Will the History and Physical Examination Help Establish That Irritable Bowel Syndrome Is Causing This Patient's Lower Gastrointestinal Tract Symptoms?

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Context Many individuals experience lower gastrointestinal tract symptoms, most commonly attributable to functional conditions. These individuals are frequently diagnosed with irritable bowel syndrome (IBS) based on their symptoms; however, some may require additional testing or referral to specialists before this diagnosis is made.

Objective To systematically review the literature of the accuracy of individual symptoms and combinations of findings in diagnosing IBS.

Data Sources Search of MEDLINE and EMBASE (up to June 2008) for prospective studies reporting on unselected cohorts of adult patients with lower gastrointestinal tract symptoms recorded before investigation.

Study Selection Studies prospectively evaluating accuracy of individual symptoms or combinations of findings compared with results from investigations of the lower gastrointestinal tract.

Data Extraction Two authors independently assessed studies and extracted data to estimate likelihood ratios (LRs) of individual symptoms and combinations of findings in diagnosing IBS.

Results Ten studies evaluating 2355 patients were identified, with a summary prevalence of IBS following investigation of 57%. Individual symptom items yielded positive LRs from 1.2 (95% confidence interval [CI], 0.93-1.6) for passage of mucus per rectum to 2.1 (95% CI, 1.4-3.0) for looser stools at onset of abdominal pain and negative LRs from 0.29 (95% CI, 0.12-0.72) for no lower abdominal pain to 0.88 (95% CI, 0.72-1.1) for no passage of mucus per rectum in diagnosing IBS. The Manning criteria had a summary positive LR of 2.9 (95% CI, 1.3-6.4) and a summary negative LR of 0.29 (95% CI, 0.12-0.71). The Rome I criteria had a positive LR of 4.8 (95% CI, 3.6-6.5) and a negative LR of 0.34 (95% CI, 0.29-0.41). The Kruis scoring system provided a summary positive LR of 8.6 (95% CI, 2.9-26.0) and a summary negative LR of 0.26 (95% CI, 0.17-0.41). The Rome II and III criteria have not been studied.

Conclusions Individual symptoms have limited accuracy for diagnosing IBS in patients referred with lower gastrointestinal tract symptoms. The accuracy of the Manning criteria and Kruis scoring system were only modest. Despite strong advocacy for use of the Rome criteria, only the Rome I classification has been validated. Future research should concentrate on validating existing diagnostic criteria or developing more accurate ways of predicting a diagnosis of IBS without the need for investigation of the lower gastrointestinal tract.

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PATIENT SCENARIO

A 35-year-old woman presents with a 6-month history of lower gastrointestinal tract symptoms. She describes lower abdominal discomfort along with a long-standing fluctuating bowel habit, such that her stools often occur more frequently and with looser consistency. In addition, she experiences a sense of incomplete evacuation after defecation. She specifically denies any weight loss or the passage of blood or mucus per rectum. Her symptoms are unrelated to menstruation. She has always been healthy and is not taking any regular prescribed or over-the-counter medications. Her father was diagnosed with colorectal carcinoma at age 80 years. You notice that she is thin but without pallor. Her abdomen is soft and nontender, without palpable organomegaly or masses. Results of a digital rectal examination are normal. Complete blood cell count

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(CBC) and erythrocyte sedimentation rate (ESR) results are normal. While you suspect irritable bowel syndrome (IBS), are the symptoms convincing enough to you (and the patient) that no further investigation is necessary?

WHY IS THE CLINICAL EXAMINATION IMPORTANT?

Patients frequently experience lower gastrointestinal tract symptoms, such as lower abdominal pain or discomfort, change in bowel habit, passage of blood or mucus per rectum, or a sensation of incomplete rectal emptying, with approximately 50% of the general population reporting 1 or more of these symptoms.[1] This high prevalence means that, over a lifetime, these symptoms are experienced by everyone. When patients present to a physician for evaluation of lower gastrointestinal tract symptoms, the most common diagnosis is IBS, which is considered a functional, rather than organic, disorder, since no structural lesion accounts for the symptoms. The prevalence of IBS in the community is estimated to be between 5% and 20%.[2-4] IBS occurs more commonly in women[1,5] and younger individuals[4,6] and may be significantly associated with lower income,[7] although data are conflicting on socioeconomic status.[8]

IBS accounts for at least 3% of primary care visits,[9] with a high variability in referral rates to secondary care (between 15% and 60% in cross-sectional studies).[7,9-12] The reason for this variation is unclear but probably relates to different approaches to handling uncertainty in the underlying diagnosis. Lower gastrointestinal tract symptoms are usually attributable to IBS or to other functional disorders of the gastrointestinal tract, but occasionally they are the presentation of serious underlying organic pathology, most commonly inflammatory bowel disease (Crohn disease and ulcerative colitis) and colorectal carcinoma.[13] Diverticulosis is a structural abnormality commonly encountered during investigation of lower gastrointestinal tract symptoms, but the prevalence of this condition is also high in asymptomatic individuals.[14,15] Some gastroenterologists would therefore not consider diverticulosis an organic disease. The challenge for the primary care physician confronted with a patient who has lower gastrointestinal tract symptoms is to distinguish between the majority of patients who have IBS vs the minority who have an organic disease. Studies have shown that most patients with IBS are diagnosed and managed in primary care,[16] but concern that organic pathology may have been missed is a major problem for clinicians.[17]

Diagnostic criteria have been developed in an attempt to better identify patients with a high likelihood of having IBS. Manning et al[18] were the first to outline symptom-based criteria that suggested a diagnosis of IBS without the need for further investigation. Since the publication of the Manning criteria, other diagnostic criteria or scoring systems have been proposed (TABLE 1). The Kruis scoring system was reported in 1984[19] and is based on a combination of presence as well as duration of symptoms, negative physical examination findings, and normal laboratory investigation results. The Rome criteria were described in 1990.[20] The rationale for the development of these criteria was to reduce ordering of unnecessary diagnostic tests and to help standardize selection of patients for clinical trials of potential therapies for

Table 1. Existing Diagnostic Criteria and Statistical Models for the Diagnosis of Irritable Bowel Syndrome

Criteria or Model	Symptoms, Signs, and Laboratory Investigations Included in Criteria or Model	Symptom Duration Required
Manning et al,[18] 1978[a]	Abdominal pain relieved by defecation More frequent stools with onset of pain Looser stools with onset of pain Passage of mucus per rectum Feeling of incomplete emptying Patient-reported visible abdominal distension	None
Kruis et al,[19] 1984[b]	Symptoms (reported by the patient using a form): Abdominal pain, flatulence, or bowel irregularity Description of abdominal pain as "burning, cutting, very strong, terrible, feeling of pressure, dull, boring, or 'not so bad' " Alternating constipation and diarrhea Signs (each determined by the physician): Abnormal physical findings and/or history pathognomonic for any diagnosis other than IBS Erythrocyte sedimentation rate >20 mm/2h Leukocytosis >10 000 cells/μL Anemia (hemoglobin <12 g/dL for females or <14 g/dL for males) Impression by the physician that the patient's history suggests blood in the stools	>2 y
Rome I,[20] 1990	Abdominal pain or discomfort relieved with defecation or associated with a change in stool frequency or consistency, plus ≥2 of the following on at least 25% of occasions or days: Altered stool frequency Altered stool form Altered stool passage Passage of mucus per rectum Bloating or distension	≥3 mo
Rome II,[23] 1999	Abdominal discomfort or pain that has 2 of 3 features: Relieved with defecation Onset associated with a change in frequency of stool Onset associated with a change in form of stool	≥12 wk (need not be consecutive) in last 1 y
Rome III,[22] 2006	Recurrent abdominal pain or discomfort ≥3 d per mo in the last 3 mo associated with 2 or more of the following: Improvement with defecation Onset associated with a change in frequency of stool Onset associated with a change in form of stool	Symptom onset ≥6 mo prior to diagnosis

Abbreviation: IBS, irritable bowel syndrome.
[a] A threshold of at least 3 positive items is the cutoff most commonly used to define IBS.
[b] A logistic regression model produces the probability of IBS.

functional disorders of the gastrointestinal tract.[21] From a research perspective, the Rome criteria have become increasingly important over the last 10 years and have been revised on 2 subsequent occasions to produce the Rome II and III criteria.[22,23] These have been developed by panels of experts informed by reviews of the literature.

It is argued that, while the Rome criteria are useful for selection of patients for clinical trials, they are less relevant to physicians in primary care, because they have been developed primarily by gastroenterologists in secondary or tertiary care. A consensus panel has suggested that existing diagnostic criteria are not sufficiently broad for use in primary care,[24] and a recent survey demonstrated that few primary care physicians were aware of, or had used, any of these criteria to diagnose IBS.[25] On the other hand, some primary care–based guidelines advocate the use of both the Manning and the Rome criteria.[26,27] A quantitative review of the various diagnostic criteria for IBS is useful for identifying the most relevant clinical findings. A greater understanding of lower gastrointestinal tract symptoms will help answer the question as to which referred patient will most likely have IBS, and therefore normal results from investigations of the gastrointestinal tract, as opposed to addressing the fundamental question of which patients the primary care physician should refer.

Anatomical/Physiological Origins of Symptoms and Signs

No known structural or anatomical lesion accounts for the symptoms of IBS. The pathophysiology of the condition is poorly understood, but it seems unlikely that a unique underlying mechanism explains all the symptoms. Proposed etiologies include altered gastrointestinal tract motility causing smooth muscle spasm and change in bowel habit,[28] visceral hypersensitivity and abnormalities of central pain processing leading to abdominal discomfort,[29,30] low-grade inflammation (eg, following acute gastroenteritis) increasing gut permeability,[31] and altered gut flora.[32] In most persons with IBS it is probable that a combination of some or all of these factors contribute to the disturbance in bowel habit and abdominal pain.

How to Elicit Symptoms and Signs

Symptoms. A basic approach to history-taking should include questions that address the presence and duration of symptoms, with particular attention to the site and nature of abdominal pain, any change in bowel habit or stool form (and its relation to pain), bloating or patient-reported visible abdominal distension, the passage of mucus per rectum, or the association of symptoms with menses. Patients with alarming features such as weight loss or rectal bleeding (fresh or altered blood) should be evaluated for nonfunctional causes such as inflammatory bowel disease or colorectal carcinoma and thus require urgent investigation. It is also important to elicit any family history of either of these conditions, because this is associated with at least a 2-fold risk of lower gastrointestinal tract malignancy compared with individuals without a family history.[33] Finally, numerous over-the-counter and prescribed medications, including nonsteroidal anti-inflammatory drugs, antidepressants, antibiotics, and antidiabetic agents such as metformin, can cause abdominal symptoms including pain and disturbances in bowel habit; the use of these should be recorded.

Signs. The physical examination should consist of a basic abdominal examination to identify any obvious abnormalities rather than to confirm a diagnosis of IBS, although a lack of physical findings may be reassuring to both physician and patient. The examination should commence with inspection of the abdomen for evidence of previous surgery, obvious visible distension, or mass. Before palpating the abdomen, the patient should be asked to identify the predominant site where pain is typically experienced, as well as if pain is currently present, because this will affect how the remainder of the physical examination is carried out. Palpation of the abdomen should begin with a general examination to rule out a palpable mass. This should be followed by a focused search for liver enlargement or splenomegaly, although this gives limited additional information in this situation.[34,35] Given the differential diagnosis of lower gastrointestinal tract symptoms and the possibility of underlying colorectal cancer, digital rectal examination to exclude a palpable rectal cancer is advisable.

METHODS

Search Strategy

The systematic review was performed according to the Cochrane Methods Group on Screening and Diagnostic Tests guidelines.[36] A search of the medical literature was conducted using MEDLINE (1950 to June 2008) and EMBASE (1980 to June 2008). Studies on lower gastrointestinal tract disease were identified with the terms *irritable bowel syndrome* and *functional diseases, colon* (both as Medical Subject Heading and free-text terms), and *IBS* and *functional* adj5 *bowel* (both as free-text terms). These studies were combined using the "OR" set operator with studies evaluating diagnostic criteria in lower gastrointestinal tract disease, identified using the terms *Kruis*, *Manning*, *Rome 1*, *Rome I*, *Rome 2*, *Rome II*, *Rome 3*, and *Rome III* (all as free-text terms).

The bibliographies of identified studies were used to perform a recursive search of the literature. Studies were required to report prospectively on unselected cohorts of adult (older than 16 years) patients with lower gastrointestinal tract symptoms who were attending for investigation (colonoscopy, barium enema, or computed tomographic colography); studies had to record symptoms prior to investigation. Studies that compared the accuracy of individual clinical findings, or combinations of findings, with the results from investigations of the lower gastrointestinal tract were eligible for inclusion (BOX 1).

Combinations of findings were analyzed in 2 ways. In the simplest approach, investigators created a check-

Box 1. Eligibility Criteria for Study Inclusion

Adult patients (more than 95% of participants aged >16 years) with lower gastrointestinal tract symptoms

Cross-sectional design (not case-control)

Patients not specially selected[a]

Lower gastrointestinal tract symptoms recorded[b]

Symptoms and diagnosis recorded prospectively

Patients undergo complete investigations of the lower gastrointestinal tract, with diagnosis recorded[c]

Symptoms and investigative diagnosis compared

≥50 Patients included

[a]Patients could be selected by age or by primary care physician's referral but not by other criteria (eg, only patients without rectal bleeding).
[b]This includes individual symptoms and combinations of findings as either diagnostic criteria or statistical models.
[c]Colonoscopy, barium enema, computed tomographic colography.

list of diagnostic criteria, and patients who exceeded a threshold for a certain number of findings were diagnosed as having IBS (Table 1). In a more complicated approach, investigators collected the results of many clinical findings and then developed statistical models to select out the independently useful items. These models generated a threshold score above which patients were considered to have IBS. For either approach, when a threshold is identified, the sensitivity, specificity, and likelihood ratios for the individual finding or combination of findings can be calculated. Greater confidence can be placed in the data when these thresholds are also validated prospectively by other researchers.

Articles were independently assessed by 2 researchers (A.C.F., P.M.) according to the prospectively defined eligibility criteria. Any disagreement between investigators was resolved by consensus. The quality of studies was evaluated similarly to that of other articles in the Rational Clinical Examination series, according to whether assessors were blinded, cases were consecutive, and sample sizes were adequate (we considered studies with sample sizes ≥200 to be sufficiently large); these factors have been shown to influence the outcome of diagnostic studies.[37] Data were extracted onto predesigned forms and checked by a second reviewer (P.M.).

Reference Standard

Organic lower gastrointestinal tract disease was defined as colorectal carcinoma, inflammatory bowel disease, microscopic colitis, diverticular disease, and colorectal adenoma by included studies. All other findings at colonoscopy, barium enema, or computed tomographic colography were classified as functional.

Statistical Analysis

The primary goal was to describe the performance of individual symptoms or combinations of findings (diagnostic criteria and statistical models) in evaluating IBS vs organic disease of the lower gastrointestinal tract. The sensitivity, specificity, positive likelihood ratio (LR), negative LR, and their 95% confidence intervals (CIs) were calculated for each symptom using Microsoft Excel, XP professional edition (Microsoft Corporation, Redmond, Washington) and checked using StatsDirect version 2.4.4 (StatsDirect Ltd, Cheshire, England). The same approach was used for combinations of findings. In the case of statistical models that generated a score, the cutoff point that gave the highest diagnostic odds ratio (positive LR/negative LR) for the diagnosis of IBS was chosen for analysis. Data were pooled using a random-effects model,[38] and StatsDirect was used to generate forest plots of sensitivities, specificities, and positive and negative LRs. Heterogeneity between studies was assessed using the χ^2 and I^2 statistics, with values greater than 50% indicating clinically important heterogeneity.[39]

RESULTS

The search strategy identified 16 079 studies, of which 17 were possibly relevant to the systematic review and retrieved (FIGURE 1).[18,19,40-54] There was good agreement between reviewers (88% agreement, $\kappa = 0.73$) when eligibility criteria were assessed, and 10 studies evaluating a total of 2355 patients were eligible for inclusion (TABLE 2), with a summary prevalence of IBS of 57% (95% CI, 45%-68%).[18,19,41,43-47,50,53] Of the 7 excluded studies, 5 did not provide extractable data,[48,49,51,52,54] 1 excluded patients at study entry on the basis of symptoms,[40] and 1 used the presence of nongastrointestinal symptoms to predict a diagnosis of IBS.[42]

Final diagnosis among all individuals with organic disease was provided by 9 of the included studies.[18,19,41,43-45,47,50,53] Some studies classified diverticulosis and colorectal adenomas as organic disease, even though these conditions may not cause symptoms. Four studies classed diverticular disease as an organic disease of the lower gastrointestinal tract,[41,45,47,53] though in 3 of the studies the proportion of individuals with organic disease who had diverticular disease was 15% or less (range, 5%-35%).[45,47,53] Four studies categorized individuals with colorectal adenoma as having organic disease,[19,41,44,45] though only 3 reported these data.[19,41,44] In 2 studies the proportion of individuals with organic disease who had colorectal adenoma was between 3% and 5%,[19,44] while in the third study it was 33%.[41]

Prevalence of IBS

The prevalence of IBS in the eligible studies varied from 21% to 78%. Only 1 study was partly based in primary care, and this reported a prevalence of IBS of 60% among patients with lower gastrointestinal tract symptoms,[41] compared with a pooled prevalence of 57% in the 9 secondary care–based studies. Six of the studies reported prevalence of IBS according to sex.[19,41,43-45,50] The pooled prevalence of IBS in males was 42% (95% CI, 26%-60%), compared

with 57% (95% CI, 38%-75%) in females. Only 1 study reported a higher prevalence of IBS in males (74%) compared with females (71%).[50] Four studies compared mean age between patients with IBS and those with organic disease,[41,43,44,50] and this was lower in those with IBS in all 4 cases, though only 1 study stated that this was statistically significant.[41]

Accuracy of Individual Symptoms

Seven individual symptom items were collected as part of the statistical models or diagnostic criteria common to at least 3 of the studies (TABLE 3). These were the presence of lower abdominal pain, passage of mucus per rectum, feel-

Figure 1. Assessment of Studies Identified in Systematic Review

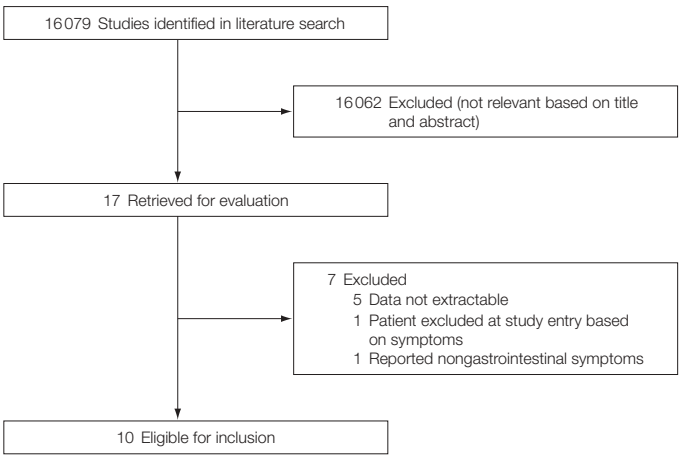


Table 2. Characteristics of Included Studies

Source	Country	Patients, No.	Reference Standard	IBS Prevalence, No. (%)	Criteria or Model Used	Patient Referral for Lower Gastrointestinal Tract Symptoms	Setting	Assessors Blinded	Quality Level[a]
Manning et al,[18] 1978	England	65	Colonoscopy or barium enema	32 (49)	Manning criteria	To outpatient clinic, unclear who referred	Gastroenterology and surgical clinic in a single hospital	Yes	3
Kruis et al,[19] 1984	Germany	317	Colonoscopy or barium enema	108 (34)	Kruis model	To outpatient clinic by external physician	Internal medicine clinic in a single hospital	Yes	1
Mazumdar et al,[47] 1988	India	75	Colonoscopy	55 (73)	Statistical model[b]	To outpatient clinic, unclear who referred	Gastroenterology clinic in a single hospital	Yes	2
Bellentani et al,[41] 1990	Italy	254	Colonoscopy or barium enema	152 (60)	Statistical model[c]	Consulted PCP or referred to outpatient clinic	14 PCPs and a gastroenterology clinic in a single hospital	Yes	1
Frigerio et al,[44] 1992	Italy	253	Colonoscopy	52 (21)	Statistical model[c]	To outpatient clinic by PCP	Gastroenterology clinic in a single hospital	Yes	1
Jeong et al,[46] 1993	Korea	74	Colonoscopy or barium enema	58 (78)	Manning criteria	To outpatient clinic, unclear who referred	Internal medicine clinic in a single hospital	Yes	2
Rao et al,[50] 1993	India	88	Colonoscopy or barium enema	65 (74)	Manning criteria	To outpatient clinic, unclear who referred	Gastroenterology clinic in a single hospital	Unclear	4
Doğan and Unal,[43] 1996	Turkey	347	Colonoscopy or barium enema	165 (48)	Manning criteria and Kruis model	To outpatient clinic, unclear who referred	Gastroenterology clinic and internal medicine clinic in 2 hospitals	Yes	3
Tibble et al,[53] 2002	England	602	Colonoscopy or barium enema	339 (56)	Rome I criteria	To outpatient clinic by PCP	Gastroenterology clinic in a single hospital	Yes	1
Hammer et al,[45] 2004	Australia	280	Colonoscopy	214 (76)	Statistical model[b]	To outpatient clinic by PCP primarily, but also by surgeons and internists	Gastroenterology clinic in a single hospital	Yes	1

Abbreviation: PCP, primary care physician.
[a] Quality levels are consistent with those used in The Rational Clinical Examination series, with level 1 indicating the highest quality (independent blinded comparison of test with a valid criterion standard in a large number [≥200] of consecutive patients). Level 2 studies were similar to level 1 studies but enrolled <200 patients. Level 3 studies also used an independent blinded comparison of the findings with a valid criterion standard but enrolled nonconsecutive patients. Level 4 studies used a nonindependent comparison of a test with a valid criterion standard among a "convenience" sample of patients believed to have the condition in question.
[b] Derived from patients enrolled in the study.
[c] Compared Kruis model with a model derived from patients enrolled in the study.

ing of incomplete evacuation, passage of looser stools at commencement of abdominal pain, passage of more frequent stools at commencement of abdominal pain, abdominal pain relieved by defecation, and patient-reported visible abdominal distension. Lower abdominal pain had a high sensitivity but very low specificity for the diagnosis of IBS and also provided the best negative LR. The 3 other symptom items relating to abdominal pain had better specificity but poorer sensitivity and yielded the best positive LRs, though no symptom item had a positive LR greater than 2.2.

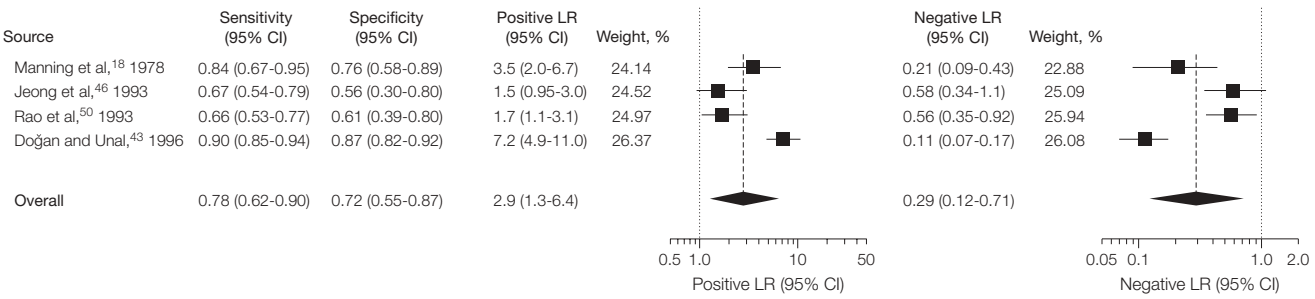
Other items such as the passage of mucus per rectum and patient-reported visible abdominal distension failed to demonstrate good discriminatory value between IBS and organic disease. Individual symptoms are therefore insufficiently accurate to diagnose IBS. This suggests that combinations of findings in the form of a general clinical opinion, diagnostic criteria, or statistical models generating a score that indicates the probability of IBS may be more accurate.

Table 3. Sensitivity, Specificity, and Positive and Negative Likelihood Ratios (LRs) of Individual Symptoms for the Diagnosis of Irritable Bowel Syndrome

Symptom and Source	Symptom Frequency, No./Total (%)	Sensitivity (95% CI)	Specificity (95% CI)	LR (95% CI)	
				Positive	Negative
Lower abdominal pain					
Manning et al[18]	61/65 (94)	0.97 (0.84-1.0)	0.09 (0.02-0.24)	1.1 (0.92-1.3)	0.34 (0.05-2.3)
Kruis et al[19]	218/317 (69)	0.96 (0.91-0.99)	0.45 (0.39-0.52)	1.8 (1.6-2.0)	0.08 (0.03-0.20)
Frigerio et al[44]	174/253 (69)	0.87 (0.74-0.94)	0.36 (0.29-0.43)	1.4 (1.1-1.6)	0.38 (0.18-0.73)
Hammer et al[45]	215/280 (77)	0.80 (0.74-0.85)	0.33 (0.22-0.46)	1.2 (1.0-1.5)	0.60 (0.40-0.94)
Summary measure		0.90 (0.79-0.97)	0.32 (0.21-0.44)	1.3 (1.1-1.7)	0.29 (0.12-0.72)
Passage of mucus per rectum					
Manning et al[18]	22/65 (34)	0.47 (0.29-0.65)	0.79 (0.61-0.91)	2.2 (1.1-4.7)	0.67 (0.45-0.96)
Jeong et al[46]	14/74 (19)	0.19 (0.10-0.31)	0.81 (0.54-0.96)	1.0 (0.36-3.2)	1.0 (0.80-1.4)
Rao et al[50]	66/88 (75)	0.78 (0.67-0.88)	0.35 (0.16-0.57)	1.2 (0.92-1.8)	0.62 (0.31-1.3)
Hammer et al[45]	99/280 (35)	0.36 (0.29-0.42)	0.65 (0.52-0.76)	1.0 (0.71-1.5)	0.99 (0.82-1.2)
Summary measure		0.45 (0.22-0.69)	0.65 (0.47-0.81)	1.2 (0.93-1.6)	0.88 (0.72-1.1)
Feeling of incomplete evacuation					
Manning et al[18]	30/65 (46)	0.59 (0.41-0.76)	0.67 (0.48-0.82)	1.8 (1.0-3.2)	0.61 (0.37-0.97)
Jeong et al[46]	56/74 (76)	0.78 (0.65-0.87)	0.31 (0.11-0.59)	1.1 (0.85-1.8)	0.72 (0.33-1.8)
Rao et al[50]	70/88 (80)	0.85 (0.74-0.92)	0.35 (0.16-0.57)	1.3 (1.0-1.9)	0.44 (0.21-0.99)
Hammer et al[45]	193/280 (69)	0.72 (0.66-0.78)	0.42 (0.30-0.55)	1.3 (1.0-1.6)	0.65 (0.46-0.94)
Summary measure		0.74 (0.66-0.82)	0.45 (0.31-0.60)	1.3 (1.1-1.5)	0.62 (0.48-0.80)
Looser stools at onset of pain					
Manning et al[18]	33/65 (51)	0.81 (0.63-0.93)	0.73 (0.54-0.88)	3.0 (1.7-5.8)	0.26 (0.12-0.52)
Jeong et al[46]	40/74 (54)	0.59 (0.45-0.71)	0.63 (0.35-0.85)	1.6 (0.89-3.3)	0.66 (0.42-1.2)
Rao et al[50]	34/88 (39)	0.48 (0.35-0.60)	0.87 (0.66-0.97)	3.7 (1.4-11.0)	0.60 (0.45-0.82)
Hammer et al[45]	127/280 (45)	0.50 (0.43-0.57)	0.70 (0.57-0.80)	1.7 (1.2-2.5)	0.72 (0.59-0.90)
Summary measure		0.58 (0.46-0.69)	0.73 (0.64-0.81)	2.1 (1.4-3.0)	0.59 (0.45-0.79)
More frequent stools at onset of pain					
Manning et al[18]	32/65 (49)	0.74 (0.55-0.88)	0.70 (0.51-0.85)	2.5 (1.5-4.6)	0.37 (0.19-0.67)
Jeong et al[46]	38/74 (51)	0.57 (0.43-0.70)	0.69 (0.41-0.89)	1.8 (0.96-4.1)	0.63 (0.41-1.0)
Rao et al[50]	25/88 (28)	0.35 (0.24-0.48)	0.91 (0.72-0.99)	4.1 (1.3-15.0)	0.71 (0.56-0.92)
Hammer et al[45]	134/280 (48)	0.51 (0.44-0.58)	0.62 (0.49-0.74)	1.3 (0.98-1.9)	0.79 (0.63-1.0)
Summary measure		0.53 (0.41-0.66)	0.72 (0.58-0.84)	1.9 (1.2-2.9)	0.67 (0.54-0.84)
Pain relieved by defecation					
Manning et al[18]	31/65 (48)	0.71 (0.52-0.86)	0.70 (0.51-0.85)	2.4 (1.4-4.4)	0.41 (0.22-0.72)
Jeong et al[46]	39/74 (53)	0.59 (0.45-0.71)	0.69 (0.41-0.89)	1.9 (1.0-4.2)	0.60 (0.39-1.0)
Rao et al[50]	53/88 (60)	0.66 (0.53-0.77)	0.57 (0.34-0.77)	1.5 (0.99-2.6)	0.60 (0.37-1.0)
Hammer et al[45]	140/280 (50)	0.55 (0.48-0.62)	0.67 (0.54-0.78)	1.7 (1.2-2.4)	0.67 (0.54-0.86)
Summary measure		0.60 (0.54-0.67)	0.66 (0.57-0.73)	1.8 (1.4-2.2)	0.62 (0.52-0.75)
Patient-reported visible abdominal distension					
Manning et al[18]	26/65 (40)	0.59 (0.41-0.76)	0.79 (0.61-0.91)	2.8 (1.4-5.8)	0.52 (0.32-0.78)
Jeong et al[46]	29/74 (39)	0.40 (0.27-0.53)	0.63 (0.35-0.85)	1.1 (0.57-2.3)	0.97 (0.67-1.6)
Rao et al[50]	17/88 (19)	0.22 (0.12-0.33)	0.87 (0.66-0.97)	1.7 (0.59-5.1)	0.90 (0.75-1.2)
Summary measure		0.39 (0.20-0.60)	0.77 (0.64-0.88)	1.7 (0.90-3.2)	0.79 (0.56-1.1)

Abbreviation: CI, confidence interval.

Figure 2. Summary Random-Effects Meta-analyses of the Manning Criteria for Diagnosis of Irritable Bowel Syndrome



Presence of ≥3 criteria considered positive. I^2=90% and $P<.001$ for both analyses. CI indicates confidence interval; LR, likelihood ratio.

Accuracy of a High Clinical Suspicion of Non–IBS-Related Disease From the History and Physical Examination

Kruis et al[19] included the item "abnormal physical findings and/or history pathognomonic for any diagnosis other than irritable bowel syndrome." This represents a clinical gestalt that the patient has organic pathology that explains the symptoms. Examples of such findings were not given by the authors, but the item was statistically significant in a logistic regression model. However, because the item was reported in a logistic regression model, its impact can be evaluated only in the context of the other included variables.

The overall prevalence of patients with IBS and no suggestion of organic pathology in the study was 34%. When a patient endorsed no other symptom, the presence of an abnormal physical finding, history pathognomonic for any diagnosis other than IBS, or both lowered the predicted probability of IBS to approximately 2%. If there were no pathognomonic findings, the predicted probability of IBS was approximately 71%. The LR for pathognomonic findings can be back-calculated from the prevalence of disease and the predicted probability. The absence of pathognomonic findings for other conditions had an LR of 4.8 (95% CI, 3.7-6.3) and increased the likelihood of IBS. In contrast, the presence of pathognomonic findings was even more important and made IBS much less likely, with an LR of 0.04 (95% CI, 0.02-0.12).

Table 4. Combinations of Findings for the Diagnosis of Irritable Bowel Syndrome—Rome I Criteria and Statistical Models Other Than Kruis Model[a]

Source	Sensitivity (95% CI)	Specificity (95% CI)	LR (95% CI) Positive	LR (95% CI) Negative
Diagnostic criteria (Rome I)				
Tibble et al,[53] 2002	0.71 (0.66-0.76)	0.85 (0.80-0.89)	4.8 (3.6-6.5)	0.34 (0.29-0.41)
Statistical models (other than Kruis)				
Mazumdar et al,[47] 1988	0.91 (0.80-0.97)	1.0 (0.83-1.0)	38 (4.7-362)	0.10 (0.04-0.21)
Bellentani et al,[41] 1990	0.76 (0.68-0.82)	0.82 (0.74-0.89)	4.3 (2.9-6.7)	0.30 (0.22-0.39)
Frigerio et al,[44] 1992	0.69 (0.55-0.81)	0.91 (0.86-0.95)	7.7 (4.8-12)	0.34 (0.22-0.49)
Hammer et al,[45] 2004	0.96 (0.93-0.98)	0.53 (0.40-0.65)	2.1 (1.6-2.7)	0.07 (0.03-0.14)

Abbreviations: CI, confidence interval; LR, likelihood ratio.
[a]The Rome criteria evaluations were based on summing the number of findings. A positive test result exceeded the threshold value for number of findings. The remaining studies evaluated statistical models that produced a threshold score that could be translated to a probability of irritable bowel syndrome. In either case, the threshold value was used to calculate the sensitivity, specificity, and LRs.

Accuracy of Combinations of Findings

Of the 10 studies included, 5 reported the accuracy of diagnostic criteria for distinguishing IBS from organic disease of the lower gastrointestinal tract in 1176 patients.[18,43,46,50,53] Four of these studies assessed the accuracy of the presence of 3 or more of the Manning criteria in 574 patients, with a summary prevalence of IBS of 62% (95% CI, 45%-78%).[18,43,46,50] Physicians making assessments were blinded to questionnaire data in 3 studies,[18,43,46] but in the other study blinding was unclear.[50] Using a threshold of at least 3 findings, the Manning criteria performed best at diagnosing IBS in the original study,[18] and in the validation conducted by Doğan and Unal,[43] who found a positive LR of 7.2 (95% CI, 4.9-11.0) and a negative LR of 0.11 (95% CI, 0.07-0.17). However, the Manning criteria performed poorly in the remaining 2 validation studies, in which positive LRs were just greater than 1.0 and negative LRs greater than 0.50.[46,50] Overall, the summary LRs when at least 3 Manning criteria were present nearly tripled the likelihood of IBS (LR, 2.9; 95% CI, 1.3-6.4; I^2=90%; $P<.001$), while the presence of fewer than 3 Manning criteria made IBS less likely (LR, 0.29; 95% CI, 0.12-0.71; I^2=90%; $P<.001$) (FIGURE 2). We conducted a sensitivity analysis excluding the original validation study[18] to assess the impact this had on the accuracy of the Manning criteria. The summary LR for the presence of at least 3 Manning criteria was slightly lower (LR, 2.7; 95% CI, 0.92-7.8; I^2=93%; $P<.001$), and the summary LR for the presence of fewer than 3 increased (LR, 0.33; 95% CI, 0.11-1.0; I^2=93%; $P<.001$). The difference

between the positive and negative LRs when the original validation study was included in or excluded from the analysis were not statistically significant ($P=.91$ and $P=.86$, respectively).

The fifth study reporting on the accuracy of diagnostic criteria evaluated the Rome I criteria in 602 patients, 339 (56%) of whom had IBS (TABLE 4).[53] Clinicians were blinded to questionnaire data. The positive LR of the Rome I criteria was 4.8 (95% CI, 3.6-6.5), and the negative LR was 0.34 (95% CI, 0.29-0.41). No identified eligible studies assessed the accuracy of either the Rome II or the Rome III criteria in distinguishing IBS from organic pathology of the lower gastrointestinal tract.

Six of the 10 eligible studies evaluated the accuracy of a statistical model in diagnosing IBS in 1526 patients.[19,41,43-45,47] The summary prevalence of IBS in these studies was 52% (95% CI, 34%-69%). Two of the studies validated the Kruis scoring system,[19,43] 2 developed statistical models derived from patients enrolled in the study,[45,47] and 2 compared the Kruis scoring system with a model developed from the patients enrolled in the study (Table 2).[41,44] Physicians making assessments were blinded to questionnaire data in all 6 studies.

Kruis et al[19] described a model that included a combination of symptoms, physical findings, and laboratory results (Table 1 and TABLE 5). While the presence of blood in the stool (determined by the physician taking the patient's history) was not statistically significant, the authors retained that variable and created a recalibrated score (Table 5, column 3). Each item was assigned a coefficient, and all items were summed to obtain a total score. The authors proposed a score of at least 44 as the optimum cutoff for diagnosing IBS. For example, a patient with duration of symptoms greater than 2 years (score=16), self-reported features of the pain using the descriptors in Table 1 (score=23), and alternating constipation and diarrhea (score=14) has a total score of 53, which exceeds the threshold value of 44 and makes IBS the likely diagnosis.

Since all of the patients in the study by Kruis et al[19] had abdominal pain, flatulence, and a change in bowel habit, we reanalyzed their logistic regression model by forcing these variables into the constant term (Table 5, column 2). The probability of IBS can be calculated by summing up the coefficients for these findings and adding them to the constant term (0.93). The probability of disease is then derived from the logistic function, where estimated probability of IBS = exp(score)/[1 + exp(score)]. When only abdominal pain, flatulence, and a change in bowel habit are present, the probability of IBS is 72%. However, if in addition the symptom duration is greater than 2 years, the features of pain are consistent with those described in Table 1, and alternating diarrhea and constipation are also present, the probability of IBS is almost 100%.

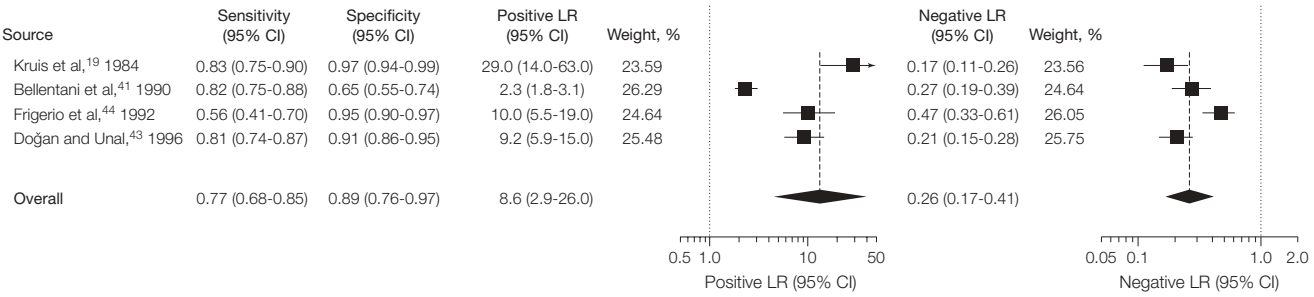
The Kruis scoring system was used in 3 other studies. Thus, between the original report of the Kruis scoring system[19] and the 3 validation studies,[41,43,44] 1171 patients were evaluated, with a summary prevalence of IBS of 40% (95% CI, 25%-56%). Three of the studies showed high LRs for Kruis scores of at least 44, suggesting utility for making the diagnosis of IBS. The summary LR for a Kruis score of at least 44 was 8.6 (95% CI, 2.9-26.0; $I^2=95\%$; $P<.001$), while a score less than 44 had a summary LR of 0.26 (95% CI, 0.17-0.41; $I^2=85\%$; $P<.001$)

Table 5. Symptoms, Physical Findings, and Laboratory Results in Kruis Model

Finding	Coefficient[a]	Score
Findings self-reported on form filled out by patient		
Abdominal pain, flatulence, or bowel irregularity	NA[b]	34
Duration of symptoms >2 y	1.644	16
Description of abdominal pain as "burning, cutting, very strong, terrible, feeling of pressure, dull, boring, or 'not so bad' "	2.31	23
Alternating constipation and diarrhea	1.466	14
Findings determined by physician and recorded on checklist		
Abnormal physical findings and/or history pathognomonic for any diagnosis other than IBS	−4.692	−47
Erythrocyte sedimentation rate >10 mm/h[c]	−1.264	−13
Leukocytosis >10 000 cells/μL	−4.908	−50
Anemia (hemoglobin <12 g/dL for females or <14 g/dL for males)	−9.768	−98
History of blood in stool	NA[d]	−98
Score	0.93 + sum of all findings present	Sum of the transformed value
Result	Probability of IBS = exp(score)/[1 + exp(score)]	Positive score for IBS ≥44 points

Abbreviations: IBS, irritable bowel syndrome; NA, not available.
[a] Coefficients modified from Kruis et al.[19]
[b] The original logistic regression model reported included a term for row 1, but all patients had to have this finding. Thus, the coefficient for the finding is included in the constant value (0.93) for calculating the score.
[c] The original study reported a rate of >20 mm/2 hours. Most measurements of erythrocyte sedimentation rate are now performed over a 1-hour period, so half the value was assumed.
[d] The history of blood in the stool was not independently significant in the logistic model. The authors forced the result into a final model for calculating the score shown in column 3.

Figure 3. Summary Random-Effects Meta-analyses of the Kruis Scoring System for Diagnosis of Irritable Bowel Syndrome



Score ≥44 considered positive. For positive likelihood ratio, I^2=95% and $P<.001$; for negative likelihood ratio, I^2=85% and $P<.001$. CI indicates confidence interval; LR, likelihood ratio.

(FIGURE 3). A sensitivity analysis of the Kruis scoring system excluding the original validation study[19] provided an LR of 5.9 (95% CI, 2.0-17.0; I^2=94.5%; $P<.001$) for scores of 44 or greater and an LR for a score less than 44 of 0.30 (95% CI, 0.18-0.49; I^2=86%; $P=.001$). Again, the differences between positive and negative LRs were not statistically significant ($P=.63$ and $P=.67$, respectively).

Frigerio et al[44] developed a modified version of the Kruis scoring system, differing in the threshold hemoglobin level applied to define anemia (11 g/dL for females, 13 g/dL for males). The other 3 statistical models differed greatly from the Kruis scoring system (BOX 2). Rectal bleeding was common to all 4 models and abdominal pain to 3 of the models. Of the 4 other statistical models reported, only that of Mazumdar et al[47] gave better positive and negative LRs, due to a high sensitivity and a specificity of 100%. The model of Hammer et al[45] gave a better negative LR as a result of a very high sensitivity for the diagnosis of IBS.

SCENARIO RESOLUTION

Recalling the original clinical scenario and using the data from the studies evaluated in this review, the symptoms, taken individually, are not particularly helpful. Since the patient has only 1 of the Manning criteria clearly present (incomplete emptying), the likelihood of IBS decreases (LR, 0.29). While she meets the Rome III criteria for IBS (has 2 of the 3 findings, with fluctuation in frequency and form of stool), these have not been subjected to rigorous testing, so the LRs are unknown. While it seems unlikely that she has serious underlying pathology, a more detailed history should be obtained, focusing more on the items from the Kruis score, such as having her describe the pain more completely and determining if she has constipation alternating with diarrhea. The lack of physical findings is reassuring, and the normal CBC and ESR results provide additional evidence to support IBS rather than organic pathology. If a more detailed history were to provide further clinical information and produce a Kruis score of 44 or greater, then the likelihood of IBS would be greatly increased (positive LR, 8.6). The Kruis model is complex for use in routine clinical practice but indicates that a reasonably confident diagnosis of IBS can be made if the symptoms of abdominal pain and change in bowel habit have been present for some time, the clinician does not strongly suspect organic disease, and the CBC and ESR results are normal.

The patient's age alone (younger than 50 years) does not suggest a need for colonoscopy to exclude malignancy. Furthermore, she specifically denies weight loss, a recent change in bowel habit, or rectal bleeding, all of which are thought to predict a diagnosis of colorectal cancer, although their utility has been shown to be suboptimal.[55] Nor does she report diarrhea, which also would require investigations of the lower gastrointestinal tract due to a higher a priori concern of organic disease. She does have a family history of colorectal carcinoma. A patient's report of a positive family history of colon cancer is reliable,[56] but this patient's young age makes this diagnosis very unlikely, and she does not yet meet criteria for screening.[57] To meet the patient's needs and to address any specific concerns that may have led her to visit a physician as a result of these symptoms, one should direct the interview to get a better understanding of the patient's perceptions about the cause of her symptoms and her expectations about the medical evaluation.

THE BOTTOM LINE

The absence of abdominal pain reduces the likelihood of IBS as the explanation of lower gastrointestinal tract symptoms. Abdominal pain is built into most definitions of IBS, thereby maximizing sensitivity and optimizing the negative LR. Other symptoms related to abdominal pain have better positive LRs than symptoms such as passage of mucus per rectum and feeling of incomplete evacuation, owing to their lower frequency in individuals with organic disease, and thus higher specificity for the diagnosis of IBS. However, individual symptoms are poor at distinguishing IBS from organic disease of the lower gastrointestinal tract, so

Box 2. Items Incorporated in Statistical Models Differing From the Kruis Scoring System

Bellentani et al[41] Model

Patient-reported visible abdominal distension
First-degree relative with "colitis"
Feeling of distension
Flatulence
Irregular bowel habit
Increased erythrocyte sedimentation rate
Blood in the stool
Age >45 y
Increased white cell count
Fever (temperature between 37°C and 38°C)
First-degree relative with "neoplastic disease"

Hammer et al[45] Model

Age >50 y
Female sex
Blood on toilet paper
Severe pain
Pain more than 6 times in the last year
Radiating pain
Pain with looser bowel movements
Diarrhea
Reflux

Mazumdar et al[47] Model

Abdominal pain
Early morning abdominal pain
Postprandial abdominal pain
Poorly localized pain
Food aggravating pain
Pain relieved by passage of flatus/defecation
Nocturnal diarrhea
Alternating constipation/diarrhea
Repeated attempts to pass stool
Straining at defecation
Feeling of incomplete evacuation
Food precipitating bowel movement
Stress factor
Excess mucus in the stool
Blood in stool
Blood uniformly mixed with stool
Blood after stool
Gas bloating/belching
Borborygmi

combinations of findings are required. The accuracy of nocturnal diarrhea, which is often used by physicians in everyday clinical practice in distinguishing between organic disease and IBS, was not reported in any of the eligible studies.

Diagnostic criteria have become the recommended method for making a positive diagnosis of IBS in both primary and secondary care, rather than exhaustive investigation to exclude an underlying organic cause. This approach is endorsed by both the American College of Gastroenterology and the British Society of Gastroenterology.[58,59] It is perhaps surprising that so few studies examined the utility of the various published diagnostic criteria in differentiating IBS from organic disease.

We found only 4 studies that reported on the accuracy of the Manning criteria,[18,43,46,50] despite these first being described 30 years ago. The use of a set number of Manning criteria as a cutoff to define the presence of IBS was never validated as part of the original study, and all the studies identified in this systematic review used a varying number of the symptoms that constitute the Manning criteria to diagnose the condition. We used the presence of at least 3 Manning criteria as the threshold to define IBS in our analysis because all of the studies reported on the accuracy of this particular number. Accuracy of the Manning criteria in distinguishing between organic disease and IBS was modest and was reduced when the original validation study was excluded from the analysis, though this difference was not statistically significant.

We found only 1 eligible study that reported on the Rome I criteria,[53] and no studies that reported on the Rome II or Rome III criteria. Two studies that we excluded examined the accuracy of the Rome II criteria,[40,54] but in one the organic disease group was highly selected and consisted of only 6 patients[40] (and any inferences drawn from these data would therefore have been limited); in the other, data were not extractable.[54] While the Rome III criteria were described only recently,[22] the Rome II criteria were published 9 years ago,[23] so it is disappointing to find that their utility has yet to be analyzed prospectively. It is also of some concern, as the use of these criteria has in recent years become universally accepted to the exclusion of other diagnostic criteria in the research arena.

Statistical models, which use a combination of patient demographics, results of laboratory investigations, items from the clinical history and physical examination, and symptom items from questionnaires to calculate the probability of IBS, might be expected to have greater accuracy than diagnostic criteria. Our analysis suggests this is the case, but there are insufficient data to be certain, and no statistically significant difference in likelihood ratios exists between the diagnostic criteria and the statistical models. This greater accuracy may be because statistical models more accurately reflect usual clinical practice, because physicians often combine other items from the clinical history, such as patient age and any relevant family history, with the patient's symptoms as part of the diagnostic process. However, this observation could also be the result of the fact that the diagnostic criteria were selected and defined a priori. This is in contrast to the statistical models, which often were validated as an integral part of the study process, with the final model being chosen on the basis that it best fit the study data. Such models require validation in populations other than the one used to generate the model, and the Kruis scoring system has been prospectively validated in 3 studies[41,43,44] with no statistically significant difference in LRs when only

these 3 studies were included in the analysis.

Symptom duration longer than 2 years, one of the variables in the Kruis statistical model, probably explains some of the model's accuracy, because this is likely to be a highly efficient way of ruling out serious underlying pathology. However, the patient's description of pain was a more significant symptom variable in the model. The variables collected by the physician were more important than those reported by the patient, strengthening the argument for obtaining a CBC (and perhaps an ESR). The combination of 4 items self-reported by the patient with a basic history, physical examination, and simple laboratory tests (a CBC and ESR) performed by the physician holds significant appeal for simplifying the diagnosis of IBS. Unfortunately, several of the symptom items from the Kruis scoring system, such as irregularities of bowel habit and alternating constipation and diarrhea, are not clearly defined; others, such as the description of abdominal pain and stool properties, are open to numerous interpretations and therefore may not be reproducible between individual patients. Compared with the Manning criteria, the only other combination of findings evaluated in more than 1 study, the Kruis scoring system had broader CIs for the positive LR but narrower CIs for the negative LR. The other statistical models seem complicated for routine clinical use, because they contain far more variables. In addition, they have not been prospectively and independently validated.

A major limitation of the studies we identified is that they were conducted in patients referred for investigations of the gastrointestinal tract, making spectrum and referral bias highly likely. Indeed, the Kruis score performed least well in the study conducted in primary care by Bellentani et al.[41] Their validation of the Kruis scoring system (positive LR, 2.3; 95% CI, 1.8-3.1; negative LR, 0.27; 95% CI, 0.19-0.39) provides the most applicable data for the patient presenting to a physician in primary care with lower gastrointestinal tract symptoms. Overrepresentation of organic disease, a marker for spectrum bias, appears in many of the included studies, with approximately 40% of individuals found to have "organic disease." This is a higher prevalence than would be expected in patients presenting in primary care.

Some studies classified individuals with diverticular disease, colorectal adenomas, or both as having organic disease,[19,41,44,45,47,53] so the extent of spectrum bias is not as great as it first appears. Colorectal adenomas are unlikely to be responsible for lower gastrointestinal tract symptoms in individuals undergoing investigation. Diverticulosis is an organic disease in that it is a structural abnormality of an aging colon, but it is often asymptomatic. However, diverticulitis is an acute inflammatory condition that can cause symptoms both at initial presentation and subsequently, due to stricture and abscess formation or following postinflammatory modulation of neuromuscular function.[60,61] Unfortunately, only 1 of the included studies made a distinction between diverticulitis and diverticulosis.[44]

These issues highlight another problem with evaluating the accuracy of clinical features in diagnosing IBS—namely, the lack of a reference standard for this disorder. An analysis excluding individuals with adenoma or diverticular disease from the organic disease category was not possible due to the reporting of data in the original studies. While this may have led to the misclassification of individuals with IBS as having organic disease, in most studies the proportion of individuals with organic disease who had either of these conditions was small, and this issue is therefore unlikely to have had a major impact on our findings. However, one study reporting on the Kruis scoring system classified larger numbers of individuals with either diverticular disease or colorectal adenoma as having organic disease,[41] so this may have led to underestimation of the model's accuracy when results were pooled.

Only 3 studies examined stool specimens for evidence of infection. One study examined specimens in all patients[47] and reported 2 cases of amoebic colitis; the other 2 studies examined specimens only in patients presenting with diarrhea.[19,53] One of these studies found 9 cases of infective diarrhea.[53] Because this test was not performed routinely in all studies, the possibility exists that some individuals classified as having IBS—in the absence of a structural cause for their symptoms—may have had underlying chronic infections of the gastrointestinal tract. Again, the numbers involved are probably small, so any misclassification is unlikely to have had a significant effect on our results. None of the studies routinely tested individuals for celiac disease with serology or distal duodenal biopsy, so the possibility also exists that this diagnosis was missed in some of those labeled as having IBS. However, current guidelines for the management of IBS do not recommend routine screening for celiac disease in this situation.[58,59]

A final problem with the data we identified is the statistically significant heterogeneity between study results. The small number of studies identified meant that we could not perform sensitivity analyses to explore possible reasons for the variability. Nonetheless, the summary measures are useful in describing the confidence that primary care clinicians can have in individual clinical features and in combinations of findings.

The Manning and Rome criteria may not be used explicitly by most primary care clinicians. Given the available data, this may be appropriate. The statistical models identified in this review appear to perform better. Key features from these models may help to inform future clinical practice. The Kruis scoring system, in particular, points to the importance of a long duration of abdominal pain and altered bowel habit, a lack of symptoms that would strongly suggest organic disease, and normal CBC and ESR results. These features were associated with a high probabil-

ity of IBS among patients referred for investigations of lower gastrointestinal tract symptoms, although this scoring system has several important limitations. Existing criteria used to distinguish IBS from organic diseases of the lower gastrointestinal tract performed only modestly in our analyses. In the future, either more accurate ways of diagnosing IBS without the need for investigation need to be developed, or existing diagnostic criteria for the condition need to be validated by high-quality studies.

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Author Contributions: Drs Ford and Moayyedi had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Ford, Talley, Veldhuyzen van Zanten, Vakil, Simel, Moayyedi.
Acquisition of data: Ford, Moayyedi.
Analysis and interpretation of data: Ford, Simel, Moayyedi.
Drafting of the manuscript: Ford, Veldhuyzen van Zanten, Vakil, Moayyedi.
Critical revision of the manuscript for important intellectual content: Ford, Talley, Vakil, Simel, Moayyedi.
Statistical analysis: Ford, Simel, Moayyedi.
Administrative, technical, or material support: Veldhuyzen van Zanten, Moayyedi.
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Philosophy has had from its earliest days two different objects which were believed to be closely interrelated. On the one hand, it aimed at a theoretical understanding of the structure of the world; on the other hand, it tried to discover and inculcate the best possible way of life.

—Bertrand Russell (1872-1970)