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Increased psychological distress and somatization in patients with irritable bowel syndrome compared with functional diarrhea or functional constipation, based on Rome IV criteria

Mohamed G. Shiha¹ | Zohaib Asghar^{1,2} | Mo Thoufeeq¹ | Matthew Kurien^{1,2} | Alex J. Ball¹ | Anupam Rej¹ | Foong Way David Tai¹ | Shima Afify¹ | Imran Aziz^{1,2} 

¹Academic Department of Gastroenterology, Sheffield Teaching Hospitals, Sheffield, UK

²Department of Infection, Immunity and Cardiovascular Disease, University of Sheffield, Sheffield, UK

Correspondence

Imran Aziz, Academic Department of Gastroenterology, Sheffield Teaching Hospitals & Department of Infection, Immunity and Cardiovascular Disease, University of Sheffield, Sheffield, UK.
Email: imran.aziz1@nhs.net

Abstract

Background: The Rome IV criteria for disorders of gut-brain interaction define irritable bowel syndrome (IBS) as a functional bowel disorder associated with frequent abdominal pain of at least 1 day per week. In contrast, functional diarrhea (FD) and functional constipation (FC) are relatively painless. We compared differences in mood and somatization between Rome IV IBS and FC/FD.

Methods: A total of 567 patients with Rome IV defined IBS or FD/FC completed a baseline questionnaire on demographics, abdominal pain frequency, mood (hospital anxiety and depression scale, HADS), and somatization (patient health questionnaire, PHQ-12). The primary analysis compared differences in mood and somatization between IBS and FC/FD, and the relative influence of abdominal pain frequency on these extra-intestinal symptoms. The secondary analysis evaluated differences across individual IBS subtypes, and also between FC and FD.

Key Results: Patients with IBS—in comparison to those with FC/FD—had significantly higher mean PHQ-12 somatization scores (9.1 vs. 5.4), more somatic symptoms (6.0 vs. 4.3), abnormally high somatization levels (16% vs. 3%), higher HADS score (15.0 vs. 11.7), and clinically abnormal levels of anxiety (38% vs. 20%) and depression (17% vs. 10%). Increasing abdominal pain frequency correlated positively with PHQ-12, number of somatic symptoms, and HADS; $p < 0.001$. No differences in mood and somatization scores were seen between individual IBS subtypes, and nor between FC and FD.

Conclusion & Inferences: Based on the Rome IV criteria, IBS is associated with increased levels of psychological distress and somatization compared with FD or FC. Patients reporting frequent abdominal pain should be comprehensively screened for psychosomatic disorders, with psychological therapies considered early in the disease course.

Mohamed G. Shiha and Zohaib Asghar are joint first authors

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KEYWORDS

functional constipation, functional diarrhea, HADS, IBS, PHQ-12, Rome IV, Somatization

Key points

- Based on Rome IV criteria, IBS is associated with increased levels of psychological distress and somatization compared with FD or FC.
- The frequency of abdominal pain correlates positively with psychological distress and somatic co-morbidity.
- Patients with functional bowel disorders, and in particular those who report abdominal pain, should be routinely and comprehensively screened for extra-intestinal ill-health.
- Future research studies should consider evaluating the role of psychological therapies early in the disease course for IBS, whilst evaluating both bowel- and mental- health related end points.

1 | INTRODUCTION

Functional bowel disorders belong to the spectrum of disorders of gut-brain interaction.¹ They are defined as chronic lower gastrointestinal symptoms that occur in the absence of organic disease to explain the symptoms.¹ Recent large-scale epidemiological studies report functional bowel disorders to affect 1-in-4 adults, in whom the vast majority are represented by either irritable bowel syndrome (IBS), functional constipation (FC), or functional diarrhea (FD).² The Rome Foundation has, over the last 30 years, provided clinicians and researchers with symptom-based criteria to aid toward the recognition of functional gastrointestinal disorders.³ As of May 2016, the Rome IV criteria was released which differs markedly from the previous Rome III iteration with regards to the diagnosis of IBS.^{4,5} The Rome IV criteria defines IBS as a functional bowel disorder associated with frequent abdominal pain of at least 1 day per week, which contrasts to the relatively lax Rome III criteria where a diagnosis of IBS was based on abdominal pain or discomfort at least 2–3 day per month.^{4,5} This change in criteria has reduced the prevalence of IBS by almost half, going from 9.0% under Rome III to 4.6% under Rome IV.² Those individuals no longer satisfying a diagnosis of IBS under Rome IV are instead re-classified as having another functional bowel disorder, such as the relatively painless FD and FC. Indeed, following the change in criteria from Rome III to Rome IV, the prevalence of FD has subsequently risen from 0.9% to 4.4% and FC has risen from 5.6% to 7.8%.²

The relevance of this update in criteria to Rome IV, which in essence differentiates IBS from FC or FD on the basis of frequent abdominal pain, is unclear with regards to the role of psychological distress, an important factor associated with disorders of gut-brain interaction.^{1,3} While functional abdominal pain has historically been linked with mood disturbances,⁶ a recent study comprising 100 patients found no difference in psychosomatic symptoms between patients with IBS-D and FD based on the Rome IV criteria.⁷ However, this study evaluated the diarrhea subtypes only and, moreover, 77% of patients labeled as having FD were experiencing abdominal

pain (with almost 40% having abdominal pain at least once a week) which questions whether they should have been classed as IBS-D instead.⁷ Elsewhere, multiple groups have shown that subjects with Rome IV IBS have higher levels of psychological and somatic distress compared with those who do not meet Rome IV criteria for IBS, although these studies have methodological limitations.^{8–11} For example, some have evaluated datasets of Rome III defined IBS patients and applied a surrogate marker to identify, or rather assume, which patients may or may not have IBS under the Rome IV criteria,^{9,10} whereas others have recruited online participants self-reporting IBS without verifying the diagnosis.¹¹ Moreover, those subjects deemed unlikely to have Rome IV IBS have not been distinctly defined as having FD or FC, but rather pooled under the spectrum of any other functional bowel disorder, thereby limiting our understanding of their particular disease subtype.^{8–11}

We therefore undertook a study to compare levels of psychological distress and somatization between IBS and FC/FD based on the Rome IV criteria. We hypothesized that Rome IV IBS, a bowel disorder characterized by frequent abdominal pain, will be strongly associated with mood disturbances and high levels of somatization, compared with the relatively painless FD or FC.

2 | METHODS

2.1 | Study design and participants

This prospective observational study took place at Sheffield Teaching Hospitals, United Kingdom, during the course of 2019. All English-speaking adults, aged 18 years and over, referred at the clinical discretion of their GI physician for an out-patient colonoscopy (excluding those as part of the national bowel cancer screening program) were eligible to participate. Individuals were invited to self-complete a baseline questionnaire collecting demographic and symptom-based data followed by undergoing a colonoscopy.

2.2 | Baseline questionnaire

The following items were collected prior to colonoscopy:

- a. Demographic data—participants entered their age, sex, and ethnicity.
- b. Past gastrointestinal history—patients were asked whether they had any of the following illnesses or interventions: coeliac disease, inflammatory bowel disease, colon cancer, microscopic colitis, and bowel surgery. For verification, all clinical records were reviewed
- c. The Hospital Anxiety and Depression scale (HADS)¹²—this 14-item instrument contains seven questions for anxiety and seven questions for depression. Each question is scored from 0 to 3, providing a minimum score of 0 (no symptoms) and a maximum score of 21 (maximal severity of symptoms) on each subscale. A subscale score of ≥ 11 is used to indicate a clinically significant level of anxiety or depression.
- d. The Patient Health Questionnaire (PHQ)-12 evaluates the severity of extra-intestinal somatic symptoms. The twelve non-GI symptoms assessed are back pain, limb pain, headaches, chest pain, dizziness, fainting spells, palpitations, breathlessness, menstrual cramps, dyspareunia, insomnia, and lethargy.¹³ Subjects were asked to rate how much they had been troubled by these twelve symptoms over the last four weeks as 0 ("not bothered at all"), 1 ("bothered a little"), or 2 ("bothered a lot"). The PHQ-12 responses can be used to calculate a) the number of sites reporting somatic symptoms (ranging from 0 to 12), and b) the PHQ-12 somatization severity score (ranging from 0 to 24), the latter which can be further categorized as minimal (PHQ-12 score ≤ 3), low (4–7), medium (8–12) and high (≥ 13) somatization severity.
- e. The Rome IV bowel disorder questionnaire¹⁴—this validated tool was used to identify patients who had symptoms compatible with one of the following functional bowel disorders; IBS and its subtypes (IBS-constipation, IBS-diarrhea, IBS-mixed), and FD and FC.⁴ This differentiation was based on evaluating stool pattern and the reported frequency of abdominal pain (never, ≤ 2 –3 days a month, 1 day a week, 2–3 days a week, most days to every day, or multiple times per day), with the 1 day per week of abdominal pain being the relevant cutoff point to distinguish IBS from FC/FD.

Moreover, for those with symptoms of constipation, individuals completed questions on how frequently they experienced hard or lumpy stools (type 1 or 2 on the Bristol stool form scale), strained with defecation, had a sensation of incomplete evacuation, and performed manual maneuvers to facilitate digitation. In contrast, for those with symptoms of diarrhea, individuals completed questions on how frequently they experienced loose or watery stools (type 6 or 7 on the Bristol stool form scale) and had fecal urgency. A value of 30% or greater for any of the aforementioned bowel symptoms was the threshold used to define an abnormal frequency within the clinical setting.

2.3 | Colonoscopy

The endoscopists performing the colonoscopies were blinded to the baseline questionnaire data. A normal colonoscopy was defined as no endoscopic and histological evidence of colon cancer, inflammatory bowel disease, or microscopic colitis. We did not take diverticulosis into consideration and, moreover, any association with functional bowel disorders is controversial.¹⁵

2.4 | Definitions of functional bowel disorders

We have recently used this dataset to report on the diagnostic outcomes of colonoscopy in patients with symptoms compatible with a Rome IV functional bowel disorder.¹⁶ For the purpose of the current study, a diagnosis of IBS, FC, or FD was reached in those subjects with compatible symptoms (as per the Rome IV diagnostic questionnaire) and had a normal colonoscopy examination and a negative past gastrointestinal history. Patients not fulfilling this criteria were deemed not to have a functional bowel disorder. None of the patients had functional abdominal bloating/distension.

2.5 | Statistical analysis

The primary analysis compared differences in mood and somatization scores between Rome IV IBS and FC/FD, and the relative influence of abdominal pain frequency on these extra-intestinal symptoms. However, prior to undertaking this main analysis, we compared difference in mood and somatization scores between those patients with and without a Rome IV functional bowel disorder. The secondary analysis evaluated differences across individual IBS subtypes, and also between FC and FD.

Statistical analysis was carried out using SPSS version 25.0 software, with significance set at a *p*-value of < 0.05 . Categorical variables were summarized by descriptive statistics, including total numbers and percentages, with comparisons between groups performed using the chi-square test or Fisher exact test, and adjusted odds ratios (AOR) with 95% confidence intervals (95% CI) presented when appropriate. Continuous variables were summarized by mean and standard deviation, with difference between two independent groups performed using the unpaired Student *t* test, and between multiple groups using 1-way analysis of variance. Correlations were assessed using Spearman's test.

2.6 | Ethics

The study commenced following ethical approval by Sheffield Teaching Hospital (protocol number: STH20572) and the Health Research Authority (IRAS project ID: 253210). The study was conducted in accordance with the STROBE statement. Patients who

TABLE 1 Comparison of basic demographics, mood, and somatization between those with and without a Rome IV functional bowel disorder (FBD)

	No FBD (n = 762)	Rome IV FBDs (n = 567)	p-value
Demographics			
Mean age, years (SD)	59 (15)	56 (16)	<0.001
Female (%)	366 (48%)	349 (62%)	<0.001
White race (%)	722 (95%)	525 (93%)	0.43
Symptoms scores			
HADS			
Mean HADS-anxiety score (SD)	6.1 (4.5)	7.9 (4.8)	<0.001
Mean HADS-depression score (SD)	4.6 (4.1)	5.8 (4.3)	<0.001
Mean HADS-total score (SD)	10.7 (7.8)	13.6 (9.6)	<0.001
Abnormal HADS-anxiety levels (%)	126 (16.5%)	169 (30%)	<0.001
Abnormal HADS-depression levels (%)	63 (8%)	79 (14%)	0.001
Somatization			
Mean PHQ-12 score (SD)	5.2 (3.6)	6.9 (4.1)	<0.001
Number of somatic symptoms (SD)	4.1 (2.5)	5.3 (2.6)	<0.001
Level of somatization severity (%)			
Minimal	291 (38%)	129 (23%)	
Low	286 (37.5%)	199 (35%)	<0.001
Medium	153 (20%)	180 (32%)	
High	32 (4%)	59 (10.4%)	

returned their questionnaire consented for their data to be used for analysis.

3 | RESULTS

3.1 | Study participants

We sent out 3000 questionnaires of which 1329 were returned with complete dataset and underwent colonoscopy. Of these, 567 patients had a final diagnosis of a Rome IV functional bowel disorder, whereas the remaining 762 patients did not (513 known or new diagnosis of colonic disease, and 249 normal). Of the 567 patients with

TABLE 2 Comparison of basic demographics, mood, and somatization between Rome IV IBS and FD/FC

	FD/FC (n = 249)	IBS (n = 318)	p-value
Demographics			
Mean age, years (SD)	61 (13)	51 (7)	<0.001
Female (%)	130 (52%)	219 (62%)	<0.001
White race (%)	236 (95%)	289 (91%)	0.37
Symptoms scores			
HADS			
Mean HADS-anxiety score (SD)	6.7 (4.4)	8.8 (4.9)	<0.001
Mean HADS-depression score (SD)	5.0 (3.8)	6.3 (4.5)	<0.001
Mean HADS-total score (SD)	11.7 (7.4)	15 (8.6)	<0.001
Abnormal HADS-anxiety levels (%)	50 (20%)	119 (38%)	<0.001
Abnormal HADS-depression levels (%)	25 (10%)	54 (17%)	0.02
Somatization			
Mean PHQ-12 score (SD)	5.4 (3.4)	9.1 (4.2)	<0.001
Number of somatic symptoms (SD)	4.3 (2.4)	6 (2.6)	<0.001
Level of somatization severity (%)			
Minimal	88 (35%)	41 (13%)	
Low	90 (36%)	109 (34%)	<0.001
Medium	64 (26%)	116 (36.5%)	
High	7 (3%)	52 (16%)	

a Rome IV functional bowel disorder, 318 had IBS (further stratified as 133 with IBS-D, 118 with IBS-M, 67 with IBS-C) and 249 patients had either FD (n = 147) or FC (n = 102).

3.2 | Comparison in demographic and symptom scores between subjects with and without a Rome IV functional bowel disorder

Patients with a Rome IV functional bowel disorder—compared to those without—were significantly younger (mean age 56 vs. 59 years, $p < 0.001$), had a higher female representation (62% vs. 48%, $p < 0.001$), and reported greater levels of psychological distress and somatization (Table 1). The increased associations for clinically abnormal levels of anxiety, depression, and moderate-high somatization scores seen in those with a functional bowel disorder persisted despite adjusting for age and gender; data not shown.

TABLE 3 Comparison of basic demographic and symptom scores between Rome IV IBS-D and FD

	IBS-D (n = 133)	FD (n = 147)	p-value
Mean-age, years (SD)	52 (15.1)	60 (13.1)	<0.001
Female	92 (69%)	71 (48%)	<0.001
HADS			
Mean HADS-anxiety score (SD)	9.2 (5.1)	6.7 (4.4)	<0.001
Mean HADS-depression score (SD)	6.4 (4.2)	4.7 (3.7)	<0.001
Mean HADS-total score (SD)	15.7 (8.4)	11.5 (7.5)	<0.001
Abnormal HADS-anxiety levels (%)	55 (41%)	31 (21%)	<0.001
Abnormal HADS-depression levels (%)	24 (18%)	11 (11%)	0.04
Somatization			
Mean PHQ-12 score (SD)	8 (4)	5.2 (3.3)	<0.001
Number of somatic symptoms (SD)	5.9 (2.5)	4.2 (2.3)	<0.001
Level of somatization severity (%)			
Minimal	17 (13%)	55 (37%)	
Low	46 (34.5%)	51 (35%)	<0.001
Medium	52 (39%)	37 (25%)	
High	18 (13.5%)	4 (3%)	
Bowel symptoms (>30% of the time)			
Type 6-7 loose/watery stools	27 (20%)	52 (35%)	0.005
Urgency	114 (86%)	89 (60.5%)	<0.001

3.3 | Comparison in demographic and symptom scores between Rome IV IBS and FC/FD

As outlined in Table 2, patients with IBS were significantly younger than those with FD/FC (mean age 51 years vs. 61 years, $p < 0.001$) and had a higher female predominance (62% vs. 52%, $p < 0.001$). Furthermore, patients with IBS had a significantly higher HADS score (15.0 vs. 11.7, $p < 0.001$), and clinically abnormal levels of anxiety (38% vs. 20%, $p < 0.001$) and depression (17% vs. 10%, $p = 0.02$). They also had a significantly higher mean PHQ-12 somatization score (9.1 vs. 5.4, $p < 0.001$), abnormally high somatization levels (16% vs. 3%, $p < 0.001$) and a greater number of somatic symptoms (6.0 vs. 4.3, $p < 0.001$). With regards to individual somatic symptoms, 11 out of the 12 items listed on the PHQ-12 at a level of "bothered a lot" were reported at a significantly greater frequency by IBS patients compared with FC/FD (Table S1). Following adjustments for age and gender, IBS subjects were still significantly more likely than their FD/

TABLE 4 Comparison of basic demographic and symptom scores between Rome IV IBS-C and FC.

	IBS-C (n = 67)	FC (n = 102)	p-value
Mean Age, years (SD)	53 (18.1)	62 (13.7)	<0.001
Female	47 (70%)	59 (58%)	0.11
HADS			
Mean HADS-anxiety score (SD)	8.6 (4.5)	6.6 (4.3)	0.005
Mean HADS-depression score (SD)	5.9 (4.8)	5.4 (3.8)	0.42
Mean HADS-total score (SD)	14.6 (8.7)	12.1 (7.2)	0.06
Abnormal HADS-anxiety levels (%)	24 (36%)	19 (19%)	0.01
Abnormal HADS-depression levels (%)	10 (15%)	14 (9.5%)	0.40
Somatization			
Mean PHQ-12 score (SD)	8.3 (4.2)	5.5 (3.4)	<0.001
Number of somatic symptoms (SD)	6.1 (2.4)	4.3 (2.3)	<0.001
Level of somatization severity (%)			
Minimal	6 (9%)	33 (32%)	
Low	26 (39%)	39 (38%)	<0.001
Medium	22 (33%)	27 (26%)	
High	13 (19%)	3 (3%)	
Bowel Symptoms (>30% of the time)			
Type 1-2 hard/lumpy stools	62 (92.5%)	73 (72%)	0.001
Straining	57 (85%)	81 (79%)	0.35
Incomplete emptying	57 (85%)	81 (79%)	0.35
Manual digitation	23 (34%)	26 (25.5%)	0.22

FC counterparts to have clinically abnormal levels of anxiety (AOR 2.9, 95% CI: 1.3-3.0), depression (AOR 1.9, 95% C.I 1.13-3.3), and moderate-high levels of somatization (AOR 2.65, 95% C.I 1.8-3.8).

3.4 | Comparison between IBS-D and FD, and between IBS-C and FC

Patients with IBS-D were younger, had a greater female representation, experienced more psychosomatic distress, and reported increased stool urgency than those with FD (Table 3). Following adjustments for age, gender, and bowel habit, patients with IBS-D were more likely than FD to have abnormal levels of anxiety (AOR

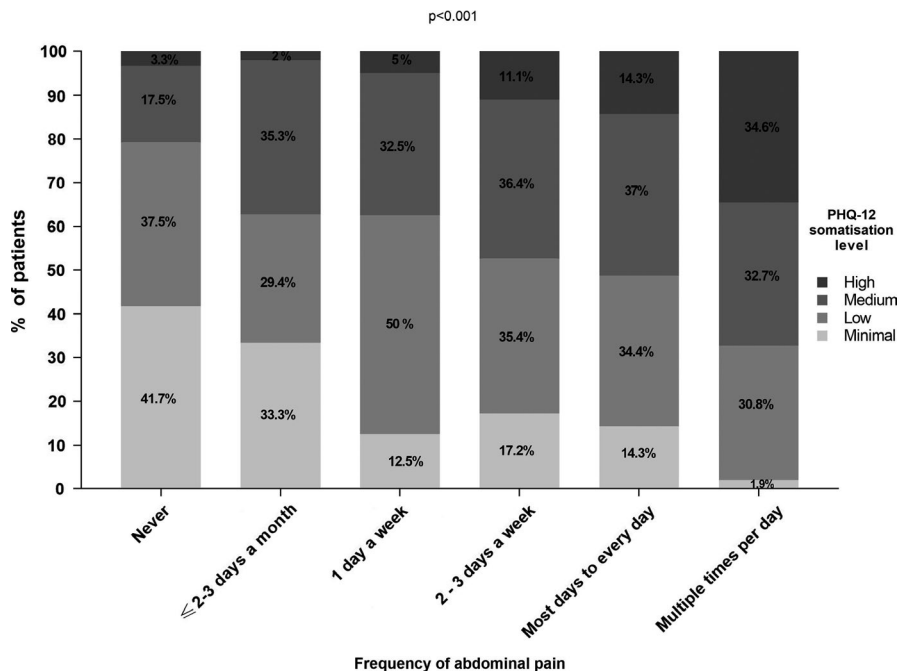


FIGURE 1 Prevalence of different levels of PHQ-12 somatization among patients with Rome IV functional bowel disorders according to the frequency of abdominal pain

2.4, 95% C.I 1.3–4.4), depression (AOR 2.3, 95% C.I 1.0–5.0), and moderate-high somatization (AOR 2.7, 95% C.I 1.5–4.7).

Patients with IBS-C were younger, experienced more psychosomatic distress, and reported type 1/2 stools more frequently than those with FC. However, there was no difference between the groups with regards to straining, incomplete emptying and manual digitation (Table 4). Following adjustment for age and bowel habit, patients with IBS-C were more likely than FC to have abnormal levels of anxiety (AOR 2.3, 95% C.I 1.1–4.9) and moderate-high somatization (AOR 2.1, 95% C.I 1.1–4.3).

We found no statistical differences in mood and somatization symptom scores between FC and FD, and nor between individual IBS subtypes (supplementary tables B/C).

3.5 | Correlation between the frequency of abdominal pain and psychosomatic symptoms

Increasing abdominal pain frequency correlated positively with PHQ-12 score ($r = 0.4$, $p < 0.001$), number of somatic symptoms ($r = 0.37$, $p < 0.001$), and HADS score ($r = 0.23$, $p < 0.001$). The proportion of individuals experiencing high levels of somatization increased from 3.3% in those without abdominal pain, to 34.6% to those reporting abdominal pain multiple times per day; Figure 1. Similarly, clinically abnormal levels of anxiety increased from 18.3% to 46.2%, and depression from 10% to 25%, with the change in abdominal frequency from never to multiple times per day; Figure 2.

4 | DISCUSSION

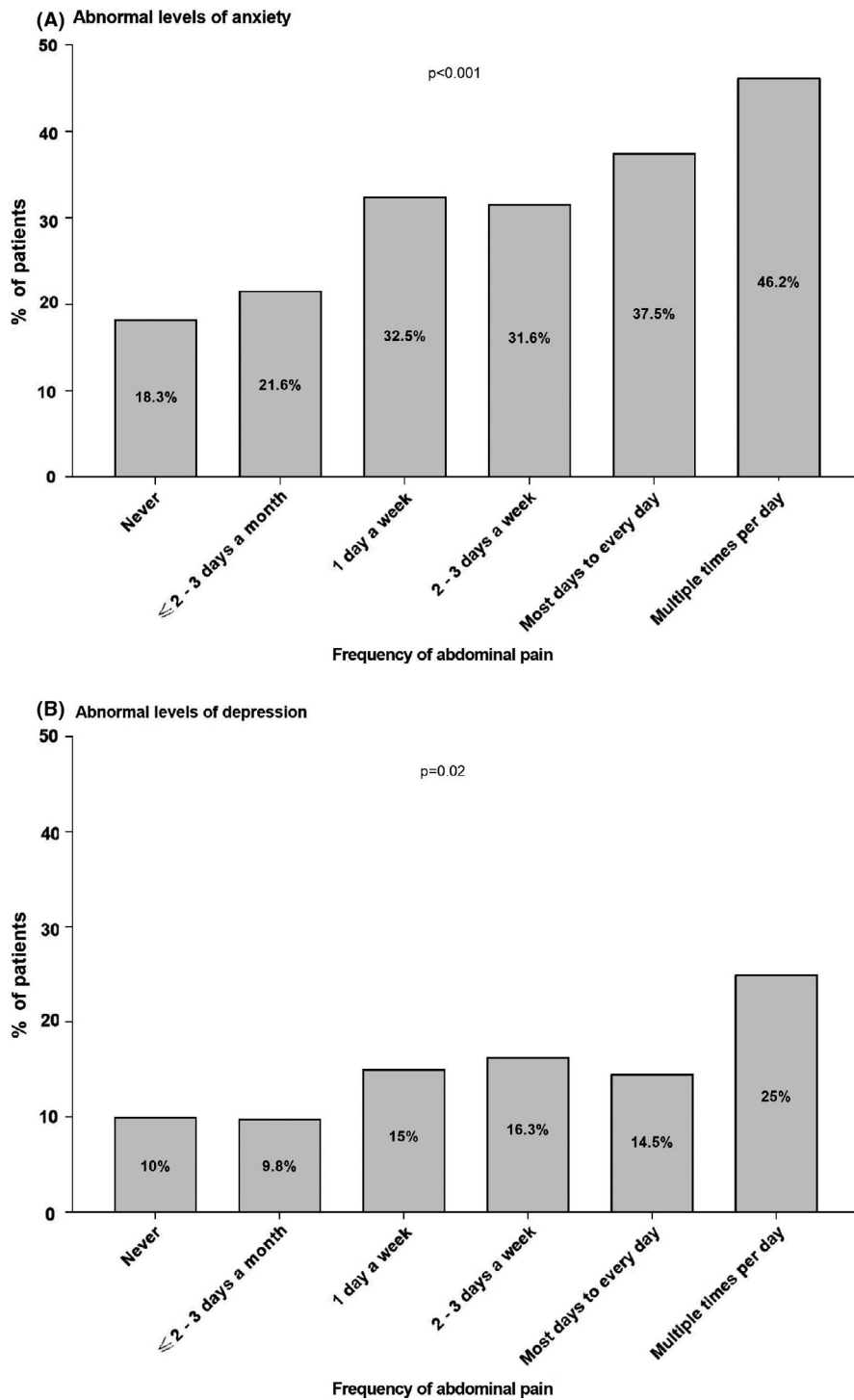
By undertaking a large cross-sectional observational study, we have shown that individuals with Rome IV IBS have significantly greater

levels of anxiety, depression, and somatization compared with Rome IV FC or FD, and that increasing abdominal pain frequency correlates positively with psychological distress and somatization.

Our findings are in keeping with systematic reviews reporting a high prevalence of psychosomatic distress in IBS patients,^{17,18} with observational data showing this to occur to a greater extent than in FD or FC.¹⁹ However, the definition of IBS in these studies was based on historic criteria, such as the Rome I-III iterations, which were far more accommodating and thus comprised a heterogeneous pool of patients compared with the stringent Rome IV criteria. Recent groups have since attempted to compare levels of psychosomatic distress in subjects with and without Rome IV IBS, demonstrating conflicting results and with certain limitations related to patient selection and functional bowel disorder classification.^{7–11} In contrast, the strength of our study is that we included a well-defined cohort of patients with IBS and FC/FD using the validated Rome IV diagnostic questionnaire, and having excluded organic bowel disease via a negative colonoscopy.

The association between increasing abdominal pain frequency and psychosomatic distress is in line with a Swedish community-based survey which linked anxiety and depression to functional abdominal pain in both IBS patients and healthy subjects.⁶ Combined with our own findings, this suggests the need to consider adopting different clinical and therapeutic strategies between Rome IV IBS and FC/FD. Firstly, patients with IBS—and in particular those experiencing frequent abdominal pain—should be routinely screened for psychological ill-health and somatic symptoms, and not just bowel-related symptoms. This concept would be supported by the Rome committee who advocate a multidimensional clinical profile approach to help characterize the full breadth of the patient's illness state.³ Secondly, as somatic symptom reporting in IBS is independently associated with increased rates of unnecessary surgical interventions, clinicians must be wary of this link to prevent its occurrence.^{20,21} Thirdly, studies should consider evaluating

FIGURE 2 Prevalence of abnormal levels of clinical (A) anxiety and (B) depression among patients with Rome IV functional bowel disorders according to the frequency of abdominal pain



the role of psychological therapies (ie, neuromodulators and behavioral psychotherapy) earlier in the treatment paradigm for IBS, as opposed to them being reserved for individuals refractory to standard gut-directed or peripherally acting therapies (eg, antispasmodics, laxatives, diet etc). The National Institute of Health and Clinical Excellence currently recommend psychological therapies for patients who remain symptomatic following medical treatment but only after 12 months have elapsed, although evidence to support this approach is sparse.²² Psychological therapies exert their beneficial effects via the release of neurotransmitters leading to changes in visceral hypersensitivity,

neuroplasticity, pain modulation, and mood.²³ They have been shown to be among the most effective strategies for IBS with a number needed to treat of 4.^{24,25} Moreover, a recent network meta-analysis of randomized controlled trials (of soluble fiber, antispasmodic drugs, peppermint oil, and gut-brain neuromodulators for IBS) ranked tricyclic antidepressants first for efficacy when abdominal pain was used as the outcome measure.²⁶ Finally, integrating psychological therapy within a multidisciplinary clinical care package is superior to gastroenterologist-only care in relation to symptoms, psychological state, quality of life, and cost of care for the treatment of functional gastrointestinal

disorders.²⁷ Hence, there is growing support for earlier deployment of psychological therapies within functional gut disorders, in particular for IBS, although a limiting factor has historically been attributed to a lack of familiarity with the use of neuromodulators among gastroenterologists, and the practical constraints associated with delivering face-to-face behavioral psychotherapy over a prolonged time period within a busy healthcare service. To address these issues, there has been recent guidance from the Rome Foundation Working Team educating and empowering gastroenterologists towards becoming comfortable with prescribing neuromodulators.²³ There is also promising data to show minimal-contact cognitive behavioral therapy, which participants can self-administer at home via telephone or web (thereby reducing clinic service pressures) is efficacious at improving IBS symptoms and has sustained benefit at 24-month follow-up.^{28,29} Despite the data supporting the use of psychological therapies in IBS, it is worth highlighting that many clinical trials generally exclude patients with underlying psychological co-morbidities or fail to screen for them. Moreover, they tend to use neuromodulators at low doses to treat abdominal pain and bowel habit, not psychological illnesses. In summary, given that an appreciable subset of patients with IBS under the Rome IV criteria have high levels of psychological distress and somatic co-morbidity, we suggest that future trials in this field should consider: a) earlier interventions with psychological therapies, b) include those with psychological co-morbidity, c) evaluate higher doses of psychological therapies where appropriate, and d) assess for both bowel- and mental health-related end points. In contrast, patients with FC and FD may mainly benefit from peripherally gut-directed therapies given that they appear to have less central involvement, although those with psychological distress should be recognized and treated accordingly.

Our study had limitations. Firstly, all included patients completed the questionnaire prior to colonoscopy, and it is therefore conceivable that levels of psychological distress may have been heightened due to the presence of alarm features, severe symptoms, and the concern regarding the potential endoscopic diagnosis. However, this is unlikely to explain the difference in psychological distress and somatization seen between those subsequently diagnosed with and without a functional bowel disorder, and between Rome IV IBS compared with FD or FC. Secondly, despite population-based studies having previously demonstrated high levels of psychosomatic disorders in community subjects with IBS,^{6,17,18} our results should not be generalized to patients managed in the primary- or secondary-care out-patient clinic setting, many of whom will be a younger cohort with mild symptoms and no red flags to warrant a colonoscopy. Thirdly, while a colonoscopy excluded organic disease within the colon, it is possible that subjects with diarrhea may have had coeliac disease or primary bile acid diarrhea which can account for roughly 4% and 25% of cases, respectively, although testing for the latter is not routine international practice.³⁰⁻³² For those with symptoms of constipation, we did not mandate testing for dysenergetic defecatory disorders, although its presence would not alter the diagnosis of IBS-C or FC. Finally, this was a cross-sectional observational study, and the association noted between IBS and psychosomatic distress cannot be evaluated further to identify the direction of causality.

Previous studies have shown that in one-third of individuals a mood disorder precedes gut symptoms, but in two-thirds gut symptoms precede the mood disorder.³³

In conclusion, IBS is associated with increased levels of psychological distress and somatization compared with FD or FC, based on the Rome IV criteria. Patients with functional bowel disorders, and in particular those who report abdominal pain, should be routinely and comprehensively screened for extra-intestinal ill-health. Future research studies should consider evaluating the role of psychological therapies early in the disease course for IBS, while evaluating both bowel- and mental health-related end points.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR CONTRIBUTIONS

IA designed the study and its conduct. All authors collected data. IA, MGS and ZA analyzed the data and wrote the initial manuscript. All authors revised the manuscript and approved the final version of the article. IA is guarantor of the article.

ORCID

Imran Aziz  <https://orcid.org/0000-0003-3833-2302>

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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