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Presentation and Characteristics of Abdominal Pain Vary by Irritable Bowel Syndrome Subtype: Results of a Nationwide Population-Based Study

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Abstract

INTRODUCTION: Abdominal pain is a cardinal feature of irritable bowel syndrome (IBS); however, differences in abdominal pain among IBS subtypes remain unknown. We aimed to characterize abdominal pain symptoms among established IBS subtypes using data from the National Gastrointestinal (GI) Survey.

METHODS: Individuals participating in the National GI Survey completed National Institutes of Health GI Patient- Reported Outcomes Measurement Information System (GI-PROMIS) questionnaires. Adults meeting modified Rome III IBS criteria and reporting abdominal pain in the previous 7 days were eligible. Outcomes included abdominal pain severity, bothersomeness, interference with daily activities, frequency, and location. Results were stratified by subtype (diarrhea [IBS-D], constipation [IBS-C], and mixed [IBS-M]). Regression models adjusted for demographics and comorbidities.

RESULTS: One thousand one hundred fifty-eight individuals (245 IBS-D, 232 IBS-C, and 681 IBS-M) with active IBS symptoms (defined as abdominal pain in the past 7 days) were included. Demographics were similar among the subtypes except for age, race/ethnicity, education, and marital status. The GI-PROMIS score was lower for IBS-D (percentile score of 68.6, SD = 25.1; $P = 0.001$) and IBS-M (69.1, SD = 25.1; $P < 0.001$) compared with IBS-C (75.5, SD = 20.7). Abdominal pain was more bothersome ($P = 0.001$), caused more interference with daily activities ($P = 0.03$), and was more frequent ($P = 0.047$) for individuals with IBS-C compared with

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CONFLICTS OF INTEREST

Potential competing interests: B.M.S. and W.D.C. are consultants for Ironwood Pharmaceuticals and Allergan. B.M.S. and W.D.C. are patent holders and previously were principals at My Total Health. C.V.A. has a stock option grant in My Total Health. E.D.S. has no relevant disclosures.

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individuals with IBS-D. No differences in these domains were seen between individuals with IBS-D and IBS-M. Individuals with IBS-C and IBS-M had more widespread pain compared with those with IBS-D.

DISCUSSION: In this population-based study, we found that abdominal pain characteristics differ between the IBS subtypes. Namely, individuals with IBS-C experience more bothersome, frequent, and diffuse abdominal pain compared with those with IBS-D.

INTRODUCTION

Irritable bowel syndrome (IBS) requires the presence of both abdominal pain and bowel symptoms (diarrhea and/or constipation) (1). The Rome IV diagnostic criteria and clinical trial endpoints recommended by the US Food and Drug Administration (FDA) classify IBS into subtypes based on the prevailing bowel symptom of diarrhea (IBS-D) or constipation (IBS-C) (2–4). Although abdominal pain is a cardinal symptom of IBS, the Rome IV diagnostic classification system does not subtype individuals with IBS on differences in how abdominal pain is experienced. Furthermore, the current FDA definition for weekly abdominal pain response is the same for both IBS-D and IBS-C: “decrease in the weekly average of worst abdominal pain in the past 24 hours score (measured daily) of at least 30% compared with baseline weekly average.”(4,5)

Abdominal pain can be the most intrusive and bothersome symptom of IBS (6) and is often accompanied by only mild diarrhea or constipation (7). Other individuals experience alternating diarrhea and constipation (mixed-type IBS, IBS-M), a subtype which may account for more than 40% of all IBS cases (8). In both scenarios, treatments primarily targeting the underlying bowel symptom (such as constipation) may unintentionally cause the opposite motility effect (such as diarrhea) (9) or may leave significant abdominal pain symptoms undertreated. Conceptually, focusing management on abdominal pain rather than bowel symptom might be sensible in these individuals with relatively mild or alternating bowel symptoms.

At present, it is unknown whether IBS-D and IBS-C subtypes merely represent differences in bowel symptoms or whether patterns of abdominal pain also vary by subtype on factors such as location or severity of pain which are elicited on a usual clinical history. Differences in intestinal permeability (10), mucosal immune activation (11–13), and the gut microbiota (14) between IBS-D and IBS-C contribute to the growing evidence underlying the importance of maintaining the distinction between IBS subtypes and support that the distinction between the subtypes likely involves much more than just the underlying bowel habit. Just as bowel symptoms are managed differently between patients with IBS-D or IBS-C, it would thus be important to understand whether abdominal pain also manifests differently by subtype because this may lead to important and specific treatment targets for IBS-D or IBS-C abdominal pain. To determine whether a more nuanced approach toward evaluating and managing abdominal pain on the basis of IBS subtype might be justified, we aimed to determine whether abdominal pain is characterized differently among established IBS subtypes using data from the National Gastrointestinal (GI) Survey.

METHODS

We conducted an analysis of abdominal pain symptoms using data from a nationwide population-based survey called the National GI Survey which was conducted to evaluate gastrointestinal symptoms among 71,812 community-dwelling individuals (adults ≥ 18 years of age) (15,16). Recruitment in the original study used an opt-in, incentivized list managed by a survey research firm (Cint, New York, NY) adjusted for age, sex, and location, as previously described in detail elsewhere (15,16). Respondents who were eligible met modified Rome III IBS criteria (Figure 1) and experienced abdominal pain within 7 days of the survey (consistent with standard recall length for PROMIS instruments). The modifications were specifically intended to limit our study population to actively symptomatic individuals. Moreover, this recall length minimizes effects of recall bias while ensuring enough days to support ecological validity (17,18). Eligible respondents were stratified based on IBS subtypes: diarrhea (IBS-D), constipation (IBS-C), or mixed-type (IBS-M). The National GI Survey was conducted using the MyGiHealth application (mygi.health). Demographic data included age, sex, ethnicity, education, marital status, employment status, household income, and number of comorbid medical conditions that can affect the gastrointestinal tract (including GI malignancy, Celiac disease, constipation, cirrhosis, Crohn's disease, diabetes mellitus, endometriosis, gallstones, gastroesophageal reflux, human immunodeficiency virus, pancreatitis, peptic ulcer, thyroid disease, ulcerative colitis, and other).

Abdominal pain symptoms were assessed using the National Institutes of Health (NIH) GI Patient-Reported Outcomes Measurement Information System (GI-PROMIS) (15,19,20). This instrument provides a percentile abdominal pain score representing a composite evaluation of severity, bothersomeness, interference with daily activities, and frequency to capture the complete abdominal pain symptom domain in actively symptomatic individuals (defined as having symptoms within the past 7 days), each using a 5-point Likert response scale. Refer to www.healthmeasures.net for the actual item bank (19). Methodology to assess content and construct validity and internal consistency reliability in an IBS population were reported in the original validation study for this instrument (20).

Our primary endpoint was the composite GI-PROMIS percentile score (0–100) for abdominal pain for each IBS subtype. Secondary endpoints included abdominal pain severity (At its worst, how would you rate your belly pain?), bothersomeness (How much did belly pain bother you?), interference with daily activities (How much did belly pain interfere with your day-to-day activities?), frequency (How often did you have belly pain?), and location, each analyzed by IBS subtype. Abdominal pain location was divided into 9 regions (right upper quadrant, epigastric, left upper quadrant, right midabdomen, periumbilical, left midabdomen, right lower quadrant, suprapubic, and left lower quadrant).

Demographic differences among IBS subtype were evaluated using a χ^2 test for nominal variables. Descriptive statistics using mean with SD and proportions were used to report scores for GI-PROMIS, abdominal pain severity, bothersomeness, impact on day-to-day activities, frequency, and location. Multivariable regression models were performed on our outcomes to adjust for potentially confounding demographic variables. All analyses were

performed using Stata 13.1 software (StataCorp, College Station, TX). This study was approved by the Cedars-Sinai Institutional Review Board (Pro41586), and all respondents agreed to the use of their deidentified data for research purposes.

RESULTS

Of 71,812 individuals completing the nationwide survey, 1,158 eligible respondents reported abdominal pain symptoms within the previous 7 days of the survey and met modified Rome III criteria for IBS. Of these, 245 (21.2%) had IBS-D, 232 (20.0%) had IBS-C, and 681 (58.8%) had IBS-M. Sex, employment status, annual income, and number of medical comorbidities were similar among IBS subtypes; however, there were differences regarding distributions of age, race/ethnicity, education, and marital status (Table 1). The prevalence of specific individual comorbidities affecting the GI tract was similar among subtypes, except for Crohn's disease and gallstones which were more frequent in patients with IBS-D and for self-reported chronic constipation which was less frequent in IBS-D (see Table 1, Supplementary Digital Content 1, <http://links.lww.com/AJG/B353>).

Composite GI-PROMIS scores

Regardless of IBS subtype, respondents with IBS had abdominal pain GI-PROMIS scores higher than the median (i.e., 50th percentile) among all symptomatic individuals in the community. The GI-PROMIS score, as a composite measure of abdominal pain severity, bothersomeness, interference with daily activities, and frequency, was higher for IBS-C (75.5, SD = 20.7) compared with IBS-D (percentile score of 68.6, SD = 25.1; $P = 0.001$) or IBS-M (69.1, SD = 25.1; $P < 0.001$). GI-PROMIS scores were not significantly different between IBS-D and IBS-M subtypes ($P = 0.70$).

Comparison of abdominal pain severity, bothersomeness, interference with daily activities, and frequency among IBS subtypes

There were no significant differences in abdominal pain "severity at its worst" based on responses from a 5-point Likert scale among IBS subtypes (Table 2). However, when compared with those with IBS-D, respondents with IBS-C noted more bothersomeness ($P = 0.001$), interference with daily activities ($P = 0.03$), and frequency ($P = 0.047$) of abdominal pain symptoms. Those with IBS-C were also more likely to note that their pain was more bothersome ($P = 0.009$) and frequent ($P < 0.001$) and had a larger impact on day-to-day tasks ($P = 0.04$) vs those with IBS-M. No differences in these domains were seen between individuals with IBS-D and IBS-M.

Localization and anatomic distribution of abdominal pain stratified by IBS subtype

Table 3 and Figure 2 present the localization of painful abdominal regions by IBS subtype. The most common individual areas in all subtypes were the suprapubic, periumbilical, right lower, and left lower regions. The mean number of abdominal pain regions, of 9 total, was 3.0 for IBS-D (SD = 1.9), 3.4 for IBS-C (SD = 2.0), and 3.5 (SD = 2.0) for IBS-M (Table 2). Adjusting for demographic variables, IBS-C was associated with a greater number of abdominal regions affected by pain than IBS-D ($P = 0.03$) but not IBS-M ($P = 0.65$). IBS-D was associated with a greater number of abdominal regions affected by pain than IBS-M (P

= 0.002). More individuals with IBS-C (52.2% of individuals with IBS-C) also reported diffuse abdominal pain or pain affecting the entire abdomen compared with those with IBS-D (40.8%, $P = 0.004$) but not IBS-M (54.5%). Individuals with IBS-M were significantly more likely to report diffuse abdominal pain than those with IBS-D ($P = 0.001$). There was no statistically significant difference in prevalence of diffuse abdominal pain between IBS-C and IBS-M subtypes ($P = 0.90$). We also found no differences in the proportion of individuals with only upper-mid abdominal pain (regions 1–6) among the various subtypes.

DISCUSSION

In this study, we identified differences in severity and characteristics of abdominal pain among IBS subtypes in a nationwide representative sample of individuals in the United States. Individuals with IBS-C had a higher composite GI-PROMIS score vs those with IBS-D and IBS-M. When looking at the individual components of GI-PROMIS, we found that those with IBS-C reported more bothersome and frequent abdominal pain as well as more interference with daily activities than individuals with either IBS-D or IBS-M. The IBS-C subtype was also associated with more diffuse abdominal pain compared with the IBS-D subtype. We also noted that although abdominal pain severity is similar between IBS-D and IBS-M subtypes, those with IBS-M are more likely to have diffuse abdominal pain.

IBS is a symptom-based diagnosis requiring 2 types of symptoms: abdominal symptoms (pain) and bowel symptoms (constipation/diarrhea). As our findings suggest that abdominal pain in IBS-D and IBS-C manifests differently, there is now evidence that both abdominal and bowel symptoms differ between IBS subtypes. Given that IBS is diagnosed based on symptoms alone, both of the cardinal symptoms of IBS manifest very differently between IBS-D and IBS-C. Physiologic mechanisms appear to differ between subtypes (10–14), lending credence to the notion that IBS-D and IBS-C might represent distinct entities as opposed to being true subtypes of the same disease. What IBS-D and IBS-C do have in common is that both subtypes are associated with the presence of visceral hypersensitivity, supported most recently by Melchior et al. who found that individuals meeting Rome III criteria for IBS-D or IBS-C had increased rectal hypersensitivity using a standard barostat technique compared with healthy controls (21). The severity of pain in IBS arising from visceral hypersensitivity may be modulated by serotonin signaling pathways (22). Although abdominal pain amplified by visceral hypersensitivity is shared across IBS subtypes, differences in how abdominal pain manifests in the first place may be explained by differences in both the etiology of the underlying condition and neural processing pathways involved in regulating abdominal pain. Multiple studies identified differences in brain activation changes on functional MRI associated with painful stimuli between IBS-D and IBS-C, suggesting that neural processing pathways for visceral pain differ (23–25). Future efforts to improve clinical trial design may benefit from recognizing differences in abdominal pain between IBS-D and IBS-C supported by differences in etiology and central pain processing, rather than simply differences in the prevailing bowel habit. Recent drug approvals may provide ample opportunity to learn how abdominal pain management based on the IBS subtype might be optimized, through a variety of neurobiological mechanisms including abnormal brain-gut interactions (26,27), small intestinal bacterial overgrowth (28), guanylate cyclase C agonism (29), and opioid receptor modulation (30).

Rome IV defines IBS-M by requiring that stool consistency be Bristol Stool type 1 or 2 during greater than 25% of bowel movements, as well as Bristol Stool type 6 or 7 in at least another 25% of bowel movements (3). Unfortunately, in clinical trials, there is no regulatory mechanism to evaluate prescription drugs for what may be an unstable clinical phenotype (31). It is possible that abdominal symptoms may provide a more stable therapeutic target for individuals with IBS-M, compared with the moving target of bowel complaints. Our findings suggest similarities in the presentation of abdominal pain between IBS-D and IBS-M, specifically that both conditions are associated with pain that is less bothersome, not as frequent, and causes less interference with daily activities compared with IBS-C. These findings contrast with those of Palsson et al. (32), which followed patterns of IBS symptoms among individuals with IBS-M, IBS-D, or IBS-C for an average of 73 days. In that study, individuals with IBS-M reported more days with abdominal pain (47.7% of days) compared with those with IBS-D (35.2%). The difference in findings may be related more to study design because our study focused on evaluating the severity and location of pain precisely when individuals were actively symptomatic and stratified subtypes during enrollment. Despite similarities between IBS-D and IBS-M symptoms, there is evidence that IBS-C and IBS-M might share similar stool microbiota signatures (33). At the same time, history of acute gastroenteritis, methanogen production, are similarly lower between IBS-D and IBS-M compared with IBS-C (34). Whether individuals with IBS-M on therapy respond more similarly to IBS-C (35) or IBS-D (36) remains unknown. Although the underlying etiology and rationale for managing IBS-M remains undecided, our findings are important in at least characterizing the most stable defining symptom (i.e., abdominal pain) of this rather unstable phenotype of IBS.

Several previous studies have evaluated differences in abdominal pain between IBS-D and IBS-C. In a survey of consecutive IBS individuals, Talley et al. found that individuals with IBS-C reported lower abdominal pain more frequently than those with IBS-D (40.8% vs 24.4%, $P=0.05$). This study did not use the Rome criteria nor were abdominal pain regions visually defined (37). In a prospective cohort of individuals with Rome III IBS followed for a mean of 73 days, Palsson et al. identified more days with abdominal pain in IBS-C compared with IBS-D. Unlike our study which was primarily focused on characterizing abdominal pain in IBS, the focus of the Palsson study was on confirming the episodic nature of symptom patterns in IBS, and further pain characteristics were not reported (32). Melchior et al. (21) recently reported that individuals with IBS with increased visceral hypersensitivity derived by barostat were more likely to have lower as opposed to diffuse abdominal pain; however, distributions and severity of pain were not reported for IBS subtypes. One previous study similarly evaluated localization of abdominal pain; however, symptom data in this study were based on patient recall, enrollment was based on a referral population with nondiagnostic endoscopic examination, and Rome criteria were not uniformly applied (38).

We found that IBS-M was the most prevalent subtype among individual with active symptoms, which contrasts with a previous systematic review by Ford et al. in which IBS-M was least common subtype among studies which categorized 3 subtypes of IBS (IBS-D, IBS-C, and IBS-M) (8). However, Ford et al. included all individuals with IBS, rather than limiting to solely actively symptomatic individuals. Although not the intent of our study, our

findings could imply the possibility that IBS-M is more likely to be actively symptomatic than IBS-D or IBS-C. This may be supported by the lack of FDA-approved therapies for IBS-M, as opposed to IBS-D and IBS-C, and that several IBS treatments cause the bowel side effects opposite the predominant bowel complaint (i.e. too much constipation in a patient treated for IBS-D and *vice versa*). At the same time, the overall prevalence of IBS was unmeasured in our study, so further studies should measure both the overall prevalence of IBS and the prevalence of actively symptomatic (and inactive) IBS to clarify the clinical significance of these findings.

Our findings are potentially limited by the use of modified Rome III criteria to determine study eligibility rather than strict Rome III definitions. These modifications were intended to restrict analysis to individuals with active abdominal pain symptoms, as opposed to IBS without active pain symptoms or the total IBS population. Although these modifications likely explain the low apparent prevalence of actively symptomatic IBS (1.6%) in our study (39), (i) our methodology limited the influence of recall bias and (ii) our study was not intended to assess IBS prevalence (40). We also did not assess ongoing medications and supplements which can impact the severity of IBS. It is possible that our findings could be due to higher rates of medication use for pain episodes among individuals with IBS-D compared with individuals with IBS-C or IBS-M, resulting in less bothersome pain in IBS-D. However, this effect may be limited by the broader underuse of medications to treat IBS pain episodes (with medication use in fewer than 30% of pain episodes in 1 study) regardless of IBS subtype (41). It is also possible that our findings might relate to possible variation among subtypes in the frequency of comorbid mood disorders, as well as coping skills including pain catastrophizing behaviors, somatization, and anxiety sensitivity which were not assessed in our study (42,43). Prospective studies to understand why abdominal pain varies by subtype are needed to understand whether these findings are explained by variation in the direct mechanisms of IBS or whether these findings are due to variation in coping skills or comorbidities which impact how abdominal pain is experienced. Regardless of reason, however, abdominal pain experiences do seem to vary by subtype in our nationwide, representative sample.

Study strengths include our use of the GI-PROMIS instrument which is validated for use in evaluating the abdominal pain symptom domain for individuals with IBS. Furthermore, the study evaluated abdominal pain symptoms experienced only within the previous 7 days, consistent with PROMIS methodology to limit recall bias (44). Although the prevalence of IBS in this nationwide cohort was lower than that reported in the literature (8), this derives specifically from our study design and use of the GI-PROMIS instrument requiring individuals to be actively or recently symptomatic to limit recall bias associated with survey data. Furthermore, our study was conducted from a nationwide cohort using recruitment quotas for age, sex, and location.

In summary, this study reports the results of a nationwide population-based survey to characterize abdominal pain symptoms among individuals with IBS based on the contemporary motility-based subtype framework. Abdominal pain appears more severe in IBS than in the general population. Our findings also show that abdominal pain is more severe and generalized within the IBS-C subtype, compared with IBS-D or IBS-M subtypes.

Our findings support the Rome IV framework of subtyping IBS based on the predominant bowel habit, but add that more effort is needed to understand and address abdominal symptoms specific to each subtype.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Study Highlights**WHAT IS KNOWN**

- Abdominal pain is a cardinal feature of IBS.
- Differences in abdominal pain among IBS subtypes based on bowel pattern remain unknown.

WHAT IS NEW HERE

- The typical pattern of abdominal pain varies significantly by IBS subtype.
- Individuals with constipation-predominant IBS experience more bothersome, frequent, and widespread abdominal pain than those with diarrhea-predominant IBS.

Figure 1.
Study eligibility criteria.

Figure 2.

Anatomical distribution of abdominal pain for each IBS subtype presented using heat maps. Results are presented for diarrhea-predominant IBS (IBS-D) (**a**), constipation-predominant IBS (IBS-C) (**b**), and mixed-type IBS (IBS-M) (**c**). The assigned color for each abdominal region ranges from yellow (least involved) to red (most involved) based on the prevalence of abdominal pain within each abdominal pain region. IBS, irritable bowel syndrome.

Table 1.

Demographics of survey participants stratified by IBS subtype (N = 1,158)

	IBS with diarrhea (n [%])	IBS with constipation (n [%])	Mixed-type IBS (n [%])	P
Age				0.008
18–24 years	28(11.4)	20 (8.6)	93 (13.7)	
25–44 years	123 (50.2)	114(49.1)	386 (56.7)	
45–64 years	92 (37.6)	94 (40.5)	192 (28.2)	
65+ years	2 (0.8)	4(1.7)	10(1.5)	
Sex				0.07
Female	176 (71.8)	179 (77.2)	539 (79.2)	
Male	69 (28.2)	53 (22.8)	142 (20.9)	
Race/ethnicity				0.02
Non-Hispanic white	217 (88.6)	181 (78.0)	586(86.1)	
Non-Hispanic black	4(1.6)	14 (6.0)	21 (3.1)	
Hispanic	20 (8.2)	23 (9.9)	46 (6.8)	
Asian	1 (0.4)	2 (0.9)	7(1.0)	
Other	3(1.2)	12(5.2)	21 (3.1)	
Education				0.009
Less than high school	7(2.9)	13(5.6)	16 (2.4)	
High school	54 (22.0)	48 (20.7)	134 (19.7)	
Some college	103 (42.0)	96(41.4)	231 (33.9)	
College graduate	65 (26.5)	61 (26.3)	240 (35.2)	
Graduate degree	16(6.5)	14 (6.0)	60 (8.8)	
Maritalstatus				0.001
Never married	37(15.1)	33 (14.2)	134 (19.7)	
Divorced/separated/widowed	39 (15.9)	55 (23.7)	86(12.6)	
Married/long-term relationship	169 (69.0)	144(62.1)	461 (67.7)	
Employment status				0.13
Not employed	98 (40.0)	112(48.3)	282(41.4)	
Employed or full-time	147 (60.0)	120 (51.7)	399 (58.6)	
Annualincome				0.07
\$0–\$50,000	143 (58.4)	133 (57.3)	342 (50.2)	

	IBS with diarrhea (n [%])	IBS with constipation (n [%])	Mixed-type IBS (n [%])	P
\$50,001–\$100,000	75 (30.6)	74 (31.9)	231 (33.9)	0.23
\$100,001–\$200,000	16 (6.5)	14 (6.0)	72 (10.6)	
\$200,001 or more	4 (1.6)	0 (0.0)	6 (0.9)	
Prefer not to say	7 (2.9)	11 (4.7)	30 (4.4)	
No. of medical comorbidities				
0	69 (28.2)	85 (36.6)	244 (35.8)	0.23
1	89 (36.3)	81 (34.9)	226 (33.2)	
2	51 (20.8)	38 (16.4)	107 (15.7)	
3 or more	36 (14.7)	28 (12.1)	104 (15.3)	

IBS, irritable bowel syndrome.

Table 2.

Bothersomeness, interference with daily activities, frequency, and distribution of abdominal pain vary among common IBS subtypes^a

	IBS with diarrhea (n = 245)	IBS with constipation (n = 232)	Mixed-type IBS (n = 681)
Abdominal pain severity rating at its worst, 5-point Likert scale (0 = not bad at all; 4 = very bad)	2.3 ± 1.0 (reference)	2.5 ± 0.9 (<i>P</i> = 0.001 vs IBS-D)	2.5 ± 1.0 (<i>P</i> = 0.22 vs IBS-D) (<i>P</i> = 0.009 vs IBS-C)
Abdominal pain bothersomeness, 5-point Likert scale (0 = not at all; 4 = very much)	2.4 ± 1.0 (reference)	2.7 ± 0.9 (<i>P</i> = 0.001 vs IBS-D)	2.5 ± 1.0 (<i>P</i> = 0.22 vs IBS-D) (<i>P</i> = 0.009 vs IBS-C)
Abdominal pain interference with daily activities, 5-point Likert scale (0 = not at all; 4 = very much)	2.0 ± 1.1 (reference)	2.3 ± 1.0 (<i>P</i> = 0.03 vs. IBS-D)	2.0 ± 1.1 (<i>P</i> = 0.57 vs IBS-D) (<i>P</i> = 0.04 vs IBS-C)
Abdominal pain frequency, 5-point Likert scale (0 = never; 4 = always) ^b	2.6 ± 0.8 (reference)	2.8 ± 0.8 (<i>P</i> = 0.047 vs IBS-D)	2.5 ± 0.8 (<i>P</i> = 0.10 vs IBS-D) (<i>P</i> = <0.001 vs IBS-C)
No. of painful anatomic abdominal regions (0–9)	3.0 ± 1.9 (reference)	3.4 ± 2.0 (<i>P</i> = 0.03 vs IBS-D)	3.5 ± 2.0 (<i>P</i> = 0.002 vs IBS-D) (<i>P</i> = 0.65 vs IBS-C)
Individuals with diffuse abdominal pain ^b	100 (40.8%) (reference)	121 (52.2%) (<i>P</i> = 0.004 vs IBS-D)	371 (54.5%) (<i>P</i> = 0.001 vs IBS-D) (<i>P</i> = 0.90 vs IBS-C)
Individuals with only upper-mid abdominal pain (regions 1–6)	43 (17.6%) (reference)	32 (13.8%) (<i>P</i> = 0.28 vs IBS-D)	100 (14.7%) (<i>P</i> = 0.44 vs IBS-D) (<i>P</i> = 0.58 vs IBS-C)

Bold entries represent statistically significant findings (*P* < 0.05).

Individuals with IBS-C reported more bothersome, frequent, and diffuse abdominal pain, and more interference with daily activities, than those with IBS-D than those with IBS-D, but there was no difference in severity. Individuals with IBS-M reported more diffuse pain than those with IBS-D, but otherwise, there were no differences in severity, bothersomeness, interference with daily activities, or frequency of abdominal pain between IBS-M and IBS-D.

Data are presented as mean ± SD or n (%).

IBS, irritable bowel syndrome.

^a All multivariable regression models adjusted for IBS subtype, age, sex, race/ethnicity, education, marital status, employment status, household income, and number of comorbid conditions.

^b Diffuse abdominal pain is defined as pain that crossed 1 horizontal or vertical planes.

Table 3.

Localization of painful abdominal regions by IBS subtype

	IBS with diarrhea n = 245, n (%)	IBS with constipation n = 232, n (%)	Mixed-type IBS n = 681, n (%)
Diffuse, ^a but not entire abdomen	94 (38.4)	109 (47.0)	337 (49.5)
Entire abdomen (regions 1–9)	6(2.5)	12 (5.2)	34 (5.0)
Right upper quadrant (region 1)	1 (0.4)	0 (0.0)	2 (0.3)
Epigastrium (region 2)	7(2.9)	2 (0.9)	9(1.3)
Left upper quadrant (region 3)	1 (0.4)	2 (0.9)	1 (0.2)
Right midabdomen (region 4)	3(1.2)	2 (0.9)	2 (0.3)
Periumbilical(region 5)	13 (5.3)	5 (2.2)	14 (2.1)
Left midabdomen (region 6)	0(0.0)	1 (0.4)	5(0.7)
Right lower quadrant (region 7)	1 (0.4)	2 (0.9)	6(0.9)
Suprapubic (region 8)	30 (12.2)	16 (6.9)	62 (9.1)
Left lower quadrant (region 9)	1 (0.4)	3(1.3)	4(0.6)
Upper abdomen (regions 1–3)	1 (0.4)	2 (0.9)	4(0.6)
Midabdomen (regions 4–6)	4(1.6)	6 (2.6)	12(1.8)
Lower abdomen (regions 7–9)	38(13.9)	23 (9.9)	59 (8.7)
Right abdomen (regions 1, 4, 7)	3(1.2)	0 (0.0)	8(1.2)
Midline abdomen (regions 2, 5, 8)	39(15.1)	41 (17.7)	115(16.9)
Left abdomen (regions 3, 6, 9)	3(1.2)	6 (2.6)	7(1.0)

IBS, irritable bowel syndrome.

^aDiffuse abdominal pain is defined as pain that crossed 1 horizontal or vertical planes.