncompliance. Multivariable logistic regression analysis was performed to examine the association between noncompliance and the outcomes of interest.

Results:

There were 28,337 pediatric Crohn's disease hospitalizations identified with 1,028 (3.6%) hospitalizations having a diagnosis of both Crohn's disease and noncompliance. The mean age of the study population was 15.9 years and 48.9% were girls. Black patients (multivariable adjusted odds ratio, aOR,2.27; 95% CI:1.84-2.79) and those in the lowest income quartile (aOR 1.57; 95% CI:1.20-2.05) had an increased likelihood of a noncompliance diagnosis than respective comparison groups. Noncompliant patients had an increased likelihood of concurrent depression, nutritional deficiency, and anemia. Patients with a diagnosis of noncompliance had lower rates of intestinal obstruction (4.0% vs 6.3%), intraabdominal abscesses (2.0% vs 4.2%), and underwent

fewer major surgical procedures (aOR 0.40; 95% CI:0.31-0.53) and large bowel resections (aOR 0.44; 95% CI:0.31-0.64) than patients without this diagnosis.

Conclusions:

We found significant differences in socioeconomic status and race among hospitalized children with Crohn's disease with, as compared to those without, a diagnosis of noncompliance. Children with noncompliance have different comorbidities, disease-related complications, and are managed differently. Possible explanations for observed treatment differences include a reluctance to offer surgery to those with a diagnosis of noncompliance, a refusal of intervention by noncompliant patients, or implicit bias. Further investigation is warranted to better define noncompliance in this population and to determine the implications of this diagnosis.

Key words:

Crohn's disease; Noncompliance; Pediatric

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Preface:

Other works that will not be presented as part of this thesis:

Manuscripts:

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Chapter I: Introduction

Pediatric Crohn's Disease

Crohn's disease (CD), also known as regional enteritis, is an inflammatory disease which can affect any part of the gastrointestinal tract from the mouth to anus. It has a relapsing nature and frequently involves the ileum, ileum and cecum, or ileum and entire colon. In Western countries, between 20-30% of patients with CD are diagnosed before age 20 with a peak incidence of inflammatory bowel disease (IBD) occurring between the ages of 15 and 30 years [1-4]. There is some evidence that suggests that there has been an increase in the incidence of IBD worldwide over the past several decades [5-9].

Pediatric patients with CD face a more extensive and severe disease course than adults[10], coupled with unique long-term risks. With disease-related malabsorption, maldigestion, and reduced caloric intake coinciding with a developmentally critical time, young patients with CD are at high risk of osteopenia, growth failure, failure to thrive, and delayed puberty[11-13].

This clinical syndrome is associated with psychosocial complications which compound the physical manifestations. Approximately 63% of adolescents with CD meet criteria for a psychiatric disorder compared with 18% of the general adolescent population[14] with adjustment disorder, major depressive disorder, and anxiety disorders predominating at 29%, 24%, and 10% respectively[15]. CD is associated with lower quality of life in adolescents which has been directly associated with increased disease activity[16].

Treatment Noncompliance In Pediatric Crohn's Disease

Remission for patients with CD is commonly achieved and maintained through the stepwise escalation of anti-inflammatory and immunosuppressant medications (Figure 1). Medication

adherence is critical to reducing disease activity but lacks a universal definition. Adherence in this context can be defined as the extent to which patients take medications they are prescribed whereas “compliance” suggests that the patient is passively following the instructions and that the treatment plan is not necessarily equal commitment from both parties [17]. Additionally, the term persistence is used in some situations to refer to the number of days taking the prescribed medication or following the planned treatment regimen [18]. Several studies of young patients with inflammatory bowel disease (IBD) have demonstrated volitional nonadherence or noncompliance in 35% of adolescents [19]. Unfortunately, most studies cannot differentiate nonadherence from noncompliance from nonpersistence. The net outcome for noncompliance, nonadherence or nonpersistence, however, is the same – failure to follow a prescribed treatment regimen.

One study in children and adolescents with newly diagnosed IBD defined adherence as taking at least 80% of prescribed medications [20]. Analysis of prescription refill rates in pediatric CD has shown that 60% of patients do not fill at least 80% of required medications[21]. Among adherent pediatric CD patients, 80% achieve disease remission compared with 34% of non-adherent patients[21]. Among noncompliant patients with pediatric CD and ulcerative colitis (UC), 25% experience therapy escalation and 13% require hospitalization for IBD sequelae, compared to 3% and 3% of compliant patients, respectively[21]. Additionally, a study of predominately adult patients found that patients who delayed refilling their anti-tumor necrosis factor (TNF) medications by more than two days on average every two weeks significantly increased their risk of experiencing a CD flare[22]. The association between CD treatment noncompliance and medical comorbidities, complications, and surgical interventions in the pediatric CD population is poorly understood.

Overview of the Kids' Inpatient Database (KID):

The KID is the largest publicly available administrative all-payer national sampling of pediatric (≤ 20 years of age) inpatient discharges and is managed as part of the Healthcare Cost and Utilization Project (HCUP) by the Agency for Healthcare Research and Quality (AHRQ)[23]. Each iteration of the KID involves between $>3,700$ hospitals, and >6.7 million national discharges among children and adolescents aged < 21 years. The number of participating states were 38, 44, and 44 for the study years of 2006, 2009, and 2012, respectively. The KID is produced triennially and includes data from non-federal hospitals, short-term stay hospitals, academic medical centers, and specialty hospitals. Hospitals not included in the dataset are federal hospitals, rehabilitation hospitals, psychiatric hospitals, or substance treatment centers. The KID represents a sample of approximately 80% of all pediatric discharges during the years under study.

The KID contains over 100 sociodemographic and clinical variables and utilizes an International Classification of Diseases, Ninth Revision (ICD-9) classification system of both diagnoses and procedures. It also includes variables regarding payer, geographic region, hospital charges, length of stay, and hospital characteristics including size and teaching status (Figure 2). Due to the nature of the KID as a discharge-level database, patients hospitalized multiple times have multiple records in the KID.

Specific Aims:

The primary aim of this observational study was to examine, among children and young adults with CD, the characteristics of patients who received a diagnosis of treatment noncompliance as compared with those who did not. The secondary aims of the study were to evaluate the effect of noncompliance on associated comorbidities, complications, and treatment interventions. We

utilized the Kids' Inpatient Database for the years 2006, 2009, and 2012 to examine these outcomes among children and young adults (<21 years) who had a diagnosis of CD.

Chapter II: Methods

Data Source

Using the Kids' Inpatient Database (KID), a cross-sectional analysis was performed after combining the three study years of 2006, 2009, and 2012 into a single dataset.

Case Selection

Patients were identified using ICD-9 diagnosis codes related to CD. We utilized the following ICD-9 codes – 555, 555.0, 555.1, 555.2, and 555.9 in either the primary or secondary diagnostic positions. This study population was further stratified according to the ICD-9 code of V15.81 – a personal history of noncompliance with medical treatment, presenting hazards to health. To identify procedures and comorbidities, we used the ICD-9 and single-level Clinical Classifications Software (CCS) (Appendix I and II). The CCS is a diagnosis and procedure categorization scheme developed by AHRQ as part of HCUP[24].

Children and young adults with CD were excluded from the study if there was a concern for indeterminate colitis (presence of ICD-9 codes for both UC and CD), if the hospitalization involved trauma (as defined by ICD-9 E-codes), and if there were missing data from critical variables including age, gender, race, primary payer, mortality, total hospital charges, and median income quartile by zip code. If coding abnormalities in the ICD-9 codes were identified using STATA 15.0 statistical software (2017; College Station, TX), those cases were also excluded. Overall, 24.4% of cases were excluded, and the main reasons for exclusion were due to missing data on race (63.9%) and trauma (14.7%).

Trauma	2601 E Codes: Cut/pierce 2602 E Codes: Drowning/submersion 2603 E Codes: Fall 2604 E Codes: Fire/burn 2605 E Codes: Firearm
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2606 E Codes: Machinery
2607 E Codes: Motor vehicle traffic (MVT)
2608 E Codes: Pedal cyclist; not MVT
2609 E Codes: Pedestrian; not MVT
2610 E Codes: Transport; not MVT
2611 E Codes: Natural/environment
2613 E Codes: Poisoning
2614 E Codes: Struck by; against
2615 E Codes: Suffocation

Independent and Dependent Variables

Patient characteristics included age, gender, race, health insurance type, income quartile by median income by zip code, and whether the admission was elective or otherwise. Hospital course variables included the length of stay (LOS) and total hospital charges (USD\$), which were standardized to 2018 U.S. Dollar values[25]. Age was evaluated both continuously and categorically with four age groups that were defined by school-age: elementary school (<10 years, ES), middle school (11-13 years, MS), high school (14-18 years, HS) and post-high school (19-20 years). Patient location was defined as urban (central and fringe counties of ≥ 1 million population), suburban (counties in metro areas of 250k- <1 million and counties 50k - <250k), and rural (micropolitan or non-core counties). Payer information was consolidated into private, government (Medicaid, Medicare), and other. Four distinct hospital regions were defined by the U.S. Census Bureau definitions[26]. Major surgical procedure is an HCUP-defined variable in the KID indicating the presence of a major therapeutic or diagnostic procedure that occurred during hospitalization. The comorbidities and interventions assessed were defined using ICD-9 codes. The comorbidities assessed included anxiety, anemia, depression, nutritional deficiency, intestinal obstruction, perianal disease, peritonitis, peritoneal or intestinal abscess, and presence of an ostomy. The interventions examined included having either an upper gastrointestinal endoscopy (EGD) colonoscopy, vascular catheterization, or a small or large bowel resection performed, receipt of a blood transfusion, and use of supplemental parenteral or enteral nutrition.

Diagnosis	ICD-9 Code
Anemia	285.9 – Anemia 285.29 – Anemia of chronic disease 280.0 – Iron deficiency anemia secondary to chronic blood loss 280.9 – Iron deficiency anemia
Anxiety	300.0 – Anxiety states 300.00 – Anxiety state, unspecified 300.01 – Panic disorder without agoraphobia 300.02 – Generalized anxiety disorder 300.09 – Other anxiety states
Depression	311 – Depressive disorder, not elsewhere classified
Intestinal Obstruction	560.8 – Other specified intestinal obstruction 560.81 – Intestinal or peritoneal adhesions with obstruction (postoperative) (postinfection) 560.89 – Other specified intestinal obstruction 560.9 – Unspecified intestinal obstruction
Perianal Disease	565.0 – Anal fissure 565.1 – Anal fistula 566 – Abscess of anal and rectal regions
Peritonitis	567.0 – Peritonitis in infectious diseases classified elsewhere 567.2 – Other suppurative peritonitis 567.21 – Peritonitis (acute) generalized 567.29 – Other suppurative peritonitis 567.3 – Retroperitoneal infections 567.31 – Psoas muscle abscess 567.38 – Other retroperitoneal abscess 567.39 – Other retroperitoneal infections 567.8 – Other specified peritonitis
Peritoneal or Intestinal Abscess	567.22 – Peritoneal Abscess 569.5 – Abscess of intestine
Ileostomy	PRCCS 73 – Ileostomy and other enterostomy V44.2 – status post ileostomy V55.2 – Attention to ileostomy
Presence of Ileostomy	V44.2 – status post ileostomy V55.2 – Attention to ileostomy
Noncompliance	V15.81 – Personal history of noncompliance with medical treatment, present hazards to health

Procedures	PR-CCS Code (ICD-9)
Upper Gastrointestinal Endoscopy	70 – Upper gastrointestinal endoscopy, biopsy
Colonoscopy	76 – Colonoscopy and Biopsy
Vascular Catheterization	54 – Other vascular catheterization; not heart
Blood Transfusion	222 – Blood transfusion
Parenteral or Enteral Nutrition	223 – Enteral and parenteral nutrition
Any Small Bowel Resection	75 – Small bowel resection
Any Large Bowel Resection	78 – Colorectal Resection
Diagnosis	CCS Code (ICD-9)
Nutritional Deficiencies	52

Statistical Analysis

We examined differences in the distribution of categorical variables, using chi-square tests, and Student's t-test for continuous variables, between children and young adults with CD with a diagnosis of noncompliance in comparison with those who were defined as compliant. All statistical tests were two-sided with statistical significance considered as a p-value <0.05 . The data were weighted, using HCUP-provided weights, to be representative of all U.S. inpatient discharges using the STATA svy function. A multivariable logistic regression analysis was performed to assess patient characteristics (gender, race, age group, patient location, income quartile, and health insurance payer) associated with a diagnosis of noncompliance. To assess our secondary aims, separate independent multivariable logistic regression analyses were performed to examine the association between a diagnosis of noncompliance with comorbidities and interventions; this model adjusted for the following potentially confounding variables: gender, race, age group, patient location, income quartile, and health insurance payer. These factors were selected based on differences between the comparison compliant and noncompliant patient populations. All statistical analyses were performed using STATA 15.0 statistical software.

Ethical Considerations:

The Institutional Review Board at the University of Massachusetts Medical School deemed this study exempt from IRB review due to the de-identified nature of the data. In compliance with the KID data use agreement, this study does not report information where the number of observations is less than or equal to 10.

Chapter III: Results

There were a total of 28,337 pediatric hospitalizations involving CD during the three years under study (2006, 2009, and 2012). Among these, 1,028 (3.6%) hospitalizations had a diagnosis of noncompliance. The overall population of patients with a diagnosis of CD was predominately male, non-Hispanic white, resided in the South, in the highest income quartile, had private health insurance, lived in urban environments, and had a mean age of 15.9 years (Table 1). The frequency of a diagnosis of noncompliance in hospitalized children and young adults with CD slightly increased from 3.3% in 2006 to 3.9% in 2009.

Patient Characteristics Associated with A Diagnosis Of Noncompliance

In examining differences in various characteristics between children with, as compared to those without, a diagnosis of noncompliance (Table 1), boys were significantly more likely to carry a diagnosis of noncompliance, and noncompliant children were less likely to be non-Hispanic white, Asian, or Pacific Islander than girls and whites, respectively (Table 1). On the other hand, black children and young adults with CD were more likely to have a diagnosis of noncompliance than non-Hispanic white children. In addition, children in ES and MS were significantly less likely, whereas post-high school students were significantly more likely, to have a diagnosis of noncompliance. Patients with a diagnosis of noncompliance were significantly less likely to have an elective hospitalization or private health insurance. The highest proportion of those with a documented diagnosis of noncompliance was in the lowest income quartile (33.9%) (Table 1).

Comorbidities, Complications, And Interventions Associated With A Diagnosis of Noncompliance

Compared to those without a diagnosis of noncompliance, there were higher rates of anemia, anxiety, depression, and nutritional deficiency in those diagnosed with noncompliance (Table 3). The rates of intestinal obstruction and peritoneal or intestinal abscess were significantly higher in those without the noncompliance diagnosis. The rates of perianal disease and peritonitis were similar.

The rates of small bowel resection, non-cardiac vascular catheterization, and the use of enteral or parenteral nutrition were similar between the two comparison groups. Patients with the diagnosis of noncompliance underwent significantly fewer upper gastrointestinal endoscopies, colonoscopies, large bowel resections, and major surgical procedures than patients without a diagnosis of noncompliance. However, there were higher rates of blood transfusions in patients with a noncompliant diagnosis.

Logistic Regression Analysis Evaluating Factors Associated With A Diagnosis Of Noncompliance

After performing multivariable adjusted logistic regression analysis, several factors were identified as being associated with a diagnosis of noncompliance (Table 2). Males were 29% more likely than females to be diagnosed with noncompliance and post-high school aged patients were 45% more likely to receive a diagnosis of compliance compared with those in HS. Compared to non-Hispanic whites, blacks were 2.26 times (95% CI 1.83-2.77) more likely to receive a diagnosis of noncompliance. Both ES and MS patients were significantly less likely than HS patients to have received a diagnosis of noncompliance. Patients residing in suburban and rural settings were less likely to receive a diagnosis of noncompliance than those in urban settings. In evaluating the

relationship between income quartile and receiving a diagnosis of noncompliance, individuals in the lowest quartile (59%) had a higher likelihood of receiving the diagnosis compared to the highest income quartile. Patients with government health insurance were 2.34 times more likely (95% CI 1.90-2.88) to receive a diagnosis of noncompliance than those with private health insurance.

Logistic Regression Evaluating The Association Between Comorbidities, Complications, And Interventions With A Diagnosis Of Noncompliance

After multivariable adjusted logistic regression analysis, patients with a diagnosis of noncompliance had a significantly increased odds of being diagnosed with anxiety (59%), anemia (61%), depression (92%), and nutritional deficiencies (65%), but had a decreased odds of intestinal obstruction (40%), peritoneal and intestinal abscesses (41%), and having an ostomy (54%) than children and young adults without the diagnosis of noncompliance. (Table 4).

Those with a noncompliant diagnosis were significantly less likely to have undergone a major surgical procedure or a large bowel resection but had a higher odds of receiving a blood transfusion. Patients with a noncompliant diagnosis were 29% lower odds to undergo a colonoscopy than those without the diagnosis.

Chapter IV: Discussion

To the best of our knowledge, this is the first study to describe and compare the demographic characteristics of hospitalized pediatric patients in the United States with CD who received, as compared with those who did not receive, a diagnosis of noncompliance and to examine the associated comorbidities, disease-related complications, and interventions associated with this diagnosis. We found that there was an increased risk of comorbidities, complications and subsequent interventions associated with the diagnosis of noncompliance in hospitalized children and young adults with CD.

Patient Characteristics Associated With A Diagnosis Of Noncompliance

This study demonstrated that males were 29% more likely to be diagnosed with noncompliance than females (Table 2). This contrasts with one recent pediatric IBD study in which females were more non-adherent with medication than males [21]. Pediatric transplantation, another chronic disease state with a strong emphasis on medication compliance, has shown mixed results with several studies suggesting girls[27, 28] had more noncompliance while others failed to find any differences in compliance between boys and girls[29, 30]. Similarly, studies in adults with IBD have shown mixed results regarding gender differences[31, 32]. Additional longitudinal research will need to determine whether there are gender differences in noncompliance/nonadherence among the population of patients with pediatric IBD.

Studies in adults with IBD have shown that African-Americans have both lower compliance[33] and adherence[34] than non-Hispanic whites. In the present study, black children with CD were significantly more likely to receive a diagnosis of noncompliance than non-Hispanic whites. This finding is consistent with the results of the current literature among children and

young adults with other chronic diseases that have shown non-whites to be significantly more likely to be noncompliant/nonadherent than whites[29, 35, 36]. The reasons for these differences are unclear, but possible explanations include differences in socioeconomic status, access to medications or healthcare providers, health literacy, family structure, or an implicit bias in the use of the diagnosis itself. Some of these factors have been studied with tailored interventions showing improvements in compliance[35, 37], but few have addressed the possibility of implicit bias. Implicit bias refers to attitudes and ideas that are outside of one's awareness, cannot be recalled, and can be considered "unconscious." The prejudice they impart may subtly alter treatment decisions[38]. Implicit bias has been demonstrated in the management of common pediatric disease states[39], and its impact in the present study cannot be excluded.

Older patients with CD had a significantly higher likelihood of being diagnosed with noncompliance as compared to those in HS whereas children in ES and MS were significantly less likely to receive this diagnosis. We believe that this is due to the increased role of parents in managing medical therapy in the younger age groups and the reluctance of health care providers to assign a diagnosis of noncompliance to a younger child when the challenges of care might involve the parents or caregivers more than the child themselves. Our findings that older adolescents were more likely to be diagnosed as noncompliant is consistent with the existing literature indicating a significant decrease in adherence with CD medications with increasing age[20].

Comorbidities Associated with Crohn's Disease and Noncompliance

Pediatric patients with IBD who are nonadherent to prescribed medical regimens have been demonstrated to achieve lower rates of symptom remission and have more hospitalizations than

patients who are adherent [21]. The increased likelihood of being diagnosed with both anemia and non-compliance in the present study was an interesting finding. Potential explanations include symptom escalation (and/or persistence), inadequate medical therapy or other potential comorbidities. However, due to the limitations of the KID, we cannot accurately assess all factors potentially associated with anemia. Additionally, we found blood transfusions were given more frequently to patients with a noncompliance diagnosis, which was expected given their higher rates of anemia. It is possible that the higher likelihood of having depression and anxiety in the noncompliant group reflects symptomatic CD. This finding would be consistent with the existing literature which indicates that children with symptomatic CD have more severe depressive symptoms and a higher incidence of depressive mood diagnoses than children with CD not experiencing active symptoms[40].

Complications Associated with Crohn's Disease and Noncompliance

We hypothesized that patients with a diagnosis of noncompliance would have a higher prevalence of disease complications due to the failure of the medications to achieve remission of symptoms, [20]. Surprisingly, we found lower rates of intestinal obstruction and peritoneal or intestinal abscesses in the noncompliant group. One hypothesis regarding the association between obstruction and anti-TNF agents (a mainstay of CD treatment) suggests that in stricturing-type CD anti-TNF agents, such as infliximab, cause rapid luminal healing resulting in fibrosis and scarring of the bowel wall with subsequent stenosis or obstruction. An early case series[41] raised this concern, but a study analyzing two long-term observational trials found that, after multivariable analysis, infliximab was not associated with intestinal stricture or obstruction[42]. An alternative explanation is that children might preferentially be started on infliximab by providers who have

concerns about their compliance. The opportunity to directly observe the intravenous infusion of infliximab as an outpatient mitigates the risk of patients becoming noncompliant with oral medications. A limitation of the KID prevents evaluating medications taken by the patients, and so we cannot assert that the reason for lower rates of intestinal obstruction seen in the noncompliant group was from not taking anti-TNF agents but raises the opportunity for further study.

Interventions Associated With Crohn's Disease And A Diagnosis Of Noncompliance

Patients with a diagnosis of noncompliance were less likely to undergo colonoscopy, a major surgical procedure, and large bowel resection than those without the diagnosis. Generally, in CD, surgery is reserved for the management of complications or failures of medical therapy. It is surprising that noncompliant patients, who are more symptomatic, would undergo less critical interventions for which we offer two possible explanations. First, it is possible there is a reluctance on the part of providers to provide endoscopic or surgical intervention in a patient who is deemed noncompliant whether that be due to perceived higher risks associated with the intervention or due to the patient having more severe disease. Additionally, patients who carry a diagnosis of noncompliance may do so because of the refusal of medical therapy, and, by extension, they may be more likely to refuse endoscopic or surgical intervention. The lower rates of endoscopic or surgical intervention may be directly related to the diagnosis of noncompliance within that hospitalization.

Future Areas of Research

Further research in the area of treatment noncompliance within the pediatric IBD community is necessary to develop a universal definition and understanding of what entails one being

noncompliant with treatment. This will allow clinicians and researchers a universal definition from which to study clinical outcomes and ways to improve the care of children and young adults. Once a universal definition has been created, interventions and educational initiatives could be developed to reduce the rates of treatment noncompliance in this population.

Study Strengths and Limitations

The most significant advantage of this study is the utilization of the KID. It is the single largest national all-payer administrative dataset of children < 20 years of age within the United States. With over 3,500 participating hospitals, the KID is significantly larger than alternative data sources such as the Pediatric Health Information System (PHIS, ~ 45 participating hospitals) and the American College of Surgeons National Surgical Quality Improvement Program Pediatric (ACS NSQIP Peds, ~ 44 participating hospitals). The large size of the dataset allows for the study of disease states which would be challenging to study at a single institution.

There are several limitations to this study – the reliance on ICD-9 codes, absence of disease-specific variables, the impact of missing data, and the lack of a longitudinal design. Diagnoses and procedures of interest were determined using ICD-9 codes. It cannot be determined whether the comorbidities or complications were present on admission or not. Additionally, one cannot be sure how thoroughly these diagnoses were captured, and any observed change may be more reflective of increased documentation and awareness as opposed to changes in practice or management. We did observe a slight increase in the percentage of cases with a diagnosis of compliance annually from 2006 to 2012 but cannot conclude if that is due to generally increased noncompliance among pediatric CD patients or if greater awareness of billing and coding resulted in this finding. There are several disease-specific variables which would further our understanding

of these findings but are not available in the dataset. For example, there are limitations to the ICD-9 codes regarding the location of CD within the intestinal tract, and no variables indicating the severity of the disease. Furthermore, the disease duration for each patient would be a helpful metric in understanding a diagnosis of noncompliance in perspective of the patient's overall disease course. However, there are no national CD specific databases spanning multiple years to the best of our knowledge. The presence of missing data represents a significant challenge and is predominately due to individual state's decision not to include variables, particularly race. However, the prevalence of noncompliance within the excluded cases was similar to the included cases (3.6% vs. 2.9-4.8%). Finally, the KID is not a patient-level database nor longitudinal in design, and it is not possible to determine whether patients had one or multiple hospitalizations in the same year or in subsequent years with similar diagnoses, to track re-admissions, or track medication use.

Chapter V: Conclusions

A diagnosis of treatment noncompliance has a substantial impact on the care of hospitalized pediatric patients with CD. We observed significant variation in the application of this diagnosis with a predominance of blacks, urban residents, low income, and government health insured patients being labelled with this term. Additionally, there appears to be a difference in the inpatient management and interventions for those with a diagnosis of noncompliance compared to those without. The long and short-term adverse sequelae of noncompliance with medical therapy pose significant health concerns including the risk of escalation of comorbidities and disease-related complications. This highlights the importance of interventions to improve compliance and adherence in this population. Uniform guidelines should be developed to better define noncompliance and nonadherence in the pediatric IBD community. To improve care and eliminate bias, an understanding of the risks associated with these diagnoses will provide the necessary insight to ensure that these children are most effectively treated and not left behind.

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Tables:

Table 1: Patient Characteristics According to a Diagnosis of Noncompliance

	Noncompliant (n = 1,028)	Compliant (n = 27,309)	p-value
	n (%)	n(%)	
Age, mean (years, ± Std. Dev)	17.6 (3.0)	15.8 (4.6)	<0.01
School Age Groupings:			
Elementary (0-10 years)	19 (1.8)	2,543 (9.3)	<0.01
Middle School (11-13 years)	51 (5.0)	3,769 (13.8)	<0.01
High School (14-18 years)	492 (47.9)	12,827 (47.0)	0.65
Post-High School (19+ years)	466 (45.3)	8,171 (29.9)	<0.01
Male	570 (55.4)	13,915 (51.0)	0.04
Race			
Non-Hispanic White	524 (51.0)	19,684 (72.1)	<0.01
Black	381 (37.0)	4,019 (14.7)	<0.01
Hispanic	81 (7.9)	2,117 (7.8)	0.90
Asian or Pacific Islander	NR	333 (1.2)	0.02
Native American	NR	83 (0.3)	0.69
Other	35 (3.4)	1,074 (3.9)	0.56
Region			
Northeast	298 (29.0)	7,888 (28.9)	0.95
Midwest	175 (17.0)	5,166 (18.9)	0.33
South	399 (35.6)	9,687 (35.5)	0.14
West	144 (14.1)	4,148 (15.2)	0.46
Elective Admission	103 (10.1)	4,954 (18.2)	<0.01
Length of Stay, mean (days, ± Std. Dev)	5.5 (7.0)	5.5 (8.2)	0.93
Median Income Quartile by Zip Code			
1st	349 (33.9)	5,763 (21.1)	<0.01
2nd	217 (21.1)	5,845 (21.4)	0.83
3rd	249 (24.2)	6,661 (24.4)	0.92
4th	214 (20.8)	9,040 (33.1)	<0.01
Setting			
Urban	713 (69.4)	16,363 (59.9)	<0.01
Suburban	219 (21.3)	7,092 (26.0)	0.01
Rural	79 (7.7)	3,417 (12.5)	<0.01
Payer			
Private	402 (39.1)	17,972 (65.8)	<0.01
Government	476 (46.3)	6,867 (25.1)	<0.01
Other	150 (14.6)	2,471 (9.1)	<0.01
Percent of cases by year			
2006	231 (3.3)	6,744 (96.7)	0.28
2009	354 (3.6)	9,576 (96.4)	0.77
2012	443 (3.9)	10,990 (96.1)	0.21

NR = Not Reported in conjunction with data use agreement

Table 2: Logistic Regression Analysis of Factors Associated With A Diagnosis Of Noncompliance

	Odds Ratio	95% Confidence Interval
Gender		
Male	1.29	(1.08, 1.54)
Female	Reference	
Race		
Non-Hispanic White	Reference	
Black	2.26	(1.83, 2.77)
Hispanic	0.94	(0.63, 1.40)
Asian or Pacific Islander	0.26	(0.06, 1.05)
Native American	1.60	(0.38, 6.81)
Other	1.02	(0.61, 1.71)
School Age Groups		
Elementary (0-10 years)	0.19	(0.11, 0.25)
Middle School (11-13 years)	0.37	(0.24, 0.55)
High School (14-18 years)	Reference	
Post-High School (19+ years)	1.45	(1.22, 1.73)
Setting		
Urban	Reference	
Suburban	0.71	(0.57, 0.89)
Rural	0.49	(0.35, 0.68)
Median Income Quartile by Zip Code		
1st	1.59	(1.22, 2.08)
2nd	1.29	(0.98, 1.69)
3rd	1.45	(1.12, 1.89)
4th	Reference	
Payer		
Private	Reference	
Government	2.34	(1.90, 2.88)
Other	1.97	(1.53, 2.53)

Table 3: Comorbidities, Complications And Interventions Associated with A Diagnosis Of Noncompliance

	Noncompliant	Compliant
	N (%)	N (%)
Associated Comorbidities		
Anxiety	55 (5.4)	1,031 (3.8)
Anemia	380 (36.9)	6,553 (24.0)
Depression	84 (8.2)	1,109 (4.1)
Nutritional Deficiency	142 (13.8)	2,207 (8.1)
Disease-Related Complications		
Intestinal Obstruction	41 (4.0)	1,715 (6.3)
Perianal Disease	59 (5.7)	1,191 (4.4)
Peritonitis	NR (0.4)	325 (1.2)
Peritoneal/Intestinal Abscess	37 (3.6)	1,579 (5.8)
Ostomy	20 (2.0)	1,136 (4.2)
Interventions		
Upper gastrointestinal endoscopy	130 (12.7)	4,652 (17.0)
Colonoscopy	156 (15.2)	5,764 (21.1)
Vascular Catheterization	126 (12.2)	3,394 (12.4)
Blood Transfusion	105 (10.2)	1,602 (5.9)
Enteral/Parenteral Nutrition Use	114 (11.1)	3,115 (11.4)
Major Surgical Procedure	98 (9.6)	5,647 (20.7)
Small Bowel Resection	20 (1.9)	748 (2.7)
Large Bowel Resection	44 (4.3)	2,474 (9.16)

NR = Not Reported in conjunction with data use agreement

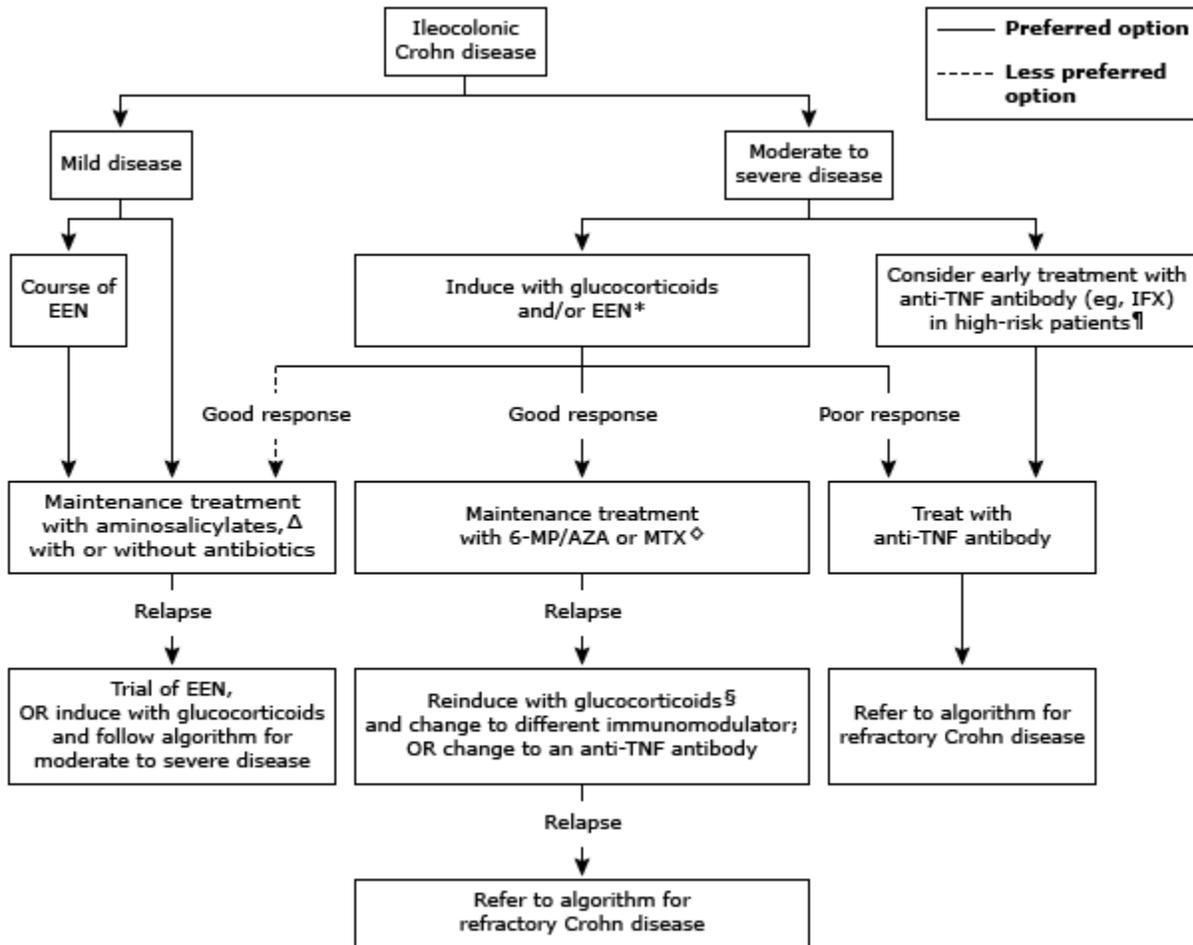
Table 4: Logistic Regression Analysis Of Comorbidities, Complications, And Interventions Associated With A Diagnosis Of Noncompliance

	Crude Odds Ratio	95% Confidence Interval	Adjusted Odds Ratio*	95% Confidence Interval
Associated Comorbidities				
Anxiety	1.45	(1.05, 2.01)	1.59	(1.12, 2.24)
Anemia	1.85	(1.57, 2.19)	1.61	(1.36, 1.92)
Depression	2.11	(1.55, 2.86)	1.92	(1.39, 2.66)
Nutritional Deficiency	1.82	(1.46, 2.28)	1.65	(1.31, 2.08)
Disease-Related Complications				
Intestinal Obstruction	0.62	(0.40, 0.94)	0.60	(0.39, 0.94)
Perianal Disease	1.34	(0.95, 1.89)	1.30	(0.91, 1.86)
Peritonitis	0.35	(0.11, 1.11)	0.36	(0.11, 1.15)
Peritoneal/Intestinal Abscess	0.61	(0.40, 0.92)	0.59	(0.38, 0.90)
Ostomy	0.47	(0.28, 0.79)	0.46	(0.26, 0.80)
Interventions				
Upper gastrointestinal endoscopy	0.71	(0.54, 0.84)	0.82	(0.63, 1.06)
Colonoscopy	0.67	(0.54, 0.84)	0.71	(0.56, 0.90)
Vascular Catheterization	0.98	(0.78, 1.24)	1.04	(0.82, 1.33)
Blood Transfusion	1.82	(1.41, 2.35)	1.57	(1.19, 2.06)
Enteral/Parenteral Nutrition Use	0.97	(0.73, 1.25)	1.14	(0.87, 1.47)
Major OR Procedure	0.41	(0.31, 0.53)	0.40	(0.31, 0.53)
Small Bowel Resection	0.69	(0.39, 1.21)	0.76	(0.43, 1.34)
Large Bowel Resection	0.45	(0.32, 0.65)	0.44	(0.31, 0.64)

*Adjusted for gender, race, age group, patient location, income quartile, and health insurance payer

Figures

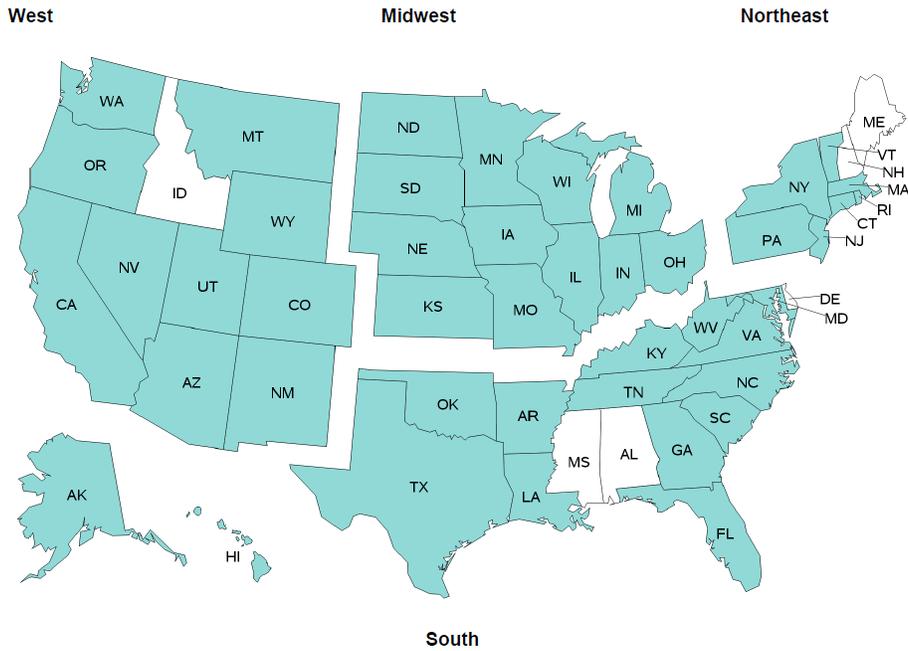
Figure 1 – Algorithm For Management Of Ileocolonic Crohn Disease In Children



Source:

<https://www-uptodate-come.ezproxy.umassmed.edu/contents/images/PEDS/64031/AlgoileocoloncCrohnchild.gif>

Figure 2 – Map of U.S. States by U.S. Census Bureau Regions



All States, by Region¹²

Region	States
1: Northeast	Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont.
2: Midwest	Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin.
3: South	Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia.
4: West	Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, Wyoming.