

# Abdominal Pain and Anxious or Depressed State Are Independently Associated With Weight Loss in Inflammatory Bowel Disease

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**Background:** Many factors impact nutritional status in inflammatory bowel disease (IBD). We undertook this study to evaluate the potential role that abdominal pain has on weight loss and dietary behavior in IBD.

**Methods:** This is a retrospective cohort study utilizing data from an IBD registry at our institution between January 1, 2015 and August 31, 2018. Pain scores and nutritional outcomes were derived from validated questionnaires while key associated clinical data were derived from the medical record.

**Results:** Three hundred and three patients (154 females; 206 Crohn's disease) were included in this study. Ninety-six patients (31.7%) had experienced a 6-lb or greater weight loss in the prior month. On multivariate analysis, abdominal pain and anxious/depressed state were independently associated with weight loss, while female gender and NSAID use were inversely associated with weight loss ( $P < 0.05$ ). IBD patients with abdominal pain also reported significantly poorer dietary behavior than those without this symptom.

**Conclusions:** Abdominal pain is more likely to result in negative dietary outcomes and independently associated with weight loss in IBD. IBD providers should screen for malnutrition when patients report abdominal pain.

## Lay Summary

We demonstrated that IBD patients with abdominal pain, anxious or depressed state have poorer nutritional outcomes, regardless of disease activity state. These findings reinforce the importance of screening for malnutrition in IBD patients with one or more of these symptoms.

**Key Words:** abdominal pain, diet, weight loss, nutritional outcomes, inflammatory bowel disease

## INTRODUCTION

The inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic

inflammatory disorders of the gut that often adversely impact patient dietary habits and nutritional status. Previous estimates suggest that 20% report decreased appetite during most of their disease course<sup>1</sup> and up to 88% of CD patients and 60% of UC patients experience at least 5 pounds of weight loss during the course of their disease.<sup>2,3</sup> Thus, it is not surprising that 20%–85% of IBD patients qualify for having protein-energy malnutrition,<sup>4,5</sup> while up to 65% exhibit signs of deficiencies in at least one micronutrient (ie, vitamin or mineral).<sup>6,7</sup> While many of these studies have been undertaken in active IBD populations, similar findings have been demonstrated in quiescent patients,<sup>8,9</sup> highlighting the chronic impact that IBD has on even seemingly healthy individuals. Thus, it is also not surprising that malnutrition is a persistent negative contributor to IBD patient disease course, morbidity and mortality.<sup>10</sup>

Many factors have previously been associated with the development of malnutrition in IBD including (a) active inflammation, (b) reduction in food intake (related to reduced appetite and/or sitophobia), (c) nutrient malabsorption, and (d) even exudative loss of nutrients.<sup>4,11</sup> These elements may themselves be influenced by other factors, including patient symptoms. For example, abdominal pain has also been linked to poor nutritional outcomes, including reduction in appetite, weight loss, and macro- and micronutrient deficiencies.<sup>12,13</sup> As

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abdominal pain is relatively common in IBD, affecting 70% or more of IBD patients with active disease<sup>14</sup> and 20% or more of patients with quiescent disease.<sup>14, 15</sup> It is possible that this symptom may serve as a primary driver of malnutrition in these populations. It is also possible that pain may be serving as a proxy for other disease-related factors, including active inflammation and complications such as strictures and abscesses.<sup>14, 16, 17</sup> No study to date has attempted to discern the influence of these various factors on nutritional status in IBD patients. Thus, uncertainty remains as to whether abdominal pain serves as a surrogate or a determinant of nutritional outcomes rather than the disease activity itself.

This question is important as the answer may (a) provide new insights into how abdominal pain impacts individuals with IBD and (b) influence how IBD providers manage their patients. For example, abdominal pain has been demonstrated to negatively influence other key health-related factors in IBD, such as quality of life,<sup>13, 18</sup> and clinical and research tools have been developed to account for these relationships.<sup>19, 20</sup> Routine incorporation of abdominal pain assessment may also be important for malnutrition screening in IBD. Current management paradigms do not regularly account for a link between pain and nutritional status in IBD patients. The revelation of such a relationship could also spur the use of more aggressive and innovative pain management strategies and prompt the inclusion of nutritional specialists in the care of IBD patients with abdominal pain earlier in the course of their disease.

Accordingly, we undertook this study to determine whether abdominal pain independently influences dietary behavior and nutritional outcomes in IBD patients. We hypothesized that patients with IBD experiencing abdominal pain would have poor nutritional outcomes, irrespective of disease activity.

## MATERIALS AND METHODS

### Study Population

We performed a retrospective analysis of consecutive patients enrolled in the Intestinal Diseases Natural History Database at Pennsylvania State University Hershey Medical Center (PSHMC) between 1/1/2015 and 8/31/2018. Of note, this database is comprised of clinical and research information related to the encounters of IBD patients receiving clinical management at Pennsylvania State University Hershey Medical Center, a tertiary care referral hospital with a dedicated IBD center that cares for over 6000 patients with these disorders.

Inclusion criteria for enrollment in this study were as follows: (a) adult (ie, >17 years old), (b) established diagnosis of CD, UC or IBD colitis of indeterminate nature (IC) (based upon standard clinical criteria routinely used to identify IBD<sup>21</sup>), and (c) participants needed to have undergone an ileocolonoscopy and completed contemporaneous surveys on abdominal pain experience, dietary behavior and nutritional status (see below). UC patients were excluded if they had previous colonic surgery.

### Abdominal Pain Assessment

Abdominal pain frequency scores were derived from the sub-score associated with question #4 of the short inflammatory bowel disease questionnaire (SIBDQ) (“How often during the last two weeks have you been troubled by pain in your abdomen”) (SIBDQ Pain Score or SPS). Patients respond using a frequency-based inverse Likert scale, with 1 representing pain “all of the time” and 7 representing pain “none of the time”). An SPS score of <6 was defined as having clinically significant abdominal pain. We made this determination after performing correlative analyses comparing the SIBDQ pain score (SPS) with the pain scores derived from other widely used scales (Harvey–Bradshaw and PROMIS pain surveys). These analyses demonstrated a strong correlation between the SPS and the other two scales (ie, suggesting that SPS could be used as a proxy measure of the other measures).

### Dietary Behavior and Nutritional Assessment

In order to assess patient appetite and general dietary behavior, the following selected questions were asked from the Council on Nutritional Assessment Questionnaire (CNAQ):<sup>22</sup> (1) “How is your appetite?,” (2) “How does food taste to you, in general?,” (3) “During meals, how soon do you feel full?,” and (4) “How often do you normally eat?.” Patients provided individual answers for each question based upon separate 5-point Likert scales that include descriptors allowing patients to define their relative health or level of impairment. We also asked the following question from the Short Nutritional Assessment Questionnaire (SNAQ)<sup>23</sup>: (1) “Did you use supplemental drinks or tube feeding over the last month?.” Patients were asked to answer “yes” or “no” to this question. Note that [Supplementary Addendum](#) provides an overview of the questions, potential responses and the answers considered to be abnormal or pathological.

The primary measure of nutritional status was weight loss, which was defined as an unintentional patient-reported drop of 6-lb or more in body weight over the month preceding survey completion. Please note, we relied upon patient reports rather than direct measures of weight because the vast majority of patients did not have two reliable recorded weights within the study period to verify the findings in each case. We also evaluated body mass index (BMI) and serum albumin levels.

### Disease Activity Assessment

Inflammatory bowel disease activity was based upon direct endoscopic evaluation of the intestinal mucosa in the area of previously established activity in each patient. Endoscopic activity in UC was determined using the Mayo endoscopy subscore, which ranges from 0–3, with 0 = no disease (“quiescent”) and 3 = severe disease. In CD, we used the Simple Endoscopic Score for CD (SES-CD), where 0–6 is mild, 7–15 is moderate and >15 is severe. Hence “moderate to severe disease activity”

was defined as a Mayo endoscopy sub-score of 2–3 in UC and Simple Endoscopic Score for CD of 7 or greater in CD.

### Other Demographic and Clinical Data

Age, gender, IBD duration, IBD extent/location (eg, organ involvement, based upon the Montreal classification system,<sup>24, 25</sup> disease complications (including stricture, intra-abdominal fistula, abscess and cancer development), extraintestinal manifestations (EIMs) (including inflammatory arthritides, IBD-associated dermatopathies (including pyoderma gangrenosum), erythema nodosum, uveitis, episcleritis, and primary sclerosing cholangitis), endoscopic severity (as defined by the Mayo Index endoscopy sub-score or the Simple Endoscopic Scale for CD as appropriate), medication use (including antidepressant/anxiolytic, corticosteroid, mesalamine, immunomodulator (azathioprine, 6-mercaptopurine and/or methotrexate) and biologic therapy (infliximab, adalimumab, certolizumab, golimumab, vedolizumab, and/or ustekinumab), opioids and “other” pain medications (acetaminophen, NSAIDs, dicyclomine and/or tricyclic agents)), surgical history, laboratory values (platelet count, white blood cell count (WBC), sedimentation rate (ESR), C-reactive protein (CRP), and albumin), and tobacco use were obtained from the record. Platelet count  $> 400 \times 10^9/L$ , WBC  $> 10 \times 10^9/L$ , CRP  $> 1.0 \text{ mg/dL}$ , and ESR  $> 20 \text{ mm/hour}$  were each considered to be pathologically elevated. The presence of anxiety or depression symptoms were determined based upon responses to the Hospital Anxiety and Depression Scale (HADS), which were completed at the time of the clinical encounter. Of note, this 14-question survey (seven apiece for anxiety and depression) was developed as a screening tool to evaluate for anxiety and depression in the outpatient clinical setting.<sup>26</sup> It has since been validated for use as a screening tool of both anxious and/or depressed states in IBD<sup>27</sup> and is widely used for both clinical and/or research purposes to investigate these symptoms in this population and in other chronic inflammatory disorders.<sup>28–30</sup> In our study, anxiety or depression sub-scores of 8 or greater (out of a potential total of 21) were considered clinically significant, as these scores have previously been associated with each respective diagnosis.<sup>26, 31</sup>

### Statistical Analysis

Data were extracted and analyzed using GraphPad Prism version 8 (San Diego, CA) or SAS version 9.4 (Cary, NC). The primary outcome of interest was weight loss (each as defined above). Initially, demographic and clinical variables were compared using univariate analysis (eg, Student's *t*-test, Chi-square test, or Fisher's exact test as appropriate) between two distinct cohorts: (1) IBD patients with weight loss and (2) IBD patients without weight loss. A multivariable logistic regression model was then created, incorporating each significant ( $P < 0.05$ ) or near significant ( $P = 0.05–0.10$ ) variable identified during the univariate analysis comparing the two cohorts above in order to

examine the odds ratio of experiencing weight loss. As described in the Results section, we initially incorporated age, female gender, presence of anxious and/or depressed state, presence of abdominal pain, presence of moderate-severe inflammation (on endoscopic examination), and NSAID use into our model to derive the results for Table 2. We also developed a separate multivariable logistic regression model that incorporated all of the factors described in Table 2 while also accounting for pathological elevations of the inflammatory markers described in the previous paragraph (eg, platelet count, WBC, ESR, and CRP) in 136 patients that had undergone laboratory testing within 3 months of the endoscopic evaluation (Supplemental Table 1). A Hosmer and Lemeshow goodness-of-fit test was used to check the appropriateness of data for multivariate logistic regression and a concordance (“C”) statistic was calculated.

Secondary outcomes of interest were (a) patient appetite, (b) food taste experience, (c) fullness after eating, (d) frequency of meals, and (e) use of supplemental nutrition in patients with and without abdominal pain. Univariate analyses were also used to individually compare demographic and clinical variables between cohorts with and without abnormalities in any of these factors. Values listed represent means  $\pm$  SEM, unless indicated otherwise. *P* values of  $< 0.05$  were considered significant unless signified otherwise.

### Ethical Considerations

This work was performed in accordance with the rules and regulations set forth by the Pennsylvania State University College of Medicine Institutional Review Board and carried out under protocol PRAMSHY98-057.

## RESULTS

### Clinical and Demographic Information

Three hundred and three patients completed the abdominal pain and CNAQ/SNAQ questions described above. Ninety-six patients (32%) experienced at least a 6-lb weight loss over the preceding month. Patients with weight loss were less commonly female (41.7% vs 55.1%,  $P < 0.05$ ). There was also a trend toward a lower mean age in patients with weight loss (40.7 vs 44.7 years,  $P = 0.05$ ). There was no significant difference in disease type, duration, or location between those with and without weight loss (Table 1). There was also no detectable difference in the incidence of moderate to severe inflammation, complications in CD (eg, stricture and/or intra-abdominal fistula), or current EIM (Table 1). Use of IBD-directed therapies (eg, corticosteroids, mesalamines, immunomodulators, and biologics) and history of surgeries were comparable as was the use of other substances and medications with the exception of NSAIDs, which were less commonly used by those with weight loss (10.4 vs 23.8%,  $P < 0.01$ ). Notably, patients with weight loss were much more likely to exhibit a concurrent anxious

**TABLE 1. IBD patients With and Without Weight Loss**

Demographic variables	IBD without weight loss (n = 207)	IBD with weight loss (n = 96)	P-value
Age (years)	44.7±1.2	40.7±1.6	0.05
Gender (f/m)	114/93	40/56	<b>&lt;0.05</b>
BMI	29.7±0.6	25.2±0.7	<b>&lt;0.0001</b>
Disease type			
CD	136 (65.7%)	70 (72.9%)	0.20
UC	66 (31.9%)	24 (25.0%)	0.22
Indeterminate nature	5 (2.4%)	2 (2.1%)	0.84
Disease location			
CD			
L1	44 (32.3%)	21 (30.0%)	0.75
L2	21 (15.4%)	12 (17.2%)	0.84
L3	71 (52.3%)	36 (51.4%)	0.99
L4	0 (0.0%)	1 (1.4%)	0.34
UC			
E1	5 (7.6%)	0 (0.0%)	0.32
E2	19 (28.8%)	8 (33.3%)	0.80
E3	42 (63.6%)	16 (66.7%)	0.99
Disease duration (years)	13.1±0.9	10.6±1.2	0.10
Moderate–severe inflammation (endoscopic exam)	73 (35.2%)	42 (44.0%)	0.21
Strictures ± fistula(e) (CD)	85/136 (62.5%)	42/70 (60.0%)	0.76
Current EIM	72 (34.8%)	38 (39.6%)	0.44
Anxious ± depressed state	85 (41.1%)	61 (63.5%)	<b>&lt;0.001</b>
Abdominal pain	117 (56.5%)	73 (76.0%)	<b>&lt;0.01</b>
Laboratory values			
CRP (mg/dL)	1.5±0.2	2.3±0.3	<b>&lt;0.05</b>
ESR (mm/hour)	19.3±1.5	24.5±2.6	0.06
Platelets (×10 <sup>9</sup> /L)	276.2±7.8	322.8±14.5	<b>&lt;0.01</b>
WBC (×10 <sup>9</sup> /L)	7.7±0.3	8.6±0.4	<b>&lt;0.05</b>
Albumin (mg/dL)	4.1±0.1	3.8±0.1	0.07
Elevated CRP (yes/no)	44/55	29/23	0.23
Elevated ESR (yes/no)	44/81	30/30	0.08
Elevated platelets (yes/no)	14/130	16/71	0.07
Elevated WBC (yes/no)	24/120	20/61	0.16
IBD-directed therapy			
Corticosteroid use	26 (12.6%)	15 (15.6%)	0.48
Mesalamine use	53 (25.7%)	21 (21.9%)	0.57
Immunomodulator use	47 (22.8%)	27 (28.1%)	0.32
Biologic use	116 (56.3%)	57 (59.4%)	0.71
IBD-related surgery	53 (5.7%)	25 (26.0%)	0.99
Medication and substance use			
Tobacco use	19 (9.2%)	14 (14.6%)	0.17
Alcohol use	75 (36.2%)	26 (27.1%)	0.19
Marijuana use	10 (4.8%)	9 (9.4%)	0.13
Opiate use	19 (9.2%)	14 (14.6%)	0.17
NSAID use	49 (23.8%)	10 (10.4%)	<b>&lt;0.01</b>
Antidepressant/anxiolytic use	62 (30.1%)	26 (27.1%)	0.68



**TABLE 2. Logistic Regression Analysis: Weight Loss**

Variable	OR (95% CI)	P-value
Age	0.99 (0.96–1.01)	0.37
Female gender	<b>0.53 (0.31–0.90)</b>	<b>0.02</b>
State of anxiety ± depression	<b>1.85 (1.06–3.24)</b>	<b>0.03</b>
Presence of abdominal pain	<b>2.06 (1.12–3.81)</b>	<b>0.02</b>
Moderate-to-severe inflammation	1.29 (0.76–2.17)	0.35
NSAID use	<b>0.40 (0.18–0.89)</b>	<b>0.02</b>

Items in bold are considered statistically significant.

and/or depressed state (63.5 vs 40.9%,  $P < 0.001$ ) though it was noted that antidepressant/anxiolytic use was similar between the cohorts (Table 1).

Patients with weight loss did have a significantly higher mean CRP (2.3 vs 1.5 mg/dL,  $P < 0.05$ ), platelet count ( $322.8$  vs  $276.2 \times 10^9/L$ ,  $P < 0.01$ ) and WBC ( $8.6$  vs  $7.7 \times 10^9/L$ ,  $P < 0.05$ ), and a trend toward having a higher mean ESR (24.5 vs 19.3 mm/hour,  $P = 0.05$ ). Of note, however, there were no statistically significant differences in rates of pathological elevation of these laboratory values (eg, CRP  $> 1.0$  mg/dL, ESR  $> 20$  mm/hour, platelet count  $> 400$   $10^9/L$  and WBC  $> 10 \times 10^9/L$ ) between the cohorts (Table 1). There was also no significant difference in mean albumin between the cohorts (Table 1).

On multivariate logistic regression, while adjusting for age, gender, presence of anxious and/or depressed state, presence of abdominal pain, presence of moderate-severe inflammation, and NSAID use, we found that presence of anxious and/or depressed state and abdominal pain were each independently associated with a 6-lb. or greater weight loss over the prior month ( $P < 0.05$ ). We also found that female gender and NSAID use were negatively associated with weight loss ( $P < 0.05$ ) (Table 2). For this model, the Hosmer and Lemeshow goodness-of-fit test demonstrated a chi-square value of 0.64 and a “*s*-statistic” of 0.701. Additionally, we ran a similar analysis including only patients who had provided contemporary (within 3 months) laboratory values for CRP, ESR, platelet count, and WBC ( $n = 136$ ), dichotomizing cases based upon the presence or absence of a pathologic elevation of the value in question (see Materials and Methods section). When incorporating these factors, we found that the only statistically significant association was a negative relationship with female gender ( $P < 0.01$ ) (Supplementary Table 1). In this model, the Hosmer and Lemeshow goodness-of-fit test demonstrated a chi-square value of 0.90 and a “C-statistic” of 0.75.

### Perception of Nutritional Status, Dietary Behavior, and Abdominal Pain

As we were interested in further evaluating the relative impact of abdominal pain on diet and nutritional status in IBD, we compared CNAQ/SNAQ respondents based upon the

presence or absence of this symptom. In our study cohort, 190 patients (56.5%) reported clinically significant abdominal pain (defined as a 5 or lower on the SPS). Of note, IBD patients with abdominal pain described having a poor or very poor appetite (25.4% vs 6.2%,  $P < 0.0001$ ), fullness after a third or less of a meal (32.8% vs 7.1%,  $P < 0.0001$ ) and consuming one or fewer meals per day (10.1% vs 3.6%,  $P < 0.05$ ) more frequently than those without abdominal pain. There was no significant difference in perceived taste of food when comparing these cohorts (4.2% vs 2.7%,  $P = 0.75$ ). However, IBD patients with abdominal pain were more likely to report using supplemental nutritional drinks or tube feeds over the prior month (21.0% vs 10.6%,  $P < 0.05$ ) than those without pain (Fig. 1A–E).

Given the findings of our multivariable analysis, we also evaluated these responses in individuals who did and did not have an anxious and/or depressed state (AD). One hundred and forty-six patients (48.2%) met criteria for having an anxious and/or depressed state (defined as a total score of 8 or higher on the Hospital Anxiety and Depression Scale). Patients with AD were more likely than those without AD to have a poor or very poor appetite (30.1% vs 7.0%,  $P < 0.0001$ ), to experience fullness after a third or less of a meal (34.9% vs 12.1%,  $P < 0.0001$ ), to experience changes in the perceived taste of food (6.9% vs 0.6%,  $P < 0.01$ ), and to consume one or fewer meals per day (13.7% vs 1.9%,  $P < 0.0001$ ) more frequently than those without abdominal pain. There was also a trend toward increasing likelihood of using supplemental nutritional drinks or tube feeds over the prior month (21.2% vs 12.9%,  $P = 0.07$ ) in those with AD (Supplemental Fig. 1A–E).

## DISCUSSION

This is one of the first studies demonstrating that abdominal pain and symptoms of anxiety and/or depression are independently associated with weight loss in patients with IBD. Our investigation also reinforced that IBD patients are more likely to experience multiple deleterious effects in their dietary behavior in the setting of abdominal pain. Additionally, this is the first study to demonstrate an inverse association between weight loss in IBD and female gender or NSAID use.

No prior report in adult IBD patients has simultaneously elucidated these specific clinical relationships. However, at least some of our findings match those of a previous retrospective study focused on pediatric IBD patients, which demonstrated independent associations between depression, weight loss and abdominal pain.<sup>12</sup> Our results also reinforce previous studies demonstrating that key symptoms such as abdominal pain and anxiety and depression frequently persist, even in the absence of ongoing luminal disease activity.<sup>15, 30</sup> Additionally, these findings support previous expert opinions suggesting that patients can detrimentally impact their diet and overall nutritional status due to fear of inducing abdominal pain.<sup>4, 5</sup> In fact, there are well-described eating disorders (particularly in adolescents), such as avoidant/restrictive food intake disorder

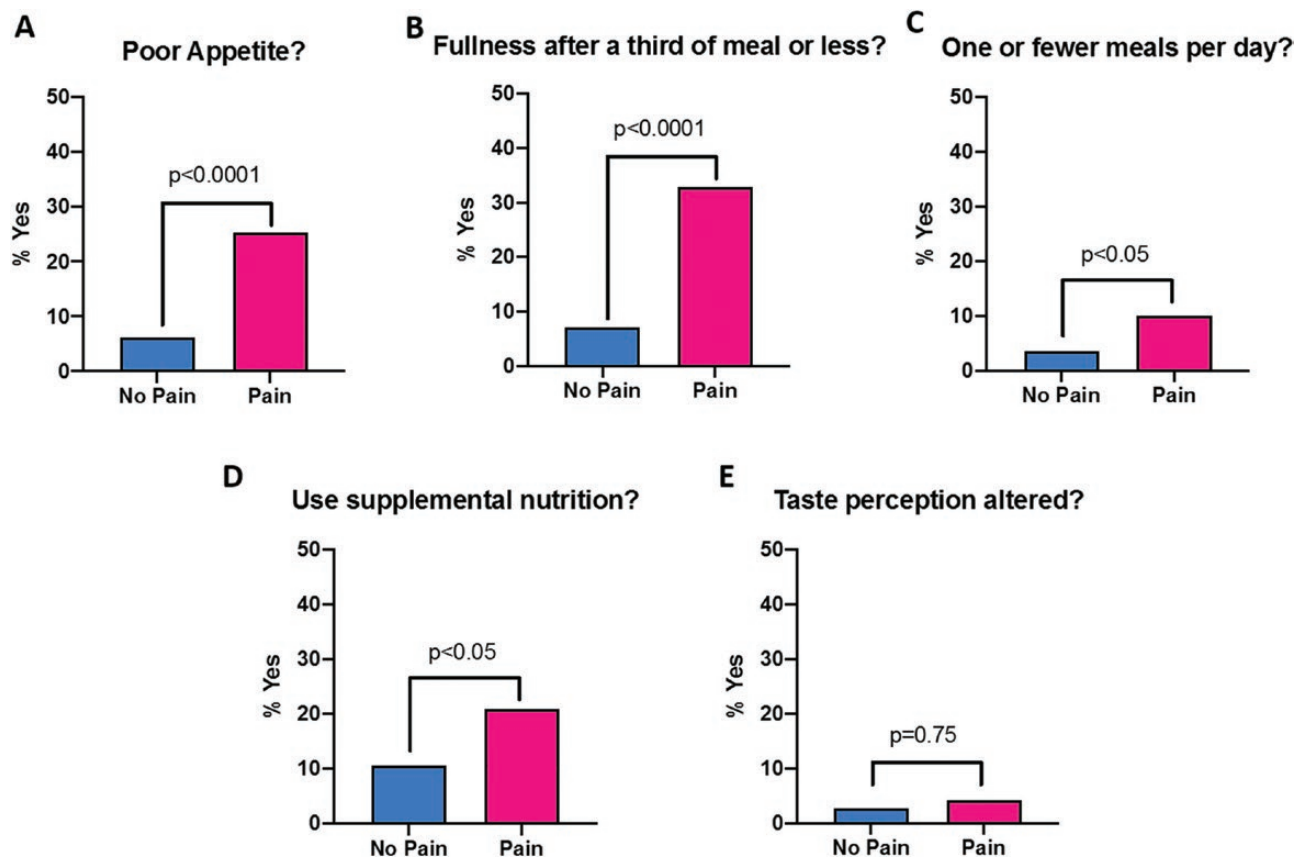


FIGURE 1. (A–E) Dietary behavior in IBD patients with and without abdominal pain

(ARFID), that are strongly associated with this behavior.<sup>32, 33</sup> Importantly, the converse can also be true, as patients may also experience reduction in appetite or taste as a result of anxiety and/or depression.<sup>34, 35</sup>

The findings associated with gender and NSAID use are harder to interpret. Our study was the first to suggest that female gender may be protective against weight loss in IBD. While it is clear that men and women experience unique nutritional challenges in the setting of IBD,<sup>36</sup> previous studies evaluating gender and weight loss in IBD have provided mixed results. One recent large-scale investigation found that women initiated on antitumor necrosis factor medications demonstrated a significantly smaller (though not clinically relevant) change in weight when compared to men on the same therapy.<sup>37</sup> A separate study demonstrated that men with low BMI are at increased risk of developing CD.<sup>38</sup> How NSAID use may be protective against weight loss is less clear. Our findings were surprising because NSAIDs are classically associated with increased disease activity and complications in IBD.<sup>39, 40</sup> One possibility is that NSAID users were achieving an analgesic benefit from these medications that may have allowed them to maintain their nutritional status. This seems less likely, though, given the lack of a similar positive effect in opioid and antidepressant/anxiolytic medication users. In brief, there is no clear explanation for why female gender or NSAID use should be protective in this regard, but these results warrant further investigation.

No matter how the data are interpreted, though, these results do not establish a cause and effect relationship. Notably, several previous studies demonstrate that weight loss and various nutritional deficiencies can impact the likelihood of developing abdominal pain and psychiatric symptoms. For example, changes in body weight and nutrient intake have long been described in the context of depression and anxiety<sup>41</sup> and individuals participating in long term weight loss programs have demonstrated an increased incidence of depression.<sup>42</sup> Micronutrient deficiencies, including those associated with vitamin D and zinc, have been directly and indirectly associated with increased incidences of anxiety, depression and abdominal pain, including in the context of IBD.<sup>43–45</sup> Thus, malnutrition may have as much potential for driving these symptoms and being driven by them.

We did provide circumstantial evidence, though, that abdominal pain and/or anxious or depressed state may be at least partially responsible for some of these nutritional outcomes. Our study demonstrated that patients with these symptoms had significantly increased risks of several deleterious dietary behaviors/outcomes, including poor appetite, early satiety, reduced food intake, and increased reliance on supplemental nutrition resources. These findings supported those of previous studies, which demonstrated that reductions in appetite and food intake are common in IBD patients<sup>1</sup> and that these patients frequently

adjust their dietary choices to avoid symptoms such as abdominal pain.<sup>46</sup> In fact, at least one prior investigation found that over 80% of IBD patients experience food-related issues, including anxiety over dietary selection, restricting their quality of life.<sup>47</sup> Unsurprisingly, several studies have shown that many IBD patients practice selective or discriminatory dietary practices, specifically hoping to positively impact their disease course and/or reduce problematic symptoms.<sup>47-50</sup> Unfortunately, there is a lack of evidence supporting general application of these dietary approaches to the IBD population and it is possible that patients may be doing more harm than good.

There are several strengths to this study. This is one of the largest studies of its kind. This is also one of the few investigations to evaluate key nutritional parameters in an adult IBD population, simultaneously assessing both CD and UC cohorts. Additionally, this study was performed at a dedicated IBD center within a tertiary care center, providing specialized care to this population. We also used rigorous assessments of IBD disease activity in the form of direct endoscopic assessments. This helped to reduce potential mistakes associated with more subjective IBD activity assessment tools like those based on patient symptom reporting.

There are also several limitations to this study. Our investigation involved retrospective data retrieval methods, including questionnaires, which increase the potential for, among other issues, recall, and selection bias. This work was also conducted at a single center, tertiary referral center with a majority Caucasian population. Thus, our findings may not be generalizable to the broader community. Beyond this, we used a 6-lb weight loss as our primary outcome. While this measure has previously been associated with other poor nutritional outcomes,<sup>23</sup> it may not be as meaningful as other measures, such as change in BMI. Additionally, we obtained information on weight loss through use of a patient-reported survey response rather than by directly weighing each patient. Thus, there is the possibility that recall bias impacted these results. We were also unable to evaluate levels of many potentially relevant micronutrients, including some with the potential to impact patient abdominal pain experience (eg, Vitamin D<sup>45</sup>). Finally, while we were able to evaluate both CD and UC patients, it is likely that the respective cohort sizes for each disease cohort were too small for adequate sub-analysis of various clinical factors on weight loss and dietary behaviors.

While larger scale, prospective studies would be helpful to confirm the results of this study, the findings shared here are important because they highlight the significant, independent impact that abdominal pain and psychiatric symptoms, such as anxiety and depression, can have on nutritional outcomes and dietary behavior in IBD. This investigation also reinforces the importance of regularly screening IBD patients for these symptoms as well as incorporating consistent assessments of nutritional status and dietary behavior. IBD providers need to be cognizant of these relationships and be

prepared to optimize management of abdominal pain, anxiety and depression, even when gastrointestinal disease activity seems to be in remission. Given the chronicity and complexity of managing these issues, it is important to consider employing a multi-disciplinary approach that incorporates mental health, nutrition, and pain specialists as soon as possible (preferably as integrated services within the same clinic or as separate referrals to providers with experience caring for patients with IBD or digestive disease). Regardless of the management approach, providers should remember that even when IBD appears quiescent, there are certain persistent symptoms and comorbid complications (eg, abdominal pain, anxiety, depression, and weight loss) that still require our careful attention.

## SUPPLEMENTARY MATERIAL

Supplementary data are available at *Crohn's & Colitis 360* online.

## DATA AVAILABILITY

The data associated with this article was derived from the Penn State College of Medicine Colorectal Diseases Data Registry and Biorepository. No further data was generated as a part of this study.

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