

# Narcotic Use for Inflammatory Bowel Disease and Risk Factors During Hospitalization

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**Background:** Growing evidence demonstrates the adverse effects of narcotics in inflammatory bowel disease (IBD). We sought to study the relationship between narcotic use, objective measures of disease activity, and other associated factors in hospitalized patients with IBD.

**Methods:** We performed a retrospective cohort study of all adult IBD patients admitted to a general medical or surgical ward service at a United States tertiary care center over a 1-year period. We collected demographic and disease-specific information, inpatient narcotic use, and disease activity measurements from endoscopic and radiologic reports. Bivariate comparisons were made between characteristics and narcotic use. Logistic regression was used to evaluate the independent effects of characteristics on narcotic use.

**Results:** A total of 117 IBD patients were included. Narcotics were given to 70.1% of hospitalized patients. Factors significantly associated with any inpatient narcotic use: Crohn's disease (CD);  $P \leq 0.01$ , duration of IBD,  $P = 0.02$ , prior psychiatric diagnosis,  $P = 0.02$ , outpatient narcotic use,  $P \leq 0.01$ , current smoking,  $P \leq 0.01$ , prior IBD-specific surgery,  $P < 0.02$ , and prior IBD / irritable bowel syndrome (IBS) diagnosis,  $P = 0.02$ . Narcotic use was not significantly associated with disease severity on computed tomography (CT) scan or endoscopy. On multivariate analysis, smoking (odds ratio [OR] 4.34, 95% confidence interval [CI] 1.21–15.6) and prior outpatient narcotic use (OR 5.41, 95% CI 1.54–19.0) were independently associated with inpatient narcotic use.

**Conclusions:** A majority of patients with IBD are prescribed narcotics during hospitalization in spite of data on increased complications. Risk factors for narcotic use include CD and associated factors (disease duration, surgeries), substance abuse (outpatient narcotics and smoking), psychiatric diagnoses, and IBD-IBS.

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**Key Words:** IBD, narcotics, complications

Many patients with inflammatory bowel disease (IBD) suffer from chronic abdominal pain. The perception of pain in those with IBD can vary significantly. As many as 20% of patients with resolving inflammation and clinical remission can still have chronic pain.<sup>1</sup> In the past narcotics were often contraindicated in patients with IBD for fear of precipitating toxic megacolon. Now, narcotics are increas-

ingly prescribed for chronic pain in nonmalignant disease, and thus are commonly used in the IBD population. The United States is estimated to use 80% of the world's opioids, in spite of only representing 4.6% of the world's population.<sup>2</sup> For example, retail sales of opioids have skyrocketed in the past decade; prescriptions for methadone have increased 1177% from 1997–2006.<sup>3</sup> It is estimated that  $\approx 5\%$ – $13\%$  of patients with IBD are on chronic narcotics in the outpatient setting.<sup>4,5</sup> Similarly, in patients with irritable bowel syndrome (IBS), national surveys have estimated that 8% of the population are on chronic narcotics.<sup>6</sup>

Several factors have been associated with outpatient narcotic use in the IBD population. These factors include psychiatric comorbidities such as depression and anxiety, a history of abuse, female gender, and clinical disease activity when measured by symptoms.<sup>4,5,7</sup> Cross et al<sup>5</sup> used the Harvey–Bradshaw Index to assess disease activity, which includes measurements of general well-being and abdominal pain, which may not necessarily be associated with active inflammation. Many of the symptoms in scales of IBD disease activity are also symptoms of IBD-IBS.<sup>2</sup> IBS can coexist with IBD, as can chronic widespread pain.<sup>8</sup>

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The prevalence of IBS symptoms in patients with IBD is estimated to be 2–3 times higher than that of the general population. Approximately 57% of patients with Crohn's disease (CD) and 33% of patients with ulcerative colitis (UC) report IBS-like symptoms.<sup>9</sup> IBD-IBS is defined by disproportionate degrees of pain and diarrhea relative to the observed disease activity.<sup>10</sup> The overlap of IBD-IBS may be partially responsible for chronic abdominal pain in IBD and may be a risk factor for narcotic use.

Little is known about narcotic use in patients hospitalized with IBD. One recent study of the association between narcotic use and colectomy in UC found that only 19.7% of patients required narcotic analgesics prior to colectomy.<sup>11</sup> Because narcotics have been associated with complications of IBD and are also associated with significant mortality,<sup>12</sup> rates of narcotic use in both UC and CD and risk factors for use during hospitalization need to be quantified. We therefore sought to quantify narcotic use in patients hospitalized for a primary indication of IBD at a single tertiary care center. We also aimed to describe the relationship between narcotic use, objective measures of disease activity, and other associated factors, including prior diagnosis of IBD-IBS, in hospitalized patients with IBD.

## MATERIALS AND METHODS

### Study Design

We performed a retrospective cohort study of all patients  $\geq 18$  years old admitted to the University of North Carolina at Chapel Hill from May 1, 2008 to April 30, 2009 for a primary indication of IBD and seen by the adult gastroenterology consultation service. At our institution, patients with IBD are admitted to an adult general medical ward service or a specialized gastrointestinal (GI) surgery service, with consultation by the medical gastroenterology service. Primary medication prescriptions are provided by the ward services. As a different system of practice is in place for pediatric patients at our institution, these patients were excluded from the study. Each unique patient was only included in the study for their first hospitalization over the study period. Information on narcotic use and demographic and clinical information was abstracted from the electronic medical record. For any patient who ultimately underwent surgery during his or her admission, data were censored at the time of surgery.

### Patient Selection

All patients  $\geq 18$  years old whose initial consultation for IBD was not within 1 month post-operation for IBD and who did not have an intraabdominal abscess during the studied admission were included in the study population. Postoperative and intraabdominal abscess patients were excluded related to specific increased narcotic requirements for pain control in these conditions.

### Assessment of Exposures

Demographic information including age, gender, tobacco and alcohol use, marital status (as a measure of social support), and health insurance status were abstracted from the medical record. Disease characteristics including type of IBD (CD versus UC), duration of IBD, prior IBD-specific surgeries, presence of active perianal disease, a prior diagnosis of IBD-IBS, presence of a stricture on computed tomography (CT) scan or colonoscopy during this admission, whether a surgery was performed during the admission, and hospital length of stay were also collected. IBD-IBS was defined as disproportionate degrees of pain and diarrhea relative to the observed disease activity and had to be diagnosed by a physician prior to the admission.<sup>10</sup> Additionally, we recorded whether patients had a prior psychiatric diagnosis, defined as depression or anxiety disorder, and whether they were on psychiatric medications prior to admission. Psychiatric medications included any tricyclic antidepressant, selective serotonin reuptake inhibitor (SSRI), selective norepinephrine reuptake inhibitor (SNRI), antipsychotic, atypical antipsychotic, or benzodiazepine class of medication. Body mass index (BMI) was also abstracted when available. If a patient went to surgery during the admission, all data, including hospital length of stay, were censored at the time of surgery.

### Assessment of Disease Severity

Disease severity was measured for endoscopic (colonoscopy, ileoscopy, or pouch exam) and radiologic (CT scan) tests performed in the week prior to or during admission by two separate gastroenterologists (M.L. and H.H.). The physicians were blinded to narcotic requirements and other clinical characteristics during the hospitalization. Endoscopic findings were defined as normal, mild, moderate, or severe based on endoscopic reports, photographs, and pathology results. Findings on CT scan were classified as normal (no abnormal bowel or intraabdominal findings), mild/moderate (thickening of bowel wall only), or severe (thickening of bowel wall with evidence of extraluminal inflammatory changes or dilation of bowel). A stricture on endoscopic or radiologic test was classified separately. Endoscopic severity was then categorized as low (normal or mild) or high (moderate or severe). In order to be placed in the high category, both reviewers had to score the findings as at least moderate. Radiologic severity was categorized as low (normal or mild/moderate) or high (severe). In order to be placed in the high category, both reviewers had to score the findings as severe.

### Assessment of Outcome (Narcotic Use)

Many narcotic orders for inpatients are written in an as-needed format. Because of this, we used billing records rather than medical orders to determine narcotics received during hospitalization. Any billing record for a narcotic analgesic (see Appendix for complete list) and the date and time of delivery for each study patient were electronically retrieved.

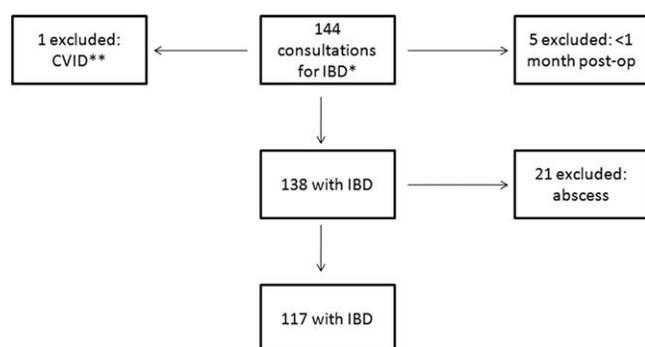


FIGURE 1. Patients included in the study population. \*For patients with >1 hospitalization, only the first hospitalization is included. \*\*Common variable immunodeficiency.

Those medications given for conscious sedation for a procedure were excluded (most often fentanyl). Any patient who underwent surgery during the admission was censored at the time of surgery, so that postoperative pain management was not included in the assessment of narcotic use. All narcotics were converted to intravenous (IV) morphine equivalents using MedCalc.<sup>13</sup> As there is no direct conversion for transdermal fentanyl patch, conversion was performed via the method of Donner et al,<sup>14</sup> with a conversion rate of oral morphine to transdermal fentanyl of 100:1. This conversion method has been validated in a population of patients with malignant pain. For those patients requiring a patient-controlled analgesia (PCA) pump, billing records were only able to provide the total amount of narcotics placed in the pump; therefore, actual delivered dosing for these patients could not be obtained. Total narcotic use was reported as average mg/day (total IV morphine requirements / total hospital length of stay). Peak narcotic use was defined as highest mg of IV morphine equivalents required over a 24-hour period. Narcotic use was also classified into a dichotomous variable (any/none). This variable was used in all analyses, as we were able to definitively determine whether narcotics were given from billing records.

### Statistical Analysis

Bivariate comparisons were made between exposures, disease severity measurements, and categories of narcotic use (any/none) using Pearson's chi-squared test statistic or Wilcoxon rank sum test as appropriate. For assessment of disease severity via radiologic or endoscopic reports, only those obtaining the test during the hospitalization were included in analyses. Logistic regression modeling was used to determine risk factors independently associated with narcotic use. Candidate variables for the model were selected a priori from the literature. For all analyses, a *P* value of 0.05 (2-sided) was considered statistically significant. Stata 11.0 (College Station, TX) was used for all analyses. The Institutional Review Board at the University of North Carolina at Chapel Hill approved the study protocol.

### RESULTS

A total of 144 consultations in unique patients for an indication of IBD occurred over the 1-year study period from May 1, 2008 to April 30, 2009. A total of five patients were excluded due to an IBD-specific surgery <1 month prior to hospitalization, one was excluded due to ultimate diagnosis of combined variable immunodeficiency rather than IBD, 21 were excluded related to an intra-abdominal abscess at the time of hospitalization, leaving 118 unique patients with IBD in the study population (Fig. 1). The majority of the population had CD (71.8%). For both CD and UC, the majority of those hospitalized were female. Nearly one-fourth of those with CD had a prior psychiatric diagnosis, and >one-third were on a psychiatric medication prior to admission did not have a prior psychiatric diagnosis. In this group, benzodiazepines were the most commonly prescribed agent. Additionally, >one-third of patients with CD were current smokers, in spite of evidence that smoking may exacerbate underlying CD. Characteristics of the population by CD or UC status are shown in Table 1. Patients with CD had significantly longer disease duration, were older, had more prior surgeries, perianal disease, and strictures. CD patients also had significantly more psychiatric medications and less evidence of endoscopic disease severity.

A total of 70.1% of patients with IBD received narcotics for pain control during their admission. Among those patients who did receive narcotics in an as-needed or scheduled format, the median peak (over 24 hours) narcotic use in IV morphine equivalents was 12 mg, interquartile range (IQR) 6–20 mg. The median daily average narcotic use (total amount averaged over total number of days of hospitalization) was 7.5 mg/day, IQR 2.5–12.7 mg/day. In addition, a total of 7.7% of the population required a PCA pump during hospitalization. Billing records for those using PCAs could not provide the delivered narcotic dose; these records only reported the total in the pump. Because of this, narcotic amounts for those on PCAs were not included in peak or average daily narcotics calculations. These calculations therefore represent an underestimation of actual narcotics given during hospitalization for IBD.

Characteristics of the population by any narcotic use are shown in Table 2. Several features were significantly associated with any narcotic use during hospitalization. These factors included: CD, duration of IBD, prior psychiatric diagnosis, outpatient narcotic use, current smoking, prior IBD-specific surgery, and prior diagnosis of IBD-IBS. Interestingly, requirement for surgery during the hospitalization was not significantly associated with narcotic use. When the IBD-IBS population was compared to the IBD population, 100% versus 67% required narcotics during

**TABLE 1.** Characteristics of the Hospitalized Population by Crohn's Disease Versus Ulcerative Colitis

Characteristic	CD (n=84)		UC (n=33)		P-value <sup>a</sup>
	n	Median( IQR) or %	n	Median (IQR) or %	
Duration of IBD (years)	83	9 (3-16)	33	5 (1-9)	<0.01
Psychiatric diagnosis <sup>b</sup> (% yes)	19	22.6	3	9.1	0.09
Psychiatric med prior <sup>c</sup> (% yes)	30	35.7	5	15.5	0.03
Outpatient narcotics prior (% yes)	31	36.9	7	21.2	0.10
Female gender (%)	49	58.3	23	69.7	0.26
Age (years)	84	33 (26-43)	33	29 (21-35)	0.04
Body Mass Index (continuous)	73	24.9 (22-29)	30	24.5 (22-30)	0.79
Alcohol use (any/none) % any	21	25	11	33.3	0.36
Illicit drugs (any/none) % any	3	3.6	0	0	0.27
Smoking <sup>d</sup> (any/none) % any	32	38.1	4	12.1	<0.01
Health insurance (any/none) (% any)	72	85.7	30	90.9	0.45
Married (% yes)	30	36.1	11	34.4	0.86
Prior IBD surgery (% yes)	49	58.3	4	12.1	<0.01
Surgery this admission (% yes)	8	9.5	5	15.2	0.38
Perianal disease (% yes)	11	13.3	0	0	0.03
Stricture <sup>e</sup> (% yes)	23	27.4	1	3.0	<0.01
IBD-IBS <sup>f</sup> (% yes)	10	11.9	1	3.0	0.14
CT scan severity <sup>g</sup> (% high)	25	39.7	4	44.4	0.79
Endoscopic severity <sup>h</sup> (% high)	23	36.5	22	78.6	<0.01

<sup>a</sup>P value by Pearson's chi squared test statistic for categorical variables, Wilcoxon rank sum or Student's *t*-test as appropriate for continuous variables, IQR (interquartile range).

<sup>b</sup>Depression or anxiety.

<sup>c</sup>Any SSRI, SNRI, tricyclic antidepressant, atypical antipsychotic, antipsychotic or benzodiazepine class of medication.

<sup>d</sup>Defined as any current smoking.

<sup>e</sup>As visualized on colonoscopy or CT scan.

<sup>f</sup>Prior diagnosis of IBD-IBS, defined as disproportionate degrees of pain and diarrhea relative to the observed disease activity.

<sup>g</sup>CT severity categorized into low (no or mild findings as judged by blinded gastroenterologist) and high (moderate or severe findings), CT severity only assessed in those who underwent CT scan.

<sup>h</sup>Endoscopic severity categorized into low (no or mild/moderate findings) and high (severe), endoscopic severity only assessed in those who underwent endoscopic evaluation.

admission ( $P = 0.02$ ). Disease severity as assessed by endoscopic or radiologic criteria was not significantly associated with narcotic use.

A total of 45.3% ( $n = 53$ ) of patients were discharged from the hospital with a prescription for a narcotic pain medication. A quarter (24.5%,  $n = 13$ ) of these patients underwent surgery during the hospitalization. Factors significantly associated with narcotics prescribed at discharge included: chronic outpatient narcotics prior to admission, receipt of narcotics during hospitalization, surgery during the admission, and perianal disease (data not shown).

Multivariate logistic regression was used to evaluate the independent effects of factors associated with narcotic use during hospitalization. Prior substance abuse, either via smoking (odds ratio [OR] 4.34, 95% confidence interval [CI] 1.21–15.6) or outpatient narcotic use (OR 5.41, 95% CI 1.54–19.0), was independently associated with narcotic

use during hospitalization. While not significant, prior psychiatric diagnoses were also associated with narcotic use (2.15, 95% CI 0.40–11.6) (Table 3).

## DISCUSSION

This referral-based retrospective cohort study demonstrates that a majority of patients with IBD (>70%) received narcotics during hospitalization. Even though calculated daily average doses of morphine likely represent an underestimation due to the inability to capture data from PCA pumps, a significant daily dose was still received. Not only are IBD patients receiving narcotics, they are receiving substantial doses over the course of hospitalization for pain control. Thus, it is important to understand what kinds of factors affect narcotic prescribing for IBD, as narcotics may be a risk factor for increased infectious complications and even increased mortality.<sup>12</sup> In this study we were able to quantify narcotic use and also describe risk factors

**TABLE 2.** Risk Factors by Any Narcotic Use During Hospitalization in Patients with Inflammatory Bowel Disease

Characteristics	No Narcotics (n=35)		Any Narcotics (n=82)		P-value <sup>a</sup>
	n	Median( IQR) or %	n	Median( IQR) or %	
Type of IBD					
Crohn's disease	18	21.4	66	78.6	<0.01
Ulcerative colitis	17	51.5	16	48.5	
Duration of IBD (years)	34	5.5 (1-12)	82	9 (3-16)	0.02
Psychiatric diagnosis <sup>b</sup> (% yes)	2	5.7	20	24.4	0.02
Psychiatric med prior <sup>c</sup> (% yes)	7	20.0	28	34.2	0.12
Outpatient narcotics prior (% yes)	4	11.4	34	41.5	<0.01
Female gender (%)	21	60.0	51	62.2	0.82
Age (continuous years)	35	29 (22-38)	82	33 (26-44)	0.08
Body Mass Index (continuous)	33	24.1 (22-28)	70	25.6 (21-30)	0.32
Alcohol use (any/none) % any	8	22.9	24	29.3	0.48
Illicit drug use (any/none) % any	0	0	3	3.7	0.25
Smoking <sup>d</sup> (any/none) % any	4	11.4	32	39.0	<0.01
Health insurance (any/none)(% any)	33	94.3	69	84.2	0.13
Married (% yes)	15	42.9	26	32.5	0.29
Prior IBD surgery(% yes)	10	28.6	43	52.4	0.02
Surgery this admission (% yes)	4	11.4	9	11.0	0.94
Perianal disease (% yes)	1	2.9	10	12.4	0.11
Stricture <sup>e</sup> (% yes)	6	17.1	18	22.0	0.56
IBD-IBS <sup>f</sup> (% yes)	0	0	11	13.4	0.02
CT scan severity <sup>g</sup> (% high)	7	41.2	22	40.0	0.93
Endoscopy severity <sup>h</sup> (% high)	18	60.0	27	43.3	0.16

<sup>a</sup>P value by Pearson's chi squared test statistic for categorical variables, Wilcoxon rank sum or Student's *t*-test as appropriate for continuous variables, IQR (interquartile range).

<sup>b</sup>Depression or anxiety.

<sup>c</sup>Any SSRI, SNRI, tricyclic antidepressant, atypical antipsychotic, antipsychotic or benzodiazepine class of medication.

<sup>d</sup>Defined as any current smoking.

<sup>e</sup>As visualized on colonoscopy or CT scan.

<sup>f</sup>Prior diagnosis of IBD-IBS, defined as disproportionate degrees of pain and diarrhea relative to the observed disease activity.

<sup>g</sup>CT severity categorized into low (no or mild findings as judged by blinded gastroenterologist) and high (moderate or severe findings), CT severity only assessed in those who underwent CT scan.

<sup>h</sup>Endoscopic severity categorized into low (no or mild/moderate findings) and high (severe), endoscopic severity only assessed in those who underwent endoscopic evaluation.

present on admission for receipt of narcotics during the hospitalization. These risk factors include psychiatric diagnoses, smoking, prior outpatient narcotic use, IBD-IBS, CD rather than UC, and prior IBD-related surgery. Most of these risk factors are independent of IBD diagnosis and disease activity. When we compared narcotic use by objective measures of disease activity, we did not find a significant association. Therefore, the most severe disease activity findings do not necessarily correlate with narcotic requirements. In fact, all patients with a prior diagnosis of IBD-IBS, defined as painful symptoms in the absence of disease activity, received narcotics during hospitalization. Interestingly, in the overall hospitalized IBD population 61.5% were female, which differs from the known equal incidence of IBD among men and women. IBS is more prevalent

**TABLE 3.** Adjusted Multivariate Analyses of Independent Effects of Risk Factors for Narcotic Use

Characteristic	OR <sup>a</sup>	95% CI <sup>b</sup>
Gender (female)	0.77	0.28-2.10
Crohn's disease	2.19	0.77-6.22
Current smoking	4.34	1.21-15.6
Psychiatric diagnosis	2.15	0.40-11.6
Duration of IBD (years)	1.04	0.98-1.11
Prior IBD surgery	1.04	0.32-3.42
Outpatient narcotic use	5.41	1.54-19.0

<sup>a</sup>Odds ratio via logistic regression, variables selected a priori from the literature.

<sup>b</sup>95% CI (confidence interval).

among women. When we excluded the IBD-IBS group, 57.6% of the population was female. Therefore, IBD-IBS is the likely cause of the gender disproportion. When we investigated factors associated with narcotics at discharge, factors such as prior narcotic use and surgery were significant predictors. Interestingly, perianal disease was associated with discharge narcotic prescriptions. This may be related to the fact that this is an external manifestation of IBD that can be visualized by the treating physician and is recognized as a “valid” source of pain amenable to such treatment. By recognition of risk factors for narcotic use, alternative pain control therapies could be implemented earlier in the course of hospitalization. Pain is not necessarily a marker of intestinal inflammation, but can by itself represent an illness symptom.<sup>15</sup> Severe inflammatory activity can be painless. Thus, the treatment approach to pain in IBD should include balanced therapies targeting the brain and the gut.

Narcotics can have adverse complications in patients with chronic GI conditions, such as IBD. Opioids can be associated with reduced GI motility, nausea, vomiting, constipation, secondary intestinal pseudo-obstruction, and gastroparesis.<sup>2,16</sup> Pain control in patients with IBD can be difficult, as other traditional agents for pain control such as nonsteroidal antiinflammatory drugs (NSAIDs) have been associated with flares of IBD in epidemiologic studies.<sup>17</sup> For this reason, there may be a role for antidepressants and psychological support in pain management in IBD. The central analgesic effects of antidepressant medications can be beneficial. This underrecognized mechanism of pain control is often used in patients with functional GI disorders, often in combination with psychological interventions. These treatments have overarching effects on pain regulation, regardless of the source of pain. Patients with IBD on narcotics are also at risk for development of narcotic bowel syndrome (NBS). NBS is defined by chronic or recurrent abdominal pain that worsens with continued or escalating dosages of narcotics.<sup>2</sup> In our study sample, a total of six IBD patients (5.1%) were diagnosed with NBS during hospital admission and required a detoxification protocol. This entity is important to recognize, as increasing doses of narcotics will actually cause or aggravate the pain that is being treated. Instead, medications such as tricyclic antidepressants or SNRI antidepressants can be used as centrally acting agents to treat the pain.<sup>2</sup>

In 2001 the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) introduced the concept that pain was the “fifth vital sign.” The purpose was to increase the awareness and therapy of pain in the hospitalized patient.<sup>3</sup> However, this may have resulted in the overmedication of a group of patients<sup>3,18</sup> and may have additionally influenced opioid prescribing patterns in patients with IBD. When notified regularly of elevated pain

scores, hospital physicians and trainees may be more inclined to prescribe as-needed narcotics. Additionally, there are national trends influencing narcotic prescriptions in both the ambulatory and hospital settings. Since the mid 1990s, physicians have been encouraged to become more active in identifying and treating chronic pain. Since 1990, opioid use has increased by a factor of 10.<sup>19</sup> Aggressive marketing of controlled release opioid pain medications has contributed to this phenomenon. As an unintended consequence, there has been a marked increase in deaths from unintended drug overdoses.<sup>19</sup> This prescribing pattern may represent a generational change, where younger physicians are being trained in a climate where narcotic use abounds. Narcotic use is therefore accepted as a normal component of both the inpatient and outpatient practice of medicine. In this increasing climate of narcotic use and abuse throughout the United States, it is not surprising that narcotic use is so common among hospitalized patients with IBD.

In our sample, prior psychiatric diagnosis was associated with narcotic use on bivariate analysis, and presumably increased pain. Psychological distress and poor coping can act via central nervous system pathways to produce central disinhibition of incoming visceral signals, thus amplifying the pain experience and exacerbating other GI symptoms.<sup>10,20</sup> Furthermore, stress and other psychosocial factors can increase pain for all medical conditions including IBD.<sup>21</sup> Walker et al<sup>22</sup> have previously shown that IBD patients with psychiatric disorders have increased GI and other medically unexplained symptoms despite no differences in severity of IBD. Additionally, Guthrie et al<sup>23</sup> showed that concurrent psychological disorders in patients with IBD contribute to poor health-related quality of life, independent of IBD disease severity. Drossman et al<sup>24</sup> reported that psychological distress and poor general well-being lead to increased physician visits in patients with IBD. Therefore, psychiatric disorders and psychological distress have been associated with ongoing symptoms and symptom behaviors such as health-care-seeking, regardless of the severity of the underlying IBD. We have demonstrated that psychiatric diagnoses are also associated with inpatient narcotic use in patients with IBD. It is also likely that more rigorous assessment of psychosocial factors including levels of psychological distress and coping may provide a greater understanding of psychosocial contributing factors. Importantly, early recognition and attention to psychosocial difficulties in patients with IBD may impact a patient’s pain perception and requirement for narcotics. In these situations early identification may lead to more focused treatment options.

Prior studies have evaluated outpatient chronic narcotic use in patients with IBD. To our knowledge, quantification of inpatient narcotic use and risk factors in this population has not been previously described. One of the

original descriptions of narcotic use in patients with IBD was a case series by Kaplan and Korelitz<sup>25</sup> describing patients with IBD referred for psychiatric evaluation. They found relatively high rates of narcotic drug dependence, a majority had CD, and many were diagnosed with borderline personality disorder. Edwards et al<sup>4</sup> described a series of patients with IBD on chronic narcotics without demonstrable organic pathology and also found a high prevalence of psychiatric disorders in this group (67%). Hanson et al<sup>7</sup> performed a case-control study of IBD patients on outpatient narcotics compared to those without narcotics. They demonstrated that chronic narcotic use in IBD patients is associated with female gender, >2 previous surgeries, moderate to severe pain, substance abuse, clinical disease activity, depression, anxiety, and abuse (physical, emotional, or sexual). Importantly, narcotic use was not associated with disease activity when measured by endoscopic, radiologic, or histologic severity. Our results in the inpatient setting were similar to Hanson et al's in the outpatient setting. We found that inpatient narcotic use was significantly associated with prior psychiatric diagnosis, prior IBD surgery, and substance abuse (outpatient narcotic use and smoking). Additional factors in our analysis associated with inpatient narcotic use included CD, disease duration, and IBD-IBS. We, too, found no association between narcotic use and objective measures of disease activity.

Cross et al<sup>5</sup> found that outpatient narcotic users with IBD were more likely to be female, had higher rates of disability, took more medications, and had a longer duration of disease. Similar to a trend in our study, Cross et al found a higher prevalence of neuropsychiatric drug use among narcotic users. However, they found that CD patients receiving narcotics had increased levels of disease activity as measured by the Harvey-Bradshaw Index (HBI; 9.1 vs. 5.0,  $P < 0.001$ ). Several of the components of the HBI are subjective. The HBI is heavily weighted on general well-being and level of abdominal pain.<sup>26</sup> These are also symptoms that would be exacerbated by IBS or visceral hypersensitivity. The lack of association we found in our study was likely related to our use of objective measures of disease activity: endoscopic and radiologic findings. Abnormal motility, visceral hypersensitivity, and psychosocial factors all may play a role in functional GI symptoms in patients with IBD.<sup>10</sup> Therefore, the association found by Cross et al could have been an association between narcotic use and functional GI symptoms.

There are several strengths to our study. First, we were able to capture all inpatient gastroenterology consultations for a diagnosis of IBD over the 1-year study period. We were also able to determine the prevalence of narcotic use with certainty, as information came directly from billing records. We were able to obtain detailed clinical exposure data including concurrent medications, disease

characteristics, and comorbidities. The assessment of disease severity on endoscopy and CT scan was done independently by two gastroenterologists in a blinded fashion, rather than via a subjective disease severity measurement. We were also able to describe the hospitalizations of a large number of consecutive patients with IBD.

There are also several limitations to this study. This represents a single tertiary care center referral population, which may limit generalizability to other populations. This may represent a more severe population of patients with IBD, or a more severe population of patients with coexisting functional GI conditions. Additionally, all data were collected retrospectively in this cohort; therefore, we were limited by medical record documentation. For example, psychiatric diagnoses were obtained from the medical record, rather than from formal testing. We also did not have the indication for psychiatric medications, as these could have been initiated for IBS symptoms and/or depression. For disease severity measurements, although the endoscopic and radiologic reviewers were blinded to the patients' narcotic use, the scoring system remains subjective. The scoring of radiologic tests was done by gastroenterologists and not radiologists. These limitations could have affected the lack of association between narcotic use and disease activity. We also could not completely ascertain doses of narcotics for patients on PCA pumps for pain control. In general, this subset of patients had the highest narcotic demands, which we were unable to specifically quantify. However, we could determine with certainty whether narcotics were received, which is why analyses focused on any narcotic use. Finally, we were not able to include pediatric IBD patients in our cohort, as different systems of practice are in place at our children's hospital. Little is known about the role of narcotics in children hospitalized with IBD, and this is an important area for future research.

In summary, the results of our study are important in that we have now shown that a majority of patients hospitalized for IBD receive narcotics. Narcotics have been associated with increased complications and also increased mortality in patients with IBD. It has been previously proposed that narcotics may be a marker for more severe disease, which could explain these increased risks. In our study, we did not find an association between severe disease activity and narcotic use, albeit we were limited by sample size. It is also possible that narcotics themselves precipitate complications such as increased mortality related to known side effects on the GI tract. We were also able to determine risk factors present at the time of admission that are associated with narcotic use during hospitalization. Recognition of these risk factors may allow for early interventions during the hospitalization, such as the addition of centrally acting antidepressants and

avoidance of significant narcotic use, which may ultimately improve pain control and possibly avoid complications of narcotic use.

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### APPENDIX

#### Narcotics Abstracted from Billing Records Categorized by Route

##### Oral:

- Percocet (oxycodone/acetaminophen)
- Vicodin (oxycodone/acetaminophen)
- Lortab (hydrocodone/acetaminophen)
- Hydrocodone
- Oxycodone
- Dilaudid (hydromorphone)
- Methodone
- Codeine
- MS Contin (morphine sulfate)
- Morphine sulfate immediate release
- Darvocet (acetaminophen/propoxyphene napsylate)
- Tylenol #3/4 (acetaminophen/codeine)
- Demerol (meperidine)

##### Transdermal:

Fentanyl patch

##### Intravenous/intramuscular:

- Morphine
- Dilaudid (hydromorphone)
- Fentanyl
- Demerol (meperidine)
- Nubain (nalbuphine)