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TITLE PAGE

Title: Prognosis of Patients with Rome IV-defined versus Physician-diagnosed Irritable Bowel Syndrome: Longitudinal Follow-up Study.

Short running head: Rome IV Versus Physician-diagnosed IBS.

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Abbreviations:

HADS	hospital anxiety and depression scale
IBS	irritable bowel syndrome
IBS-SSS	irritable bowel syndrome severity scoring system
PHQ-12	patient health questionnaire-12
SeHCAT	23-seleno-25-homo-tauro-cholic acid

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ABSTRACT

Introduction: Little is known about the differences between patients diagnosed with irritable bowel syndrome (IBS) by a physician who meet the Rome IV criteria for IBS and those who do not. We conducted a longitudinal follow-up study examining this.

Methods: We collected complete gastrointestinal, extraintestinal, and psychological symptom data from 577 consecutive adult patients with suspected IBS in a single UK gastroenterology clinic. We compared baseline characteristics between patients who met Rome IV criteria for IBS, and those who had IBS according to a physician's diagnosis but who did not meet Rome IV criteria, as well as examining whether meeting Rome IV criteria at baseline influenced evolution of symptoms under therapy.

Key results: Of 455 patients diagnosed with IBS by a physician, 375 (82.4%) met Rome IV criteria and 80 (17.4%) did not. Those who met Rome IV criteria were more likely to report severe symptoms (67.6%, vs 30.0%, $p<0.001$) and that symptoms limited activities ≥50% of the time (63.0%, vs 37.5%, $p<0.001$). Patients with Rome IV IBS were more likely to have abnormal anxiety scores (50.8%, vs. 35.9%, $p=0.007$) and higher levels of somatoform symptom-reporting (29.4%, vs. 12.5%, $p<0.001$). Despite this, during longitudinal follow-up, there was no significant difference in mean number of appointments required subsequently, or IBS symptom severity.

Conclusions & Inferences: Although patients who met the Rome IV criteria had more severe symptoms at baseline and were more likely to exhibit psychological comorbidity, they did not appear to have a worse prognosis than those with physician-diagnosed IBS.

Key words: irritable bowel syndrome; physician's diagnosis; Rome IV criteria; prognosis

INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic functional bowel disorder, affecting between 5% and 10% of the world's population.[1, 2] It is characterized by recurrent abdominal pain associated with a change in stool form or frequency.[3] Although it affects quality of life to the same degree as organic gastrointestinal disorders, such as inflammatory bowel disease,[4] IBS does not seem to confer an increased mortality risk.[5] The pathophysiology remains incompletely understood,[6] and hence, current treatment strategies focus on relieving the predominant symptom, or symptoms. In recognition of the significant role that mood and psychological health plays in development and persistence of IBS symptoms,[7-10] the Rome Foundation has redefined IBS as a disorder of gut-brain interaction.[11]

In the early 1990s the Rome process, which was based on consensus among a group of experts in functional bowel disorders, proposed symptom-based criteria to help clinicians make a positive diagnosis of IBS.[12] Since then, these have undergone three revisions, the latest iteration being the Rome IV criteria published in 2016.[13] The aim of the most recent change was to increase the specificity of the Rome IV criteria over prior iterations.[14] The three main changes were the removal of abdominal discomfort from the definition, an increase in the threshold frequency of abdominal pain required to meet criteria for IBS from 3 days per month to 1 day per week, and the recognition that abdominal pain was related to, rather than just relieved by, defecation.[15] These changes appear to have led to a more severe spectrum of gastrointestinal, extraintestinal, and psychological symptoms among people with Rome IV-defined IBS.[16-18]

Over the last three decades, the Rome criteria for IBS have been used to confirm the presence of IBS among patients recruited into research studies. In clinical practice, although physicians may use the Rome criteria as a guide to facilitate a diagnosis of IBS, it is rare that they apply these rigorously. Instead, they are more likely to come to a diagnosis themselves,

based on the presence of typical symptoms.[19, 20] In fact, management guidelines do not advocate using the Rome criteria to diagnose IBS in clinical practice.[21, 22] However, little is known about the differences in routine clinical practice, if any, between patients who have IBS according to a physician's diagnosis and those who meet the Rome criteria for IBS. This information is important because patients who have symptoms compatible with IBS, but who do not meet the Rome criteria for IBS, are often prescribed drugs licensed for IBS whose efficacy has been demonstrated in clinical trials recruiting only patients with Rome-defined IBS. In addition, given the changes made to the Rome IV criteria appear to select a subgroup of patients with more severe symptoms and higher levels of psychological comorbidity, the evolution of symptoms of the condition under therapy may differ in individuals with IBS who meet these criteria, compared with those who do not. We, therefore, examined these issues in a longitudinal follow-up study conducted among patients diagnosed with IBS in secondary care.

MATERIALS AND METHODS

Participants and Setting

We conducted a longitudinal follow-up study in the specialist IBS clinic at Leeds Teaching Hospitals NHS Trust, Leeds, UK, between September 2016 and March 2020. The hospital serves a local population of 800,000, and the clinic provides a rapid diagnosis and treatment for patients with suspected IBS referred by primary care physicians, rather than taking tertiary referrals from other centers. Four experienced gastroenterologists provide their services to this clinic. We recruited all unselected, consecutive new patients aged ≥16 years referred to our IBS clinic. We have reported data from this cohort previously.[14] There were no exclusion criteria, other than an inability to understand written English. All patients were provided with a detailed questionnaire as part of their clinical evaluation at the first appointment. As all data were collected to facilitate selection of appropriate therapy in routine clinical practice, ethical approval was not required.

Data Collection and Synthesis

Demographic and Lower Gastrointestinal, Extraintestinal, and Psychological Symptom Data

At the initial clinic appointment, we collected all demographic data, as well as lower gastrointestinal, extraintestinal, and psychological symptom data prior to consultation with a gastroenterologist and referral for investigations. Lower gastrointestinal symptom data were captured using the Rome IV questionnaire for IBS, assigning the presence or absence of Rome-IV defined IBS among all patients according to the proposed criteria (Table 1).[23] We assessed symptom severity using the IBS severity scoring system (IBS-SSS),[24] a validated questionnaire measuring the presence, severity, and frequency of abdominal pain, presence and severity of abdominal distension, satisfaction with bowel habit, and degree to which IBS

symptoms are affecting, or interfering with one's life. The IBS-SSS carries a maximum score of 500 points with <75 points indicating remission, 75-174 points mild symptoms, 175-299 points moderate symptoms, and ≥300 points severe symptoms. We measured the impact of IBS symptoms, in terms of the proportion of time that they limited normal daily activities using the Rome IV questionnaire,[23] and dichotomized this at a threshold of interference with daily activities of ≥50% of the time. Finally, we provided all patients with a list of possible management strategies (education about IBS, dietary assessment, medication, psychological therapy, or hypnotherapy), allowing them to select their preferred option(s).

We collected somatization data using the patient health questionnaire-12 (PHQ-12),[25] derived from the validated patient health questionnaire-15.[26] The total PHQ-12 score ranges from 0 to 24. We categorized severity into high (total PHQ-12 ≥13), medium (8-12), low (4-7), or minimal (≤3) somatic symptom disorder. We collected anxiety and depression data using the hospital anxiety and depression scale (HADS).[27] The total HADS score ranges from a minimum of 0 to a maximum of 21 for either anxiety or depression. Severity for each was categorized into normal (total HADS depression or anxiety score 0-7), borderline abnormal (8-10), or abnormal (≥11).

Investigative Work-up and Follow-up

Patients underwent relatively standardized work-up for their symptoms, which has been described elsewhere.[14] Briefly, all patients had full blood count, C-reactive protein, and coeliac serology checked, regardless of predominant bowel habit, either by their general practitioner or at their first clinic appointment. Those aged <40 years who reported diarrhea had a fecal calprotectin level checked and underwent a colonoscopy if it was ≥100mcg/g. Colonoscopy was requested in those aged 40 years and over with diarrhea, or if atypical features were present, such as nocturnal symptoms. 23-seleno-25-homo-tauro-cholic acid

(SeHCAT) scanning was requested in patients with diarrhea, and anorectal physiology studies were requested in those with symptoms suggestive of obstructive defecation or fecal incontinence. Given that the diagnosis of IBS is not one of exclusion,[21] any other investigations, such as fecal elastase or small bowel imaging, were at the discretion of the consulting doctor. A physician's diagnosis of IBS was made in patients by the consulting gastroenterologist based on typical symptoms of lower abdominal pain in association with altered stool form or frequency elicited during the clinical history at the first outpatient clinic appointment, in a patient who exhibited no evidence of organic gastrointestinal disease after the investigative algorithm described above, as per current guidelines.[21] This was communicated to the patient using unambiguous language during the consultation.

Follow-up in the clinic was at the discretion of the consulting doctor. Typically, those patients requiring limited investigation prior to a formal diagnosis of IBS or evaluation for symptom improvement after commencement of therapy once a diagnosis had been made received further follow-up appointments. At the last point of follow-up, all patients were invited to complete a second, shorter, questionnaire assessing the severity of their symptoms, again using the IBS-SSS.

Statistical analysis

We only included patients who were felt to have IBS according to a physician's diagnosis in our analyses. We compared baseline characteristics between patients who had IBS according to a physician's diagnosis and who also met the Rome IV criteria for IBS, and those who had IBS according to a physician's diagnosis but did not meet Rome IV criteria. We compared the baseline characteristics of patients who required subsequent follow-up with those who did not. Finally, we examined whether meeting Rome IV criteria for IBS at baseline influenced subsequent evolution of symptoms under therapy. We used a χ^2 test for

categorical data and an independent samples *t*-test for continuous data. Due to multiple comparisons, a 2-tailed *p* value of <0.01 was considered statistically significant for all analyses. We performed all analyses using SPSS for Windows (version 26.0 SPSS Inc., Chicago, IL, USA).

RESULTS

We recruited all 577 patients attending the clinic during the study period. The mean age of recruited patients was 36.6 years (range 16 to 88) and 436 (75.6%) were female. Of these, 122 had either an organic gastrointestinal disorder or another disorder of brain-gut interaction according to the consulting gastroenterologist. Organic diseases detected included bile acid diarrhea in 18 patients, pancreatic insufficiency in three patients, small bowel Crohn's disease in one patient, ulcerative proctitis in one patient, and microscopic colitis in one patient. Other disorders of brain-gut interaction diagnosed included functional bloating in eight patients, functional constipation in eight patients, functional diarrhea in seven patients, functional dyspepsia in five patients, and unspecified functional bowel disorder in three patients. Therefore, 455 (78.9%) patients (mean age, 35.4 years (range 16 to 88), 347 (76.3%) female) were diagnosed with IBS by a physician. Of these 375 (82.4%) met the Rome IV criteria. Among the 80 patients with physician-diagnosed IBS who did not meet the Rome IV criteria, 44 (55.0%) did not meet the minimum abdominal pain frequency criteria, 22 (27.5%) did not meet the minimum symptom duration, and 14 (17.5%) did not meet one or more of the other required criteria.

Characteristics of Patients Meeting Rome IV Criteria, Compared with Those Who Did Not, in Those with a Physician's Diagnosis of IBS.

We examined the characteristics of the 375 patients with a physician's diagnosis of IBS and who met the Rome IV criteria for IBS, comparing them with the 80 patients with a physician's diagnosis of IBS but who did not meet Rome IV criteria (Table 2). All patients with Rome IV IBS had, by definition, abdominal pain for at least 6 months compared with only 50 (62.5%) of those who did not meet the Rome IV criteria ($p<0.001$). There was no difference in IBS subtypes between the two groups, but a significantly higher proportion of

patients with Rome IV IBS had severe symptoms according to the IBS-SSS (67.6% severe, vs. 30.0%, $p<0.001$). In addition, those with Rome IV IBS were more likely to experience continuous abdominal pain (63.0%, vs 37.5%, $p<0.001$) and to report that symptoms impacted on normal daily activities ≥50% of the time (63.0%, vs 37.5%, $p<0.001$). In terms of psychological comorbidity, patients with Rome IV IBS were more likely to have abnormal anxiety scores (50.8%, vs. 35.9%, $p=0.007$), there was a trend towards higher depression scores (22.4%, vs. 10.3%, $p=0.018$), and higher levels of somatoform symptom-reporting (29.4%, vs. 12.5%, $p<0.001$). Finally, in terms of preference for different management strategies selected at their initial clinic appointment, there was a trend for those with Rome IV IBS to prefer medication (39.5%, vs. 28.0%), or hypnotherapy (7.8%, vs. 2.7%), or more than one treatment option (10.1%, vs. 4.0%) but not dietary assessment (36.3%, vs. 58.7%) ($p=0.011$).

Severity of IBS Symptoms at Last Point of Follow-up

In total, 220 (48.4%) of 455 patients required follow-up, of whom 179 (81.4%) met Rome IV criteria. Those followed up had more severe IBS symptoms compared with those who were discharged after their initial consultation (69.0% severe, vs. 53.4%, $p<0.001$) (Table 3), but there were no other significant differences observed. Two patients did not provide complete data during follow-up, meaning that 218 patients were available for subsequent analyses. There was no significant difference in the mean number of follow-up appointments in those with Rome IV IBS, compared with those with a physician's diagnosis only (2.84 vs. 2.80, $p=0.85$) (Table 4). In terms of severity of symptoms at last point of follow-up, there were greater proportions of patients with Rome IV IBS with moderate or severe symptoms on the IBS-SSS (32.8% vs. 29.3%, and 48.6% vs. 43.9%, respectively), but this was not statistically significant. Mean IBS-SSS scores were also higher (290.7 vs. 256.7,

p=0.077), but this was not statistically significant. The proportion of patients experiencing a drop in IBS-SSS of ≥50 (53.3% vs. 43.9%), ≥75 (40.1% vs. 34.1%), or ≥100 (32.3% vs. 29.3%) points was higher in those with Rome IV-defined IBS, but again not significantly so. The mean change in IBS-SSS scores at last point of follow-up was greater among those with Rome IV-defined IBS (65.9 vs. 34.6, *p*=0.096), although again this was not statistically significant. However, the mean decrease in IBS-SSS scores from baseline to follow-up was significant in those with Rome IV-defined IBS (361.4 at baseline vs, 295.5 at follow-up, *p*<0.001) but not among those with a physician's diagnosis (291.2 at baseline vs. 256.7 at follow-up, *p*=0.045).

DISCUSSION

This study has examined the characteristics of over 450 patients diagnosed with IBS by a physician, in a single clinic in a secondary care setting, using the presence of typical symptoms compatible with IBS in the absence of an organic cause of symptoms after a relatively standardized work-up.[21] Almost one-in-five patients diagnosed with IBS by a physician did not meet Rome IV criteria for IBS. By definition, those meeting Rome IV criteria for IBS were more likely to have experienced abdominal pain for at least 6 months. They were also more likely to have continuous abdominal pain, and to have severe symptoms of IBS, which had a significantly greater impact on activities of daily living, as well as higher levels of anxiety and somatoform symptom-reporting. Almost 50% of patients required a follow-up appointment after their initial visit. Those who required follow-up had more severe IBS symptoms at baseline than those who were discharged after the first clinic appointment, but there were no other significant differences. Among those who were followed up, there was no significant difference in number of appointments required, IBS symptom severity, or degree of improvement in IBS symptoms at the last point of follow-up in patients meeting Rome IV criteria compared with those who did not. However, the mean decrease in IBS-SSS score from baseline to follow-up was significant in those with Rome IV-defined IBS, but not in those with a physician's diagnosis of IBS.

This study recruited over 450 patients with physician-diagnosed IBS with near complete gastrointestinal, extraintestinal, and psychological symptom data. The patients were referred by their general practitioner to a specialist IBS clinic in secondary care. We made a pragmatic positive diagnosis of IBS according to recommendations from guidelines, rather than carrying out extensive investigations,[21, 22, 28] performing further tests, such as colonoscopy, SeHCAT scan, anorectal physiology, or fecal elastase, only where this was felt

to be indicated due to atypical features. This approach means that the patients diagnosed with IBS in our clinic are likely to represent patients seen in a similar setting.

Weaknesses of our study include the fact that we did not mandate an exhaustive list of investigations to exclude organic disease in all patients. However, we feel it is unlikely that these patients had an underlying organic explanation for their symptoms, given previous studies using a panel of routine blood tests or small bowel imaging, in patients with suspected IBS have demonstrated a very low pick up rate for organic disease of ≤1%.[29, 30] In addition, the yield of routine colonoscopy in unselected patients with suspected IBS is very low.[31] Apart from those with atypical or red flag symptoms, we only performed colonoscopy in patients with risk factors for microscopic colitis.[32, 33] We performed SeHCAT scanning in most patients with diarrhea, as symptoms of bile acid diarrhea may mimic those of IBS-D in approximately 25% of patients.[34, 35] We also performed anorectal physiology tests in patients with suspected obstructive defecation or fecal incontinence. We have previously reported investigations carried out on all 577 recruited patients from clinic in our Rome IV validation study,[14] and excluded those patients with organic disease in our analyses in the current study. Given the rigorous tests carried out in certain situations and the fact that our practice is in line with current guidance on diagnosis of IBS it is, therefore, likely that our patients have IBS. Although we studied the degree of psychological comorbidity among all patients seen, we only applied the Rome IV questionnaire for functional bowel disorders, rather than the entire Rome IV questionnaire. We cannot, therefore, assess the degree of overlap of other disorders of gut-brain interaction and whether this was more extensive in those meeting the Rome IV criteria for IBS. As this study was conducted in a specialist IBS clinic, run by gastroenterologists experienced in diagnosing and managing the condition, the proportion of patients diagnosed with IBS not meeting Rome IV criteria is likely to be a conservative estimate, compared with patients seen in a more general gastroenterology clinic setting. This

meant that the group of patients with a physician's diagnosis of IBS was smaller and may have limited our ability to detect significant differences between the two groups, particularly during longitudinal follow-up. We also did not mandate who required follow up in our clinic; this was left at the discretion of the consulting doctor. Finally, we did not record the exact duration of follow-up in both groups of patients, only the total number of follow-up appointments. Because this is, therefore, an observational study, one should exercise caution when interpreting data from the patients we followed-up.

There have been previous studies examining the characteristics of individuals with Rome IV IBS. These have demonstrated that, compared with individuals with Rome III IBS, those with Rome IV IBS in both the community and in secondary care have more severe symptoms.[16-18] These differences were consistent over 12 months of follow-up in one study.[36] However, to the best of our knowledge, this is the first study examining the differences between patients with IBS diagnosed with IBS by a physician who meet the Rome IV criteria and those who do not. Our study shows that almost 20% of patients felt to have IBS according to a physician did not meet the Rome IV criteria. Of these, 55% did not meet the abdominal pain frequency of at least once per week, and 27.5% the minimum symptom duration of 6 months. Those with Rome IV IBS had more severe IBS symptoms, based on the IBS-SSS, which includes questions related to both abdominal pain severity and frequency.[24] These differences probably relate to the fact that the Rome IV criteria select patients with abdominal pain at a higher frequency. Those with Rome IV IBS also exhibited higher levels of psychological comorbidity compared with those with IBS according to a physician. Again, this may relate to the higher frequency of abdominal pain in Rome IV IBS, which correlates positively with psychological distress and somatization.[37]

Among those who required follow-up, IBS symptoms were more severe at baseline, but there were no other significant differences, including the proportion who met Rome IV

criteria. Despite having more severe gastrointestinal, extra-intestinal, and psychological symptoms at their initial appointment, those with Rome IV IBS required an almost identical number of subsequent appointments, and a similar proportion of patients had severe symptoms, according to the IBS-SSS, at follow-up, compared with those with physician-diagnosed IBS. However, mean IBS-SSS scores were still higher at follow-up among those with Rome IV IBS, although this difference was not statistically significant. The proportions of patients with a ≥50, ≥75, or ≥100-point decrease in IBS-SSS was numerically higher among those with Rome IV IBS, but again this was not statistically significant. These observations may relate to a loss of power, with 218 of the total population of 455 patients requiring follow-up, although the absolute difference in proportions experiencing a ≥100-point decrease between the two groups was only 3%. Finally, the significant decrease in IBS symptom scores seen in those with Rome IV-defined IBS between baseline and follow-up may relate to higher efficacy of treatment in this group or, alternatively, may represent regression to the mean, given their symptoms were more severe at baseline.

In summary, in this longitudinal follow-up study conducted in our specialist IBS clinic one-in-five patients diagnosed with IBS according to a physician did not meet the Rome IV criteria. This is likely to be even higher in non-specialist gastroenterology settings, underlining the importance of recent recommendations for a pragmatic diagnosis of IBS to be used in clinical practice,[21] with the use of the Rome IV criteria restricted to a research setting. Patients who met the Rome IV criteria had more severe symptoms at baseline and were more likely to exhibit psychological comorbidity. Despite this, those with Rome IV IBS had a similar prognosis to those with physician-diagnosed IBS at follow-up. During follow-up, the mean number of appointments required, and the proportion of patients with severe symptoms, was similar between those with Rome IV-defined IBS and those diagnosed by a physician. However, those with Rome IV IBS demonstrated greater improvement in symptoms at the

last point of follow-up, although this may relate to the increased symptom severity seen at baseline.

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CONFLICTS OF INTEREST/STUDY SUPPORT

Guarantor of the article: ACF is guarantor.

Specific author contributions: VCG, OFG, DJG, CJB, and ACF conceived and drafted the study. CJB collected all data. ACF analyzed and interpreted the data. VCG and ACF drafted the manuscript. All authors have approved the final draft of the manuscript.

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Table 1. Rome IV diagnostic criteria for IBS.

Rome IV IBS Diagnostic Criteria
1. Recurrent abdominal pain, on average, at least **1 day per week** in the last 3 months and associated with two or more or the following:
a. **Related** to defecation
b. Associated with a change in frequency of stool
c. Associated with a change in form of stool
2. Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Table 2. Characteristics of Patients with Rome IV-defined versus Physician-Diagnosed IBS.

	Rome IV IBS (n = 375)	**Physician-diagnosed IBS (n= 80)**	**P value***
Mean age (SD)	34.8 (14.0)	38.3 (15.0)	0.047
Female gender (%)	288 (76.8)	59 (73.8)	0.56
Abdominal pain for at least 6 months at baseline (%)	375 (100)	50 (62.5)	<0.001
IBS subtype at baseline (%)			
Constipation	88 (23.7)	25 (31.3)	
Diarrhea	129 (34.8)	29 (36.3)	
Mixed stool pattern	145 (39.1)	26 (32.5)	
Unclassified	9 (2.4)	0 (0.0)	0.24
IBS-SSS severity at baseline (%)			
Remission	0 (0.0)	3 (3.8)	
Mild	20 (5.5)	17 (21.3)	
Moderate	98 (26.9)	36 (45.0)	
Severe	246 (67.6)	24 (30.0)	<0.001
Mean IBS-SSS at baseline (SD)	343.3 (93.3)	248.0 (100.5)	<0.001
Continuous abdominal pain at baseline (%)	233 (63.0)	30 (37.5)	<0.001
IBS limits activities ≥50% of the time at baseline (%)	323 (86.1)	48 (60.8)	<0.001
Meal-related symptoms ≥50% of the time at baseline (%)	298 (79.9)	54 (68.4)	0.025

HADS-A categories at baseline (%)			
Normal	106 (29.1)	37 (47.4)	
Borderline	73 (20.1)	13 (16.7)	
Abnormal	185 (50.8)	28 (35.9)	0.007
Mean HADS-A score at baseline (SD)	10.6 (4.9)	8.7 (4.5)	0.02
HADS-D categories at baseline (%)			
Normal	205 (56.8)	57 (73.1)	
Borderline	75 (20.8)	13 (16.7)	
Abnormal	81 (22.4)	8 (10.3)	0.018
Mean HADS-D score at baseline (SD)	7.2 (4.8)	5.3 (4.2)	0.01
PHQ-12 severity at baseline (%)			
Low	20 (5.4)	8 (10.0)	
Mild	82 (22.1)	31 (38.8)	
Moderate	160 (43.1)	31 (38.8)	
Severe	109 (29.4)	10 (12.5)	<0.001
Mean PHQ-12 score at baseline (SD)	10.2 (4.4)	8.1 (3.6)	<0.001
Preferred management strategy (%)			
Medication	137 (39.5)	21 (28.0)	
Dietary assessment	126 (36.3)	44 (58.7)	
Psychological therapy	12 (3.5)	3 (4.0)	
Hypnotherapy	27 (7.8)	2 (2.7)	
Education about IBS	10 (2.9)	2 (2.7)	
More than one	35 (10.1)	3 (4.0)	0.011

*P value for independent samples *t*-test for continuous data and Pearson χ^2 for comparison of categorical data.

Table 3. Characteristics of Patients with IBS Requiring Follow-up in Secondary Care Compared with Those Who Did Not.

	Required Follow-up in Secondary care (n = 220)	**Did not Require Follow-up in Secondary care (n= 235)**	**P value***
Mean age (SD)	36.7 (14.9)	34.3 (13.4)	0.067
Female gender (%)	174 (79.1)	173 (73.6)	0.17
Abdominal pain for at least 6 months at baseline (%)	204 (92.7)	221 (94.0)	0.57
Met Rome IV criteria for IBS at baseline (%)	179 (81.4)	196 (83.4)	0.57
IBS subtype (%)			
Constipation	64 (29.2)	49 (21.1)	
Diarrhea	77 (35.2)	81 (34.9)	
Mixed stool pattern	75 (34.2)	96 (41.4)	
Unclassified	3 (1.4)	6 (2.6)	0.15
IBS-SSS severity at baseline (%)			
Remission	0 (0.0)	3 (1.3)	
Mild	7 (3.3)	30 (12.8)	
Moderate	58 (27.6)	76 (32.5)	
Severe	145 (69.0)	125 (53.4)	<0.001
Mean IBS-SSS at baseline (SD)	346.8 (89.9)	307.5 (107.5)	<0.001
Continuous abdominal pain at baseline (%)	130 (59.6)	133 (57.3)	0.57
IBS limits activities ≥50% of the time at baseline (%)	183 (83.2)	188 (80.3)	0.43
Meal-related symptoms ≥50% of the time at baseline (%)	170 (78.0)	182 (77.8)	0.96

HADS-A categories at baseline (%)			
Normal	62 (29.1)	81 (35.4)	
Borderline	44 (20.7)	42 (18.3)	
Abnormal	107 (50.2)	106 (46.3)	0.37
Mean HADS-A score at baseline (SD)	10.5 (4.8)	10.1 (5.0)	0.35
HADS-D categories at baseline (%)			
Normal	126 (59.4)	136 (59.9)	
Borderline	46 (21.7)	42 (18.5)	
Abnormal	40 (18.9)	49 (21.6)	0.62
Mean HADS-D score at baseline (SD)	6.9 (4.6)	6.8 (4.8)	0.90
PHQ-12 severity at baseline (%)			
Low	14 (6.4)	14 (6.0)	
Mild	49 (22.4)	64 (27.6)	
Moderate	93 (42.5)	98 (42.2)	
Severe	63 (28.8)	56 (24.1)	0.54
Mean PHQ-12 score at baseline (SD)	10.0 (4.1)	9.7 (4.4)	0.58
Preferred management strategy (%)			
Medication	91 (44.2)	68 (31.3)	
Dietary assessment	74 (35.9)	96 (44.2)	
Psychological therapy	7 (3.4)	8 (3.7)	
Hypnotherapy	15 (7.3)	14 (6.5)	
Education about IBS	5 (2.4)	7 (3.2)	
More than one	14 (6.8)	24 (11.1)	0.11

*P value for independent samples *t*-test for continuous data and Pearson χ^2 for comparison of categorical data.

Table 4. Evolution of Symptoms Under Therapy During Longitudinal Follow-up Among Patients with Rome IV-defined versus Physician-Diagnosed IBS.

	Rome IV IBS (n = 177)	**Physician-diagnosed IBS (n= 41)**	**P value***
Mean number of follow-up appointments (SD)	2.84 (1.15)	2.80 (1.21)	0.85
IBS-SSS symptom severity at follow-up (%)			
Remission	6 (3.4)	2 (4.9)	
Mild	27 (15.3)	9 (22.0)	
Moderate	58 (32.8)	12 (29.3)	
Severe	86 (48.6)	18 (43.9)	0.71
Mean IBS-SSS at follow-up (SD)	290.7 (111.0)	256.7 (107.3)	0.077
Change in IBS-SSS from baseline to follow-up (%)			
≥50 points	89 (53.3)	18 (43.9)	0.28
≥75 points	67 (40.1)	14 (34.1)	0.48
≥100 points	54 (32.3)	12 (29.3)	0.71
Mean change in IBS-SSS at follow-up (SD)	65.9 (102.1)	34.6 (107.1)	0.096

*P value for independent samples *t*-test for continuous data and Pearson χ^2 for comparison of categorical data.