

Posttraumatic Stress in Patients With Inflammatory Bowel Disease: Prevalence and Relationships to Patient-Reported Outcomes

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Supported by: Digestive Health Foundation of Northwestern Medicine.

Conflicts of interest: TT: speaker for Abbvie, ownership interest in Oak Park Behavioral Medicine LLC, consultant for Healthline. SQ: speaker, Pri-Md. SBH: advisor or consultant for Centocor, Procter & Gamble, Otsuka, Abbott Labs, Protein Design Labs, and Shire; grants for clinical research from Centocor, Otsuka, Procter & Gamble, Abbott Labs, Protein Design Labs, and Shire; speaker for Centocor, Procter & Gamble, and Shire. SJ, MS, EAM: Nothing to disclose.

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Background: Patients with chronic illness are at increased risk for traumatic stress because of medical trauma. Initial studies of posttraumatic stress (PTS) in patients with inflammatory bowel disease (IBD) have found that approximately one-third of patients may experience significant PTS symptoms including flashbacks, nightmares, hypervigilance, disrupted sleep, and low mood. We aim to better characterize PTS in IBD and its relationship with patient outcomes in a large cohort of patients with IBD.

Methods: Adult patients registered with the Crohn's & Colitis Foundation/University of North Carolina IBD Partners database were invited to complete a supplementary survey between February and July 2020. The Post Traumatic Stress Disorder Checklist-5th edition was administered as a supplemental survey. Additional data from IBD Partners included disease severity, surgery and hospital history, demographics, and health care utilization.

Results: A total of 797 patients participated (452 with Crohn disease, 345 with ulcerative colitis). No impacts on response patterns because of the COVID-19 pandemic were found. Although 5.6% of the sample reported an existing PTS diagnosis because of IBD experiences, 9.6% of participants met the full IBD-related PTS diagnostic criteria per the Post Traumatic Stress Disorder Checklist-5th edition. Female patients, younger patients, those with less educational attainment, non-White patients, and Hispanic patients reported higher levels of PTS symptoms. Patients with higher PTS symptoms were more likely to have been hospitalized, have had surgery, have more severe symptoms, and not be in remission. Increased PTS was also associated with increased anxiety, depression, pain interference, fatigue, and health care utilization.

Conclusions: The present findings support prior research that approximately one-quarter to one-third of patients with IBD report significant symptoms of PTS directly from their disease experiences, and certain demographic groups are at higher risk. In addition, PTS is associated with several IBD outcomes. Patients with higher PTS symptoms are less likely to be in remission and may utilize more outpatient gastrointestinal services. Intervention trials to mitigate PTS symptoms in patients with IBD are warranted.

Key Words: inflammatory bowel disease, post-traumatic stress, medical trauma

Introduction

Chronic psychological sequelae from a traumatic experience, including post-traumatic stress disorder (PTSD), are widely studied phenomena.¹ At-risk groups include combat veterans, victims of crime or terrorism, and those surviving natural disasters. Traumatic stress reactions may become pervasive and chronic without proper treatment, with approximately 10% of the U.S. population diagnosed with PTSD.²⁻⁴ Trauma can also occur with medical events, such as a hospitalization in an intensive care unit⁵ or a near-death experience from severe illness. In medical patients, posttraumatic stress (PTS) is the most widely accepted and studied construct.

The symptoms of PTS mirror those of PTSD but may be less severe (ie, subclinical) or may not include every criterion from the *Diagnostic and Statistical Manual for Mental Disorders*, 5th edition (DSM-5). However, people with PTS

may experience pervasive flashbacks, nightmares, emotional numbing or irritability, avoidance of triggering situations, and physiological hyperarousal.¹ Traumatic stress occurs in 9% to 27% of patients who experience an acute medical event. Medical PTS is most often explored among patients with cancers,^{6,7} cardiovascular disease,^{8,9} and HIV/AIDS,^{10,11} with multiple studies showing persistent trauma symptoms. Because patients with severe inflammatory bowel disease (IBD) often have repeated emergency department visits and emergency surgeries and may utilize treatments with rare but serious adverse effects, it is possible that a proportion of these patients will develop PTS.

Only 2 studies to date have evaluated PTS in patients with IBD. In 2010, a study of a large Swiss cohort of 597 patients with Crohn disease (CD) found that 19.5% of patients had symptoms consistent with PTSD.¹² Those patients were 4.3

times more likely to experience disease exacerbation than patients with milder traumatic stress symptoms and 13 times more likely to have an IBD flare-up than those reporting no symptoms of PTSD. In 2019, our study of 131 patients with IBD in the United States found that 32% reported significant PTS symptoms, with patients with CD more likely to experience PTS than those with ulcerative colitis (UC).¹³ Risk factors for PTS included IBD severity, negative hospital experiences, and surgery leading to an ileostomy.

Chronic traumatic stress is associated with poor outcomes in other diseases. These include decreases in health-related quality of life and treatment adherence and increases in health care utilization (HCU). Anxiety, depression, substance abuse, and suicide^{14,15} are also possible. In IBD, very little is known about PTS and IBD outcomes. For example, untreated PTS can affect disease severity. Chronic inflammation is consistently implicated in PTSD via elevations in acute-phase proteins, pro- and anti-inflammatory cytokines (eg, interleukin-6, interleukin-1 β , tumor necrosis factor α , and interferon γ), innate immune cells, and white blood cell counts.¹⁶⁻²⁰ Many of the inflammatory mechanisms in PTSD overlap with those in IBD. In addition, the brain-gut-microbiome axis is implicated in chronic PTSD,^{21,22} suggesting that PTS may have multifactorial, deleterious effects on outcomes for patients with IBD.

This study aims to look at a national, large, representative sample from the Crohn's & Colitis Foundation IBD Partners database. Specifically, we aim to (1) measure the prevalence of PTS symptoms with a validated measure using DSM-5 criteria; (2) determine how PTS symptoms may relate to IBD, disease activity, and 2 specific outcomes that drive the costs of care—namely, the number of hospitalizations and surgeries; and (3) evaluate how PTS symptoms relate to psychological distress, pain interference, sleep and fatigue, and HCU via visits to primary care or gastroenterology clinics in the past year. We hypothesize that PTS symptoms are associated with poorer patient outcomes and increased HCU.

MATERIALS AND METHODS

A cross-sectional observational study was conducted with patients registered in the IBD Partners database (<https://ccfa.med.unc.edu/>) between February and August 2020. IBD Partners is a research-dedicated national database of the Crohn's & Colitis Foundation of >13,000 adult patients with IBD with a robust existing dataset designed to supplement additional surveys. After completing the standard questionnaires for IBD Partners, patients were given the option to participate in the present study. Participants were invited to participate if they lived in the United States and had a record of at least 1 surgery or 1 hospitalization because of IBD or had ever scored higher than 220 on the Simple Crohn's Disease Activity Index for CD or higher than 5 on the Simple Colitis Clinical Activity Index (SCCAI) for UC or indeterminate IBD. Before completing the study questions, participants were screened for pre-existing PTSD not related to IBD. Those who endorsed a non-IBD-related PTSD diagnosis were excluded, and participants who endorsed a PTS diagnosis related to IBD were included.

Those who agreed and met the inclusion criteria completed the following additional questionnaire. The PTSD Checklist-5 (PCL-5)²³ is a standardized questionnaire that measures symptoms of PTSD outlined in the DSM-5 over the past month using the prompt "In the past month, how

much were you been bothered by..." The PCL-5 contains 20 items (eg, "Repeated, disturbing, and unwanted memories of the stressful experience?" and "Feeling jumpy or easily startled") that encompass the 4 DSM-5 symptom groups of PTSD (intrusive memories, avoidance, negative changes in thinking and mood, changes in physical and emotional reactions). Responses are ranked on a 5-point Likert scale (0 = not at all to 4 = extremely). Participants are instructed to think about IBD-related traumatic events and avoid thinking about traumatic events that are not related to their disease when answering the questions. A total score of 80 is obtained by summing the 20 items. A DSM-5 symptom group severity score is obtained by summing items within that given criterion (B: intrusion/re-experiencing = items 1-5; C: avoidant symptoms = items 6-7; D: negative mood/thoughts = items 8-14; E: increased arousal = items 15-20). A provisional diagnosis of PTS is made by counting the number of items in each cluster rated as "moderately" or higher and following the DSM-5 criteria: 1 B item, 1 C item, 2 D items, and 2 E items. A suggested cutoff score of 31 is indicative of PTSD but is not fully validated and was therefore not used in this study.

Data Extracted From the Main IBD Partners Database

Disease severity

For patients with CD, the total score of the patient version of the Harvey-Bradshaw Index (pHBI) was computed with a cutoff for remission as pHBI < 5. For patients with UC, the total score of the SCCAI was calculated with a cutoff for remission as SCCAI < 5. Two additional categorical questions about disease activity in the last 6 months (constant, no symptoms, 1-2 days a week, 1-2 days a month, few days, no symptoms) and in the last week (severely active, moderately active, mildly active, minimal, remission) were included.

Hospitalizations and surgeries

Any history of hospitalization or surgery for IBD was dichotomized (yes, no), and the number of hospitalizations or surgeries was reported on a continuous scale.

HCU

Patients self-reported the number of visits they had to their primary care physician and to their gastroenterologist in the past year. Responses were categorical (never, 1-2, 3-4, 5 or more) for each variable.

Additional IBD Partners variables

Sex, age, age at diagnosis, race, ethnicity, highest level of education, state of residence, type of gastrointestinal (GI) clinic (university, private practice, Veterans Administration), anxiety, depression, sleep quality, fatigue, and pain interference were also recorded.

Ethical Considerations

This study was approved by the Institutional Review Board of Northwestern University and the University of North Carolina/IBD Partners. All participants completed an online consent before completing the study questionnaires.

Statistical Analyses

A priori power analyses for the planned statistics, assuming a power of 0.80, a Cohen's *d* effect size of 0.30, and an error

probability of $P < 0.01$, indicated that a minimum sample of 526 patients was needed. Data were exported from the IBD Partners database into a Microsoft Excel workbook and were then imported into SPSS v.26 for Macintosh (Chicago, IL) for analyses. Total scores for the PCL-5 and the DSM-5 symptom groups were calculated. Participant responses were coded 1 = yes and 0 = no for each criterion rated as “moderately” or higher. Tests for normal distribution and nonparametric tests were conducted using skewness/kurtosis cutoffs of ± 2.0 . Given the small number of the cohort, the patients with indeterminate IBD were pooled with the UC group.

Descriptive statistics are presented as mean (SD) for continuous and percentage (frequency) for categorical variables. States were organized into the 4 geographic regions of the U.S. Census: northeast, south, midwest, and west. The PCL-5 total score was nonnormally distributed. Therefore, DSM-5 symptom group scores were dichotomized to yes/no for each criterion (re-experiencing, avoidance, negative mood/thoughts, and increased arousal) and to meeting the full DSM-5 criteria for PTS as outlined above. Chi-square analyses with the Fisher exact test (where appropriate) evaluated differences when we compared categorical variables (eg, IBD diagnosis, sex, education, prior surgery). Independent-samples t tests examined relationships between PTSD symptom groups for continuous variables (age, number of hospitalizations, number of surgeries). The number of hospitalizations was also nonnormally distributed. As such, differences between groups were evaluated using the Mann-Whitney U test with median and interquartile range (IQR) reported.

Binary logistic regression models were used to evaluate the relationship of PTS symptoms and hospitalization history and PTS symptoms and surgical history (each dichotomized as no = 0, yes = 1). Any demographic or clinical variables also associated with these 2 outcomes were also entered into the regressions model to control for their effects. The models were organized by demographic and clinical variables, where appropriate, with each PTS symptom category and full IBD-related PTS diagnosis. Odds ratios (ORs) with 95% confidence intervals (CIs) are reported with forest plots.

Separate hierarchical linear regression models were used to evaluate the relationship between PTS symptoms and the following outcome variables: (1) symptom severity in the past week, (2) symptom severity in the past 6 months, (3) primary care physician (PCP) visits in the past year, (4) GI clinic visits in the past year. Any demographic or clinical variables also associated with each outcome were entered into the regression model first to control for their effects. Standardized beta weights are reported for each model. Statistical significance was set to $P < 0.05$ for all analyses.

COVID-19 Pandemic Impact

Participants were coded by the study date/time stamp for survey completion as “pre-COVID” and “post-COVID” using a date of March 31, 2020. Mann-Whitney U test and chi-square analyses evaluated differences between the pre- and post-COVID groups for PCL-5 scores and symptom cluster. No significant differences existed based on survey timing during the COVID-19 pandemic for the PCL-5 score ($P = 0.894$), the proportion meeting the PTS diagnostic cutoff ($P = 0.333$), and the proportion scoring moderately or higher on any PTS symptom criterion ($P = 0.121-0.404$).

RESULTS

Study Sample

During the study period, 1352 patients were presented with the option to enroll. Of these, 914 (68%) agreed to participate. An existing PTS/PTSD diagnosis was reported by 107 people (94 women, 13 men). Sixty-two out of 107 people indicated that their PTSD was not related to IBD and were therefore excluded from the study. Fifty-five participants did not complete the PCL-5, which left a final sample of 797 participants (452 with CD, 345 with UC). Demographic and clinical characteristics of the sample are outlined in Tables 1 and 2, respectively. Patients in the sample were predominantly White, non-Hispanic, middle aged (mean [SD] = 49.22 [15.14]), female, and college educated. Participants were evenly divided across the 4 major geographic regions of the United States (west, south, midwest, northeast), and no significant differences existed for PTS. Participants tended to be diagnosed with IBD in their late 20s. The majority (80%) had at least 1 prior hospitalization, and half (54%) had at least 1 prior surgery because of IBD. On average, patients reported 4.15 prior surgeries and 3.03 prior hospitalizations. Less than 10% had an ostomy or J-Pouch. Almost all participants had both a primary care physician (PCP) and a gastroenterologist, with most patients receiving treatment from a private practice or university/academic hospital clinic.

Prevalence of PTS Symptoms in IBD

Based on the self-report item “Have you ever been diagnosed with PTS/PTSD and is this because of your IBD?” 5.6% of participants in the sample had a diagnosis of IBD-related PTS. However, 9.6% of participants met the full diagnostic criteria for PTS, or all symptom criteria having the minimum number of items rated at “moderately” or higher on the PCL-5 (Fig. 1). When examining each symptom group (re-experiencing, avoidance, negative mood, increased arousal), we found that the proportion of participants with a positive score ranged from 21% to 26%; no significant differences

Table 1. Demographic Information for Study Sample

	N = 797
Age (y)	49.22 (15.14)
Sex	
Male	27.6% (220)
Female	72.4% (577)
Race	
White	95.1% (723)
Black/African American	1.4% (11)
Asian	1.1% (8)
Multiracial	1.8% (14)
Other	0.5% (4)
Unknown	4.6% (37)
Ethnicity	
Hispanic	2.3% (18)
Non-Hispanic	97.7% (754)
Education	
Less than college	22.3% (173)
College graduate or higher	77.8% (604)
Unknown	2.5% (20)

Table 2. Clinical Characteristics of Study Sample

	N = 797
Age at diagnosis (y)	28.53 (13.47)
CD	56.7% (452)
UC	43.3% (345)
Ostomy	7.9% (63)
J-Pouch	9.7% (77)
Prior surgery for IBD	53.8% (429)
Number of prior surgeries	4.15 (2.31); range, 1-14
Prior hospitalization for IBD	80.2% (639)
Number of prior hospitalizations	3.03 (2.37); range: 1-10
Duration, d (most stressful hospitalization)	
1-3	19.5% (128)
4-7	35.6% (233)
8-14	22.6% (148)
>14	19.8% (130)
Unknown	2.4% (16)
Has PCP	90.9% (720)
PCP visits in past year	
None	7.9% (57)
1-2	63.1% (454)
3-4	22.1% (159)
>5	6.9% (50)
Unknown	9.7% (77)
Has gastroenterologist	96.8% (768)
Type of GI clinic	
University/academic	29.4% (226)
Private practice	60.3% (463)
Veterans Administration	0.4% (3)
Other	8.6% (66)
Unknown	4.9% (39)
GI visits in past year	
None	7.2% (55)
1-2	60.2% (462)
3-4	23.2% (178)
>5	9.1% (70)
Unknown	3.9% (32)

existed between CD and UC. The younger a patient's age, the more PTS symptoms reported across all symptom groups and were more likely to meet the full criteria for IBD-related PTS (all $P < 0.001$).

Demographic and Illness Traits Associated With PTS

Women were significantly more likely to meet the full IBD-related PTS criteria than men, including re-experiencing the event(s) through dreams, flashbacks or intrusive thoughts, and avoidance behaviors (all $P < 0.001$; Fig. 1). Both non-White patients and non-Hispanic patients reported more avoidance behaviors than White patients ($P = 0.023$) and Hispanic patients ($P = 0.024$); these results should be interpreted with caution because of the small sample sizes for racial and ethnic minorities. Patients whose education was less than a college degree were more likely to meet the full criteria for IBD-related PTS and all symptom groups (re-experiencing, avoidance, negative mood, increased arousal; all $P < 0.004$).

Certain illness traits were also associated with IBD-related PTS. Patients with CD and a history of abscess reported more re-experiencing ($P = 0.03$) and low mood symptoms ($P = 0.05$). For patients with UC, those who reported "immediate" or higher bowel urgency reported significantly more re-experiencing, avoidance, low mood, and hypervigilance (all $P < 0.01$), whereas those who reported more frequent blood in their stool also reported more avoidance ($P = 0.023$) and low mood symptoms ($P = 0.033$). The only extraintestinal symptom associated with elevations in PTS symptoms was joint pain (all PTS symptom groups, $P < 0.05$). Those with a history of fistula or stricture did not differ regarding PTS than those without.

PTS and IBD Symptom Severity

Based on the pHBI or SCCAI scores, those with UC were less likely to be in remission compared to those with CD ($P < 0.001$). As such, patients with CD and patients with UC were evaluated separately for the relationship between PTS and remission. For CD, patients with more PTS symptoms in all categories were significantly associated with having active disease (all $P \leq 0.01$). For UC, only elevations for the re-experiencing category of PTS symptoms were associated with active disease ($P = 0.009$); avoidance, negative mood, and increased arousal were not significant. According to the logistic regression, having a CD diagnosis remained a substantial predictor of being in remission (OR = 5.57; 95% CI, 4.0-7.75; Fig. 2). The PTS symptoms of negative mood (OR = 0.60; 95% CI, 0.41-0.89) and increased arousal (OR = 0.60; 95% CI, 0.41-0.88) were associated with lower odds of being in clinical remission when controlling for IBD type (Fig. 2).

Patients with UC were more likely to report more severe and frequent symptoms over the last 6 months, compared with patients with CD ($P < 0.001$). When controlling for diagnosis in the regression models, all PTS symptom groups and those participants who met the full diagnostic criteria for IBD-related PTS were associated with more severe IBD symptoms (Table 3). Similar findings existed for symptom severity in the past week when controlling for diagnosis, sex, and race. Although a diagnosis of CD remained a predictor, the relationship between each PTS symptom group and IBD severity was considerably larger; sex and race were removed from regression models as nonsignificant predictors.

PTS and Hospitalizations

Patients with CD were more likely to ever be hospitalized for IBD than for UC ($P < 0.001$). The PTS symptoms of re-experiencing and increased arousal, along with meeting the full diagnostic criteria for IBD-related PTS, were associated with having at least 1 IBD-related hospitalization (Fig. 2). When controlling for diagnosis, patients with elevations in re-experiencing PTS symptoms were 2.18 times more likely to have been hospitalized for IBD (95% CI, 1.36-3.51), with elevations in increased arousal 2.02 times more likely (95% CI, 1.22-3.34) and meeting the full criteria for IBD-related PTS 2.16 times more likely (95% CI, 1.04-4.49).

Patients with CD were also likely to have a higher number of hospitalizations for IBD than were patients with UC (median, 3.0; IQR, 1-5 vs median, 2.0; IQR, 1-3; $P < 0.001$). Elevations in all PTS symptom categories were significantly associated with a higher number of hospitalizations for IBD (Table 4). When controlling for diagnosis, these symptoms

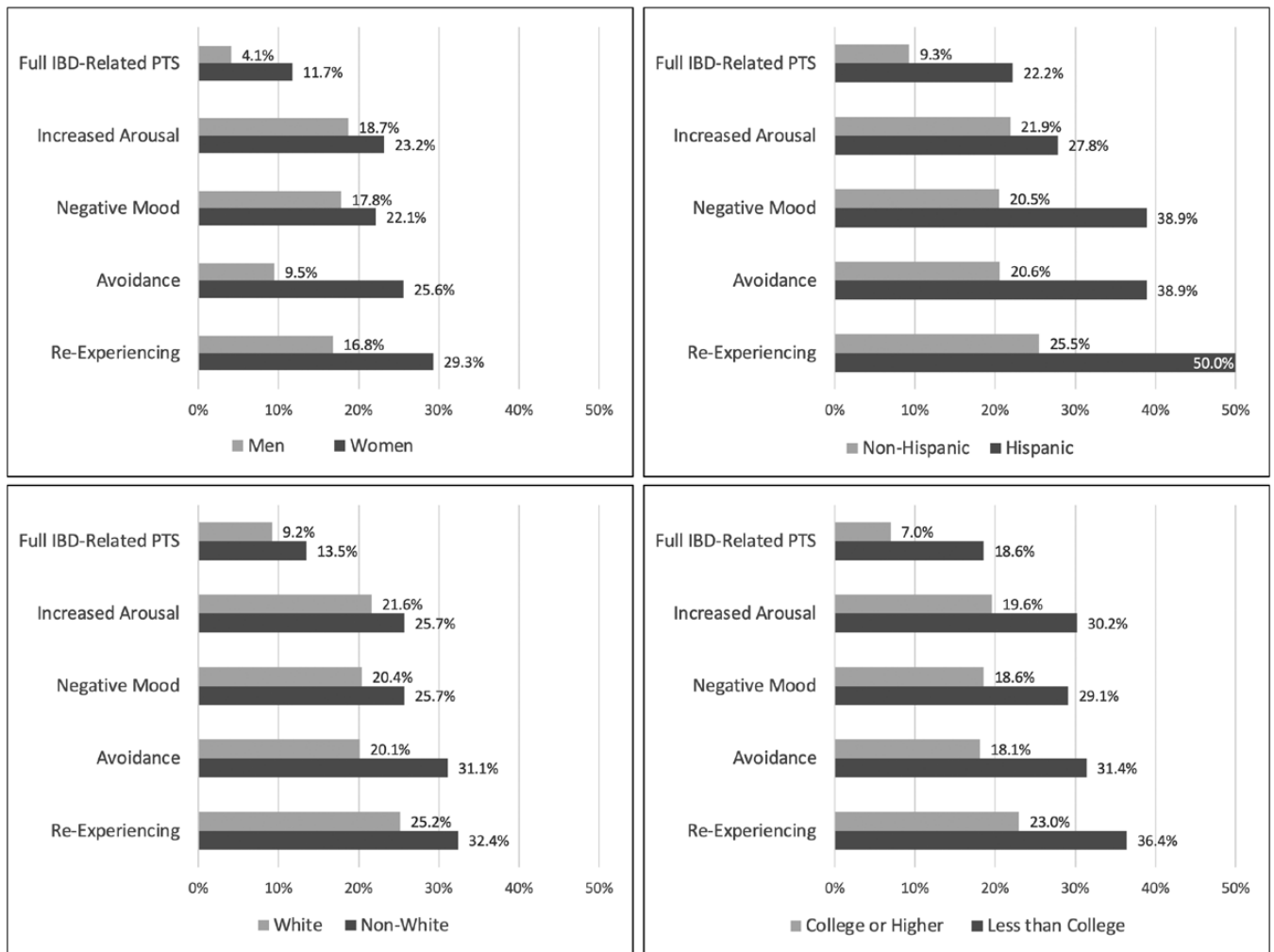


Figure 1. Percentage of patients within each demographic group meeting criteria for each PTSD symptom cluster and full PTSD.

remained significant predictors for the number of hospitalizations. However, having CD indicated a larger relationship with the number of hospitalizations than PTSD symptoms.

PTSD and Surgical History

Patients with UC were more likely to report past surgery for IBD than were patients with CD ($P < 0.001$), with women more likely than men ($P = 0.012$). The PTSD symptoms of re-experiencing and increased arousal were associated with having at least 1 IBD surgery (Fig. 2), whereas negative mood and meeting the full criteria for IBD-related PTSD were nonsignificant. Patients reporting greater re-experiencing symptoms were 1.9 times more likely to have had an IBD surgery (95% CI, 1.31-2.77), when we controlled for diagnosis and sex. Similarly, patients with elevated avoidance or elevated arousal symptoms were 1.6 times more likely (95% CI, 1.07-2.39) and 1.49 times more likely (95% CI, 1.01-2.20), respectively, to have had surgery for IBD. No differences existed by demographic or clinical variables for the number of prior IBD surgeries, and no particular PTSD symptoms were associated with the number of surgeries (all $P > 0.10$). Patients with past ostomy surgery ($P = 0.036$) or J-Pouch ($P = 0.025$) reported more of the re-experiencing type of PTSD symptoms.

No other surgery types (resection, strictureplasty, perianal repair) were associated with PTSD.

PTSD and HCU

People with less than a college degree reported more PCP visits ($P = 0.015$). All other demographic or clinical variables were not related to visits to PCPs. All PTSD symptoms and meeting the full criteria for IBD-related PTSD were associated with more PCP visits (Table 4). When controlling for education level, we found that all PTSD symptoms were predictors of the utilization of primary care. Patients with CD had more outpatient GI visits in the past year than patients with UC ($P < 0.001$). All PTSD symptoms and meeting the full criteria for IBD-related PTSD were associated with more GI visits (Table 4). When controlling for diagnosis, we found that all PTSD symptoms remained significant predictors of more GI clinic utilization.

PTSD and Psychosocial Outcomes

As expected, increased PTSD symptoms were associated with increased anxiety, depression, fatigue, and pain interference (Fig. 3). Patients with elevations across any of the symptom groups and those meeting the full criteria for IBD-related PTSD scored significantly higher across these 4 domains of psychosocial function (all $P < 0.001$). Although sleep quality was

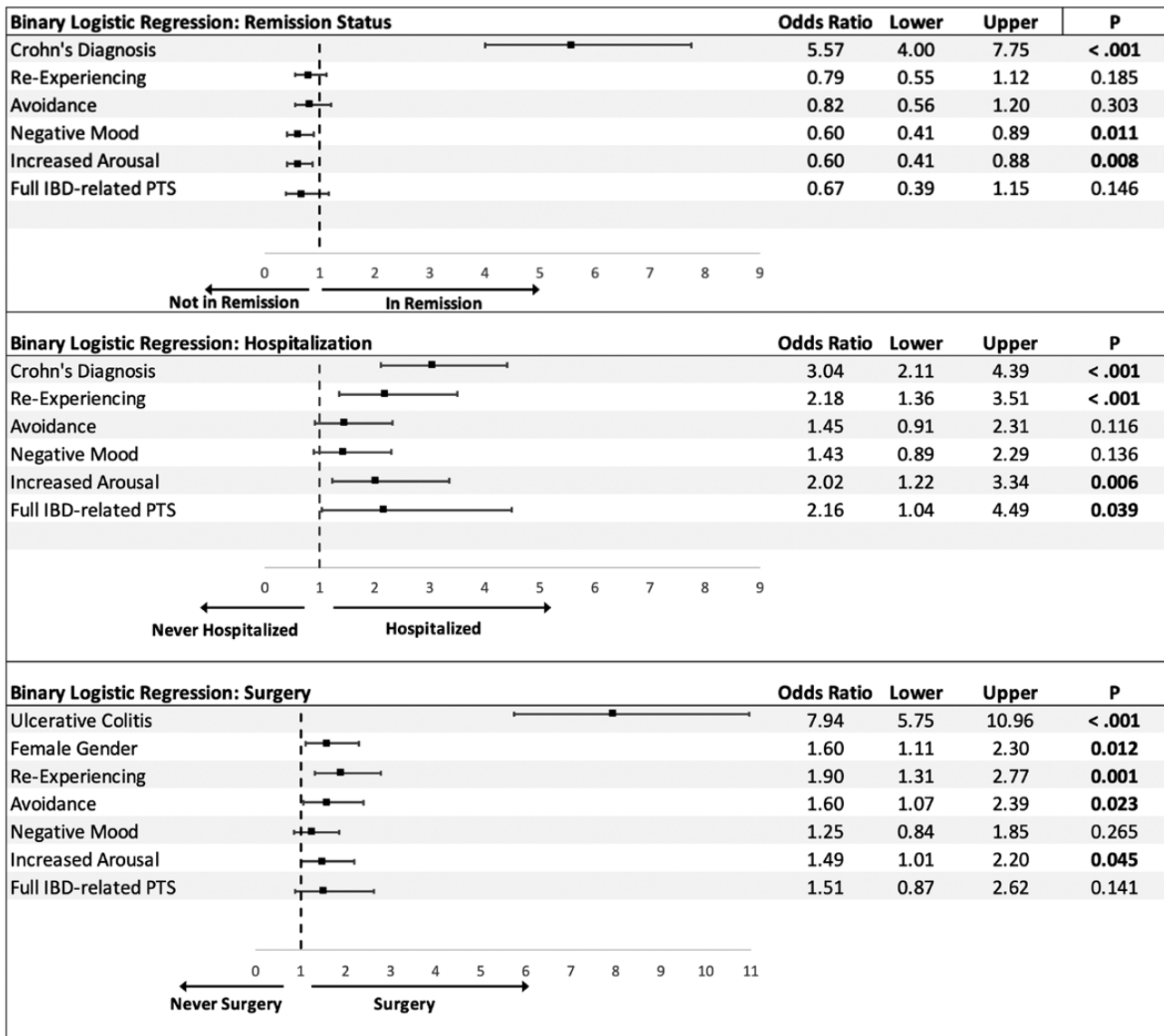


Figure 2. Relationship between PTS symptoms and remission status, history of IBD-related hospitalization, or surgery. Remission: 0 = no, 1 = yes. Diagnosis: CD = 1, UC = 2. Sex: female = 1, male = 2. Each PTS variable: 0 = no, 1 = yes.

slightly related to fatigue ($r = -0.12$; $P = 0.024$), only fatigue was substantially higher in patients with more PTS symptoms. This difference remained when controlling for symptom severity over the past week. Patients meeting the full criteria for IBD-related PTS had poorer sleep, albeit negligible, than those who did not (yes: 11.53 (1.87) vs no: 11.03 (1.67); $P = 0.028$).

Discussion

The current study sought to replicate our previous data regarding the prevalence of significant PTS symptoms with a larger cohort of patients with IBD. As hypothesized, PTS symptoms were associated with hospitalizations, IBD-related surgery, HCU, and poorer psychosocial outcomes. We found that 9.5% of patients met the full DSM-5 diagnostic criteria for IBD-related PTS, based on PCL-5 criteria. Of particular concern is the finding that 5.6% of participants reported a prestudy diagnosis of PTS because of IBD-related experiences. Our findings suggest that traumatic stress is underdiagnosed in patients with IBD. A similar percentage of patients in this

study reported significant PTS symptoms for the 4 symptom categories as in earlier research.¹³

As a whole, approximately one-quarter of patients had moderate to severe symptoms of re-experiencing the event(s), avoidance, negative mood, and increased arousal. Certain demographic groups seemed to be at increased risk, including those with less than a college education and patients of Hispanic ethnicity. Women also scored significant higher across all PTS domains than men. These findings were also consistent with the PTSD literature, which finds that women, racial and ethnic minorities, and those from lower socioeconomic backgrounds are more likely to have PTSD than comparable groups. Unfortunately, even with purposeful sampling, our cohort of participants was 95% White and 98% non-Hispanic. As such, the findings on race and ethnicity should be interpreted with caution. Future studies should focus on non-White patients with IBD to better understand the rates of PTS in these groups.

We also sought to understand how PTS symptoms relate to several self-reported patient outcomes. We found that all

Table 3. Hierarchical Multiple Regression Analysis of Relationship Between PTS and Symptom Severity Over Last Week and Last 6 Months

Symptom Severity—Past Week*					
	Univariate		Multivariate		
	χ^2	<i>P</i>	B	β	<i>P</i>
Non-White	11.233	0.024	−0.104 to −0.223	−0.048 to −0.057	All > 0.05
Female	9.845	0.043	−0.188 to −0.203	−0.041 to −0.063	All > 0.10
CD	20.448	<0.001	0.234	0.102	0.003
Re-experiencing	38.064	<0.001	0.529	0.203	<0.001
CD	20.448	<0.001	0.261	0.113	0.001
Avoidance	41.178	<0.001	0.568	0.204	<0.001
CD	20.448	<0.001	0.245	0.106	0.002
Negative mood	80.510	<0.001	0.871	0.311	<0.001
CD	20.448	<0.001	0.230	0.100	0.004
Increased arousal	45.268	<0.001	0.622	0.226	<0.001
CD	20.448	<0.001	0.267	0.116	0.001
Full IBD-related PTS	42.039	<0.001	0.721	0.186	<0.001
Symptom Severity—Past 6 Months†					
	Univariate		Multivariate		
	χ^2	<i>P</i>	B	β	<i>P</i>
UC	29.836	<0.001	0.335	0.101	0.004
Re-experiencing	40.608	<0.001	0.752	0.201	<0.001
UC	29.836	<0.001	0.376	0.114	0.001
Avoidance	38.413	<0.001	0.821	0.204	<0.001
UC	29.836	<0.001	0.346	0.105	0.002
Negative mood	75.620	<0.001	1.195	0.297	<0.001
UC	29.836	<0.001	0.326	0.099	0.005
Increased arousal	45.218	<0.001	0.828	0.210	<0.001
UC	29.836	<0.001	0.378	0.114	0.001
Full IBD-related PTS	43.841	<0.001	1.028	0.185	<0.001

*Model: diagnosis (step 1), sex + race (step 2), and each symptom cluster (step 3). Sex: female = 1, male = 2. Race: non-White = 1, White = 2. Diagnosis: CD = 1, UC = 2.

†Model: Diagnosis (step 1) and each symptom cluster (step 2). Diagnosis: CD = 1, UC = 2.

PTS symptoms were more likely to be associated with active disease, as measured by the pHBI, in patients with CD, whereas only patients with UC with re-experiencing symptoms more often reported active IBD per the SCCAI score. When controlling for these disease differences, we found that patients with greater levels of negative mood and increased arousal had significantly lower odds of being in clinical remission. Alterations in immune regulation associated with PTSD, including elevated levels of proinflammatory markers that may overlap with IBD (eg, C-reactive protein),²⁴ may explain the association between PTSD and disease activity in IBD. However, inflammation itself may be a risk factor for developing PTSD, which would place individuals with IBD at greater risk for developing PTSD or IBD-related PTS after a traumatic event. Additional research related to the relationship between inflammation, PTSD, and IBD involving longitudinal data is warranted.

We also evaluated how longer-term symptom severity (past 6 months) and short-term (past week) may be associated with PTS symptoms. Patients with UC reported greater symptoms in the past week, whereas patients with CD re-

ported more symptoms in the past 6 months. Regardless of this difference, PTS symptoms were substantially larger contributors to symptom severity in both the short and long term when controlling for diagnosis. In earlier research,¹³ symptom severity was only predictive of PTS in patients with UC, accounting for roughly one-fifth of the variance. The present findings suggest that symptom severity has an important relationship with PTS symptoms in patients with CD and with UC.

Research into the relationship of PTSD and HCU is mixed, with some studies finding a decrease in clinic visits (likely because of avoidance behaviors) and others showing increased HCU.^{10,25} Either scenario is going to increase direct costs, because deferring care, especially in the context of IBD, can lead to more severe disease and emergent treatments. Patients with CD did not differ from patients with UC for PCP visits, but patients with CD reported more GI clinic visits in the past year and more lifetime hospitalizations. Patients with less than a college degree also visited their PCP more often than those with more education. This finding is consistent with previous studies highlighting socioeconomic status-based differences

Table 4. Hierarchical Multiple Regression Analysis of Relationship Between PTS and HCU

Primary Care Visits—Past Year*					
	Univariate		Multivariate		
	χ^2	<i>P</i>	B	β	<i>P</i>
Less than college degree	9.824	0.020	−0.095 to −0.073	−0.056 to −0.043	All > 0.10
Re-experiencing	17.386	<0.001	0.225	0.139	<0.001
Avoidance	17.293	<0.001	0.190	0.109	0.004
Negative mood	21.469	<0.001	0.284	0.164	<0.001
Increased arousal	29.414	<0.001	0.271	0.159	<0.001
Full IBD-related PTS	23.645	<0.001	0.390	0.161	<0.001
GI Clinic Visits—Past Year†					
	Univariate		Multivariate		
	χ^2	<i>P</i>	B	β	<i>P</i>
CD	19.434	<0.001	−0.153	−0.099	0.005
Re-experiencing	24.723	<0.001	0.266	0.153	<0.001
CD	19.434	<0.001	−0.167	−0.109	0.002
Avoidance	16.830	<0.001	0.255	0.136	<0.001
CD	19.434	<0.001	−0.162	−0.105	0.003
Negative mood	17.641	<0.001	0.272	0.146	<0.001
CD	19.434	<0.001	−0.155	−0.101	0.005
Increased arousal	14.222	<0.001	0.223	0.122	0.001
CD	19.434	<0.001	−0.172	−0.112	0.002
Full IBD-related PTS	15.726	<0.001	0.346	0.135	<0.001
Total IBD Hospitalizations‡					
	Univariate		Multivariate		
	<i>t</i>	<i>P</i>	B	β	<i>P</i>
CD	−7.208	<0.001	−1.201	−0.248	<0.001
Re-experiencing	−2.231	0.026	0.481	0.092	0.017
CD	−7.208	<0.001	−1.223	−0.253	<0.001
Avoidance	−2.237	0.026	0.591	0.104	0.007
CD	7.208	<0.001	−1.204	−0.249	<0.001
Negative mood	−2.073	0.039	0.509	0.090	0.020
CD	7.208	<0.001	−1.174	−0.244	<0.001
Increased arousal	−3.294	0.001	0.705	0.129	0.001
CD	7.208	<0.001	−1.241	−0.256	<0.001
Full IBD-related PTS	−2.726	0.007	0.982	0.129	0.001

*Model: education (step 1) and each symptom cluster (step 2). Education: less than college = 1, college or higher = 2.

†‡ Model: diagnosis (step 1) and each symptom cluster (step 2). Diagnosis: CD = 1, UC = 2.

in HCU, surgical therapy, health-related quality of life, and clinical outcomes in patients with IBD.²⁶ However, PTS symptoms remained significant predictors of PCP use in multivariate models where education level did not. Higher PTS symptoms were predictive of more GI clinic visits and lifetime hospitalizations when controlling for IBD type and remission status. This relationship seemed to be stronger for clinic visits than hospitalizations. Attending appointments with a health care provider may provide patients with PTSD a sense of control over their symptoms or a sense that their physician is a source of safety, care, or comfort. Several studies have high-

lighted lack of social support as a risk factor for developing PTSD.^{27,28} For some patients, especially those who lack social support in the home, appointments with their medical providers may offer a sense of emotional support while being cared for by someone else.

Surgery is a common occurrence in IBD management. In this cohort, the median number of surgeries was 4, ranging from 1 to 14. Certain PTS symptoms, specifically patients with more re-experiencing of a traumatic event and arousal were 1.5 to 2 times more likely to have at least 1 IBD-related surgery. However, PTS symptoms were not associated with

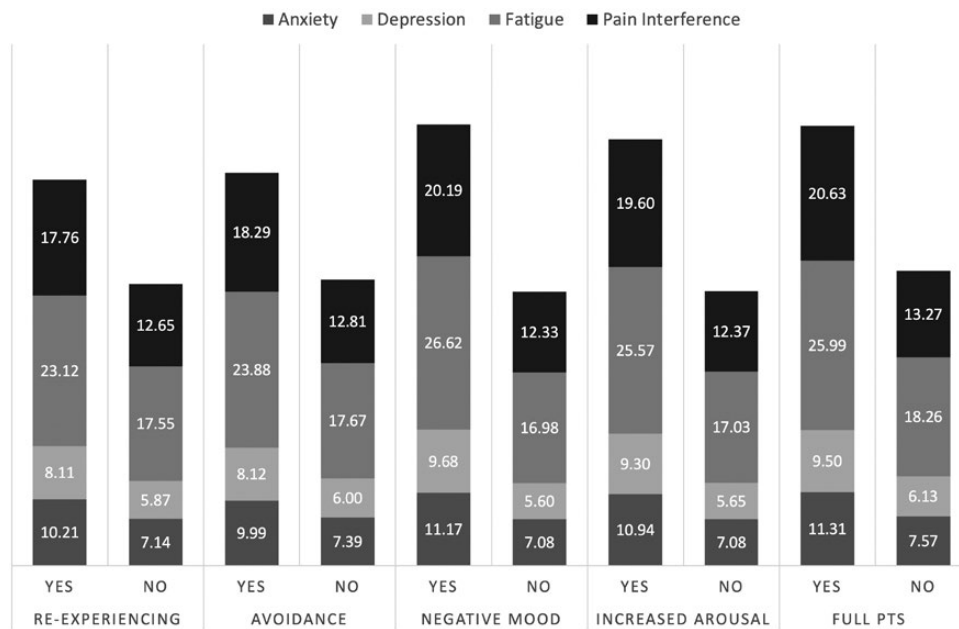


Figure 3. Mean scores for psychosocial patient-reported outcomes by PTS symptom group.

the number of surgeries. This finding suggests that the number of surgeries is less important than a particularly stressful or traumatic surgical experience in the development of PTS. Thus, patients undergoing ostomy or ileal pouch-anal anastomosis surgeries may be at higher risk compared to patients undergoing other types of IBD surgery.

Finally, PTS symptoms were associated with increased psychological distress, poorer sleep, fatigue, and pain interference. Interestingly, sleep quality was not associated with PTS, with the exception of patients meeting the full criteria for IBD-related PTS. However, fatigue was substantially higher in patients with elevations in each PTS symptom group even when controlling for IBD symptom severity over the past week. Based on this discrepancy, it seems that fatigue resulting from PTS symptoms could be a significant contributor to unexplained fatigue in IBD given a relationship that is independent of sleep quality and recent disease severity. In part, this condition may be attributable to the chronic autonomic arousal inherent in PTS.

This study has several strengths, including a large, representative national U.S. sample with a validated diagnosis of IBD via the IBD Partners database. We utilized the gold-standard measure of PTSD to evaluate IBD-related PTS and excluded individuals with a prior PTS/PTSD diagnosis not associated with their disease. This study also has some limitations. The sample was predominantly White, non-Hispanic, and female, and therefore the results may not be generalizable. Future studies of PTS should include more diverse groups. Although IBD Partners comprises a large pool of patients with IBD, these patients are motivated to participate in research and are not likely representative of the general IBD population. Because these data were collected cross-sectionally, we cannot state the true predictive nature of PTS for patient outcomes. Prospective, longitudinal research in this area is necessary. Finally, although we used specific criteria outlined for the PCL-5, a definitive diagnosis of PTSD cannot be made without a diagnostic interview. Thus, the prevalence of PTS in this study may be overestimated because some previous studies

have found higher rates of PTSD symptoms when they are measured via questionnaire vs clinician interview.²⁸

Conclusions

Results from this study suggest that approximately one-quarter of patients with IBD report substantial PTS symptoms because of their illness experiences, with women, racial and ethnic minorities, and those with less than a college degree possibly at increased risk. As expected, PTS was associated with more severe IBD, higher odds of hospitalizations and surgeries, increased outpatient HCU, and increased anxiety, depression, fatigue, and pain interference. The findings of this study underscore the need for the early detection of PTS in patients with IBD. Accordingly, patients need to be referred to appropriate mental health clinicians who can provide evidence-based treatment for PTS. In this context, referral to a clinician with expertise in trauma is preferable to referral to a GI psychologist. We recommend that IBD practices regularly screen for PTS, particularly after diagnosis, a hospitalization, or surgery and identify appropriate psychologists in their communities for referral purposes. Future studies should target which psychological therapies for IBD-related trauma are best suited for patients with CD and with UC. Perhaps, more important, additional studies should aim to prevent PTS in patients with IBD through clinician education and training.

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