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Rome III vs Rome IV criteria for irritable bowel syndrome: A comparison of clinical characteristics in a large cohort study

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Abstract

Background: The Rome criteria for irritable bowel syndrome (IBS) have been revised and are expected to apply only to the subset of Rome III IBS subjects with abdominal pain as predominant symptom, occurring at least once a week. The aim of this study was to determine the percentage of Rome III IBS subjects that fulfills Rome IV criteria and to evaluate differences between Rome IV-positive and Rome IV-negative subjects.

Methods: Four hundred and four Rome III IBS subjects completed a 14-day end-of-day symptom diary, the Gastrointestinal Symptom Rating Scale (GSRS), Hospital Anxiety and Depression Scale, and RAND 36-item Short-Form Health Survey (SF-36). Diary-based surrogate Rome IV criteria were defined as occurrence of abdominal pain at least 1 day each week with a severity of ≥ 2 (mild; definition 1) or ≥ 3 (considerable; definition 2).

Key Results: Using surrogate Rome IV criteria, 353 (87.4%, definition 1) and 249 (61.6%, definition 2) subjects were defined as Rome IV positive. These patients were more often female, younger, and recruited from secondary/tertiary care compared with Rome IV-negative subjects. They also presented with higher abdominal pain scores and gastrointestinal (GI) symptom severity on both end-of-day diary and GSRS, higher psychological symptom scores, and lower quality of life compared with Rome IV-negative subjects.

Conclusions and Inferences: The Rome IV IBS population likely reflects a subgroup of Rome III IBS patients with more severe GI symptomatology, psychological comorbidities, and lower quality of life. This implies that results from Rome III IBS studies may not be directly comparable to those from Rome IV IBS populations.

KEYWORDS

abdominal pain, irritable bowel syndrome, Rome criteria

1 | INTRODUCTION

Irritable bowel syndrome (IBS) is a functional intestinal disorder characterized by abdominal pain associated with altered bowel

habits. IBS has traditionally been subcategorized into four subtypes based on predominant stool pattern: diarrhea (IBS-D), constipation (IBS-C), a mix of diarrhea and constipation (IBS-M), or undefined predominant stool form (IBS-U). IBS is a prevalent disorder worldwide, with prevalence rates of 5%-15% in the Western population.^{1,2} Symptoms most likely result from complex interactions between

*Both authors contributed equally to the manuscript.

several biological, psychological, and social factors.^{3,4} The exact underlying mechanisms of IBS pathophysiology are, however, not completely understood, and as a consequence, accurate non-invasive biomarkers for diagnosis, disease monitoring, and treatment evaluation are not available.

At present, the diagnosis of IBS is symptom based, using the Rome criteria. The Rome Foundation, a committee of international experts in the field of functional gastroenterology, has been working on the development and revision of diagnostic criteria for IBS, among other functional gastrointestinal (GI) disorders, since 1994. Recently, Rome III criteria (2006) have been updated to Rome IV criteria (2016). Major adjustments include removal of the term abdominal discomfort (Rome III), leaving only the occurrence of abdominal pain as the key requirement for Rome IV criteria. Furthermore, abdominal pain should be present on average at least 1 day per week in the Rome IV criteria (see Box 1).^{5,6} This new frequency threshold was based on a summary report on the distribution of symptom occurrence rates for all the Rome III symptoms.⁷ Most likely, fewer patients will fulfill the new Rome criteria compared with the previously set criteria. Indeed, using Rome IV criteria, a lower population prevalence of IBS has been reported by Whitehead and colleagues.^{8,9} Furthermore, IBS subtype identification has been revised, by only taking into account symptomatic stools (i.e. loose/watery stools and hard/lumpy stools), which might result in a shift in IBS subtypes.³

Studies on previous editions of the Rome criteria have demonstrated varying IBS prevalence rates depending on the diagnostic criteria employed. Also, differences in patient characteristics and symptomatology have been reported between several criteria.¹⁰⁻¹³ As a result of the requirement of weekly symptoms, Rome IV IBS patients are likely to be those with more severe symptomatology and possibly higher prevalence of psychiatric comorbidity and lower quality of life as compared with those fulfilling Rome III criteria. However, data comparing clinical features between Rome III and Rome IV IBS populations are still lacking.

Rome criteria are widely used as a cornerstone for inclusion in IBS clinical trials and cohort studies. It is expected that in future studies

Key Points

- Rome III criteria have recently been revised to Rome IV criteria, and introduction of Rome IV criteria leads to a decrease in IBS prevalence.
- Rome IV IBS patients are younger females with higher gastrointestinal symptom severity and present with higher psychological comorbidities and lower quality of life compared with Rome III IBS patients.
- Results from Rome III IBS studies may not be directly extrapolated to Rome IV IBS populations.

only a subset of Rome III IBS patients, that is, those with more severe abdominal pain, will be eligible for study participation by introducing Rome IV criteria. In order to generalize current data to Rome IV populations and to compare results from Rome III and Rome IV studies, it is important to evaluate which Rome III patients are likely to meet the Rome IV criteria. Therefore, the aim of this study was to determine the percentage of Rome III-positive IBS subjects that is also highly likely to fulfill Rome IV criteria, based on end-of-day symptom diaries, and to evaluate whether demographical, clinical, and psychosocial differences exist between Rome IV-positive and Rome IV-negative subjects in a well-defined Rome III IBS population.

2 | MATERIALS AND METHODS

2.1 | Study design

In the current analyses, data from a well-phenotyped Dutch cohort study, the Maastricht IBS (MIBS) cohort, on the phenotypical and genotypical characterization of IBS patients,¹⁴⁻¹⁶ were evaluated. The study protocol has been approved by the Maastricht University Medical Center+ (Maastricht UMC+) Committee of Ethics in February

Box 1 Definition of IBS according to Rome III and Rome IV criteria

Rome III IBS

(1) Recurrent abdominal pain or discomfort* at least 3 days per month in the last 3 months and associated with two or more of the following:

- Improvement with defecation;
- Onset associated with a change in frequency of stool;
- Onset associated with a change in form (appearance) of stool

(2) Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

*Discomfort means an uncomfortable sensation not described as pain

Rome IV IBS

(1) Recurrent abdominal pain, on average, at least 1 day per week in the last 3 months and associated with two or more of the following:

- Related to defecation;
- Associated with a change in frequency of stool;
- Associated with a change in form (appearance) of stool

(2) Criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis

2009 and was executed according to the revised Declaration of Helsinki (64th WMA General Assembly, Fortaleza, Brazil; October 2013). Furthermore, the study has been registered in the US National Library of Medicine (<http://www.clinicaltrials.gov>, NCT00775060).

2.2 | Study participants

Between July 2009 and May 2016, IBS patients aged 18-75 years were included in the Maastricht IBS cohort at the secondary/tertiary care outpatient department of Gastroenterology-Hepatology at the Maastricht UMC+ in Maastricht and via general practitioners practices in South-Limburg, the Netherlands. All subjects fulfilled the Rome III criteria (see Box 1) for IBS and were assigned the IBS subtype based on predominant bowel habit, that is, diarrhea (IBS-D), constipation (IBS-C), a mix of diarrhea and constipation (IBS-M), or unspecified predominant bowel habit (IBS-U).^{3,17} Rome III criteria were evaluated in a face-to-face interview by a trained clinical researcher. Medical history was taken by a gastroenterologist, and if indicated, GI endoscopy, abdominal imaging and/or blood, breath or fecal analyses were performed to exclude organic disease. A history of abdominal surgery, except for uncomplicated appendectomy, cholecystectomy, or hysterectomy, was reason for exclusion. All subjects gave their written informed consent before participation.

2.3 | Data collection

As subject inclusion was performed since 2009, Rome IV criteria were not collected in a face-to-face interview at the moment of inclusion. However, all participants completed an end-of-day diary on symptom severity and bowel habits, during 14 days, at the time of inclusion. Abdominal pain, among other symptoms, was scored using a 5-point Likert scale (1 = not at all; 2 = mild; 3 = considerable; 4 = severe; 5 = extremely). Using this information, we retrospectively determined which subjects were highly likely to fulfill the Rome IV criteria, based on the presence of abdominal pain on at least 1 day in both the first and the second 7 days (i.e. abdominal pain at least once a week). Rome IV criteria do not take into account abdominal pain severity, however, as we will use surrogate Rome IV criteria to evaluate differences between Rome IV-positive and negative IBS patients, we will report on two definitions for those criteria: "Definition 1: Abdominal pain score ≥ 2 once a week in each week" and "Definition 2: Abdominal pain score ≥ 3 once a week in each week." Only symptom diaries that were completed for at least 12 of the 14 days were considered eligible for analysis.

Information on demographics was collected using a predefined self-report questionnaire. Furthermore, subjects completed the Gastrointestinal Symptom Rating Scale (GSRS),¹⁸ Hospital Anxiety and Depression Scale,^{19,20} and RAND 36-item Short-Form Health Survey (SF-36)^{21,22} for GI symptom severity, co-occurrence of depressive and/or anxiety symptoms, and general quality of life, respectively.

In addition, in a subset of participants, a rectal barostat procedure was performed. Measurement of rectal perception was performed using a standardized perception protocol, during which 17 pressure steps between 0 and 50 mm Hg, based on a semi-random staircase

protocol, were applied. During each pressure step, pain scores were reported on a 100-mm visual analogue scale. The cut-off value for visceral hypersensitivity was defined as a pain score ≥ 20 at pressure ≤ 26 mm Hg. A detailed description on the rectal barostat procedure was previously reported.²³

The end-of-day diary data were additionally used to perform an exploratory analysis on whether Rome III IBS patients, that do not fulfill (surrogate) Rome IV criteria for IBS, are likely to fulfill Rome IV criteria for other functional bowel disorders. Definitions that were used for retrospective evaluation of Rome IV diagnoses for functional constipation (FC), functional diarrhea (FD), and functional abdominal bloating/distension (FAB/D) are shown in Table S1. Since the symptom diary was designed for IBS and not specifically for assessing those other disorders, not all criteria could be definitively checked.

2.4 | Data and statistical analyses

All analyses were performed using IBM SPSS Statistics, version 23 (IBM Statistics for Macintosh, Chicago, IL, USA).

The total study population is referred to as "total." Depending on whether subgroups are highly likely to fulfill Rome IV criteria based on the end-of-day diary or not, they are referred to as "Rome IV-positive" and "Rome IV-negative," respectively. Results for "Rome IV-positive" and "Rome IV-negative" are presented separately for both definitions of fulfilling Rome IV criteria: "Definition 1: Abdominal pain score ≥ 2 once a week in each week" and "Definition 2: Abdominal pain score ≥ 3 once a week in each week."

Categorical data are presented as proportions and differences between groups are tested using χ^2 or Fisher's exact test. Continuous data are presented as medians and interquartile ranges (IQR), and groups are compared using Mann-Whitney *U* test, taking into account asymmetric distribution of the data. A *P*-value of .05 was considered statistically significant.

3 | RESULTS

3.1 | Study population

In total, 404 subjects that completed at least 12 days of the end-of-day symptom diary were included in the analyses: 293 (72.5%) were women and median age was 45 (IQR: 28-59) years. Seventy-two percent ($n = 291$) was recruited from secondary/tertiary care, and IBS subtypes (based on Rome III criteria) were distributed as follows: 140 (34.7%) IBS-D, 81 (20%) IBS-C, 159 (39.4%) IBS-M, and 24 (5.9%) IBS-U. Further characteristics of the total study population are shown in Table 1.

3.2 | IBS according to Rome IV criteria—Definition 1: abdominal pain score ≥ 2

Of the 404 IBS subjects diagnosed by Rome III criteria, 353 (87.4%) did meet the surrogate Rome IV criteria when assessed using the end-of-day symptom diary and the cut-off for abdominal pain severity of ≥ 2 .

TABLE 1 Demographical and clinical characteristics of the total study population and Rome IV-positive and -negative subjects, separated for Definition 1 and 2 of surrogate Rome IV criteria, that is, assessed using end-of-day symptom diaries

	Total n = 404	Definition 1: Abdominal pain score ≥ 2		Definition 2: Abdominal pain score ≥ 3	
		Rome IV-positive n = 353 (87.4%)	Rome IV-negative n = 51	Rome IV-positive n = 249 (61.6%)	Rome IV-negative n = 155
Female sex, n (%)	293 (72.5)	263 (74.5)	30 (58.8) [†]	195 (78.3)	98 (63.2)*
Age, median (IQR)	45 (28-59)	45 (27-58)	53 (32-65) [†]	42 (26-57)	51 (36-63)*
BMI, median (IQR)	24.03 (21.41-27.63)	23.94 (21.38-27.69)	24.62 (21.58-27.52)	24.08 (21.40-27.47)	23.96 (21.45-27.98)
Subtype Rome III, n (%)					
IBS-D	140 (34.7)	118 (33.4)	22 (43.1)	85 (34.1)	55 (35.5)
IBS-C	81 (20.0)	73 (20.7)	8 (15.7)	51 (20.5)	30 (19.4)
IBS-M	159 (39.4)	142 (40.2)	17 (33.3)	101 (40.6)	58 (37.4)
IBS-U	24 (5.9)	20 (5.7)	4 (7.8)	12 (4.8)	12 (7.7)
Secondary/tertiary care, n (%)	291 (72.0)	262 (74.4)	29 (56.9) [†]	194 (78.2)	97 (62.6)*
Hypersensitive, n (%)	87 (44.4) ^a	85 (47.5) ^b	2 (11.8) ^{c*}	72 (57.1) ^d	15 (21.4) ^{e*}
14-day mean score, median (IQR)					
Abdominal pain	2.21 (1.57-2.92)	2.36 (1.79-3.00)	1.07 (1.00-1.21)*	2.71 (2.29-3.29)	1.43 (1.17-1.77)*
Abdominal discomfort	2.43 (1.93-2.93)	2.50 (2.14-3.00)	1.50 (1.07-1.86)*	2.72 (2.36-3.21)	1.79 (1.43-2.21)*
Abdominal bloating	2.07 (1.50-2.79)	2.21 (1.64-2.86)	1.43 (1.07-2.00)*	2.43 (1.93-3.18)	1.71 (1.14-2.07)*
Flatulence	2.21 (1.71-2.86)	2.29 (1.79-2.93)	1.71 (1.29-2.33)*	2.43 (1.93-3.07)	1.93 (1.36-2.36)*
Constipation	1.29 (1.00-1.86)	1.36 (1.00-1.93)	1.00 (1.00-1.29)*	1.50 (1.07-2.07)	1.08 (1.00-1.43)*
Diarrhea	1.21 (1.00-1.64)	1.29 (1.07-1.71)	1.07 (1.00-1.29)*	1.31 (1.07-1.98)	1.08 (1.00-1.43)*
GSRS, median (IQR)					
Abdominal pain	3.33 (2.33-4.00)	3.33 (2.33-4.25)	2.67 (1.67-3.33)*	3.67 (2.67-4.33)	2.67 (2.00-3.67)*
Diarrhea syndrome	3.33 (2.00-4.33)	3.33 (2.33-4.67)	2.67 (1.67-4.00) [†]	3.67 (2.33-4.67)	3.00 (2.00-4.00)*
Constipation syndrome	3.00 (2.33-4.00)	3.00 (2.33-4.33)	2.00 (1.33-3.33)*	3.33 (2.33-4.33)	2.67 (1.67-3.67)*
Indigestion syndrome	4.00 (3.25-5.00)	4.00 (3.25-5.00)	3.75 (2.75-4.50)	4.25 (3.25-5.25)	3.75 (2.75-4.50)*
Regurgitation syndrome	1.50 (1.00-3.00)	1.50 (1.00-3.00)	1.00 (1.00-2.00) [†]	1.75 (1.00-3.50)	1.00 (1.00-2.50)*
HADS, n (%)					
Depression ≥ 8	76 (19.0)	73 (21.0)	3 (5.9)*	59 (24.1)	17 (11.0)*
Anxiety ≥ 8	142 (35.6)	131 (37.6)	11 (21.6) [†]	105 (42.9)	37 (24.0)*
SF-36, median (IQR)					
Physical Composite Score (PCS)	42.83 (33.98-50.28)	41.67 (32.98-49.11)	49.92 (41.42-53.89)*	39.23 (29.84-46.95)	48.99 (39.41-52.62)*
Mental Composite Score (MCS)	49.75 (41.23-55.82)	49.41 (41.15-55.37)	51.03 (41.98-57.73)	48.31 (40.76-54.58)	51.34 (42.16-57.19) [†]

Differences tested using Mann-Whitney *U* test for continuous data and chi-square or Fisher's exact test for categorical data. Significances are shown for both definitions of surrogate Rome IV criteria separately.

*Significant difference between Rome IV-positive and Rome IV-negative subjects ($P < .001$).

[†]Significant difference between Rome IV-positive and Rome IV-negative subjects ($P < .05$).

^{a-e}Number of subjects that underwent rectal barostat: ^a196; ^b179; ^c17; ^d126; ^e70.

Rome IV-positive subjects were more often female (74.5% vs 58.8%, $P < .05$), younger (45 vs 53 years, $P < .05$) and recruited from secondary/tertiary care (74.4% vs 56.9%, $P < .05$) compared with Rome IV-negative subjects. Additionally, visceral hypersensitivity assessed by rectal barostat was present more often in Rome

IV-positive subjects (47.5% vs 11.8%, $P < .001$). Subtype distribution (i.e. based on Rome III criteria) was not different between both groups.

With regard to GI symptoms, Rome IV-positive vs negative subjects reported higher scores in the end-of-day diary for all symptoms

assessed (i.e. abdominal pain, abdominal discomfort, abdominal bloating, flatulence, constipation, and diarrhea) and higher symptom scores for all five GSRS domains; however, this was not statistically significant for indigestion syndrome.

Furthermore, Rome IV-positive subjects showed a higher percentage of depressive (21.0% vs 5.9%, $P < .001$) and anxiety (37.6% vs 21.6%, $P < .05$) symptoms and lower physical composite scores (41.67 vs 49.92, $P < .001$) with regard to quality of life. Mental composite scores of SF-36 did not show a significant difference between the groups. Results are shown in Table 1.

3.3 | IBS according to Rome IV criteria—Definition 2: abdominal pain score ≥ 3

When using the surrogate Rome IV criteria as defined by at least 1 day of abdominal pain each week using the cut-off for abdominal pain severity of ≥ 3 , of the 404 IBS subjects diagnosed by Rome III criteria, 249 (61.6%) were Rome IV-positive.

In line with the findings above, that is, regarding the cut-off of abdominal pain severity of ≥ 2 , Rome IV-positive subjects were more often female, younger, recruited from secondary/tertiary care, more often hypersensitive on rectal barostat, showed higher symptom severity scores for all symptoms assessed in the end-of-day symptom diary, and showed higher percentages of depressive and anxiety symptoms compared with Rome IV-negative subjects, when using the cut-off of ≥ 3 . Likewise, subtype distribution (i.e. based on Rome III criteria) did not differ between the groups.

Moreover, with regard to symptom severity on GSRS, Rome IV-positive vs Rome IV-negative subjects scored significantly higher on all domains including indigestion syndrome when using the cut-off of ≥ 3 . Furthermore, Rome IV-positive subjects scored significantly lower on both physical composite score and mental composite score of SF-36 compared with Rome IV-negative subjects. Results are shown in Table 1.

3.4 | Alternative Rome IV diagnoses in Rome IV-negative (IBS) subjects

Of the Rome IV-negative (IBS) subjects, according to the surrogate Rome IV criteria using the cut-off for abdominal pain severity of ≥ 3 , 34 (23.61%) fulfilled surrogate Rome IV criteria for FC, 50 (34.25%) for FD, and 37 (25.69%) for FAB/D. Results are shown in Table S2.

4 | DISCUSSION

This study demonstrates that 61.6%–87.4% of Rome III IBS patients is likely to also fulfill the new Rome IV criteria for IBS, depending on the cut-off for abdominal pain severity used, when applying surrogate Rome IV criteria based on end-of-day symptom diaries. Regardless of the cut-off chosen, Rome IV-positive subjects were more often female, younger, and recruited from secondary/tertiary care than Rome IV-negative subjects. Not only did they present with higher abdominal

pain scores, but overall symptom severity was higher in Rome IV-positive subjects, including a higher percentage of visceral hypersensitivity as assessed by rectal barostat. In addition, higher percentages of comorbid psychological symptoms and lower quality of life were found for Rome IV-positive subjects. Taken together, the current findings imply that the Rome IV IBS population will likely reflect a subgroup of Rome III IBS patients with more severe overall GI symptomatology, psychological comorbidities, and lower quality of life.

To date, a recent study by Bai et al investigated the agreement between Rome III and Rome IV criteria for IBS in a GI outpatient population in China. They found a moderate consistency between Rome III and Rome IV criteria, with prevalences of 12.4% and 6.1% based on Rome III and Rome IV criteria, respectively.²⁴ Similarly, Whitehead and colleagues reported prevalences of 10.7% and 5.7%, respectively, in a large population-based study.^{8,9} Our current study confirms this decrease in prevalence by introducing Rome IV criteria, within a well-defined Rome III IBS population. Additionally, in line with these previously reported findings, our cut-off for abdominal pain severity of ≥ 3 may be most robust to define those subjects highly likely to fulfill Rome IV criteria, based on end-of-day diary.

We observed that Rome IV-positive subjects were more often of female gender than Rome IV-negative subjects. These differences were not demonstrated by Bai and colleagues.²⁴ Differences in symptom severity between men and women, however, have been reported previously, indicating possible differences in pathophysiological mechanisms as well as in pain perception and coping strategies. A meta-analysis by Adeyemo and colleagues demonstrated that women are more likely to report abdominal pain than men.²⁵ Furthermore, higher overall IBS symptom severity in female IBS patients has been reported by Bjorkman et al.²⁶ These previous findings could explain the higher percentage of women in our Rome IV-positive IBS population compared with the Rome IV-negative subjects.

With regard to clinical differences between Rome III and Rome IV IBS subjects, Bai et al reported higher abdominal pain scores for Rome IV, but no differences in abdominal discomfort, abdominal bloating or demographic characteristics. In contrast, our study shows significantly higher scores for abdominal discomfort, bloating, flatulence, diarrhea, and constipation, apart from abdominal pain. A possible explanation for the discrepancy between these studies is the method of data collection. Bai and colleagues retrospectively assessed the presence of above-mentioned symptoms at one time point, whereas in our study, symptom severity scores were determined daily, using an end-of-day diary during 14 days.

As a study by Engsbro et al demonstrated that IBS subtype classification differs depending on whether retrospective (i.e. Rome Diagnostic Questionnaire) or prospective methods (i.e. diary cards) are used,²⁷ we did not use the symptom diary to assess the IBS subtypes. However, we feel that the end-of-day diary provides an objective overview of present symptoms during a 14-day period and therefore can be used to identify patients highly likely to fulfill the Rome IV criteria. Furthermore, Rome IV criteria require abdominal pain to be present at least once a week on average during the last 3 months. The end-of-day symptom diary as used only provides

us with information about the past 2 weeks. However, all subjects fulfilled Rome III criteria assessed using the Rome III Diagnostic Questionnaire, which also requires the abdominal complaints to be present during the previous 3 months. Therefore, we think that the surrogate Rome IV criteria are a reliable reflection of the Rome IV Diagnostic Questionnaire.

This is the first study focusing on clinical differences between Rome III and Rome IV IBS subjects. In conclusion, this study underlines a decrease of IBS prevalence when using (surrogate) Rome IV compared with Rome III criteria. In addition to these findings, the question arises how to deal with the Rome IV-negative patient population presenting with IBS symptoms in both primary and secondary/tertiary care and with regard to future clinical and mechanistic studies.

Firstly, it might be interesting to explore whether alternative Rome IV disorders can now be diagnosed in these subjects, for example, FC, FD, or FAB/D. An exploratory analysis in this study demonstrates that 24% is likely to fulfill Rome IV criteria for FC, 34% for FD, and 26% for FAB/D. These results should, however, be interpreted with caution, since these diagnoses are based on surrogate criteria, using an IBS-specific end-of-day symptom diary. Nevertheless, this suggests that an additional $\pm 16\%$ of Rome III IBS patients will not fulfill any of these Rome IV diagnoses. Possibly, a small subset might be defined as Rome IV unspecified functional bowel disorder. However, it is very likely that patients reporting abdominal pain or bloating/distension less than once weekly (without predominant constipation or diarrhea) will not fulfill any Rome IV diagnosis due to the new frequency threshold.

Secondly, as the Rome criteria are not that universally used in routine clinical practice, in our opinion, patients with milder functional GI symptoms seeking health care, but not fulfilling one of the Rome IV diagnoses, should still be managed as functional GI disorders. With regard to future IBS research, patient inclusion should be based on the Rome IV criteria, in order to aim at agreement between studies.

Nevertheless, this study demonstrates that the Rome IV IBS population is represented by younger females with higher overall GI symptom severity, including comorbid psychological symptoms and lower quality of life compared with the Rome III IBS population. Therefore, results from Rome III IBS studies may not be directly comparable to those from Rome IV IBS populations, which have implications for future IBS research in particular.

DISCLOSURES

No competing interests declared.

AUTHOR CONTRIBUTIONS

LV, ZZRMW: study concept and design, data collection, data analysis and interpretation, manuscript writing. ZM: data collection, constructive review of manuscript. JWK: study concept and design, constructive review of manuscript. MAMH: data collection and processing. JWMM: study concept and design, constructive review of manuscript. DK, DMAEJ: study concept and design, data interpretation, constructive review of manuscript. AAMM: study concept and

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REFERENCES

1. Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clin Gastroenterol Hepatol*. 2012;10:712-21.e4.
2. Hungin AP, Whorwell PJ, Tack J, Mearin F. The prevalence, patterns and impact of irritable bowel syndrome: an international survey of 40,000 subjects. *Aliment Pharmacol Ther*. 2003;17:643-650.
3. Drossman DA. The functional gastrointestinal disorders and the Rome III process. *Gastroenterology*. 2006;130:1377-1390.
4. Enck P, Aziz Q, Barbara G, et al. Irritable bowel syndrome. *Nat Rev Dis Primers*. 2016;2:16014.
5. Foundation R. Appendix A: Rome III Diagnostic Criteria for FGIDs.885-97.
6. Mearin F, Lacy BE, Chang L, et al. Bowel disorders. *Gastroenterology*. 2016;150(6):1393-1407.
7. Whitehead W, Palsson O. *Report on the Rome III Normative Gastrointestinal Symptom Survey*. Chapel Hill, NC: University of North Carolina; 2013.
8. Palsson O, van Tilburg MA, Simren M, Sperber A, Whitehead W. *Population prevalence of Rome III and Rome IV Irritable Bowel Syndrome (IBS) in the United States (US), Canada and the United Kingdom (UK)*. Vienna: UEG Week; 2016.
9. Whitehead WE, Palsson OS, Simren M. Irritable bowel syndrome: what do the new Rome IV diagnostic guidelines mean for patient management? *Expert Rev Gastroenterol Hepatol*. 2017;11:281-283.
10. Boyce PM, Koloski NA, Talley NJ. Irritable bowel syndrome according to varying diagnostic criteria: are the new Rome II criteria unnecessarily restrictive for research and practice? *Am J Gastroenterol*. 2000;95:3176-3183.
11. Sperber AD, Shvartzman P, Friger M, Fich A. A comparative reappraisal of the Rome II and Rome III diagnostic criteria: are we getting closer to the 'true' prevalence of irritable bowel syndrome? *Eur J Gastro Hepatol*. 2007;19:441-447.
12. Park DW, Lee OY, Shim SG, et al. The differences in prevalence and sociodemographic characteristics of irritable bowel syndrome according to Rome II and Rome III. *J Neurogastroenterol Motil*. 2010;16:186-193.
13. Wang AJ, Liao XH, Hu PJ, Liu SC, Xiong LS, Chen MH. A comparison between Rome III and Rome II criteria in diagnosing irritable bowel syndrome. *Zhonghua Nei Ke Za Zhi*. 2007;46:644-647.
14. Ludidi S, Mujagic Z, Jonkers D, et al. Markers for visceral hypersensitivity in patients with irritable bowel syndrome. *Neurogastroenterol Motil*. 2014;26:1104-1111.
15. Mujagic Z, Ludidi S, Keszthelyi D, et al. Small intestinal permeability is increased in diarrhoea predominant IBS, while alterations in gastroduodenal permeability in all IBS subtypes are largely attributable to confounders. *Aliment Pharmacol Ther*. 2014;40:288-297.
16. Mujagic Z, Tigchelaar EF, Zhernakova A, et al. A novel biomarker panel for irritable bowel syndrome and the application in the general population. *Sci Rep*. 2016;6:26420.
17. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology*. 2006;130:1480-1491.
18. Svedlund J, Sjodin I, Dotevall G. GSRS—a clinical rating scale for gastrointestinal symptoms in patients with irritable bowel syndrome and peptic ulcer disease. *Dig Dis Sci*. 1988;33:129-134.
19. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67:361-370.
20. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res*. 2002;52:69-77.

21. Farivar SS, Cunningham WE, Hays RD. Correlated physical and mental health summary scores for the SF-36 and SF-12 Health Survey, V.I. *Health Qual Life Outcomes*. 2007;5:54.
22. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med Care*. 1993;31:247-263.
23. Ludidi S, Conchillo JM, Keszthelyi D, et al. Rectal hypersensitivity as hallmark for irritable bowel syndrome: defining the optimal cutoff. *Neurogastroenterol Motil*. 2012;24:729-733, e345-6.
24. Bai T, Xia J, Jiang Y, et al. Comparison of the Rome IV and Rome III criteria for IBS diagnosis: a cross-sectional survey. *J Gastroenterol Hepatol*. 2017;32:1018-1025.
25. Adeyemo MA, Spiegel BM, Chang L. Meta-analysis: do irritable bowel syndrome symptoms vary between men and women? *Aliment Pharmacol Ther*. 2010;32:738-755.
26. Bjorkman I, Jakobsson Ung E, Ringstrom G, Tornblom H, Simren M. More similarities than differences between men and women with irritable bowel syndrome. *Neurogastroenterol Motil*. 2015;27:796-804.
27. Engsbro AL, Simren M, Bytzer P. The Rome II and Rome III criteria identify the same subtype-populations in irritable bowel syndrome: agreement depends on the method used for symptom report. *Neurogastroenterol Motil*. 2012;24:604-611, e266.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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