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Impact of Nutritional Deficiencies on Children and Young Adults with Crohn's Disease Undergoing Intraabdominal Surgery



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ABSTRACT

Purpose: We examined the impact of comorbidities on length of stay and total hospital charges for children and young adults with Crohn's Disease (CD) undergoing surgery.

Methods: Patients (<21 years) were identified with a diagnosis of CD and an intraabdominal surgery in the Kids' Inpatient Database for the years 2006, 2009 and 2012. Length of stay (LOS) and total hospital charges (THC; USD \$) were stratified by anemia, anxiety, depression and nutritional deficiency. National estimates were obtained using case weighting and multivariable linear regression was performed.

Results: We identified 3224 CD admissions with an intraabdominal surgery. The population was predominantly male, non-Hispanic white, and high school aged. There was an increase in LOS and THC for nutritional deficiency in all study years, and for depression and anemia in specific years. Multivariable linear regression revealed a 3.3–5.5 day increase in LOS associated with a comorbid diagnosis of nutritional deficiency. However, no increase in THC was seen for any comorbidity under evaluation.

Conclusions: Behavioral health and, particularly, nutritional status have a significant impact on the care of children and young adults with CD. Nutritional deficiency, anemia, and depression resulted in increased LOS for those undergoing surgery. Improved presurgical management of comorbidities may reduce LOS for these patients.

Level of evidence: III.

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Crohn's disease (CD) is a chronic inflammatory bowel disease (IBD) of relapsing and remitting nature with estimated direct costs in the United States of \$3.6 billion [1]. Pediatric patients with CD typically incur greater costs as compared to adults with CD, in part owing to the higher frequency of hospital admissions in the pediatric population [1]. Approximately 40% of pediatric CD-related hospitalization costs involve surgical interventions [1] and patients with CD who undergo surgery have increased hospital-related costs and length of hospital stay (LOS) in comparison with those who are managed medically [2].

In the general adult population, depression [3], preoperative anemia [4,5] and malnutrition [5] have been associated with increased LOS and

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cost of admission after surgery. Similarly, in adult CD patients, preoperative anemia [6], and nutritional deficiency [7] have been shown to impact the LOS and hospitalization cost. Anemia, nutritional deficiency, anxiety, and depression are commonly associated comorbidities for children who are diagnosed with CD [8]. A recent study demonstrated increased postoperative complications in pediatric CD patients with worsening degrees of malnutrition [9]. Between 41 and 75% of pediatric CD patients have anemia [10] and the majority have growth restriction secondary to nutritional deficiency [11]. Data on the prevalence of depression and anxiety in pediatric patients with CD varies widely. Studies show that pediatric CD patients who are more symptomatic report more severe depressive symptoms and have a higher incidence of formal depressive mood disorder diagnoses [8]. The impact of these frequent comorbidities on the LOS and total hospital charges (THC) has not been studied within the pediatric CD population following major surgery.

This study examines the impact of four relatively common comorbidities, nutritional deficiency, anemia, anxiety, and depression on the LOS and THC among children and adolescents with CD undergoing an intraabdominal surgery.

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1. Methods

1.1. Data source

A cross-sectional analysis was performed using the Kids' Inpatient Database (KID) for 2006, 2009, and 2012. The KID is the largest publicly available all-payer national sampling of pediatric (< 21 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) [12]. There were 38, 44, and 44 states participating in 2006, 2009, and 2012, respectively representing a sample of approximately 80% of all acute care pediatric discharges during the years under study. Owing to the conversion from ICD-9 to ICD-10, the most recent iteration of the KID (2016) was excluded to ensure coding consistency. Each iteration of the KID represents 6.7–7.6 million national discharges among children.

This study was reviewed by the Institutional Review Board at our institution and was deemed to be exempt. In compliance with the data use agreement from HCUP, this study does not report information where the number of observations is less than or equal to 10 to preserve patient confidentiality.

1.2. Case selection

Patients were identified using International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes related to CD in either the primary or secondary diagnoses (555, 555.0, 555.1, 555.2, and 555.9). ICD-9 and single-level Clinical Classifications Software (CCS) were used for the identification of procedures and comorbidities (Appendix A). The CCS is a diagnosis and procedure categorization scheme developed by AHRQ as part of the HCUP [13].

Cases were excluded if there was a concern for indeterminate colitis (ICD-9 codes for both ulcerative colitis and CD) and if there was trauma involved in the reason for hospitalization (defined by ICD-9 E-codes). Cases were excluded if there were missing data from critical variables including age, gender, race, primary payer, mortality, THC, length of stay, and income quartile per zip code. Additional cases were excluded if there were coding errors within the ICD-9 codes using a built-in STATA feature (College Station, TX). These exclusion criteria eliminated 16.5% of the 2012 KID, 22.8% in 2009, and 34.3% in 2006. The predominant reasons for exclusion were a missing race (63.9%) and trauma (14.7%).

1.3. Independent and dependent variables

LOS and THC for the hospitalization were found for each of the CD-related hospitalizations. THC are reported in USD\$ and were standardized to 2018 U.S. Dollar values, according to the U.S. Bureau of Labor Statistics [14].

Four variables were selected *a priori* by the study team that were felt to impact our patient's LOS. In our experience in this population, a child's mental health state, nutritional status, or the presence of anemia has significantly impacted the LOS. We utilized ICD-9 based definitions for nutritional deficiency, anemia, anxiety, and depression (Appendix A).

Patient characteristics included age, sex, race, and elective admission. Health insurance payer consisted of three categories: private pay (including HMO), government-supported (Medicare, Medicaid), and other. The four defined age groups were elementary school (<10 years), middle school (11–13 years), high school (14–18 years), and post-high school (19–20 years). Median household income for zip codes was classified into quartiles [15]. Hospital regions were defined by U.S. Census Bureau definitions [16]. An intraabdominal procedure was defined using ICD-9 procedure codes for any one of the following surgeries: any small bowel or large bowel resection, a diagnostic

laparotomy, creation of a colostomy or ileostomy, and an exploratory laparotomy (Appendix A).

1.4. Statistical analysis

National estimates, using HCUP-provided weights, for all U.S. inpatient discharges were generated. Bivariate analysis of categorical variables was performed using Pearson's chi-square, and continuous variables were assessed using Student's t-test. All statistical tests were two-sided with statistical significance considered as a p-value < 0.05. Two regressions models were assessed. The first unadjusted model contained all four outcomes of interest (independent variables) with the dependent variables of interest. A second adjusted was generated to assess for confounding. The adjusted model was generated using stepwise linear regression with the selection of potential confounders based on a priori assumptions. The final multivariable linear regression analysis performed controlled for confounding variables including presence of perianal disease, presence of bowel obstruction, age (as a continuous variable), race, hospital region, gender, payer, setting, income quartile, elective admission, and number of procedures during hospitalization in examining the association between comorbidities of interest with LOS and THC. Multicollinearity was assessed using variance intrinsic factor with a cutoff > 2.5 considered for significance. All analyses were performed using STATA 15.0 statistical software using the svy function.

2. Results

There were a total of 3,224 pediatric hospital admissions for children and young adults with CD undergoing an abdominal surgical procedure in 2006, 2009 and 2012. The patients were predominantly male, non-Hispanic white, admitted to a hospital in the South, high school-aged, and had private health insurance (Table 1). Mean age was approxi-

Table 1Patient characteristics and demographics.

| | 2006 | 2009 | 2012 | p-value | |
|-----------------------------|------------|-------------|--------------|---------|--|
| | n (%) | n (%) | n (%) | | |
| Total | 766 | 1,073 | 1,385 | | |
| Age, mean (years, \pm Std | 16.6 (3.3) | 16.7 (3.5) | 16.6 (3.8) | | |
| Dev.) | | | | | |
| School Age Category | | | | | |
| Elementary School | 26 (3.4) | 31 (2.9) | 47 (3.4) | 0.81 | |
| Middle School | 78 (10.2) | 123 (11.4) | 162 (11.7) | 0.73 | |
| High School | 420 (54.9) | 567 (52.8) | 738 (53.3) | 0.80 | |
| Post-High School | 241 (31.4) | 353 (32.9) | 438 (31.6) | 0.88 | |
| Male | 453 (59.2) | 624 (58.2) | 796 (57.5) | 0.84 | |
| Race | | | | | |
| Non-Hispanic White | 611 (79.8) | 816 (76.0) | 1,037 (74.9) | 0.22 | |
| Black | 92 (12.0) | 161 (15.0) | 198 (14.3) | 0.37 | |
| Hispanic | 30 (3.9) | 49 (4.6) | 73 (5.3) | 0.61 | |
| Asian or Pacific Islander | 5 (0.6) | 5 (0.5) | 14 (1.0) | 0.52 | |
| Native American | 2 (0.2) | 4 (0.4) | 3 (0.2) | 0.83 | |
| Other | 27 (3.5) | 38 (3.6) | 59 (4.3) | 0.78 | |
| Hospital Region | | | | | |
| Northeast | 232 (30.3) | 311 (29.0) | 339 (24.5) | 0.50 | |
| Midwest | 127 (16.5) | 228 (21.2) | 332 (24.0) | 0.31 | |
| South | 295 (38.5) | 330 (30.7) | 505 (36.5) | 0.26 | |
| West | 91 (11.9) | 169 (15.8) | 208 (15.1) | 0.47 | |
| Elective Admission | 317 (41.7) | 506 (47.2) | 720 (52.2) | 0.01 | |
| Length of Stay, mean (days, | 10.1 (9.9) | 10.1 (13.5) | 9.7 (13.2) | | |
| ± Std Dev.) | , , | , , | , , | | |
| Hospital Charges, Mean USD | \$68,792 | \$85,909 | \$93,037 | | |
| $(\pm \text{ Std Dev.})$ | (\$77,764) | (\$127,656) | (\$169,334) | | |
| Type of Primary Insurance | | | | | |
| Private | 582 (76.1) | 767 (71.4) | 1,039 (75.0) | 0.24 | |
| Government | 127 (16.6) | 225 (20.9) | 251 (18.1) | 0.24 | |
| Other | 56 (7.4) | 82 (7.7) | 95 (6.8) | 0.83 | |
| Anemia | 129 (16.8) | 256 (23.8) | 311 (22.4) | 0.02 | |
| Anxiety | 9 (1.2) | 26 (2.4) | 66 (4.8) | 0.00 | |
| Depression | 22 (2.8) | 15 (1.4) | 48 (3.5) | 0.04 | |
| Nutritional Deficiency | 71 (9.2) | 131 (12.2) | 170 (12.3) | 0.25 | |

mately 16.6 years and did not vary significantly by year. LOS was similar across all three years (10 days). THC ranged from \$68,792 in 2006 to \$93,037 in 2012. Anemia was present in approximately 20% (range 16.8–23.8%), nutritional deficiencies in 11% (range 9.2–12.3), anxiety in 3% (range 1.2–4.8%), and depression in more than 2% of patients (range 1.4–3.5%). Increases were observed in the prevalence of nutritional deficiencies, anemia, anxiety, and depression between 2006 and 2012. There was a decrease in the proportion of patients who were between 14 and 18 years old with a concomitant increase in middle school-aged patients.

2.1. Relationship of comorbidities on mean length of stay

There was a significant increase in the mean LOS for patients who underwent an abdominal surgical procedure when there was a comorbid diagnosis of nutritional deficiency, depression (2006 only) or anemia (2009, 2012 only) compared to those without these comorbidities. The difference in the LOS between those with and without nutritional deficiency increased from approximately seven days to ten days from 2006 to 2012 (Table 2). Patients with a comorbid diagnosis of anemia experienced an increase in the mean LOS from approximately four days to five days from 2009 to 2012. There was no difference in LOS with a comorbid diagnosis of anxiety for patients with CD undergoing abdominal surgery. A significant increase in the LOS of 4.6–6.6 days was demonstrated in both 2006 and 2012 for a comorbid diagnosis of depression.

2.2. Relationship of comorbidities on mean Total Hospital charges

In evaluating THC, the presence of nutritional deficiency was associated with a significant increase in THC with a more than doubling of the charge difference compared with those without nutritional deficiencies from \$42,000 (2006) to over \$92,000 (2012). There was a significant increase in THC associated with a comorbid anemia diagnosis with an more than 50% increase in the difference in THC from 2009 to 2012 compared to those without a diagnosis of anemia. There were no significant differences in THC related to a diagnosis of anxiety in any of the years studied. A comorbid diagnosis of depression was associated with statistically significant increased THC by more than \$50,000 in 2006 only.

2.3. Multivariable analysis of the impact of the comorbidities on LOS

Multivariable linear regression analysis was performed to assess the effect of the comorbidities understudy on the LOS after adjusting for

potential confounders (Table 3). A nutritional deficiency was associated with a 3.3–5.5 day increase in the LOS during the study period after adjusting for confounders, including anemia, anxiety, bowel obstruction, perianal disease, and depression. No difference was seen in LOS for either anxiety or anemia in the adjusted model for any of the years studied. For children and young adults with CD and a comorbid diagnosis of depression, there was an increase in the LOS of approximately three days in 2006, but there was no statistically significant difference in 2009 or 2012.

2.4. Multivariable analysis of the impact of the comorbidities on total hospital charges

The same multivariate linear regression analysis was performed to assess the impact of the comorbidities understudy on THC (Table 4). While there were differences in THC observed in the crude linear regressions, there was no statistically significant difference in THC for nutritional deficiencies, anxiety, anemia or depression for the adjusted model in any of the years under study.

3. Discussion

In this study, the presence of a concomitant diagnosis of nutritional deficiency in a pediatric patient with CD undergoing an intraabdominal surgical procedure results in increased length of stay during inpatient admissions, after adjusting for confounders. However, no differences were seen in the THC for nutritional deficiencies, or for length of stay or total hospital charges for anxiety, anemia, and depression.

Prior research has shown that pediatric CD patients undergoing surgery have longer hospitalization by four days and almost double the hospital charges compared to those not undergoing surgery [17]. However, there has been limited literature evaluating how comorbidities associated with CD impact the LOS or THC incurred during these surgical hospitalizations for CD.

3.1. The impact of nutritional deficiencies

Nutritional deficiency in children with CD was associated with an adjusted, increased LOS of 3.3 days in 2006, 5.5-days in 2009 and 3.8 days in 2012 when compared to those without nutritional deficiencies. Nutritional deficiency or malnutrition in pediatric abdominal and thoracic surgery, as well as pediatric CD patients, has been

Table 2Means of length of stay and total hospital charge of all hospitalizations for patient's with Crohn's disease.

| Undergoing Intraabdominal Surgery by Comorbid Risk Factor | | | | | | | | | | |
|---|-----|-----------|-----------|---------|-----------|-----------|---------|-----------|-----------|---------|
| Calendar Year | | 2006 | | | 2009 | | | 2012 | | |
| | | Mean | Std. Dev. | p value | Mean | Std. Dev. | p value | Mean | Std. Dev. | p value |
| Length of Stay (days) | | | | | | | | | | |
| Nutritional Deficiency | Yes | 16.3 | 11.9 | < 0.01 | 18.3 | 25.2 | < 0.01 | 18.5 | 24.3 | < 0.01 |
| _ | No | 9.2 | 9.8 | | 8.8 | 9.8 | | 8.5 | 9.3 | |
| Anemia | Yes | 10.7 | 8.7 | 0.22 | 13.0 | 13.0 | < 0.01 | 13.5 | 14.9 | < 0.01 |
| | No | 9.7 | 10.6 | | 9.0 | 13.0 | | 8.6 | 11.8 | |
| Anxiety | Yes | 10.6 | 5.1 | 0.68 | 9.4 | 7.4 | 0.74 | 12.1 | 12.4 | 0.10 |
| • | No | 9.8 | 10.4 | | 9.9 | 13.2 | | 9.6 | 12.8 | |
| Depression | Yes | 16.3 | 9.7 | < 0.01 | 15.6 | 13.0 | 0.26 | 14.1 | 14.6 | 0.19 |
| | No | 9.7 | 10.3 | | 9.8 | 13.1 | | 9.5 | 12.7 | |
| Total Hospital Charge (\$) | | | | | | | | | | |
| Nutritional Deficiency | Yes | \$105.531 | \$82,340 | < 0.01 | \$139,753 | \$158,386 | < 0.01 | \$173,968 | \$256,192 | < 0.01 |
| - | No | \$63,500 | \$79,958 | | \$77,293 | \$116,217 | | \$81,741 | \$141,810 | |
| Anemia | Yes | \$78,105 | \$70,187 | 0.10 | \$108,800 | \$123,302 | < 0.01 | \$131,348 | \$210,726 | < 0.01 |
| | No | \$65,271 | \$82,288 | | \$77,388 | \$123,214 | | \$81,952 | \$145,449 | |
| Anxiety | Yes | \$69,036 | \$55,924 | 0.93 | \$75,446 | \$52,595 | 0.39 | \$109,344 | \$131,668 | 0.33 |
| - | No | \$67,397 | \$80,908 | | \$84,878 | \$125,471 | | \$92,217 | \$166,044 | |
| Depression | Yes | \$117,965 | \$99,109 | 0.02 | \$131,613 | \$164,052 | 0.26 | \$153,096 | \$350,031 | 0.19 |
| - | No | \$66,027 | \$79,424 | | \$84,024 | \$123,478 | | \$90,873 | \$153,508 | |

Table 3Linear regression model for impact of comorbidities on length of stay by year.

| Year/Comorbidity | Outcome: Length of Stay (days) | | | | | | | | |
|------------------------|--------------------------------|--------|-----------------------|---------|---------------------|--------|-----|---------|--|
| | Unadjusted | | Adjusted ^a | | | | | | |
| | Regression Estimate | 95% CI | | p value | Regression Estimate | 95% CI | | p value | |
| 2006 | | | | | | | | | |
| Nutritional Deficiency | 7.1 | 4.7 | 9.6 | < 0.001 | 3.3 | 0.8 | 5.8 | 0.009 | |
| Anemia | 0.5 | -3.2 | 4.3 | 0.784 | 0.0 | -3.4 | 3.6 | 0.982 | |
| Anxiety | 0.0 | -1.6 | 1.7 | 0.982 | -1.2 | -2.6 | 0.3 | 0.126 | |
| Depression | 6.6 | 2.7 | 10.5 | 0.001 | 2.7 | 0.1 | 5.4 | 0.043 | |
| 2009 | | | | | | | | | |
| Nutritional Deficiency | 8.7 | 4.0 | 13.4 | < 0.001 | 5.5 | 1.4 | 9.5 | 0.008 | |
| Anemia | -1.9 | -5.2 | 1.4 | 0.261 | -1.1 | -4.2 | 2.1 | 0.510 | |
| Anxiety | 2.5 | 0.3 | 4.6 | 0.024 | 0.0 | -2.3 | 2.4 | 0.976 | |
| Depression | 2.3 | -4.1 | 8.7 | 0.486 | -1.7 | -6.0 | 2.7 | 0.457 | |
| 2012 | | | | | | | | | |
| Nutritional Deficiency | 8.8 | 4.6 | 13.0 | < 0.001 | 3.8 | 0.9 | 6.7 | 0.010 | |
| Anemia | -0.1 | -2.8 | 2.5 | 0.928 | 0.5 | -1.8 | 2.8 | 0.677 | |
| Anxiety | 2.8 | 0.5 | 5.1 | 0.018 | 0.4 | -1.9 | 2.6 | 0.759 | |
| Depression | 3.0 | -1.2 | 7.2 | 0.160 | 1.8 | -1.1 | 4.7 | 0.228 | |

^a Adjusted for presence of perianal disease, presence of bowel obstruction, age, race, hospital region, gender, payer, setting, income quartile, elective admission, and the number of procedures during hospitalization.

associated with an increased risk of 30-day postoperative complications [9,18]. To date, there have been no substantial studies assessing the role of total parenteral nutrition (TPN) in the preoperative period for pediatric patients with CD. As previously discussed, owing to the limitations of the KID, we are unable to tell whether the nutritional deficiency was present before the major surgical procedure. Additionally, it is possible that children with CD are being admitted before the surgical intervention to receive nutritional supplementation because of a known nutritional deficiency. One potential confounding factor in this population is the use of steroids in the management of CD during critical growth periods which can prematurely close growth plates, and lead to inaccurate assessment of nutritional deficiencies when performing nutritional assessments using Z-scores. Unfortunately, the KID does not report on steroid use, either as an inpatient or as an outpatient, so we cannot evaluate the impact of steroids on premature growth plate closure and potential impact on Z-score analysis. Aggressive outpatient preoperative management of these comorbidities with enteral supplementation or parenteral nutrition would perhaps result in a reduction of the LOS and presumably THC. Further research into the role of perioperative parenteral nutrition or nutritional optimization for children and adolescents with CD is warranted.

3.2. The impact of anemia

In this study, after adjusting for confounders, no difference was seen in LOS or THC for the diagnosis of anemia. To the best of our knowledge, there are no existing studies assessing the impact of anemia on LOS or THC in pediatric patients with CD (or IBD as a whole) undergoing surgery. However, in adult IBD patients undergoing a surgical procedure, anemia was shown to increase the LOS by approximately four days [6]. The findings in this study differ from those found in the adult population, which might be because of the nature of the study. We assessed several factors via one model, and while may anemia may play a role in increasing LOS/THC, a difference might not have been seen owing to other factors playing a more significant role. Owing to the limitations of the KID, the exact etiology of the anemia is difficult to assess or whether it was pre- or postprocedural. Prospective research is needed to understand any potential impact a diagnosis of anemia might have on LOS

and THC for hospitalizations involving intraabdominal surgery in children and young adults with CD.

3.3. The impact of mental health comorbidities

Psychiatric comorbidities of children with CD, such as anxiety and depression, have been shown to be associated with increased rates of readmission [19] but have not been studied for their impact on a hospitalization involving an intraabdominal surgery. This study demonstrated that depression, but not anxiety, was associated with increased LOS within the 2006 KID. This association was not observed to significance for either anxiety or depression in the 2009 or 2012 KID. It is unclear the reason this increase was not seen in 2009 or 2012, but the rise in prevalence of both comorbidities from 2006 to 2012 may reflect an increase in diagnosis and awareness, which may have influenced management. Perioperative assessment and intervention for mental health illnesses associated with CD will likely not only improve the quality of life experienced by these children with CD but also may reduce the LOS associated with their care.

3.4. Economic burden of the comorbidities

In the general adult surgical population, depression [3], anemia [4], and malnutrition [20] are associated with increased THC, but this has not been explicitly studied within the pediatric CD population. A Dutch study of hospitalized children demonstrated that gastrointestinal disease-related acute and chronic malnutrition were associated with an additional 11% and 9% cost increase respectively [21]. In a U.S. study, pediatric patients with CD undergoing surgery had higher hospital charges by \$9758 than nonsurgical pediatric CD patients, but this did not assess for the presence of comorbidities [18]. In this study, a diagnosis of nutritional deficiency was captured in between 9 and 12% of the 3224 total hospitalizations and was responsible for approximately US \$26.8 million in projected increased inpatient hospital charges for children and young adults undergoing intraabdominal surgery during their inpatient hospitalization. It is interesting that we did not find an increase in THC associated with nutritional deficiencies after adjusting for confounders. It is likely that there are a multitude of factors influencing THC for which this large administrative database is not able to fully investigate. These might include that the patient underwent a staged procedure and

Table 4Linear regression model for impact of comorbidities on total hospital charge by year.

| Year/Comorbidity | Outcome: Total Hospital Charge (\$) | | | | | | | | |
|------------------------|-------------------------------------|-----------|-----------|-----------------------|---------------------|-----------|-----------|---------|--|
| | Unadjusted | | | Adjusted ^a | | | | | |
| | Regression Estimate | 95% CI | | p value | Regression Estimate | 95% CI | | p value | |
| 2006 | | | | | | | | | |
| Nutritional Deficiency | \$40,857 | \$22,141 | \$59,573 | < 0.001 | \$15,413 | -\$2,823 | \$33,649 | 0.098 | |
| Anemia | \$930 | -\$35,969 | \$37,829 | 0.961 | \$2,786 | -\$25,286 | \$30,857 | 0.846 | |
| Anxiety | \$6,448 | -\$7323 | \$20,219 | 0.359 | -\$1429 | -\$12,293 | \$9434 | 0.796 | |
| Depression | \$50,749 | \$4,634 | \$96,864 | 0.031 | \$23,774 | -\$7,739 | \$55,282 | 0.139 | |
| 2009 | | | | | | | | | |
| Nutritional Deficiency | \$55,065 | \$23,938 | \$86,192 | 0.001 | \$16,638 | -\$11,899 | \$45,175 | 0.253 | |
| Anemia | -\$19,467 | -\$43,582 | \$4,649 | 0.114 | -\$12,642 | -\$40,524 | \$15,239 | 0.374 | |
| Anxiety | \$22,177 | \$3,099 | \$41,254 | 0.023 | -\$2,619 | -\$21,775 | \$16,536 | 0.789 | |
| Depression | \$24,809 | -\$59,222 | \$108,841 | 0.563 | -\$8,749 | -\$62,565 | \$45,067 | 0.750 | |
| 2012 | | | | | | | | | |
| Nutritional Deficiency | \$79,488 | \$34,196 | \$124,780 | 0.001 | \$9,047 | -\$31,529 | \$49,263 | 0.662 | |
| Anemia | -\$14,597 | -\$50,522 | \$21,329 | 0.426 | -\$14,068 | -\$50,374 | \$22,081 | 0.445 | |
| Anxiety | \$29,887 | \$559 | \$59,214 | 0.046 | \$4,518 | -\$20,785 | \$29,860 | 0.727 | |
| Depression | \$51,419 | -\$49,862 | \$152,701 | 0.320 | \$33,120 | -\$45,755 | \$111,574 | 0.408 | |

^a Adjusted for presence of perianal disease, presence of bowel obstruction, age, race, hospital region, gender, payer, setting, income quartile, elective admission, and the number of procedures during hospitalization.

thus had multiple shorter hospitalizations which are not fully captured or linked here. Additionally, it is possible that a component of the patient's care, such as the use of TPN, has been shifted to an outpatient setting from an inpatient setting, and these costs are not captured in an inpatient database. Further research will be needed to understand better the role that common comorbidities associated with CD play during inpatient admissions involving intraabdominal surgery.

3.5. Study strengths, potential confounders, and limitations

The most significant strength of this study is the utilization of the KID and its sampling nature. It represents the single largest national all-payer dataset of children < 21 years of age within the United States. With more than 3500 participating hospitals, the KID is significantly larger than alternative data sources such as the Pediatric Health Information System, and the American College of Surgeons National Surgical Quality Improvement Program Pediatric. The size of the KID allows for a robust analysis of a variety of conditions. The adjusted model we used in this study demonstrated no concern for collinearity and included confounders that prior research has shown to impact both LOS and THC during hospitalizations for children and young adults with CD. Perianal disease was included because it has been previously demonstrated to increase LOS, cost, and surgical interventions [22]. Bowel obstruction was included owing to the study team's experience with this factor extending LOS, and potentially THC. The inclusion of these factors strengthens our findings that nutritional deficiencies play a significant role in an inpatient admission for a child with CD undergoing intraabdominal surgery.

The present study has some limitations. Firstly, ICD-9 codes were utilized to determine the presence of the comorbidities of interest in the study population, and it cannot be determined whether these comorbidities were present on admission and before the surgical procedure, or if they manifested in the postoperative period. The timing of the diagnosis relative to the surgical procedure has the potential for significant implications. Second, it cannot be determined how thoroughly these comorbidities were documented, and the rise in prevalence observed may be more reflective of increased documentation and awareness as opposed to increased prevalence. However, other longitudinal studies are subject to the same risk. Additionally, each institution and practitioner

may document and diagnose these comorbidities differently. For example, nutritional deficiency is often diagnosed based on weight changes, biomarkers (such as transferrin, albumin, prealbumin), anthropometric measurements, and Z-score calculation but it is unclear how each diagnosis was reached. Moreover, owing to the potential for variability with regards to each practitioners and institution's characterization of protein-calorie and vitamin deficiencies, and recoding of such in hospital records, we are limited in our ability to comment on the presence, magnitude, severity and duration of these disorders among patients included in the database. One, therefore, needs to be careful in the interpretation of the present findings. A further limitation of this research is the use of a pooled variable for nutritional deficiency. The authors did not feel that any single available variable accurately represented malnutrition or nutritional deficiency in the study cohort. Therefore, we chose to utilize the HCUP definition of nutritional deficiency which was designed to assist with the analysis of complex disease states where a large number of related ICD-9 codes are consolidated into a smaller number of clinically relevant categories. There are several disease-specific variables, not available in the dataset, which would further our understanding of our findings. For example, there are limitations to the ICD-9 codes regarding the location of CD within the intestinal tract, and no variables were available which would indicate the phenotype of CD or the severity of the disease. Additionally, information about the duration of each patient's disease would be a helpful metric in further understanding the impact of the nutritional deficiencies and other conditions on hospitalizations involving surgery. Finally, the KID is not a patient-level database, and it is not possible to determine whether patients had multiple hospitalizations over time.

4. Conclusions

A comorbid diagnosis of nutritional deficiencies during a hospitalization involving a major intraabdominal surgical procedure can have a significant impact on LOS for children and young adults with CD. It is important to consider associated comorbidities carefully when counseling patients and families regarding perioperative expectations. Preoperative and elective management of nutritional deficiency, anemia, anxiety, and depression may help reduce the length of stay for children with CD who undergo surgery.

Appendix A

| Exclusion Criteria | for Trauma: | | |
|---|--|--|--|
| Trauma | 2601 E Codes: Cut/pierce 2602 E Codes: Drowning/submersion 2603 E Codes: Fall 2604 E Codes: Fire/burn 2605 E Codes: Firearm 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 | | |
| Diagnosis | 2615 E Codes: Suffocation ICD-9 Code | | |
| Anemia Anxiety Depression Perianal disease Bowel Obstruction Procedure | 285.9, 285.29, 280.0, 280.9 300.0, 300.00, 300.01, 300.02, 300.09 311 565.0, 565.1, 566 560.8, 560.81, 560.89, 560.9 ICD-9 Code | | |
| Diagnostic Laparot Procedure | comy 54.21 CCS Code (<i>ICD</i> -9) | | |
| Exploratory Laparotomy Ileostomy Creation | 89 73 (46.20 46.21 46.22 46.23 46.24 46.31 46.32 46.39) | | |
| Colostomy Creation | 72 (46.10 46.11 46.12 46.13 46.14) | | |
| Small Bowel Resection Large Bowel Resection | 75 (45.61 45.62 45.63) 78 (17.31 17.32 17.33 17.34 17.35 17.36 17.39 45.71 45.72 45.73 45.74 45.75 45.76 45.79 45.8 45.81 45.82 45.83 48.40 48.41 48.42 48.43 48.49 48.5 48.50 48.51 48.52 48.59 48.61 48.62 48.63 48.64 48.65 48.69) | | |
| Diagnosis | CCS Code (ICD-9) | | |
| Nutritional Deficiencies | 52 (260, 261, 262, 263.0, 263.1, 263.2, 263.8, 263.9, 264.0, 264.1, 264.2, 264.3, 264.4, 264.5, 264.6, 264.7, 264.8, 264.9, 265.0, 265.1, 265.2, 266.0, 266.1, 266.2, 266.9, 267, 268.0, 268.1, 268.2, 268.9, 269.0, 269.1, 269.2, 269.3, 269.8, 269.9, 799.4, V12.1) | | |

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