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Prevalence of Rome IV Functional Bowel Disorders Among Adults in the United States, Canada, and the United Kingdom

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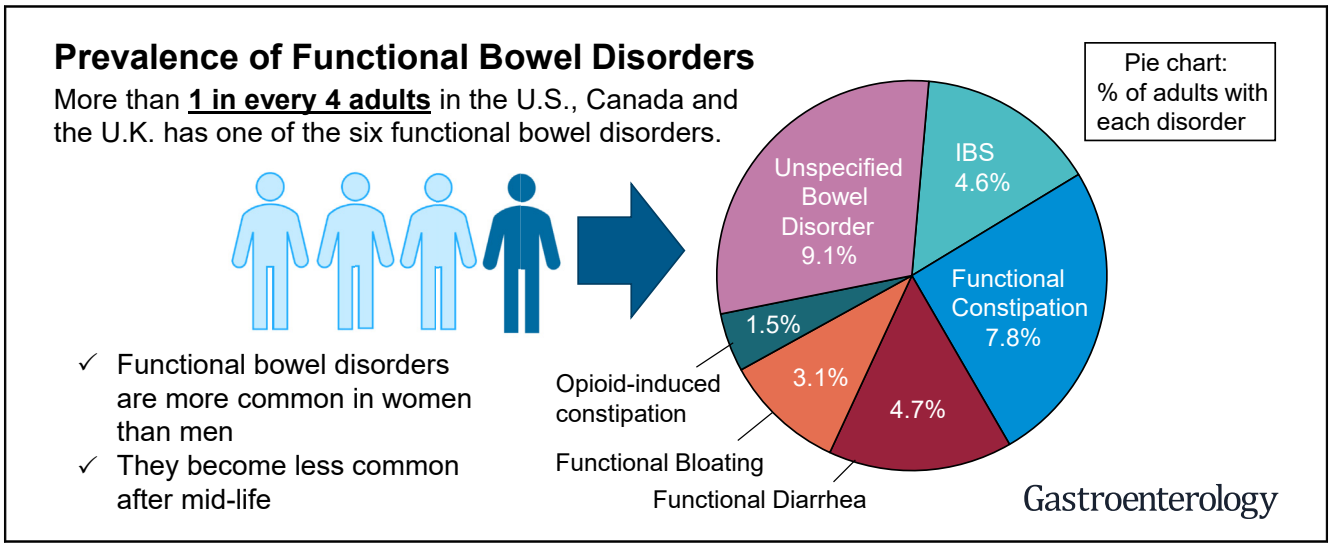

See editorial on page 1212.

BACKGROUND & AIMS: Little is known about the population prevalence or demographic distributions of Rome IV functional bowel disorders (FBDs) or their effects on quality of life. We examined these in a multinational survey. **METHODS:** We analyzed data from a population-based survey of adults in the United States, Canada, and United Kingdom (5931 valid responders; 49.2% female; mean age, 47.4 years; range, 18–92 years). The survey included the Rome IV Diagnostic Questionnaire, Rome III irritable bowel syndrome (IBS) and constipation questions, and the SF-8 quality of life questionnaire. **RESULTS:** The prevalence values of census-adjusted Rome IV FBDs were similar among the 3 countries; ranges were: 4.4%–4.8% for IBS, 7.9%–8.6% for functional constipation, 3.6%–5.3% for functional diarrhea, 2.0%–3.9% for functional bloating or distention, 1.1%–1.9% for opioid-induced constipation, 7.5%–10.0% for unspecified FBDs, and 28.6%–31.7% for any Rome IV FBD. FBDs were less common in older individuals, and all except functional diarrhea were more common in women. IBS was only half as prevalent by Rome IV as by Rome III criteria (4.6% vs 9.0% overall), primarily due to higher Rome IV minimum pain frequency. Functional diarrhea and functional constipation were more prevalent by Rome IV than Rome III criteria. Subjects with FBD had significant reductions in quality of life and reported more gastrointestinal doctor consultations than other subjects. **CONCLUSIONS:** More than 1 in 4 adults in the general population meet the Rome IV criteria for FBDs. These disorders affect quality of life and increase use of gastrointestinal health care. The switch from Rome III to Rome IV criteria reduces the prevalence of IBS by half, but increases the prevalence of functional constipation and functional diarrhea.

Keywords: Abdominal Pain; Epidemiology; Europe; GI Disorder.

The functional bowel disorders (FBDs) are a subset of a larger family of functional gastrointestinal (GI) disorders (FGIDs),[1] and involve chronic symptoms of abdominal pain, bloating, diarrhea, and constipation in the lower half of the GI tract. Like other FGID, the FBDs have no identifiable structural or biochemical abnormalities that can

Abbreviations used in this paper: **CI, confidence interval; FBD, functional bowel disorder; FC, functional constipation; GI, gastrointestinal; IBS, irritable bowel syndrome; IBS-C, IBS with predominant constipation; IBS-D, IBS with predominant diarrhea; IBS-M, IBS with mixed bowel habits; IBS-U, IBS unclassified; OIC, opioid-induced constipation; OR, odds ratio; SF-8, Short Form 8.**

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WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

Little is known about the population prevalence or demographic distributions of Rome IV functional bowel disorders (FBDs) or their effects on quality of life

NEW FINDINGS

More than 25% of adults in the general population meet the Rome IV criteria for FBDs. These disorders affect quality of life and increase use of gastrointestinal healthcare.

LIMITATIONS

This is a study of the populations of 3 countries. Studies of other populations are needed.

IMPACT

The switch from Rome III to Rome IV criteria reduces the prevalence of IBS by half, but increases the prevalence of functional constipation and functional diarrhea

account for their defining symptoms. Diagnosis therefore relies almost exclusively on symptom patterns, and the Rome diagnostic criteria are the most widely accepted standard for such symptom-based diagnoses. The latest version of those criteria, Rome IV, recognizes 6 different FBDs.[2] Five of these were also in the Rome III classification system: irritable bowel syndrome (IBS), functional constipation (FC), functional diarrhea, functional abdominal bloating/distention, and unspecified bowel disorder. The sixth disorder, introduced for the first time in Rome IV, is opioid-induced constipation (OIC), which differs from all the other FBDs in that it has an identifiable organic cause, that is, opioid use.[3]

Apart from the addition of OIC, the only notable changes between Rome III and IV definitions of FBDs were in the criteria for IBS and functional diarrhea. IBS diagnosis changed from Rome III to Rome IV in 3 main aspects[4]: (1) the qualifying symptom of "abdominal discomfort or pain" was modified to just "abdominal pain"; (2) the minimum abdominal pain frequency required for diagnosis was increased from 2 to 3 days a month to once a week; and (3) rather than tying stool consistency abnormality to pain onset as in Rome III, Rome IV diagnosis only requires association of pain with defecation or changes in stools. In addition, IBS subtypes are defined in Rome IV based on the typical type of stool consistency abnormality (diarrhea, constipation, or a mix) on days in which such abnormal stools occur, rather than on proportions of different kinds of abnormal stools out of all bowel movements as in Rome III. Rome III functional diarrhea diagnosis required at least 75% of bowel movements in the past 3 months to be loose or watery in a person with no abdominal pain or discomfort. Rome IV criteria for this disorder are far more permissive, requiring only >25% of stools to be loose or watery in the past 3 months in individuals who do not meet IBS criteria and do not have predominant symptoms of abdominal pain or bloating.

The prevalence of FBDs in the general population has remained unclear in spite of considerable research on their epidemiology. The principal reasons for this are that definitions of the disorders, survey methodologies, and the populations studied in the published research have varied greatly, resulting in very divergent and hard-to-compare findings.[5] In addition, the research focus has mainly been on only 2 of the bowel disorders, IBS and FC, with far less prevalence research published on the others. A 2012 systematic review by Lovell and Ford[6] of 81 studies of IBS, conducted in numerous countries and using a number of different criteria, concluded that the pooled global prevalence of the disorder was 11.2%, with prevalence reports ranging all the way from 1.1% to 45.0%. For FC, a 2011 systematic review by Suares and Ford[7] found a pooled prevalence of 14% in 41 study populations, with similarly extreme spread of prevalence, ranging from 1.9% to 40.1%. Little can be concluded about population prevalence rates from such a broad set of estimates based on multiple disorder definitions and sampling methods.

Practically no information is available in the literature that provides a comprehensive picture of the FBDs as a class in national populations. These disorders are a set of overlapping and interactive symptoms, and it is well recognized, as emphasized by the Rome IV bowel disorders working team,[2] that they often transition over time in the same individual. Therefore, examining their collective presence in the population as a group gives a better idea of functional health problems in the lower GI tract than merely focusing on individual diagnoses.

The heterogeneity of methodologies and case definitions in past work has made it hard to know whether the FBDs generally afflict different demographic groups at different rates. However, there has been a fairly consistent indication from multiple studies that IBS and FC tend to occur at higher rates in female than in male individuals, and that constipation is more prevalent in older than in younger adults, whereas IBS declines in prevalence in the upper half of the adult age range.[6–8] Finally, no national prevalence estimates for Rome IV bowel disorders in adults exist yet in the published literature, with the exception of a single estimate for IBS in Belgium,[9] making the provision of such data much needed to understand the scope of these health problems as they are presently defined.

The aims of this report were to describe and compare the prevalence of the Rome IV bowel disorders in the adult populations of 3 English-speaking Western countries, examine how the change from Rome III to Rome IV criteria affected the prevalence of 3 of these disorders (IBS, FC, and functional diarrhea), and assess differences in FGID prevalence between demographic subgroups and the quality of life impact of these disorders.

Materials and Methods

The analyses in this report used data from a population-based survey of 6300 adults commissioned by the Rome Foundation in the fall of 2015 as a part of the validation process for the forthcoming Rome IV diagnostic criteria.[10] The survey was conducted online, using Qualtrics Research Suite survey software (Qualtrics, LLC, Provo, UT). All survey participants were provided by Qualtrics, LLC, an international survey

company, from existing panels of individuals who had already enrolled in registries to participate in various online surveys. Survey participants were kept anonymous to the investigators.

Nationwide community samples of 2100 individual age 18 years and older were recruited in the United States, United Kingdom, and Canada. The sampling was quota-controlled to obtain an equal proportion of male and female individuals, an age group distribution of 40% of ages 18 to 39, 40% ages 40 to 64, and 20% aged 65+ in each country, and a 30% maximum quota of individuals with education equivalent to a college degree (16 years of schooling or greater).

Subjects first completed online consent, and then proceeded to complete the study survey right away. The survey questions used in the analyses in this report included the Rome IV Diagnostic Questionnaire for Adult Functional Gastrointestinal Disorders,[10] the Rome III IBS and FC diagnostic modules,[4] demographic questions (age, sex, education, relationship status, population size, and region of residence within each country), the Short Form 8 (SF-8) quality of life questionnaire,[11] and questions on GI health history and doctor consultations for GI problems. The survey also contained other supplemental questions and questionnaires not used in the present analyses.

Several methods were used to ensure good quality of the data collected:

1. To avoid self-selection bias, the survey was described only as a health survey to prospective subjects, without any mention of GI symptoms or disorders.
2. The survey was a secure, closed survey accessible only to the registered survey panel members specifically invited to participate based on their known demographic characteristics.
3. Two multiple-choice attention-test questions were built into the survey. These looked like other questions but specifically asked subjects to enter a particular response. Subjects who failed to respond appropriately to either question were terminated from the survey without completion.
4. Respondents who answered questions at more than 3 times the median completion speed (as determined by the first 10% of the sample) were excluded from the dataset.
5. Three Rome IV diagnostic questions were repeated later in the survey to assess symptom reporting consistency. Data from subjects who failed to report comparable symptom frequency on 2 or more of these 3 repeated questions were eliminated from the analysis dataset.

Identification of Rome IV and Rome III FGID Cases

Likely organic causes of bowel symptoms should generally be ruled out before making Rome functional GI diagnoses. For this reason, we chose to exclude from Rome FBD diagnoses in our analyses all subjects in the survey sample who reported having been diagnosed with any of 5 self-reported organic health problems that were likely to affect or cause bowel symptoms: celiac disease, inflammatory bowel disease, GI cancer, peptic ulcer, and diverticulitis. We also excluded from FBD diagnoses individuals who reported having had a bowel resection. After these exclusions, we identified FGID cases according to the Rome scoring instructions and Rome IV and Rome III diagnostic criteria, as summarized in Table 1.

The study was reviewed by the institutional review board at the University of North Carolina at Chapel Hill before data collection started and was deemed institutional review board exempt because of the anonymity of the survey method.

Statistical Analysis

The data were analyzed with IBM SPSS Statistics version 25.0 software (IBM Corp., Armonk, NY).

Descriptive statistics using means with 95% confidence intervals were used to characterize the rates of the disorders investigated in the overall sample, within each country, and in demographic subgroups.

Chi-square tests of independence were used for comparisons of proportions of individuals with the different bowel disorders in demographic subgroups and between countries, as well as for comparing Rome III vs Rome IV prevalence rates. Odds ratios with 95% confidence intervals were calculated for select comparisons to describe relative risk of FBDs in subgroups.

Analysis of variance with post hoc significance tests using Bonferroni correction for multiple comparisons were used to compare diagnostic groups on continuous variables.

The latest national government census figures in each of the 3 countries[12–14] were used to calculate correction weights for age (in 5-year bins) and sex proportions, to make the age and sex distributions of the survey samples proportionally equivalent to those of the national populations. These population-weighted sample data were used to produce overall census-adjusted prevalence estimates for the FBDs in each country as well as overall for the 3 countries combined.

Results

Survey Sample Characteristics

The study survey was completed by a total of 6300 individuals (2100 in each of the 3 countries). A total of 369 subjects judged to be inconsistent responders based on the 3 repeated Rome IV diagnostic questions were eliminated from the dataset. As seen in Supplementary Table 1, these inconsistent responders were on average younger, more likely to be female and slightly less educated than other survey responders. Their elimination left 5931 valid response sets for analysis (94% of the original sample). Due to quota-based sampling, there were no significant differences between the country samples in age group distributions or sex ratios. Overall, the combined total sample was 49.2% women, with a mean age of 47.4 years (range 18–92 years), and 72.0% white race. Subject participation was nationwide in each country, with the proportion of participants in different parts of their respective countries generally similar to the proportions of the national population living in those states (US), government regions (UK), or province and territories (Canada). Further details of the study sample demographics can be found in a previous publication using this sample,[15] and in Supplementary Tables 2–8.

A total of 230 subjects in the study sample (3.9%) who reported 1 or more of the 6 exclusion conditions that might account for their bowel symptoms but otherwise met criteria for

Table 1. Criteria Used to Identify Rome III and Rome IV FBD Cases in the Study

Rome IV IBS	Required abdominal pain at least weekly in the past 3 months, which also met 2 of the following conditions: was temporally related to defecation, associated with change in stool frequency, or associated with change in stool consistency. Rome IV IBS subtyping was based on responses to a single question about the usual type of stool abnormality on days when diarrhea or constipation are present, with the Bristol Stool Form Scale for reference. The 4 response options, each of which lead to classification as 1 of the 4 IBS subtypes if selected by the respondent, were "Usually constipation (like Type 1 or 2 in the picture)," "Usually diarrhea (like Type 6 or 7)," "Both diarrhea and constipation, that is, more than 1/4 of all the abnormal bowel movements were constipation and more than 1/4 were diarrhea," and "Not applicable, because I never or rarely had abnormal bowel movements."
Rome III IBS	Required abdominal discomfort or pain at least 2 to 3 days a month in the past 3 months that was at least on some occasions associated with 2 or more of the following: improvement after defecation, change in stool frequency, or harder or looser stools. Rome III subtyping depended on responses to diagnostic questions about frequency of hard or loose stools. Individuals reporting having hard/lumpy stools or loose/watery stools at least "Sometimes" (assumed in Rome III to equate 25% or greater frequency) without the opposite stool abnormality meeting that frequency threshold were classified as IBS-C or IBS-D, respectively. If hard/lumpy stools and soft/watery stools were both sometimes present, patients were subtyped as IBS-M, but as IBS-U if none of the other 3 subtype definitions were met.
Rome IV FC	Required presence of at least 2 of 6 constipation symptoms at a minimum frequency of ≥25% of all stools: lumpy or hard stools, sensation of incomplete evacuation, sensation of anorectal obstruction or blockage during defecation, infrequent defecation (fewer than 3 times per week), straining, or need for manual maneuvers to facilitate defecation. The minimum frequency for each symptom was approximated by using a 30% or greater as qualifying, as the closest 10% increment in the Rome IV response scale for FC symptoms meeting the threshold. The exception was infrequent defecation, for which a threshold of >50% of weeks was used. FC was diagnosed only if the individual did not fulfill criteria for IBS or OIC and diarrhea occurred no more than rarely without laxatives.
Rome III FC	Required the same symptom criteria as for Rome IV: 2 of the 6 constipation symptoms listed for Rome IV FC above being met at ≥25% frequency threshold. However, the response scale in the Rome III diagnostic questionnaire is simply a 5-point scale of "Never or rarely," "Sometimes," "Often," "Most of the time," and "Always." The minimum threshold was therefore set for each symptom as recommended in the standard Rome III diagnostic scoring: at least "Sometimes" for sensation of incomplete evacuation, sensation of blockage during defecation, and need for manual maneuvers to defecate, but at least "Often" for hard/lumpy stools, infrequent defecation, and straining. Furthermore, for diagnosis of Rome III FC, diarrhea must not be present more than rarely and IBS criteria must not be met.
Rome IV Functional Diarrhea	Required at least 30% of all stools (the closest approximation to >25% on the 10% increment frequency response scale) to be of Bristol Type 6 or 7 in the past 3 months, IBS criteria not to be met, and abdominal pain or bloating to not be predominant symptoms.
Rome III Functional Diarrhea	Required loose or watery stools on at least 75% of bowel movements in the past 3 months in the absence of abdominal discomfort or pain. As the exact Rome III questions to diagnose this disorder were not included in the survey, survey respondents were qualified for the diagnoses if 80% or more of their total bowel movements (the closest approximation to ≥75% on the 10% Rome IV increment frequency response scale) in the past 3 months were of Bristol Stool Form Type 6 or 7, and they also responded "Never" to the included Rome III question on frequency of abdominal discomfort or pain.
Rome IV Functional Abdominal Bloating/ Distention	Required symptoms of bloating and/or distention occurring at least weekly and reported to be the predominant symptoms in the past 3 months, in individuals not meeting diagnostic criteria for IBS, functional diarrhea, FC, or post-prandial distress syndrome.
Rome IV OIC	Required constipation symptoms equivalent to those defining Rome IV FC over the past 3 months, but where those symptoms were reported to have started or worsened in relation to beginning of, change in, or increase in, use of prescription pain medications. In addition, diarrhea must not occur more than rarely without laxatives.
Rome IV Unspecified Bowel Disorder	Required 1 or more of the key symptoms of the other FBDs (abdominal pain, bloating/distention, constipation, or diarrhea) to be present at the minimum diagnostic frequency threshold for those other disorders in the past 3 months, but criteria not met for diagnosis of any of the specific bowel disorders.

NOTE. All diagnoses also required the symptoms to have been present for 6 months.

FBD diagnosis were excluded from those diagnoses and were not counted as FBD cases in the analyses presented as follows.

Prevalence of FBDs

In the combined 3-nation study sample, 27.8% of all survey respondents (n = 1650) met criteria for a Rome IV FBD diagnosis. There was no difference between countries in this overall FBD rate (see Table 2). Women had a significantly higher prevalence of FBDs than men in each of the 3 countries as well as in the total sample, with an odds ratio (OR) of 2.0 (95% confidence interval 1.8–2.2) in the combined sample. Individuals older than 50 had significantly lower prevalence of FBDs compared with younger people, and the prevalence was lowest among individuals 65 and older (Table 3).

Irritable bowel syndrome. The Rome IV IBS prevalence was 4.6% in the whole study sample. The rate was practically identical in the 3 countries (Table 2), ranging from 4.5% in Canada to 4.7% in the United States. The Rome III IBS rate was approximately twice as high as the Rome IV

Table 2. Percent Prevalence of FBDs in the Adult Population in the United States, United Kingdom, and Canada

	Overall, N = 5931	United States, n = 1949	Canada, n = 1998	United Kingdom, n = 1994	P[a] (country difference)
Rome IV					
IBS	4.6 (4.1–5.2)	4.7 (3.8–5.7)	4.5 (3.6–5.4)	4.6 (3.7–5.5)	.96
FC[b]	7.8 (7.1–8.5)	6.9 (5.8–8.0)	7.9 (6.7–9.1)	8.6 (7.4–9.9)	.12
Functional diarrhea	4.7 (4.2–5.3)	4.9 (3.9–5.8)	5.6 (4.6–6.6)	3.8[c] (2.9–4.6)	**.02**
Functional bloating/distention	3.1 (2.7–3.6)	2.2[c] (1.5–2.8)	3.9 (3.0–4.7)	3.3 (2.5–4.1)	**.007**
OIC	1.5 (1.2–1.9)	1.7 (1.2–2.3)	1.0[d] (0.5–1.4)	1.9 (1.3–2.5)	**.03**
Unspecified bowel disorder	9.1 (8.4–9.9)	9.9 (8.6–11.2)	10.1 (8.7–11.4)	7.5[d] (6.3–8.6)	**.007**
Any bowel disorder	30.1 (29.0–31.3)	29.5 (27.5–31.5)	31.9 (29.9–34.0)	28.9 (26.9–30.9)	.09
Rome III					
IBS	9.0 (8.2–9.7)	8.6 (7.3–9.8)	9.5 (8.2–10.8)	8.8 (7.5–10.0)	.56
FC	5.6 (5.0–6.2)	4.9 (3.9–5.8)	5.0 (4.1–6.0)	6.8[e] (5.7–7.9)	**.02**
Functional diarrhea	0.9 (0.6–1.1)	0.9 (0.5–1.3)	1.0 (0.5–1.5)	0.7 (0.3–1.1)	.58

NOTE. (95% CI in parentheses)
[a]*P* values indicating significant differences are identified by bold type.
[b]The prevalence values for FC presented here and elsewhere in this article are obtained with scoring in accordance with the published Rome IV diagnostic criteria. If the stricter research diagnostic scoring suggested in the Rome IV book (Rome IV Functional Gastrointestinal Disorders: Disorders of Gut-Brain Interaction, Volume 2. Rome Foundation: Raleigh, NC. Page 1552) is used, FC rates are lower: 5.7% for the overall sample, 5.1% for the United States, 5.2% for Canada, and 6.7% for the United Kingdom.
[c]Significantly lower prevalence than in Canada.
[d]Significantly lower than in both the other countries.
[e]Significantly higher prevalence than in both the other countries.

rate: It was 9.0% in the total 3-country sample, ranging from 8.6% in the United States to 9.5% in Canada, with no significant difference between countries.

In all 3 countries sampled, and by both versions of the Rome criteria, IBS rate was significantly higher in women than men, except for Rome IV IBS in the United States, where it did not reach statistical significance ($P = .07$). The female/male OR for having IBS was 1.9 (1.5–2.5) for Rome IV IBS and 2.3 (1.9–2.7) for Rome III IBS in the total study sample. Both Rome IV and Rome III IBS rates had significantly lower prevalence among individuals aged 65 years or older compared with younger age groups (see Table 3), and this was also true for each of the 3 countries when their data were analyzed separately.

There were no significant differences between countries in the distributions of IBS subtypes among individuals qualifying for IBS diagnosis (Figure 1); however, the distribution of IBS subtypes was substantially different between the 2 versions of the Rome criteria ($P < .0001$). When Rome IV criteria were applied, IBS with predominant constipation (IBS-C), IBS with predominant diarrhea (IBS-D), and IBS with mixed bowel habits (IBS-M) all constituted similar-sized and substantial proportions of the IBS cases, whereas only 4.4% to 6.5% of them had IBS unclassified (IBS-U). In contrast, IBS-M accounted for a far larger portion of all IBS cases than any of the other subtypes in Rome III subtyping, representing more than half of the cases (see Figure 1). IBS-U was very uncommon in Rome III as in Rome IV, amounting for only 1.2% to 4.6% of all IBS cases.

The substantially lower percentage of individuals meeting Rome IV IBS criteria compared with Rome III criteria, a drop by approximately half, led us to conduct follow-up analyses to examine how the specific changes in the criteria had produced this large decrease in individuals qualifying for IBS diagnosis. As described previously, 3 main changes were made in IBS diagnosis in Rome IV compared with the Rome III criteria: elimination of the word discomfort from the question about abdominal pain, changes in criteria about the relationship of pain and stools, and increase in minimum frequency of pain to once a week. With our advantage of having answers from the same individuals to both the Rome III and Rome IV diagnostic IBS questions in the dataset, we were able to examine the impact of each of these changes independently, by altering 1 criterion at a time in the diagnostic algorithm but keeping everything else unchanged, and calculating the effects of this on diagnostic rates.

Starting with the 723 nonorganic cases who met the Rome III minimum pain/discomfort frequency threshold of 2 to 3 times a month (and who reported having had this symptom for 6 months), we first examined the difference in numbers of people meeting or exceeding that frequency threshold when asked instead about frequency of abdominal pain only (ie, the Rome IV question). We discovered that 62 fewer individuals reported abdominal pain on the Rome IV diagnostic question at the minimum frequency threshold of 2 to 3 days a month, compared with the numbers obtained using the Rome III question. This quantified the impact of dropping discomfort from the pain threshold question, in isolation from other changes made in the diagnostic criteria.

Using the remaining 661 individuals who reported abdominal pain on the Rome IV question at a frequency of 2 to 3 times a month or more, we next evaluated the size of the impact of raising the minimum frequency of abdominal pain to once a week. We found that 296 fewer people

Table 3. Percent Prevalence of Functional Bowel Disorders in Sex and Age Groups in the Combined Three-Country Population Survey Sample of 5931 Individuals

	Females	Males	p[h] (sex difference)	Age 18-34	Age 35-49	Age 50-64	Age 65+	p[h] (age group difference)
Rome IV								
Irritable bowel syndrome	6.1 (5.2-6.9)	3.2 (2.6-3.9)	**<.0001**	5.0 (3.9-6.0)	6.4 (5.1-7.7)	5.0 (3.9-6.1)	1.7[a] (1.0-2.4)	**<.0001**
Functional constipation	10.1 (9.1-11.2)	5.5 (4.7-6.4)	**<.0001**	9.9[d] (8.5-11.4)	8.0 (6.6-9.4)	6.4 (5.2-7.6)	6.5 (5.1-7.9)	**<.0002**
Functional diarrhea	5.1 (4.3-5.9)	4.4 (3.7-5.1)	.11	4.1 (3.2-5.1)	6.0[e] (4.8-7.3)	5.1 (4.0-6.1)	3.8 (2.7-4.8)	**.03**
Functional bloating/ distention	4.6 (3.8-5.4)	1.7 (1.2-2.12)	**<.0001**	3.6 (2.7-4.5)	3.6 (2.6-4.6)	3.2 (2.3-4.0)	1.9[a] (1.1-2.6)	**.04**
Opioid-induced constipation	2.1 (1.2-2.1)	1.0 (0.7-1.3)	**<.0001**	1.1 (0.6-1.6)	2.3[f] (1.5-3.1)	1.7 (1.1-2.3)	1.1 (0.5-1.6)	**.03**
Unspecified bowel disorder	10.0 (12.6-15.1)	8.3 (7.3-9.3)	**<.001**	11.3[g] (9.8-12.8)	8.6 (7.2-10.1)	8.6 (7.2-9.9)	7.4 (6.0-8.9)	**<.002**
Any bowel disorder	36.9 (35.2-38.7)	23.6 (22.1-25.1)	**<.0001**	34.1 (31.9-36.4)	33.7 (31.2-36.2)	28.9[b,c] (26.7-31.1)	22.3[a] (19.9-24.6)	**<.0001**
Rome III								
Irritable bowel syndrome	12.2 (11.0-13.4)	5.8 (5.0-6.6)	**<.0001**	9.6 (8.2-11.0)	11.2 (9.5-12-9)	9.4 (8.0-10.8)	5.0[a] (3.8-6.2)	**<.0001**
Functional constipation	7.3 (6.4-8.3)	3.9 (3.2-4.5)	**<.0001**	5.4 (4.3-6.5)	6.4 (5.1-7.8)	5.2 (4.2-6.3)	5.2 (4.0-6.5)	.44
Functional diarrhea	0.8 (0.2-1.3)	0.6 (0.1-1.1)	.43	0.5 (0.0-1.1)	0.2 (-0.2-0.6)	1.5 (0.5-2.5)	0.5 (-0.2-1.2)	.07

NOTE. (95% CI in Parentheses).
[a]Significantly lower prevalence than in all the other age groups.
[b]Significantly lower than age group 18-34.
[c]Significantly lower than age group 35-49.
[d]Significantly higher prevalence than the two oldest age groups.
[e]Significantly higher prevalence than in age groups 18-34 and 65+.
[f]Significantly higher prevalence than in age groups 18-34 and 65+.
[g]Significantly higher prevalence than in all the other age groups.
[h]P-values indicating significant differences are identified by bold type.

endorsed abdominal pain at least weekly, eliminating 40.9% of all the individuals who met a minimum threshold for pain at 2 to 3 times a month.

Finally, we compared the effects of changes made in Rome IV in questions about associations with bowel functioning on qualification for diagnosis among the 365 individuals still potentially qualifying for IBS diagnosis after meeting the weekly pain requirement. This revealed that very similar numbers qualified for Rome IV IBS regardless of whether we applied their Rome III or Rome IV responses to questions on the relationship of stools and pain. Only 9 fewer individuals qualified for diagnosis on this basis when Rome IV questions were used to determine eligibility for diagnosis, indicating that the change in wording in Rome IV IBS on those questions, such as dropping the association with relief of pain after bowel movement, has minimal effect on diagnostic rate.

In summary, our analysis found, by examining each of the 3 changes made in the Rome criteria for IBS by Rome IV separately and sequentially, that most of the relative reduction in diagnostic rate, or 80.7% (296/[62+296+9]), is accounted for by just 1 of those changes;:the increase of the minimum pain frequency threshold from 2 to 3 days a month to once a week. This is illustrated in Figure 2.

The large reduction in IBS diagnosis rate with Rome IV criteria compared with Rome III invites the question of what happens in the Rome IV diagnostic classification system to the approximately half of individuals who would receive IBS diagnosis in Rome III but are disqualified from it in Rome IV. A detailed answer to that question is provided in the pie graph in Figure 2. As shown there, fewer than one-third (28.7%) of those individuals do not qualify for any bowel disorder diagnosis in the Rome IV classification system, whereas more than two-thirds meet diagnostic criteria for 1 of the other 5 FBDs.

Functional constipation. Rome IV FC had a prevalence of 7.6% in the overall study sample. The 3 countries had equivalent constipation rates, ranging from 6.9% in the United States to 8.6% in the United Kingdom, although the UK prevalence showed a trend toward being higher than in the United States (Table 2).

The Rome III constipation prevalence in the overall study sample, although diagnosed based the same 6 symptoms as in Rome IV (see Table 1), was significantly lower than Rome IV prevalence, or 5.6%. The prevalence was significantly higher in the United Kingdom compared with the other 2 countries.

Women were more likely to have a diagnosis of FC than men in all countries and with both versions of the Rome criteria, with an OR of 1.9 (1.6–2.3) by Rome IV and 2.0 (1.6–2.5) for Rome III criteria in the combined 3-country sample. Rome IV FC rates were significantly higher in the youngest age group in the overall sample than in any of the

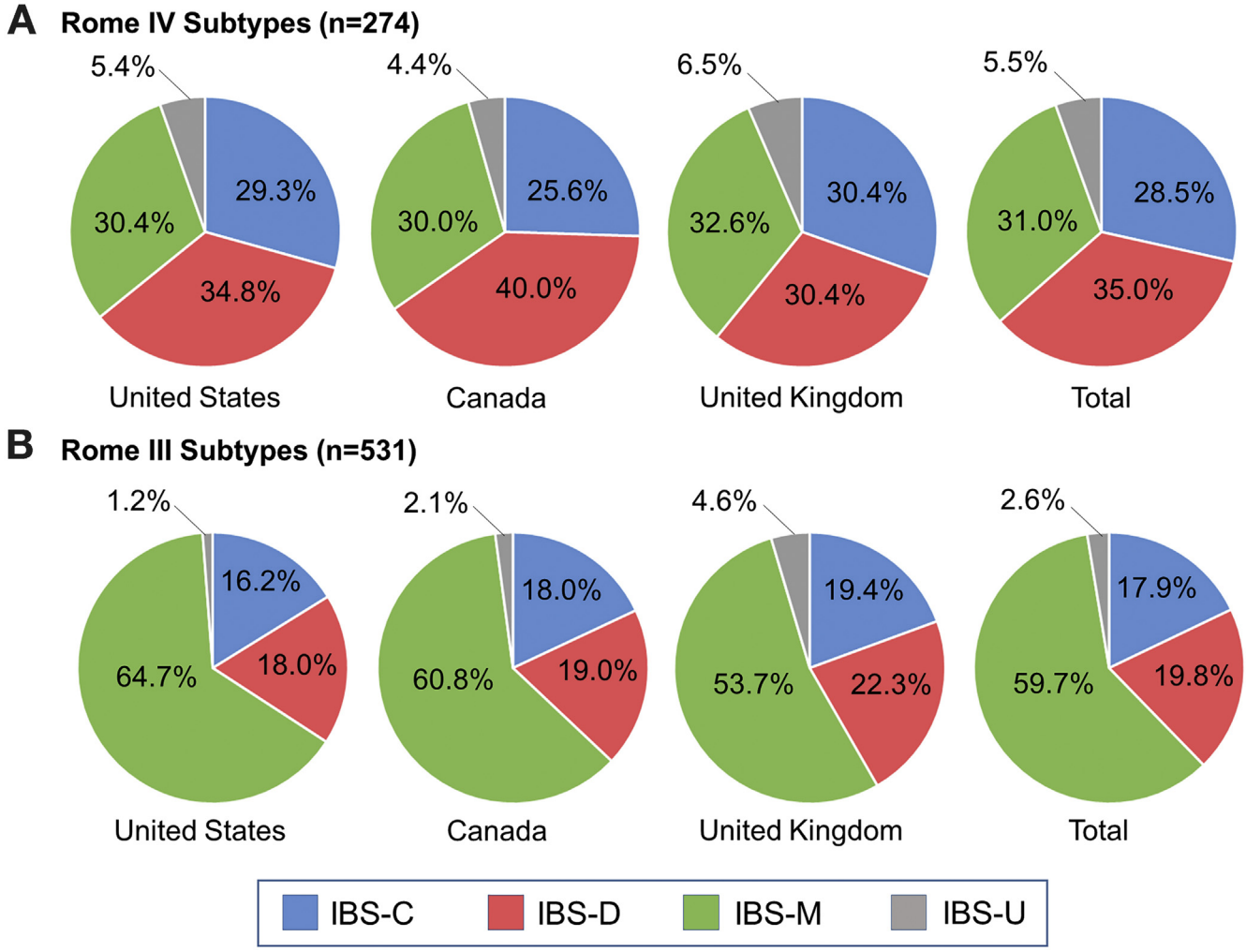

Figure 1. Distribution of IBS subtypes among individuals meeting Rome IV vs Rome III diagnostic criteria in the combined 3-country population survey sample and in each of the countries.

older groups. In contrast, that relative elevation of constipation rate in the youngest age group was not seen in FC diagnosed by Rome III criteria (see Table 3).

Functional diarrhea. Rome IV functional diarrhea had an overall prevalence of 4.7% in the total study sample, but the rate was significantly higher in Canada (5.6%) than in the United Kingdom (3.8%), with the United States in the middle and not different from either of the other countries. The prevalence was highest among individuals in the age group from 35 to 49 years, and the diarrhea prevalence in that group was significantly higher than in younger adults and those age 65 years and older. The sexes did not differ in functional diarrhea rates (Table 3).

Rome III functional diarrhea had an overall prevalence rate that was a mere one-fifth of the prevalence of that same diagnosis by Rome IV criteria, or 0.9% for the combined 3-country sample. This reflects the impact of the substantial lowering of the frequency threshold of diarrhea stools required for diagnosis in Rome IV vs Rome III; from 75% to merely >25% of all stools. There were no significant differences between age or sex groups in Rome III functional diarrhea prevalence.

Functional abdominal bloating/distention. In the total study sample, 3.1% of individuals met diagnostic criteria for functional bloating/distention. The prevalence rate was significantly higher in Canada compared to the United States, with the UK prevalence in the middle and not different from either of the other countries. Bloating/distention prevalence was substantially higher in women than men, with OR of 2.8 (2.0–3.9), and lower in individuals 65 years and older compared with other age groups.

Unspecified bowel disorder. Criteria for unspecified bowel disorder were met by 9.1% of individuals across the 3 countries in our sample. The prevalence was highest in Canada and lowest in the UK. More women than men met criteria for this diagnosis, with an OR of 1.3 (1.1–1.6) and the rates were higher among individuals younger than 35 compared with older groups.

Opioid-induced constipation. Fewer individuals in our study sample qualified for the new Rome IV OIC diagnosis compared with the other 5 Rome IV FBDs. The prevalence was 1.5% in the total sample, with all 3 countries showing less than 2% prevalence. Women were more than twice as likely as men to qualify for OIC, with an OR of 2.2

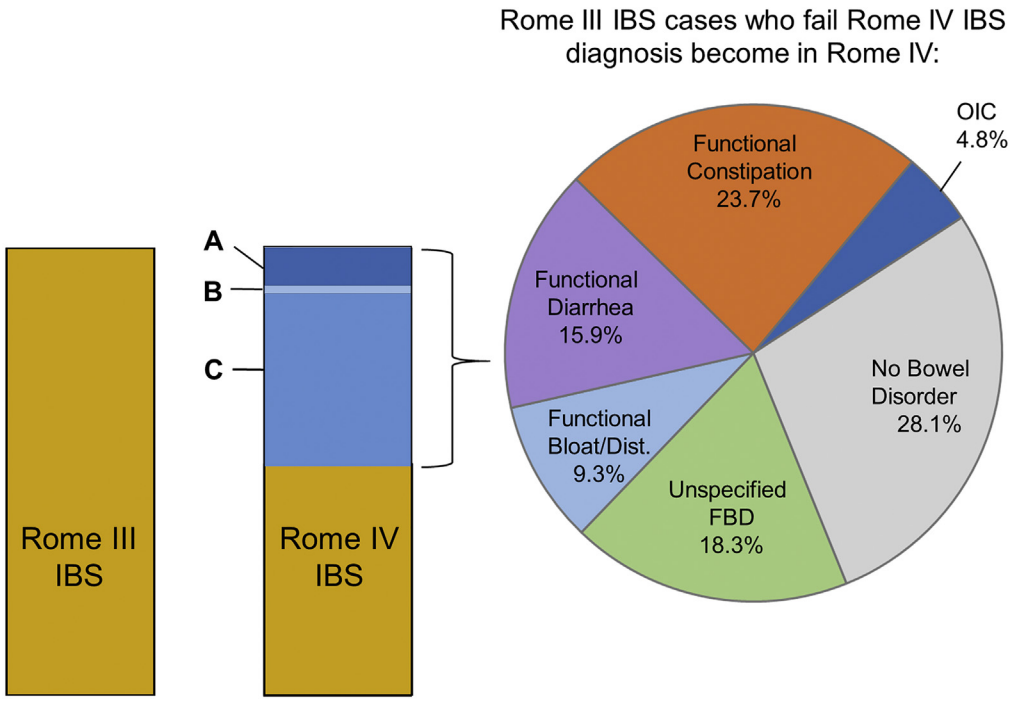

Figure 2. Comparison of the 3 different factors explaining lower Rome VI IBS prevalence compared with Rome III IBS in the combined 3-country population survey sample (*left side bars*), as percentage of all people disqualified from Rome IV IBS: A, Fewer people report abdominal "pain" than "discomfort or pain" at Rome III threshold (16.8%); B, fewer people meet stool-associated criteria in Rome IV compared with Rome III (2.5%); and C, fewer people meet 1 × week minimum than the 2 to 3 times/month pain threshold (80.7%). The *pie graph* shows the distribution of Rome IV FBD diagnoses for which the Rome III IBS cases who failed Rome IV IBS criteria qualified instead.

(1.4–3.5). Individuals in the age range from 35 to 49 had higher OIC prevalence compared with both the youngest and oldest age groups (Table 3).

Census-Adjusted Prevalence Estimates

Our national samples in this study were not entirely equivalent in age distribution to those of the nations they were drawn from, and this was likely to have some effect on the prevalence estimates for each of the 6 diagnoses we evaluated. To obtain more precise estimates of the national prevalence rates of the bowel disorders, we used the latest census data for each country to compute census weights for each participant for age and sex. As can be seen by comparing the numbers in Table 4 with those in Table 2, these census adjustments made negligible differences in the prevalence figures overall and for the individual countries, generally altering estimates for each disorder by only a fraction of percent.

Impact of the FBDs on Quality of Life and GI Health Care Seeking

To examine the subjective life impact of FBDs in the general population, we examined whether they were associated with impairment in the mental and physical dimensions of quality of life as measured with the SF-8 questionnaire. As seen in Figure 3, individuals with each of the 6 disorders had significantly impaired quality of life compared with people in our sample who did not qualify for any FBD diagnosis. People who met Rome IV IBS criteria had significantly poorer mental quality of life (SF-8 Mental Component Score) than those with all the other bowel disorders. Individuals with OIC had the lowest physical quality of life (SF-8 Physical Component Score), even lower than those with IBS, who in turn had lower physical quality of life than all other FBDs (Figure 3).

Overall, more than a third of individuals who met Rome IV criteria for any FBD in our survey reported that they had consulted a doctor about GI health problems in the past, and they were twice as likely to have done so compared with people not meeting FBD criteria (36.1% vs 17.5%; $P < .0001$). This doubling of likelihood of past GI health care consulting among FBD cases was seen for both men (32.5% vs 15.6%; $P < .0001$) and women (38.4% vs 20.4%; $P < .0001$) and in each of the 3 countries (30.1% vs 15.6% in the United States, 38.1% vs 18.6% in Canada, and 39.9% vs 18.4% in the United Kingdom; $P < .0001$ for all comparisons). People meeting IBS criteria had a significantly higher rate of GI consulting (61.3%) than those with any of the other FBDs, whereas individuals with OIC had a higher GI consultation rate (50.5%) than those with all FBDs except IBS.

Discussion

In this report, we provide a comprehensive picture of the prevalence and demographic distribution of FBDs in the national populations of 3 Western countries, using the recently launched Rome IV criteria.[1] Our findings show that this class of functional GI disorders is very common, present in 1 of every 4 adults.

We found that the rates of the bowel disorders are generally similar among the countries we surveyed. Even where differences were found between countries, the percentage differences were generally relatively modest

Table 4. Estimated Prevalence of Functional Bowel Disorders Census-Adjusted for Sex and Age in the Combined Three-Country Population Survey Sample and Each of the Three Countries Surveyed

	Overall N=5931	United States n=1949	Canada n=1998	United Kingdom n=1994
Rome IV				
Irritable bowel syndrome	4.6	4.8	4.7	4.4
Functional constipation	8.1	7.9	7.9	8.6
Functional diarrhea	4.7	5.2	5.3	3.6
Functional bloating/ distention	3.1	2.0	3.9	3.3
Opioid-induced constipation	1.6	1.8	1.1	1.9
Unspecified bowel disorder	9.1	10.0	9.6	7.5
Any bowel disorder	30.4	30.9	31.7	28.6
Rome III				
Irritable bowel syndrome	9.2	8.8	9.7	9.8
Functional constipation	5.7	5.2	5.0	6.8
Functional diarrhea	0.8	0.9	0.9	0.6

(Table 2). This suggests that our prevalence figures are likely to be reasonably close approximations of true national prevalence of FBDs as defined by Rome IV.

Perhaps the single most notable finding from our analyses was that IBS rates are reduced by half when the disorder is diagnosed by Rome IV rather than by Rome III criteria.[1,4] The fact that this halving of prevalence was seen in each of the countries separately makes clear that it is a direct function of the changed diagnostic criteria. Our analyses of the reasons for this reduction in IBS rates in Rome IV provided useful insights into the effects of changing individual aspects of the IBS criteria. They indicated that the decision to raise the minimum pain frequency threshold is the principal cause of reduced IBS rates with Rome IV, whereas eliminating the word "discomfort" from the pain criterion and changes in criteria related to association between stools and pain affected diagnostic rates only slightly. Recent retrospective surveys of clinical samples of IBS patients fulfilling Rome III criteria for the disorder highlight that the vast majority also fulfill Rome IV criteria for IBS, hence meeting the higher frequency threshold of abdominal pain required by the new criteria.[16,17] This indicates that the drop in prevalence rate seen in our population-based study from using the new version of the criteria is not likely to reduce IBS diagnoses much in specialty clinics. However, data from a recent study in China suggest that this could possibly differ between Eastern and Western countries.[18] Moreover, differences in symptom clusters defining functional GI disorders between Asia and Western countries have been proposed,[19,20] highlighting the need to assess whether the findings from this study are valid also in other parts of the world, including Asia.

Our findings regarding differences in IBS subtype distribution in Rome IV vs Rome III are clinically important. Rome IV subtyping of IBS reduces the large group of patients that has been classified as IBS-M in Rome III, dividing half of them between IBS-D and IBS-C and thereby making both of those other subtypes more prominent. This may be critically important in the management of patients with IBS, as pharmacologic treatment has offered much better options to date for treating the latter 2 subtypes.[21] The reasons for the shrinkage of the IBS-M proportion in Rome IV are unclear, but it could be due in part to Rome IV subtyping asking patients in a multiple-choice fashion what kind of stool abnormality is usual for them on days with abnormal stools. If patients experience substantial difference between amounts of diarrhea and constipation, they might be prone to choose the predominant one instead of answering "both," even if both types occur at higher than the required 25% threshold. Unlike the Rome III subtyping, which is based on separate responses about percent of diarrhea and constipation stools out of all bowel movements, the Rome IV approach might thereby possibly favor IBS-D and IBS-C over IBS-M.

Unlike the drop in IBS prevalence seen when Rome IV criteria are used instead of Rome III, we found that the newer criteria increase prevalence rate of functional diarrhea 5-fold (from 0.9% to 4.7% in the overall sample). This large Rome IV boost in functional diarrhea rates is not surprising, as the Rome IV criteria substantially lowered the diagnostic threshold for diarrhea-type stools (>25% vs 75% of all stools in the past 3 months), and unlike Rome III they do not disqualify patients from diagnosis who report abdominal pain unless they meet IBS criteria.

We also found FC rates to be higher when Rome IV criteria are applied than with Rome III. This is understandable given the large reduction in IBS diagnosis produced by Rome IV, as a portion of the individuals no longer qualifying for IBS in Rome IV will instead classify as FC, as seen in Figure 2. However, a surprising finding regarding FC diagnosis was the fact that Rome IV FC rates were significantly higher in the youngest age group (18–34 years) compared with older groups. This is at odds with prior research using earlier FC criteria, which found FC rates to be highest in the oldest age groups.[7,8] Furthermore, this elevation of FC rates in the youngest age group was not seen in our sample when Rome III FC criteria were applied. Elevation in FC among the young does seem likely to have something to do with Rome IV criteria rather than being a statistical anomaly, however, because we found higher numerical FC rates to be present in all 3 countries separately, and in both sexes. We cannot explain this, nor the general absence of the expected rise in constipation rates in the oldest age groups in our samples. Future research studies, such as the Rome Global Epidemiology Survey that has just been concluded, will need to confirm or disconfirm these unexpected constipation age effects observed in our study.

Overall, the change from Rome III to Rome IV results in reduced prevalence of IBS and increased prevalence of FC and functional diarrhea. The clinical implications of this shift are unclear, as our findings are from the general population, including large groups of individuals with FBD who have not sought health care for their bowel symptoms, and findings from existing retrospective and cross-sectional studies in clinical populations have been mixed.[16–18] However, because some of the available pharmacological agents for

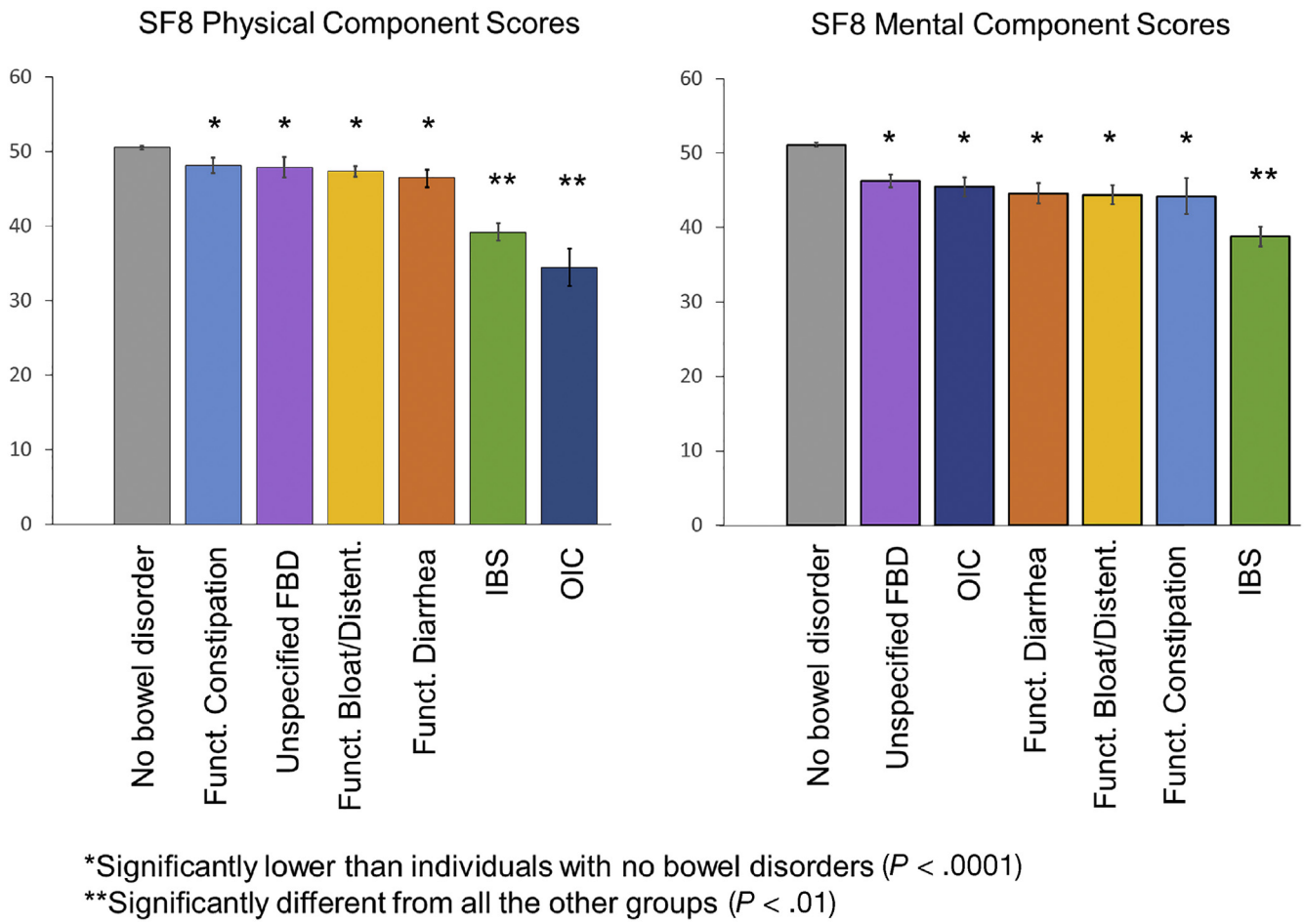

Figure 3. SF-8 quality of life scores of individuals with each of the 6 Rome IV FBDs in the 3-country survey sample (N = 5931), compared with individuals with no bowel disorder.

FBDs are approved for individual disorders only,[21] the shift among diagnoses between Rome III and Rome IV may jeopardize availability of approved drugs for a proportion of individuals with FBD.

Our analyses revealed a significant impact of the FBDs on quality of life and GI-related health care seeking. This is in agreement with numerous previous research studies.[22–24] All 6 FBDs were associated with measurable impairment in both physical functioning and mental well-being; however, IBS stands out in our results as a diagnostic entity particularly strongly associated with poor mental and physical functioning. Similarly, individuals with all the FBDs showed significantly greater tendency to have consulted doctors for GI problems than individuals without such disorders, but IBS was more strongly associated with GI consultation than any of the other disorders.

The results on OIC presented here provide the first data on the population-based presence of this new FBD. The findings show that although it is less common than the other FBDs, it is a health problem with significant adverse effects, and seems to rival IBS in quality of life impact and GI health care utilization. It is noteworthy that individuals meeting OIC criteria reported even poorer physical quality of life than those with IBS or any of the other FBDs; however, that finding should probably be interpreted with caution, as the SF-8 measures only overall physical functioning. The marked physical impairment it measures in individuals with OIC could be related more to other health problems for which they are taking opioids than bowel symptoms related to the opioid use, implicating that quality of life reduction in patients with OIC may be a multifaceted problem.[25]

The study of FBDs that we present here had some notable strengths. One of these was the multinational composition of the sample across English-speaking Western countries that share many cultural and economic similarities. It provided 3 independent side-by-side snapshots of FBDs in similar Western world populations, diagnosed based on the same questions answered by all respondents in the same language. This eliminated much of the potential confounding associated with divergent cultures, dissimilar living conditions, and differences in languages.[5] Equally important, the 3 national samples were practically identical in their sex and age group distribution by design, and each had excellent nationwide subject distribution. All of this enabled direct nation-to-nation prevalence comparisons without confounding from any major differences in demographic composition, language, or cultures. Additional methodological strengths were the fact that survey participants were unaware of the GI focus of the survey when they enrolled, and the multiple quality control methods that

prevented poor responses in the dataset, such as the built-in attention-check questions.

A limitation that our study shares with all cross-sectional population surveys is the fact that because most of the respondents who met diagnostic criteria had never visited a doctor for GI health problems, the symptoms on which diagnoses were based were largely medically uninvestigated. Some individuals to whom we assigned an FBD diagnosis may therefore have had undiscovered organic disease causing their symptoms.

Another potential limitation of this study is that it used Internet-based surveying rather than more traditional epidemiological survey methodology. However, as we know of no evidence to suggest that Internet survey-takers differ in their GI health status from other people with comparable demographic characteristics, it seems unlikely that this would affect our FBD findings. In the highly developed countries we surveyed, 88% to 90% of all adults are Internet users[26] and daily Internet use has become a normal way of life for most of the general population. For this reason, and because the demographic parameters of our national samples, including age, sex, education, and geographic distribution, were all similar to those of the actual population of those countries, we believe that the samples we obtained are likely to be representative of the general populations of the countries we studied. However, it must be acknowledged that Internet surveying does exclude the small segment of the adult population who are unable to use the Internet, such as illiterate or cognitively impaired individuals and those living in remote areas without Internet service.

Finally, one more limitation of the study methodology was that the survey was conducted at a time when the Rome IV Diagnostic Questionnaire had not yet been published or translated. This restricted the surveying to English-speaking subjects, which in particular may have limited participation among native French speakers in Canada, as some of them are not fluent in English. The fact that our survey data were obtained exclusively from English-speaking individuals in 3 Western nations with many cultural similarities means that the findings may not be generalizable to other language groups or cultural regions of the world.

In summary, the findings presented here offer the first comprehensive picture of Rome IV FBDs in the adult populations in 3 English-speaking countries. They provide estimates of the prevalence of each disorder that are likely to be reliable based on their similarities between countries and application of census-based population weights, show the relative composition of this class of health problems as defined by the current diagnostic criteria, and confirm some of the patterns of age and sex differences in FBDs previously reported by others. Furthermore, these results provide illustrations of the prevalence impact of changes introduced by Rome IV in IBS and functional diarrhea that may prove useful for guiding future development of the Rome criteria.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at http://doi.org/10.1053/j.gastro.2019.12.021.

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Conflicts of interest
The authors disclose no conflicts.

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Supplementary Table 1. Demographic Comparison of Inconsistent vs Valid Survey Respondents

Characteristic	Inconsistent[a] (n = 369)	Valid (n = 5931)
Sex (% female)	64.7 [b]	49.3
Age: Mean (SD)	39.5 (14.9)[b]	47.8 (30.5)
Percent of all subjects in each age group:		
18–34 *y*	9.0	89.0
35–49 *y*	6.9	93.1
50–64 *y*	4.4	95.6
65+ *y*	2.1	97.9
Years of education: mean (SD)	13.0 (3.7)	13.8 (3.8)

[a]Inconsistent responders were those who deviated more than one response scale step from their original response on 2 or more of 3 Rome IV GI symptom frequency questions repeated in the survey.
[b]Significantly different from valid survey responders.

Supplementary Table 2. Distribution of the US Study Subsample Across States, and Comparison With the Distribution of the US National Population (2015 US Census Estimates)

State	US sample, n	US sample, %	State % of total US population
Alabama	27	1.4	1.5
Alaska	0	0	0.2
Arizona	48	2.5	2.1
Arkansas	20	1	0.9
California	249	12.8	12.3
Colorado	30	1.5	1.7
Connecticut	25	1.3	1.1
Delaware	7	0.4	0.3
District of Columbia	4	0.2	0.2
Florida	153	7.9	6.4
Georgia	73	3.7	3.2
Hawaii	4	0.2	0.5
Idaho	15	0.8	0.5
Illinois	84	4.3	4
Indiana	42	2.2	2.1
Iowa	20	1	1
Kansas	11	0.6	0.9
Kentucky	33	1.7	1.4
Louisiana	29	1.5	1.5
Maine	3	0.2	0.4
Maryland	40	2.1	1.9
Massachusetts	41	2.1	2.1
Michigan	55	2.8	3.1
Minnesota	31	1.6	1.7
Mississippi	14	0.7	0.9
Missouri	39	2	1.9
Montana	5	0.3	0.3
Nebraska	11	0.6	0.6
Nevada	21	1.1	0.9
New Hampshire	6	0.3	0.4
New Jersey	61	3.1	2.8
New Mexico	14	0.7	0.7
New York	120	6.2	6.2
North Carolina	58	3	3.2
North Dakota	1	0.1	0.2
Ohio	78	4	3.7
Oklahoma	14	0.7	1.2
Oregon	24	1.2	1.3
Pennsylvania	103	5.3	4
Rhode Island	4	0.2	0.3
South Carolina	26	1.3	1.5
South Dakota	8	0.4	0.3
Tennessee	30	1.5	2.1
Texas	157	8.1	8.6
Utah	8	0.4	0.9
Vermont	1	0.1	0.2
Virginia	44	2.3	2.6
Washington	22	1.1	2.3
West Virginia	7	0.4	0.6
Wisconsin	25	1.3	1.8
Wyoming	4	0.2	0.2

Supplementary Table 3. Distribution of the UK Study Subsample Across the 10 Government Regions, and Comparison With the Distribution of the UK National Population (Office of UK National Statistics 2015 estimates)

Region	UK sample, n	UK sample, %	Region % of total UK population
East of England	174	8.7	9.21
London	212	10.6	12.88
Midlands	310	15.5	16.31
North East Yorkshire & the Humber	273	13.7	12.42
North West	271	13.6	11.11
Northern Ireland	33	1.7	2.95
Scotland	164	8.2	8.37
South East	288	14.4	13.6
South West	159	8	8.33
Wales	109	5.5	4.83

Supplementary Table 4. Distribution of the Canadian Study Subsample Across Provinces and Territories, and Comparison With the Distribution of the Canadian National Population (Statistics Canada Census Program 2015 estimates)

Province/Territory	Canadian sample, n	Canadian sample, %	Province/Territory % of total Canadian population
Alberta	210	10.6	11.7
British Columbia	347	17.5	13.08
Manitoba	113	5.7	3.63
New Brunswick	53	2.7	2.09
Newfoundland and Labrador	25	1.3	1.47
Nova Scotia	77	3.9	2.62
Ontario	910	45.8	38.5
Prince Edward Island	15	0.8	0.41
Quebec	171	8.6	23
Saskatchewan	65	3.3	3.17
Yukon	2	0.1	0.1
Northwest Territories	0	0	0.12
Nunavut	0	0	0.1

Supplementary Table 5. Distribution of the US Male and Female Subsamples Across Age Groups, and Comparison With Distribution of 18+ Adults in the Same Age Groups in the US Population

Age group, *y*	US male sample, n	% of US male sample	% of US male 18+ population	US female sample, n	% of US female sample	% of US female 18+ population
18–29	217	22.0	22.7	158	16.4	20.6
30–39	188	19.0	17.5	190	19.8	16.5
40–49	107	10.8	16.9	143	14.9	16.2
50–59	155	15.7	17.9	194	20.2	17.7
60–69	217	22.0	13.9	180	18.7	14.4
70+	103	10.4	11.2	95	9.9	14.3

Supplementary Table 6. Distribution of the UK Male and Female Subsamples Across Age Groups, and Comparison With Distribution of 18+ Adults in the Same Age Groups in the UK Population

Age group, *y*	UK male sample, n	% of UK male sample	% of UK male 18+ population	UK female sample, n	% of UK female sample	% of UK female 18+ population
18–29	138	13.6	20.9	223	22.8	19.3
30–39	181	17.8	16.8	234	24.0	16.2
40–49	139	13.7	17.6	128	13.1	17.2
50–59	199	19.5	16.8	153	15.7	16.4
60–69	243	23.9	13.9	165	16.9	13.9
70+	118	11.6	13.9	72	7.4	17.1

Supplementary Table 7. Distribution of the Canadian (CA) Male and Female Subsamples Across Age Groups, and Comparison With Distribution of 18+ Adults in the Same Age Groups in the Canadian Population

Age group, *y*	CA male sample n	% of CA male sample	% of CA male 18+ population	CA female sample n	% of CA female sample	% of CA female 18+ population
18–29	184	18.3	19.9	188	19.2	18.3
30–39	208	20.6	16.6	199	20.3	16.3
40–49	96	9.5	16.6	137	14.0	16.3
50–59	179	17.8	19.1	208	21.2	18.6
60–69	216	21.4	15.1	174	17.8	15.2
70+	124	12.3	12.8	73	7.4	15.4

Supplementary Table 8. Distribution of Total Study Subject Sample From the 3 Countries Across Age Groups, Compared With Distribution of the Combined Population in the 3 Countries

Age group, *y*	Total sample male, n	Total sample female, n	Total male %	Total female %	Total sample % males + females	Population % of adults 18+ y in the 3 countries
18–29	539	569	17.9	19.5	18.7	21.2
30–39	577	623	19.2	21.4	20.2	16.9
40–49	342	408	11.4	14.0	12.7	16.7
50–59	533	555	17.7	19.0	18.3	17.7
60–69	676	519	22.4	17.8	20.2	14.2
70+	345	240	11.5	8.2	9.9	13.3
All ages	3013	2918				