How the Change in IBS Criteria From Rome III to Rome IV Impacts on Clinical Characteristics and Key Pathophysiological Factors

Imran Aziz, MBChB, MD[1], Hans Törnblom, MD, PhD[1], Olafur S Palsson, PsyD[2], William E Whitehead, PhD[2] and Magnus Simrén, MD, PhD[1,2]

OBJECTIVES: **The diagnostic criteria for irritable bowel syndrome (IBS) have recently been updated from Rome III to Rome IV. Whereas in Rome III a diagnosis of IBS entailed chronic abdominal pain or discomfort at least 3 days per month, in Rome IV the term discomfort has been removed and the frequency of abdominal pain increased to at least 1 day per week. We examined how this change in IBS criteria impacts on clinical characteristics and pathophysiological factors.**

METHODS: **A total of 542 Swedish subjects with Rome III IBS completed a baseline questionnaire enquiring for the number of abdominal pain days in the last 10 days; this was subsequently used as a surrogate marker to identify Rome IV IBS, in that (a) those with 0 or 1 day of pain were classed as Rome IV-negative, and (b) those with ≥2 days of pain were classed as Rome IV-positive. Comparisons were made between Rome IV-positive and -negative IBS groups for demographics, IBS subtype, gastrointestinal and psychological symptoms, somatisation, fatigue, disease-specific quality of life, rectal sensitivity, and oro-anal transit time.**

RESULTS: **Overall, 85% of Rome III IBS patients fulfilled the Rome IV criteria for IBS, but 15% did not. Rome IV-positive subjects were significantly more likely to be female, have poorer quality of life, greater pain severity, bloating, somatisation, fatigue, and rectal sensitivity than Rome IV-negative subjects. There were no differences in severity of anxiety or depression, IBS subtypes, bowel habit dissatisfaction, or oro-anal transit time. Finally, increasing number of pain days correlated positively with symptoms and visceral hypersensitivity.**

CONCLUSIONS: **Most Rome III-positive IBS patients seeking healthcare fulfil the Rome IV IBS criteria. They constitute a more severe group than those who lose their IBS diagnosis.**

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INTRODUCTION

Irritable bowel syndrome (IBS) is a functional bowel disorder, as defined by no identifiable structural or biochemical abnormality to explain the symptoms on routine clinical tests [1]. Epidemiological surveys suggest that IBS is common, with a pooled global prevalence of 11.2%, shows a female preponderance, and mainly affects younger individuals [1–3]. IBS is frequently encountered in clinical practice, accounting for almost a third of all gastroenterology cases seen in primary care, with a subsequent third of these being referred onto secondary care for further evaluation [4]. The burden of illness with IBS is significant due to its chronic remitting-relapsing nature and its association with extra-intestinal symptoms such fatigue, anxiety, depression, and somatisation, as well as diminished quality of life [5]. The exact cause of IBS is unknown although the prevailing hypothesis is a disorder of gut–brain interaction as demonstrated by alterations in gut immunity, visceral hypersensitivity, enteric motor function disturbances, and central pain processing [5].

Guidelines for the management of IBS recommend the use of symptom-based criteria to aid clinicians towards making a positive diagnosis of IBS without the need to perform extensive investigations [6, 7]. Over the last 30 years this guidance have been provided by the Rome Foundation, an international panel of experts working in the field of functional gastrointestinal (GI) disorders,

[1]Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden. [2]Center for Functional Gastrointestinal and Motility Disorders, University of North Carolina, Chapel Hill, NC, USA. **Correspondence:** I.A. (email: imran.aziz@sth.nhs.uk)
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who update criteria for functional GI disorders every decade or so following the accumulation of high-quality scientific data.

As of May 2016 the Rome IV criteria for functional GI disorders was released, within which there was a change in symptom-based criteria for IBS compared to the previous Rome III definition (Table 1) [8, 9]. The two main differences to emerge from Rome III to Rome IV criteria pertinent to IBS are:

(1) The term "abdominal discomfort" has been removed, leaving just "abdominal pain." The justifications for removing discomfort were in view of its ambiguous interpretation, as it can also be perceived as bloating, gas, fullness, sensation of incomplete evacuation, and urgency [10]. Moreover, not all languages have a word for discomfort.

(2) The symptom frequency has increased from at least 3 days/month to at least 1 day/week, based on normative data from a survey of adults without GI disorders, who in 95% of cases reported experiencing abdominal pain less than 1 day/week [11].

As a consequence of the change in criteria it can be envisaged that a subset of subjects previously diagnosed with IBS using the Rome III criteria will no longer be defined as having IBS according to the Rome IV criteria. Indeed, this has now been evaluated by two recent studies [12, 13]. The first from a tertiary care centre in China found that roughly 50% of their subjects with Rome III defined IBS will not have IBS according to Rome IV, due to two-thirds of these reporting only abdominal discomfort and one-third having infrequent pain [12]. Moreover, this study compared those who were now Rome IV-positive for IBS against those who were Rome IV-negative, finding that Rome IV-positive subjects experienced more pain and higher overall IBS symptom severity scores, but no differences were noted for demographic characteristics, abdominal bloating, stool frequency, IBS subtype, disease duration, surgeries, or GI infection history [12]. A second study from The Netherlands, involving primary and secondary care subjects with Rome III IBS, noted that 87% could be defined as Rome IV-positive IBS and that (compared to Rome IV-negative) this group were more often female, younger, had more severe GI symptomatology (including abdominal bloating), visceral hypersensitivity, psychological co-morbidities, and lower general quality of life [13]. In all, these two studies share similarities but there were discrepancies with regards to the proportion of Rome III IBS subjects that fulfil Rome IV criteria for IBS, female demographics, and the association with abdominal bloating.

Hence, in view of the recent change in IBS definition, and the relative paucity of data with some conflicting findings, further studies are needed to substantiate how the change in diagnostic criteria for IBS from Rome III to Rome IV impacts on gastroenterology practise with regards to clinical characteristics and pathophysiological factors. We sought to address this issue using data from a large, well-characterised, cohort of Rome III IBS patients attending a Swedish gastroenterology centre.

Table 1 **The Rome III and Rome IV diagnostic criteria for IBS [8, 9]**

Rome III	Rome IV
Recurrent abdominal pain or discomfort at least 3 days/month in the last 3 months associated with two or more of the following criteria:	Recurrent abdominal pain on average at least 1 day/week in the last 3 months, associated with two or more of the following criteria:
1. Improvement with defecation	1. Related to defecation
2. Onset associated with a change in frequency of stool	2. Associated with a change in frequency of stool
3. Onset associated with a change in form (appearance) of stool	3. Associated with a change in form (appearance) of stool
Note: criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis	

MATERIALS AND METHODS

Rome III IBS subjects

We included subjects with IBS according to the Rome III criteria [8], who participated in studies assessing the relevance of pathophysiological factors for symptoms in IBS [14–17]. The patients in this study cohort were recruited from the outpatient clinic specialised in functional GI disorders at the Sahlgrenska University Hospital in Gothenburg, Sweden. The majority of them were referred to the unit by their general practitioner or through self-referral. The diagnosis of IBS was based on a typical clinical presentation, fulfilment of Rome III criteria [8], and any additional investigations if considered necessary being negative. Subtyping according to the Rome III criteria was based on information from a 2-week stool diary using the Bristol Stool Form scale (BSF) [8, 18]. Exclusion criteria were: other GI disease(s) explaining the patient's symptoms; other severe disease(s) such as malignancy, severe heart disease, kidney disease, or neurological disease; symptoms indicating other severe disease(s) such as GI bleeding, weight loss or fever; severe psychiatric disease; a history of drug or alcohol abuse within 6 months prior to enrolment; or pregnancy at the time of the study.

All patients were given study-specific verbal and written information before giving their written consent to participate in the studies. The Regional Ethical Review Board in Gothenburg approved the study prior to the start of patient enrolment. Participants then completed questionnaires followed by undertaking relevant pathophysiological studies over the ensuing few weeks. The patients were naive to IBS medication during this time period.

Identification of Rome IV IBS-positive and -negative subjects

At baseline, Rome III IBS subjects completed the IBS Severity Scoring System (IBS-SSS) questionnaire [19], of which one question asks "please enter the number of days you get abdominal pain in the last 10 days." The answer to this question was used as a surrogate marker to identify those who could be categorised as having IBS according to Rome IV. In those who answered 0 or 1 day this was considered as not fulfilling criteria for Rome IV IBS, in that (a) 0 days implies that these subjects with Rome III IBS

do not have abdominal pain but rather discomfort, and (b) 1 day of pain in 10 days suggests infrequent symptoms, which is less than once weekly. In contrast, those who answered having 2 or more days of abdominal pain in the last 10 days were categorised as being positive for Rome IV IBS as their symptom frequency would be considered to be at least weekly.

Questionnaires

Demographics. Basic demographic information about participants was obtained by a study nurse/research coordinator, using standardised case report forms. Of these variables, age and gender were used in the analyses in this study.

GI symptoms. The severity of IBS symptoms was evaluated with the widely used and validated questionnaire, IBS-SSS [19]. This questionnaire is based on five items assessing symptoms over the last 10 days; frequency and severity of abdominal pain, severity of abdominal distension, bowel habit dissatisfaction, and interference of IBS with daily life. The questionnaire uses visual analogue scales and each item is scored 0–100, which yields a total score ranging from 0 to 500, with higher scores reflecting more severe symptoms. According to validated cut-off levels, the patients can be categorised as having mild IBS (score of <175), moderate IBS (175–300), or severe IBS (>300).

In this study, we analysed the total IBS-SSS score for the entire cohort and used it for descriptive purposes. However, as the subsequent identification of Rome IV-positive or -negative IBS stemmed from using a question from the IBS-SSS questionnaire (as mentioned above, the number of days of abdominal pain in the last 10 days), we did not use total IBS-SSS scores in the Rome IV subgroups; instead, we only analysed sub-scores pertaining to pain severity, severity of abdominal distension, bowel habit dissatisfaction, and interference of IBS with daily life. Higher scores represent more severe symptoms.

Disease-specific quality of life. The 30-item IBS quality of life questionnaire [20] measures, over the preceding month, nine quality of life domains found to be of relevance for IBS: emotional health, mental health, sleep, energy, physical functioning, food/diet, social functioning, physical role, and sexual relations. Each scale score is transformed to a scale of 0–100, with 100 representing the best possible quality of life.

Psychological distress. The Hospital Anxiety and Depression scale [21] is a mood scale measuring symptoms over the last week. It has been developed for use in non-psychiatric clinical settings to identify patients with psychological distress. It consists of 14 items, evenly divided into two subscales, one for anxiety and one for depression. It uses a four-point Likert scale (0–3), which provides a minimum score of (no symptoms) and a maximum score of 21 (maximal severity of symptoms) on each subscale.

Somatisation. The Patient Health Questionnaire (PHQ)-12 somatisation score [22] is a modified version of the widely used PHQ-15 somatisation questionnaire [23] that excludes the three GI symptoms (nausea, abdominal pain, and altered bowel habit), as these are likely to be directly related to functional GI disorders. Hence, the PHQ-12 only records bothersome non-GI symptoms over the previous month. The 12 symptoms assessed are back pain, limb pain, headaches, chest pain, dizziness, fainting spells, palpitations, breathlessness, menstrual cramps, dyspareunia, insomnia, and lethargy. Subjects completing the PHQ-12 were asked to rate how much they had been troubled by these 12 symptoms over the last 4 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 the overall severity of somatic symptoms, with higher scores representing greater somatisation.

Fatigue. The Fatigue Impact Scale [24] consists of a total of 40 questions enquiring for the impact of fatigue over the preceding month. The questions can be subdivided into three sections; physical functioning (ten items), cognitive functioning (ten items) and psychosocial functioning (20 items). Each item consists of a statement, being rated by the subjects as 0 (no problem) to 4 (extreme problem). A higher score represents greater fatigue severity.

Physiologic measures

Rectal sensitivity. Balloon distensions using an electronic barostat (Dual Drive Barostat, Distender Series II; G&J Electronics Inc., Toronto, ON, Canada) were performed to assess colorectal sensitivity. In the year 2010, our department underwent a change in methodology to assess visceral sensitivity, with the phasic distension method being substituted by the ramp distension method. A detailed description of both these procedures has previously been reported [15, 17, 25].

In summary, for the initial Swedish cohort ($n=195$), an ascending methods of limits paradigm with phasic distensions of 30 s duration separated by 30 s rest intervals with the balloon at the operating pressure was used [15]. Distensions were performed with 5 mmHg stepwise increments starting at the operating pressure and increasing until the subject reported pain or when a pressure level of 70 mmHg was reached. Thresholds for rectal fullness, urge to defecate, discomfort, and pain were determined, with subjects subsequently rating on a visual analogue scale (VAS, 0–100) the severity of their symptoms, with higher scores representing greater severity. For the purpose of this study, only the pain threshold (pressure, mmHg) and its corresponding VAS pain score are reported for the phasic distension method.

For the latter Swedish cohort patients ($n=143$), an ascending method of limits ramp distension protocol starting at 0 mmHg and increasing in steps of 4 mmHg every minute up to the pain threshold or to a maximum balloon pressure of 60 mmHg was performed [17, 25]. Thresholds for first sensation, desire to defecate, urgency, and pain were assessed. Moreover, intensity ratings of these symptoms at four different sensations during random phasic distensions of 12, 24, 36, and 48 mmHg above the operating pressure were also determined. For the purpose of this study only the pain threshold (pressure, mmHg), and VAS pain score at 24 mmHg above the operating pressure, are reported for the ramp distension technique.

Colonic transit time. The ten radiopaque markers were ingested per day during six consecutive days, and on the morning of the 7th day the remaining markers were counted using fluoroscopy (Exposcop 7000 Compact; Ziemh GmbH, Nüremberg, Germany) [26]. The colonic transit time in days was obtained by dividing the number of retained markers with the daily dose, i.e. 10.

Data analysis

Statistical analysis was carried out using SPSS version 21.0 software (SPSS Inc. Chicago, Illinois, United States), with significance set at a p-value of <0.05. Data are presented as means ± standard deviations (SD) and proportions (%). As a first step we analysed the demographic profile of the Rome III IBS subjects. Following this, we identified the proportion of Rome III IBS subjects who could be considered as being positive or negative for Rome IV IBS based on the frequency of their abdominal pain. Thereafter, subsequent comparisons were made between these two groups pertaining to clinical symptoms and colorectal physiology, using the Student's T-test and Mann–Whitney U-test for parametric and non-parametric data, respectively. As a final step we used Spearman correlation to analyse how increasing number of days of abdominal pain correlated with clinical symptoms and colorectal physiology.

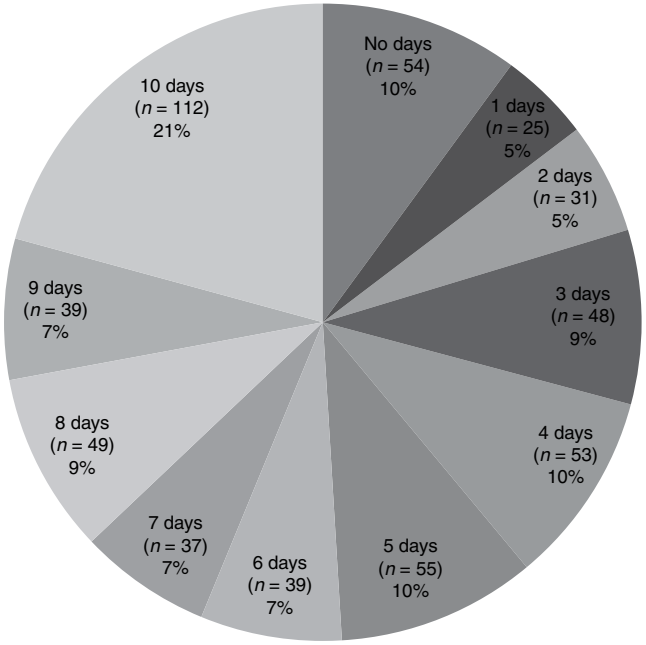

Fig. 1 Subjects with Rome III IBS reporting the "number of days with abdominal pain in the last 10 days." Note: those reporting 0 or 1 day of pain were subsequently classed as not fulfilling the criteria required for Rome IV IBS (i.e. Rome IV IBS-negative) = 15%. Those reporting ≥2 days per 10 days were classed as fulfilling Rome IV IBS criteria (i.e. Rome IV IBS-positive) = 85%

RESULTS

Subjects with Rome III IBS

We included 542 patients who fulfilled criteria for Rome III IBS, of which 402 (74%) were female. The mean age was 38 years (SD 13), ranging from 18 to 72 years. The IBS subtypes based on the Rome III criteria (BSF) were diarrhoea (35%), constipation (25%), mixed (10%), unsubtyped (21%) with missing data for 9%. The IBS-SSS was mild in 9.8%, moderate in 38.6%, and severe in 51.7%, with the overall mean score being 297 (SD 97).

The prevalence of Rome IV IBS within the Rome III IBS cohort

Figure 1 shows response to the question "please enter the number of days you get abdominal pain over the last 10 days." No days with pain during the preceding 10 days were reported by 10% ($n = 54$) of the subjects, whereas 5% ($n = 25$) of the subjects reported they had 1 day with pain. Both of these groups were subsequently used to identify those subjects with Rome III IBS who would be considered as being negative for Rome IV IBS, giving a prevalence of 15% ($n = 79$). The remaining 85% ($n = 463$) of Rome III IBS subjects reported having pain ≥2 days per 10 days, which was used as a surrogate marker to identify those who would be considered as positive for Rome IV IBS.

Demographic and clinical comparison between Rome IV-positive and -negative IBS subjects

As Table 2 shows, Rome IV-positive IBS subjects had a greater proportion of females compared to their Rome IV-negative counterparts. They also had increased pain severity, severity of abdominal distension, interference with daily life, somatisation, and fatigue compared with Rome IV-negative IBS subjects. They also reported poorer disease-related quality of life scores within most domains (Fig. 2). However, there were no differences between the groups with regards to age, IBS subtype, bowel habit dissatisfaction, anxiety, or depression.

Comparison of colorectal physiology between Rome IV-positive and -negative IBS subjects

With the phasic distension method, Rome IV-positive IBS subjects recorded a trend towards lower pain threshold, and higher VAS pain scores at that corresponding threshold, than Rome IV-negative IBS subjects. With the ramp distension method, Rome IV-positive IBS subjects recorded significantly lower pain threshold, and higher VAS pain scores during the phasic distension at 24 mmHg above the operating pressure, than Rome IV-negative IBS subjects. There were no differences in oro-anal transit times between the groups (Table 3).

Correlation between number of abdominal pain days with clinical phenotype and colorectal physiology

As shown in Table 4, increasing number of days with abdominal pain during the preceding 10 days showed positive correlations with pain severity, severity of abdominal distension, bowel habit dissatisfaction, interference with daily life, poorer quality of life, fatigue, somatisation, and depression. There was also a reduction in pain thresholds and increasing VAS pain scores with increasing numbers of pain days.

Table 2 Comparision between Rome IV-positive and -negative IBS subjects for demographics, IBS subtype, and GI and non-GI symptom severity

	Rome IV-negative IBS ($n=79$, 15%)	Rome IV-positive IBS ($n=463$, 85%)	*p*-value
Demographics			
Female	51 (65%)	351 (76%)	0.04
Mean age (SD)	38.9 (13)	37.8 (13.4)	0.4
IBS Subtype (Rome III)			
Constipation	17 (22%)	118 (25%)	0.5
Diarrhoea	31 (39%)	158 (34%)	
Mixed	5 (6%)	51 (11%)	
Unsubtyped	20 (25%)	95 (21%)	
Missing	6 (8%)	41 (9%)	
IBS-SSS (SD)			
Abdominal pain severity	17.0 (28.4)	52.5 (23.2)	<0.001
Abdominal distension	40.9 (30.2)	59.0 (26.7)	0.001
Bowel habit dissatisfaction	67.1 (27.7)	70.2 (24.7)	0.3
Interference with daily life	58.6 (26)	68.2 (22.6)	0.001
HADS (SD)			
Anxiety	6.7 (4)	7.6 (4.7)	0.1
Depression	5.1 (3.8)	5.6 (3.7)	0.3
Total	11.8 (6.5)	13.1 (7.3)	0.15
PHQ-12 somatisation (SD)	5.9 (2.8)	8.7 (4.3)	0.01
Fatigue Impact Score (SD)			
Physical	8.4 (7.8)	14.4 (10.4)	0.02
Cognitive	10.4 (8.7)	16.5 (11.3)	0.03
Psychosocial	17.2 (17.1)	29 (19.7)	0.01
Total	35.9 (31.7)	59.9 (39.4)	0.01

HADS Hospital Anxiety and Depression Scale, *IBS-SSS* IBS Severity Scoring System, *P, HQ-12* Patient Health Questionnaire

DISCUSSION

In this study, we evaluated the implications of updating the IBS diagnostic criteria from Rome III to Rome IV. We could demonstrate that 85% of subjects with Rome III IBS who visited a gastroenterology outpatient clinic will still likely have IBS according to Rome IV, whereas 15% will not. Moreover, Rome IV-positive IBS patients demonstrated more severe clinical symptoms and heightened visceral sensitivity compared to Rome IV-negative subjects. Finally, we have shown that determining the number of days with abdominal pain over the last 10 days can in itself be a useful measure to predict visceral hypersensitivity and the overall severity of ill-health within IBS subjects.

First, based on the surrogate marker adopted in our study, most subjects with Rome III IBS in a Western Gastroenterology Clinic will not lose their diagnosis when transferring over to Rome IV, hence it will not have major implications in diagnostic coding. This data are consistent with that from The Netherlands where, after using a 14-day symptom diary to assess abdominal pain frequency, 87% of Rome III IBS could be transferred over to Rome IV [13]. However, both these western studies contrast with that from a tertiary care clinic in China where subjects concurrently completed both the Rome III and Rome IV diagnostic questionnaire; in 170 patients fulfilling the Rome III criteria for IBS, 46% of these fulfilled Rome IV criteria for IBS and 54% did not [12]. The reasons for not fulfilling Rome IV IBS status was due to roughly two-thirds reporting only abdominal discomfort and not pain, and one-third reporting infrequent pain [12]. The discrepancy between the studies from the East and West may be due to differences in methodological sampling or symptom-reporting behavioural pattern [27]. It has previously been shown that bloating is very common among Asian patients consulting in clinic [28], and that its uncomfortable nature may be reported as discomfort [27]. Indeed, the imprecise interpretation of the word "discomfort" across communities was fundamental in its removal from the latest iteration of IBS diagnostic criteria [9, 10].

Second, Rome IV-positive IBS subjects show a distinct clinical phenotype compared to Rome IV-negative patients. They are more likely to be female, demonstrate increased pain severity, abdominal distension, somatisation, fatigue, and generally poorer quality of life. Moreover, they experience greater visceral sensitivity. However, there were no differences between the groups with regards to psychological distress, bowel habit dissatisfaction, and oro-anal transit time. Our findings are largely in concordance with that produced from China and The Netherlands, although some differences were noted that warrant consideration.

For example, the group from China did not find any difference with regards to gender or abdominal distension between Rome IV-positive and -negative IBS subjects [12, 13]. Admittedly, the relationship between gender and IBS symptoms is not straight forward, with men and women sharing more similarities than differences [29]. Further, where differences have been noted the effect size has been reported to be small [29]; in the instance of abdominal pain a meta-analysis has shown that women are more likely to report pain than men (odds ratio 1.12, 95% CI 1.02–1.22) [30]. In our study, the greater prevalence of females in Rome IV-positive IBS subjects was only just significant (76 vs. 65%, $p=0.04$), supporting the notion that where gender differences are observed, these are modest. Nevertheless, our findings may open the debate as to why therapeutic studies in IBS have historically shown greater efficacy in females than in males [30, 31]. This has largely been attributed to the natural history of IBS, leading to a far greater representation of females compared to males within clinical trials [30, 31]. However, we also show that females are more homogeneous in their symptom profile with regards to having abdominal pain and not discomfort, whereas males have a greater propensity to either. It can be envisaged that the Rome IV criteria for IBS will at least provide a more homogeneous group of patients, all of whom will

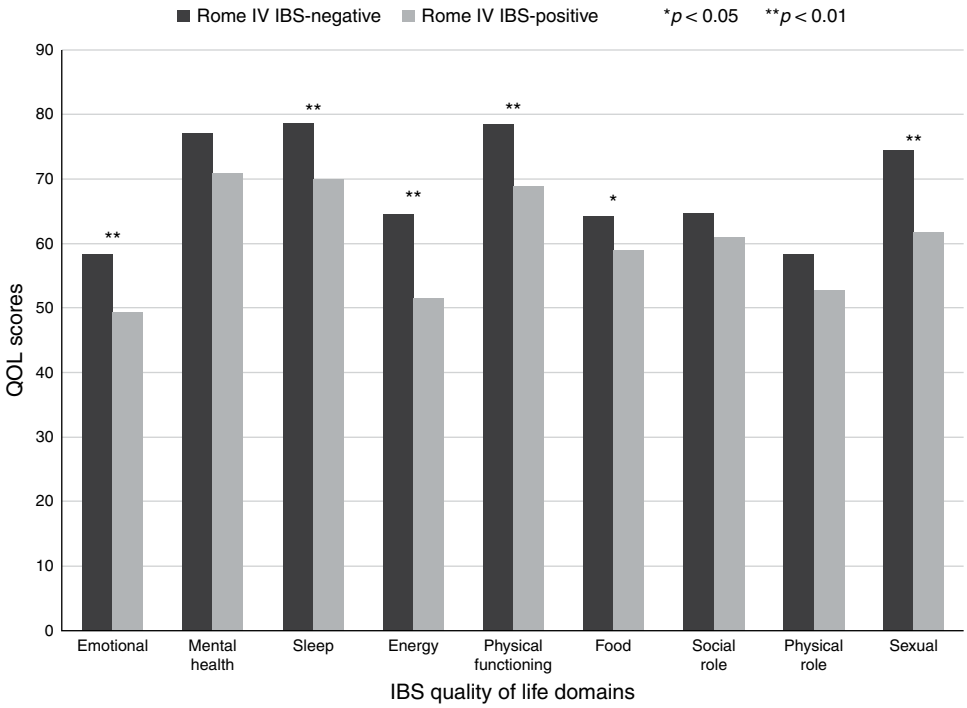

Fig. 2 IBS quality of life (QOL) domains in Rome IV-positive and -negative IBS subjects

Table 3 Colorectal physiology in Rome IV-positive and -negative IBS subjects

	Rome IV-negative IBS	Rome IV-positive IBS	p-value
Phasic distension barostat method			
Rectal pain threshold, mmHg (SD)	35.1 (14.1)	29.7 (11.9)	0.08
VAS pain score at pain threshold, mm (SD)	28.1 (27.6)	34 (22.8)	0.06
Ramp distension barostat method			
Rectal pain threshold, mmHg (SD)	32 (10.1)	26.4 (8.3)	0.01
VAS pain score at 24 mmHg distension, mm (SD)	24.1 (31.3)	51.2 (30.8)	0.001
Oro-anal transit time, days (SD)	1.4 (0.8)	1.6 (1.0)	0.1

have abdominal pain, irrespective of gender. However, results for men with IBS with probably still lag behind women due to issues with sample size. With regards to abdominal distension, the lack of significant difference seen in China between Rome IV-positive and -negative IBS groups may be due to the negative group largely being identified through having discomfort [12], which is commonly attributed to bloating [27, 28].

Next, the group from The Netherlands recorded higher psychological distress (in particular, for depression) in Rome IV-positive compared to -negative IBS subjects [13], which was not replicated in our study. This may be explained by patient recruitment in that subjects from The Netherlands with Rome IV-positive IBS were significantly more likely to be from secondary care, compared to their Rome IV-negative counterparts who had a large representation from primary care [13]. Previous studies have shown that differences exist between IBS consulters in primary and secondary care with regards to symptom severity, quality of life, and psychological symptoms [32, 33]. A key strength of our study was that this potential confounding factor was absent, as all subjects were seen in specialist care. It is also important to bear in mind that subjects with Rome III IBS who are negative for Rome IV IBS are still symptomatic and are likely to be diagnosed with an alternate functional bowel disorder; the study from The Netherlands was able to redefine these subjects as having functional constipation in 24%, functional diarrhoea in 34%, functional abdominal bloating/distension in 26%, and no diagnosis in the remaining 16% [13]. Moreover, subjects with these "other" functional bowel disorders do report psychological distress, with a large secondary care study of Rome III defined subjects showing that although IBS was associated with greater anxiety compared to functional constipation or diarrhoea, there was no difference in prevalence rates of depression between the groups [34].

However, in general, our study along with that from China and The Netherlands do suggest that the removal of discomfort and infrequent abdominal pain from the current iteration of IBS criteria identifies a subset with more severe disease activity. Yet, the culmination of these recent studies may seem completely contradictory to that initially published from the United States

Table 4 Correlation between increasing number of abdominal pain days in the last 10 days with clinical symptoms and colorectal pathophysiology

	Correlation coefficient (*r*)	*p*-value
IBS-SSS		
Abdominal pain severity	0.50	<0.001
Abdominal distension severity	0.30	<0.001
Bowel habit dissatisfaction	0.14	0.001
Interference with daily life	0.30	<0.001
Fatigue Impact Scale		
Physical	0.34	<0.001
Social	0.32	<0.001
Psychosocial	0.36	<0.001
PHQ-12 somatisation	0.30	<0.001
HADS		
Anxiety	0.08	0.07
Depression	0.10	0.02
IBS-QOL		
Emotional	−0.23	<0.001
Mental health	−0.17	<0.001
Sleep	−0.29	<0.001
Energy	−0.31	<0.001
Physical function	−0.28	<0.001
Food	−0.19	<0.001
Social Role	−0.15	<0.001
Physical Role	−0.19	<0.001
Sexual	−0.27	<0.001
Phasic distension barostat method		
Rectal pain threshold	−0.13	0.08
VAS pain scores	0.14	0.05
Ramp distension barostat method		
Rectal pain thresholds	−0.19	0.02
VAS pain scores at 24 mmHg distension	0.33	<0.001
Oro-anal transit time	−0.005	0.9

15 years ago, which evaluated subjects fulfilling Rome I criteria for IBS and compared those with pain-predominance and discomfort-predominance [35]. The investigators noted no difference in IBS symptom severity, psychological distress, quality of life, and healthcare utilisation between the groups. However, importantly, the groups were not completely exclusive as the division was based on predominant symptoms, meaning for example that subjects with discomfort-predominance did still have pain (~70%) [35]. Moreover, predominant symptoms in functional GI disorders can fluctuate, even over short periods of time [36].

Third, we noted that as the number of days with abdominal pain in the last 10 days increased, there was a significant correlation with visceral hypersensitivity and measures of ill-health related to intestinal and extra-intestinal manifestations of IBS. Indeed, a recent multi-cohort study has shown increasing visceral sensitivity to correlate positively with IBS symptoms, even after adjusting for psychological distress or somatisation [17]. Furthermore, a randomised placebo-controlled double-blind study has shown that attenuating visceral hypersensitivity, through the histamine receptor H1 antagonist Ebastine, leads to a parallel reduction in IBS symptoms [37]. Hence, asking about the frequency of abdominal pain over the preceding 10 days can be a simple and useful guide to gauge the overall severity of an individual's ill-health, and may in future clinical practise potentially be used to select individuals for treatments that address visceral hypersensitivity. With this in regard, it may be argued that increasing the pain frequency threshold further in Rome IV, to more than 1 day per week, will lead to greater homogeneity in IBS subjects; however, it is important to re-emphasise that this cut-off, albeit from the United States only, was based on normative data from a survey of adults without GI disorders, who in 95% of cases reported having abdominal pain less than 1 day per week. Finally, the frequency of abdominal pain did not correlate with oro-anal transit time, which is line with previous work from our group showing poor correlation between colonic transit time and abdominal pain in IBS, but instead good correlation with the predominant bowel habit of the patient [26].

Our study may be perceived as being limited in that we used a surrogate marker, based on the number of days of abdominal pain in the last 10 days (from the IBS-SSS questionnaire), to identify those with Rome III IBS who can be classified as being positive or negative for Rome IV IBS. The reason for using this methodological process was due to having a large number of well-characterised historical patients with Rome III IBS already under our care before the publication of Rome IV. Nevertheless, IBS has a remitting-relapsing course and hence it is possible that some subjects completing the questionnaire may have been experiencing no or infrequent abdominal pain over the last 10 days and thus classed as not having Rome IV IBS; yet, they may have had more frequent symptoms before then. Another issue is that, we identified Rome IV IBS based on subjects reporting $\geq$2 days of pain within the last 10 days, as this would suggest on average at least 1 day of pain per week as required for Rome IV. However, in its strictest sense, 2–3 days of pain per 10 days may still not meet a pain frequency threshold of at least 1 day/week if the days of pain were at the extremes of the 10 days and not in between. Future prospective studies may overcome this potential shortcoming by using 14-day symptom diaries.

Finally, our study raises additional questions. For example, whilst we investigated the major changes in IBS criteria from Rome III to IV, which being the removal of abdominal discomfort and increase in abdominal pain frequency to at least 1 day per week, we did not evaluate the subtle changes in criteria related to bowel habit (Table 1). The Rome III definition states that the onset of abdominal pain/discomfort to be associated with at least two of the following three: change in stool form, change in stool frequency, and improvement with defecation. However, Rome IV acknowledges

that some patients with IBS may experience worsening, and not an improvement, in abdominal pain following defecation. This calculation is beyond the scope of our paper as Rome III does not carry information about exacerbation of abdominal symptoms with defecation. Another noteworthy point is that whilst we show the majority of Rome III IBS patients in gastroenterology care to retain their diagnosis when transferring over to Rome IV, our findings may not be applicable to primary care where conceivably most patients with Rome III IBS will have milder symptoms. It is also unclear whether previous findings from Rome III IBS studies can be generalised to Rome IV IBS. Moreover, it is not yet known how the change in IBS criteria will impact on clinical management; it may be perceived that for Rome IV-positive IBS subjects interest will predominantly be directed towards attenuating pain plus associated intestinal/extra-intestinal symptoms, whereas those who are negative for Rome IV IBS the emphasis will be towards diagnosing an alternate bowel disorder, such as functional constipation, and focusing on improving bowel habit. However, this remains speculative and whether such an approach will lead to an improvement in clinical care, and justify the change in criteria, remains to be determined.

In conclusion, the update of criteria from Rome III to Rome IV will not have major implications in diagnostic coding in Western Gastroenterology Clinics, as only 15% of subjects with Rome III IBS will not fulfil Rome IV IBS criteria. Those who are positive for Rome IV IBS have more severe clinical symptoms and heightened visceral sensitivity, compared to Rome IV-negative IBS patients.

CONFLICT OF INTEREST

Guarantor of the article: Imran Aziz.

Specific author contributions: I.A. performed the statistical analysis of the data, and wrote the manuscript. I.A., H.T., O.S.P., W.E.W., and M.S. designed the study and interpreted the results. All authors revised the manuscript and approved the final version of the article.

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Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ The diagnostic criteria for IBS have been updated from Rome III to Rome IV.
- ✓ There is a relative paucity of data, with some conflicting findings, how this change in IBS criteria impacts on clinical characteristics and pathophysiological factors.

WHAT IS NEW HERE

- ✓ Overall, 85% of subjects with Rome III defined IBS fulfil criteria for Rome IV IBS, but 15% do not.
- ✓ Hence, the update of IBS criteria from Rome III to Rome IV will not have major implications in diagnostic coding in Western Gastroenterology Clinics.
- ✓ However, Rome IV-positive IBS patients demonstrate more severe clinical symptoms and heightened visceral sensitivity compared to Rome IV-negative subjects.

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