## Title

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# Depression Predicts Prolonged Length of Hospital Stay in Pediatric Inflammatory Bowel Disease

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## Abstract

**Objective—**Few studies report the impact of depression on inflammatory bowel disease (IBD)-related hospitalizations. We evaluated the association between depression and pediatric IBD-related hospitalizations. Our primary aim was to test the hypothesis that depression is associated with hospital length of stay (LOS); our secondary goal was to evaluate if patients with depression are at higher risk for undergoing additional imaging and procedures.

**Methods—**Data were extracted from the 2012 Kids Inpatient Database (KID), the largest nationally representative publicly available all-payer pediatric inpatient cross-sectional database in the United States. Hospitalizations for patients less than 21 years with a primary diagnosis Crohn disease (CD) or ulcerative colitis (UC) by *ICD-9* code were included. Multivariable logistic regression was used to predict long LOS controlling for patient- and hospital-level variables and for potential disease confounders.

**Results—**For primary IBD-related hospitalizations (N = 8222), depression was associated with prolonged LOS (odds ratio [OR] 1.50; 95% confidence interval [CI] 1.19–1.90) and total parenteral nutrition use (OR 1.54; 95% CI 1.04–2.27). Depression was not associated with increased likelihood of surgery (OR 0.97; 95% CI 0.72–1.30), endoscopy (OR 0.91; 95% CI 0.74–1.14), blood transfusion (OR 0.85; 95% CI 0.58–1.23), or abdominal imaging (OR 1.15; 95% CI 0.53–2.53).

**Conclusions—**Depression is associated with prolonged LOS in pediatric patients with IBD, even when controlling for gastrointestinal disease severity. Future research evaluating the efficacy of standardized depression screening and early intervention may be beneficial to improving inpatient outcomes in this population.

### Keywords

Crohn disease; inpatient; mental health; parenteral nutrition; ulcerative colitis

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The psychosocial sequelae of inflammatory bowel disease (IBD) leave pediatric patients at increased risk for depression compared with healthy population controls and other children with chronic diseases (1–3). Burke et al (4) in 1989 reported that pediatric IBD patients have a higher lifetime risk of depression than pediatric cystic fibrosis patients. Although it is difficult to determine a precise prevalence of depression in pediatric IBD patients because of sample size limitations in pediatric research, rates range from 10% to 25% in studies larger than 20 patients (5). Depression in IBD populations is associated with poor quality of life, medication nonadherence, worsened abdominal pain, and increased risk of surgery and disease relapse (3). Researchers have also noted associations with increased disease activity, steroid prescriptions, flare frequency, suicide rates, and radiation exposure (6–9).

Despite the growing rate of pediatric IBD admissions, little information exists on the effects of depression on inpatient outcomes (10). A retrospective review of over 2700 pediatric IBD-related hospitalizations showed that depression was associated with an increased rate of readmission in pediatric patients with Crohn disease (CD) (11). A similar adult study documented an association of depression with readmission rate in both CD and ulcerative colitis (UC) (12). To build on the current literature, we evaluated the impact of depression on length of stay (LOS) for IBD-related admissions using a nationally representative pediatric sample. Secondary goals include investigating the association of depression on radiologic studies, blood transfusions, endoscopic and surgical procedures, and use of total parenteral nutrition (TPN).

## METHODS

### Database

We conducted a retrospective cross-sectional review utilizing the 2012 Kids' Inpatient Database (KID), the largest nationally representative pediatric (under 21 years of age) inpatient database in the United States (13). KID is a component of the Healthcare Cost and Utilization Project (HCUP), created by the Agency for Healthcare Research and Quality. The database extracts information from administrative discharge abstracts and includes de-identified patient data (diagnoses, procedures, demographics, insurance type, and total charges) and institutional data (hospital size, ownership, location, and teaching status) from 4179 hospitals across 44 states (13). KID implements a systematic randomized sampling methodology to collect its cohort and subsequently applies a discharge-weighting algorithm to generate a nationally representative sample. Additional details regarding the sampling and weighing protocols can be accessed through HCUP (14). Diagnoses and procedures are documented through International Classification of Diseases, Ninth Revision, Clinical Modification (*ICD-9-CM*) codes. Up to 25 diagnoses (DX1-DX25) and 15 procedure codes (PR1-PR15) can be entered for each hospitalization, with the first entry (DX1) being the primary diagnosis.

### Study Population

Our study sample included all hospitalizations in which DX1, the primary reason for admission (14), involved a previously validated *ICD-9-CM* code for UC (*ICD-9*: 556.x) or CD (*ICD-9*: 555.x) (14,15). The sample was divided into hospitalizations that included a

nonprimary *ICD-9*- coded diagnosis (DX2–DX25) of depression versus those that did not. Given the lack of standardized methodology, we opted for this conservative approach to ensure that the reason for hospitalization was related to IBD and not depression (10,11,16,17). We discovered 88 hospitalization records that included diagnoses of both UC and CD; however, as the subtype of IBD was not relevant to our study, these records were included in our final analyses. *ICD-9* codes for depression were extracted from a previous validation study (18). To ensure an accurate estimation of LOS, we excluded hospitalizations that involved a transfer to or from another institution and hospital stays that ended in a patient's death (19).

## Data Analysis

The primary outcome of interest was length of hospital stay. Secondary outcomes included assessing rates of: TPN use, abdominal surgeries, endoscopic procedures, blood transfusions, cost, and abdominal imaging. A prolonged LOS was defined as >75th percentile of IBD hospitalizations, a standard used in previous literature (20). The predictor was an *ICD-9*-coded diagnosis of depression (18). For abdominal imaging, we evaluated X-rays and computerized tomography (CT) scans because of lack of specificity in *ICD-9* coding for other abdominal imaging modalities. Logistic regression was used to predict each outcome by depression.

We controlled for patient-level, hospital-level, and disease-specific confounders identified previously (10,11,16,19). Patient-specific confounders included: age, sex, race, median household income quartile of the zip code in which the patient lives, and type of insurance. Age groups were categorized based on the Paris Classification (21). Hospital-specific confounders included: bed size, geographic location, teaching status, hospital ownership, and annual volume of IBD admissions. Previous studies defined high-volume centers as those with over 20 pediatric IBD-related hospitalizations per year (10). IBD-related controls included: stricturing (B2), penetrating (B3), or perianal disease (p) as per the Paris Classification (21); extraintestinal disease; serious bacterial infections; malnutrition; anemia; and presence of an existing stoma. To control for potential confounding comorbidities, we controlled for number of chronic diseases, functional status, and the All Patient Refined Diagnosis Related Groups (ARP-DRGs) mortality risk using pre-existing variables in the KID database. We adjusted for IBD-related controls based on content expertise and previous literature. We extracted all confounder and outcome *ICD-9* codes from previous studies (10,15,22,23). Chi-squared testing was used to compare the sociodemographic and health characteristics between hospitalizations with depression and those without (Supplemental Table 1, Supplemental Digital Content, http://links.lww.com/MPG/B672). See Supplemental Table 2 (Supplemental Digital Content, http://links.lww.com/MPG/B672) for detailed *ICD-9* codes.

Although a detailed cost analysis is beyond the scope of this article, we did estimate costs of inpatient care using unweighted total hospital charges from the KID database and multiplying by the KID's cost-to-charge ratio as per previous literature (24). In line with prior studies (19), all other analyses were performed on the survey-weighted hospitalizations using Stata SE 15.1 (StataCorp, College Station, TX). For regression analysis, a *P* level

<0.05 was considered to be significant. The study was classified as nonhuman subject research by the University of California, San Francisco Committee on Human Research and was, therefore, exempt from the Institutional Review Board.

## RESULTS

The characteristics of pediatric IBD-related hospitalizations are outlined in Supplemental Table 1 (Supplemental Digital Content, http://links.lww.com/MPG/B672). There were 8222 unweighted IBD hospitalizations, which increased to 10,499 hospital stays after weighting. For hospitalizations involving IBD with comorbid depression, the median age was 17 years with an interquartile range (IQR) between 15 and 19 years. The majority of hospitalizations were female (53%), white (68.4%), and had a median household income in the fourth quartile (35.0%). The payment source for 60% of the hospital stays was private insurance. The majority of hospitalizations took place at private nonprofit (85.7%), urban teaching hospitals (79.1%) that had a large number of beds (70.2%). Hospital bed size was classified by the KID based upon the location and teaching status of the hospital (13). Geographically, 21.2% of hospitalizations were in the northeast, 24.7% in the midwest, 22% in the west, and 32.1% in the south. The majority of hospitalizations involved 2 to 4 chronic conditions (70.2%), and patients were mostly classified as having moderate loss of function (46.8%) with a minor risk of mortality (82.1%) during the hospitalization. IBD phenotype was reported as B2 in 10.7% of patients, and B3 in 3.3%. We were unable to report B2B3 as the number of hospitalizations was below the minimum required by HCUP (25). Perianal disease (p) was reported in 4.7%. A pre-existing ostomy was involved in 3.1% of hospitalizations. Comorbid complications of hospitalizations included a serious bacterial infection in 2.7%, anemia in 42.5%, and malnutrition in 19.4% (Supplemental Table 1, Supplemental Digital Content, http://links.lww.com/MPG/B672).

For hospitalizations involving IBD without comorbid depression, the median age was 16 years (IQR: 13–19 years). The majority of hospitalizations were boys (53.5%), white (61.9%), and had a median household income in the fourth quartile (33.3%). The payment source for most of the hospital stays was private insurance (64.8%). The majority of hospitalizations took place at private nonprofit (82.7%), urban teaching hospitals (78.4%) with a large number of beds (69.4%). Geographically, 23.7% of hospitalizations were in the northeast, 24.9% in the midwest, 18.2% in the west, and 33.1% in the south. Approximately half of the hospitalizations involved 2–4 chronic conditions (51.9%), and patients were mostly classified as having moderate loss of function (47.0%) with a minor risk of mortality (89.1%) during the hospitalization. IBD phenotype was reported as B2 in a smaller percentage (6.9%) but a significantly larger percentage (4.6%) had B3 ($P<0.01$). Perianal disease was reported in 3.9% of hospitalizations. A pre-existing ostomy was involved in 2.0% of hospitalizations. Comorbid complications of hospitalizations included a serious bacterial infection in 1.9%, anemia in 34.9%, and malnutrition in 13.7%. On the basis of chi-squared testing, patients with depression were more likely to have stricturing disease ($P<0.01$), anemia ($P<0.01$), malnutrition, ($P<0.01$) and more severe loss of function ($P<0.01$), and mortality risks ($P<0.01$; Supplemental Table 1, Supplemental Digital Content, http://links.lww.com/MPG/B672). We controlled for these differences in health characteristics in our logistic regression models.

In our sample of pediatric IBD-related hospitalizations, depression was associated with a prolonged LOS (odds ratio [OR] 1.50; 95% confidence interval [CI] 1.19–1.90). In our depression sample, the unweighted LOS was 5.0 ± 7.4 (median ± SD) days, whereas the IBD-only cohort had a LOS of 4.0 ± 5.0 days.

Depression was also associated with increased odds of using TPN (OR 1.54; 95% CI 1.04–2.27). However, depression was not associated with increased likelihood of surgery (OR 0.97; 95% CI 0.72–1.30), endoscopic procedures (OR 0.91; 95% CI 0.74–1.14), abdominal imaging (OR 1.15; 95% CI 0.53–2.53), or blood transfusion (OR 0.85; 95% CI 0.58–1.23; Table 1).

Unweighted total hospital charges for IBD admissions involving depression (median = $11,284.50; interquartile range [IQR] $5,720.95–$21,622.20) were higher than those that did not involve depression (median = $8,460.81; IQR $4,894.72–$15,055.30). We are, however, unable to deduce statistical significance from these charges as a formal cost analysis was outside of the scope of this study.

## DISCUSSION

Our study is one of the first to evaluate the association between depression and pediatric IBD-related hospitalization LOS. Using KID, we found that depression is associated with prolonged LOS and increased risk of initiating TPN during a hospitalization.

The strong association between depression and prolonged LOS remains despite controlling for multiple confounders. However, the cross sectional study design does not permit establishing causality. We hypothesize that overlap between the psychological and gastrointestinal diseases intensifies symptoms and induces diagnostic uncertainty that may warrant longer in-hospital monitoring. For example, depression can amplify visceral hypersensitization, and psychosocial dysfunction is known to magnify abdominal pain severity in adult IBD populations (2,3). Depression may also augment disease flares through suppression of anti-inflammatory mechanisms, thereby prolonging LOS. Inducing depression in animal models with quiescent colitis is reported to stimulate inflammatory cascades via impaired inhibition of proinflammatory cytokines by macrophages (26). Conversely, pediatric patients hospitalized for chronic medical conditions are more likely to develop depression than those admitted for an acute process (27). A study involving adolescent oncology patients revealed that disruptions in social development and roles were risk factors for developing depression, whereas meaningful relationships were deemed protective (28). We posit that these factors translate to our population. Depression with IBD is associated with missed school days, poor medication adherence, worsened fatigue, increased disease activity, and interpersonal difficulties (3,29–32). Therefore, as a result of prolonged hospitalizations that disrupt normal childhood, patients may lose some of these protective factors and be at higher risk of developing depression. The increased likelihood of starting TPN may also contribute to longer stays. This association remains statistically significant despite controlling for malnutrition, anemia, and severity of underlying gastrointestinal disease.

Historically, TPN has been used to treat severe IBD, especially in malnourished patients; however, recent pediatric guidelines suggest restricting its use to situations where enteral nutrition is insufficient to meet metabolic demand or in a pre-operative setting for an elective procedure (23). Depression in patients with IBD patients may exacerbate perceptions of disease severity and lead to earlier initiation of TPN. TPN is associated with increased cost, risk of central line infections, sepsis, deep venous thrombosis, and pulmonary embolism, and is not indicated to induce remission (23). Conversely, in pediatric CD, enteral therapy provides similar remission rates to corticosteroids (33). Our data show an association of depression with TPN use, but not with surgical or endoscopic procedures, which indicates that TPN use was likely extending beyond periprocedural time points. Previous data have highlighted barriers to adoption of new guidelines in other disease states, and we hypothesize that similar obstacles may contribute to increased TPN use in depressed patients (34,35). Pediatric gastroenterology consortia, as well as individual providers, may need to assume additional responsibility to disseminate and implement society guidelines to address disparities in care.

Similar to other trials utilizing the KID database, our study is limited by the use of *ICD-9* codes, which are specific but not sensitive for detecting conditions (36,37). *ICD-9* coding may vary between providers, which poses difficulties in standardizing our cohort. Depression is under-diagnosed in IBD populations (38), which presents a challenge in categorizing our study groups. Patients in the IBD-only cohort may have undiagnosed depression, or a depression diagnosis given in an outpatient clinic may not have transferred into the hospitalization chart. Additionally, as KID is a hospitalization-level database, a single patient may account for multiple hospitalizations. KID does not include patient-level disease-specific clinical data, which makes it difficult to comprehensively control for gastrointestinal disease severity. In addition, despite our controls, it is possible that conditions for which we did not control may influence LOS. Similarly, a patient admitted for a primary IBD-related diagnosis may subsequently require additional inpatient time to better stabilize their mental health. Given the variability in access to mental health services across hospital systems, this many contribute to increased LOS. Future research involving the severity and duration of each patient's depression, possible effects of depression on other measures of severity and mortality, and the types of treatment applied to each is needed to further elucidate the impact of mental health disorders on hospital and patient outcomes.

Our study found that depression is associated with prolonged LOS and increased TPN use in pediatric IBD-related hospitalizations using a nationally representative cohort. Further research will better characterize these correlations and can explore potential methods to mitigate discrepancies in care. An evaluation of differences in outcomes between high-volume and low-volume IBD centers can assess if IBD-specific expertise can minimize divergent outcomes in patients with depression. Present data using high-volume IBD centers showcase improved surgical outcomes and remission rates (39,40). We hypothesize that similar benefits may be seen in LOS and TPN use. Longitudinal and prospective studies are required to further elucidate the issue of causality.

A growing base of research highlights the benefits of intervention involving outpatient psychiatric care. A randomized control trial that examined the effect of 3 months of

psychotherapy on children with IBD and depression found that therapy helped reduce hospitalizations, emergency department visits, endoscopic procedures, and radiologic studies (3). Both supportive therapy and cognitive behavioral therapy (CBT) improve depressive symptoms and psychosocial functioning in pediatric IBD patients, with CBT also correlated with decreased IBD activity (2,41–43). Our study findings advocate for increased access to mental health care to investigate the effects on LOS and TPN use. Given the previously cited data, we hypothesize that outpatient interventions will reveal similarly beneficial effects.

Another avenue for future research is the development of a transitional care plan to potentially decrease LOS. Prospective trials are needed to evaluate if close postdischarge gastroenterology follow-up can facilitate an earlier discharge by allowing treatment delivery or monitoring in an outpatient setting. Care coordination models with structured postdischarge transitions plans can be effective at reducing hospital stays and costs in medically complex adult patients (44).

Annual IBD-related expenses in the United States amount to approximately $6.3 billion, with approximately 30 to 40% of the cost attributed to hospital care (3,45). Hospitalization research on other diseases, such as bronchiolitis has shown that differences in LOS of less than a single day are strongly associated with decreased healthcare expenditure (46). Our initial cost statistics suggest that IBD admissions involving depression are more expensive, but additional cost analyses are needed to validate the statistical significance of these findings.

## CONCLUSIONS

In summary, our retrospective database review of a nationally representative sample reveals that depression in pediatric IBD-related hospitalizations is associated with prolonged LOS and increased risk of initiating TPN. Future research should evaluate the causality and examine the efficacy of outpatient interventions and transitional care models to optimize inpatient outcomes.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**What Is Known**

- Pediatric inflammatory bowel disease patients are at increased risk of depression.
- Depression in inflammatory bowel disease is associated with poor quality of life, medication nonadherence, worse abdominal pain, and increase risk of surgery, relapse, and readmission.

### What Is New

- Depression correlates directly with increased length of stay in pediatric patients hospitalized for inflammatory bowel disease.
- Depression correlates directly with increased use of total parenteral nutrition.
- Depression does not correlate with an increased risk of blood transfusions, abdominal imaging, or the likelihood for endoscopic or surgical procedures in pediatric patients hospitalized for inflammatory bowel disease.

**Table 1:**

Association between depression and outcomes for pediatric inflammatory bowel disease (IBD)-related hospital stays

| Outcome | All centers OR [95% CI] | All Centers P-value |
|---|---|---|
| Prolonged length of stay * | 1.50 [1.19–1.90] | P<0.01 |
| Total parenteral nutrition | 1.54 [1.04–2.27] | P=0.03 |
| Surgery | 0.97 [0.72–1.30] | P=0.82 |
| Endoscopy | 0.91 [0.74–1.14] | P=0.43 |
| Transfusion | 0.85 [0.58–1.23] | P=0.38 |
| Abdominal Imaging | 1.15 [0.53–2.53] | P=0.72 |

Adjusted for demographics (age, gender, race, income quartile, insurance type), hospital-level variables (bed size, ownership, location, teaching status, GI disease (stricturing, penetrating, perianal disease, existing ostomy, malnutrition), comorbidities (number of chronic conditions, anemia, bacterial infection), functional status (pre-existing database variable), and mortality risk (pre-existing database variable).

* Defined as >75$^{th}$ percentile