Role of Radiologic Imaging in Irritable Bowel Syndrome: Evidence-based Review[1]

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Purpose: To critically evaluate the current literature in an effort to establish the current role of radiologic imaging (computed tomography, magnetic resonance imaging, ultrasonography [US], fluoroscopy, conventional film radiography) in irritable bowel syndrome (IBS).

Materials and Methods: The term "irritable bowel syndrome" was used to search Clinical Evidence, UpToDate, Cochrane Library, TRIP, and National Institute for Health and Clinical Excellence databases and the *American College of Physicians Journal Club* and *Evidence-Based Medicine* online. PubMed was searched by using medical subject headings ("irritable bowel syndrome;" "colonic diseases, functional;" "diagnosis;" "colonography;" "computed tomographic (CT)") and the dates January 1, 1985 to July 1, 2010. Appraisal was independently performed by two reviewers who followed the Oxford Centre for Evidence Based Medicine practice criteria.

Results: No systematic review (SR) specifically examined radiologic imaging in IBS; however, in the secondary literature, five relevant SRs or guidelines partially addressed this topic. A PubMed search identified 1451 articles, 111 of which at least partially addressed radiologic imaging. Of these, seven valid articles (two SRs and five primary research articles) were identified. The five primary research articles examined either colonic investigations (colonoscopy and barium enema examination) ($n = 5$) or US ($n = 2$) or both ($n = 2$). Structural disease found infrequently in patients with IBS-type symptoms included diverticulosis, colorectal cancer, celiac disease, inflammatory bowel disease, and ovarian cancer. The incidence of structural disease in patients with concerning symptoms was low.

Conclusion: Although widely used, there is a surprising paucity of evidence guiding radiologic imaging in IBS. Radiologic imaging may not be required in patients with IBS without potentially concerning symptoms but should be considered where such symptoms exist, and choice of imaging study should be influenced by predominant symptoms. Definitive recommendations must await further research.

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Irritable bowel syndrome (IBS) is a chronic gastrointestinal condition characterized by abdominal discomfort, bloating, and disturbed defecation (1,2). Because IBS lacks characteristic imaging features and there are currently no diagnostic biomarkers, symptom-based criteria (Manning and Rome I–III) are recommended for diagnosis (Table 1) (3–6). The Rome III (2006) criteria, for example, were reported to have a sensitivity of 70% and a specificity of 90% for IBS in a study of 328 patients with a clinical diagnosis of IBS (7).

In clinical practice, however, radiologic imaging is performed in many patients with IBS, particularly in those with so-called alarm symptoms (Table 2) (ie, symptoms concerning for underlying structural disease, which might be misclassified as IBS [9]). There is a paucity of information regarding the appropriate use of abdominal imaging in patients with IBS, and few studies have investigated typical diagnostic yields in this setting (10). As a result, the role of radiologic imaging in IBS is poorly defined, and there appears to be a lack of clinical or research interest in IBS among radiologists, with a consequential lack of IBS-related research in the radiologic literature. On one hand, clinicians, mindful of the nonspecific nature of gastrointestinal symptoms such as abdominal pain and discomfort and disturbed defecation, fear missing something, while, on the other hand, unnecessary radiologic imaging is wasteful of resources and potentially exposes patients unnecessarily to ionizing radiation. Although no data exist on this issue, it is likely, given the reported prevalence of IBS, that considerable resources are expended on unnecessary radiologic imaging in patients with IBS. It has been shown that extensive diagnostic testing in patients meeting the symptom-based criteria for IBS has a low pretest probability of finding structural disease, and this practice accounts for a considerable portion of the economic burden associated with IBS (2). With a prevalence of approximately 14%–24% in women and 5%–19% in men, IBS is responsible for 2.4–3.5 million physician visits per year in the United States at a cost of $1.6 million (2).

The purpose of this systematic review (SR) was to critically evaluate the current literature in an effort to establish the current role of radiologic imaging (computed tomography [CT], magnetic resonance [MR] imaging, ultrasonography [US], fluoroscopy, conventional film radiography) in IBS. An important step in attempting to answer the above question was to address the following issues: current recommendations guiding radiologic imaging in IBS, radiologic imaging in patients with IBS without symptoms concerning for underlying structural disease, and radiologic imaging in patients with IBS with symptoms concerning for underlying structural disease.

Advances in Knowledge

- The current evidence guiding the performance of radiologic imaging in patients with irritable bowel syndrome (IBS) is insufficient; no systematic review (SR) focusing solely on IBS exists in the literature, and further study is therefore required.
- The incidence of structural disease appears to be low in patients with IBS who do not have concerning symptoms; potentially concerning symptoms such as blood in stool, weight loss, recurrent fevers, anemia, and chronic severe diarrhea and family history of colorectal cancer, inflammatory bowel disease, or celiac sprue are poor discriminators for the presence of structural disease but should prompt further investigation, pending the generation of more robust evidence.

Implications for Patient Care

- On the basis of current, albeit limited, best evidence, we conclude that patients fulfilling the symptom-based diagnostic criteria for IBS and who do not exhibit concurrent potentially worrisome symptoms such as blood in stool, weight loss, recurrent fevers, anemia, and chronic severe diarrhea and who have no family history of colorectal cancer, inflammatory bowel disease, or celiac sprue do not require radiologic imaging.
- Current evidence suggests that radiologic imaging is required in patients with concerning symptoms who fulfill the symptom-based diagnostic criteria for IBS.
- Optimal radiologic imaging of the patient with IBS should be guided by the likely alternative diagnosis and adherence to the relevant American College of Radiology Appropriateness Criteria.
- Endoscopy appears more suitable than radiologic imaging for colonic investigation of patients with diarrhea-predominant and mixed-type IBS owing to the requirement to exclude microscopic or lymphocytic colitis by using biopsy.

Materials and Methods

Literature Search

The literature was searched and evidence was appraised independently by two reviewers, one (S.E.M.) with 7 years of radiology experience and recent completion of a 7-month course of

Published online before print
10.1148/radiol.11110423 **Content code:** GI

Radiology 2012; 262:485–494

Abbreviations:
IBS = irritable bowel syndrome
SR = systematic review

Author contributions:
Guarantors of integrity of entire study, O.J.O., S.E.M., F.S., M.M.M.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, O.J.O., S.E.M., S.O., F.S., M.M.M.; statistical analysis, S.M., S.O., E.M.M.Q., M.M.M.; and manuscript editing, O.J.O., S.E.M., S.M., F.S., E.M.M.Q., M.M.M.

Potential conflicts of interest are listed at the end of this article.

Table 1

Symptom-based Criteria for the Diagnosis of IBS

Parameter	Criteria
Manning	Abdominal pain relieved by defecation; looser stools with the onset of pain; more frequent stools with the onset of pain; abdominal distention; passage of mucous; incomplete defecation
Rome	At least 12 weeks of continuous or recurrent symptoms; abdominal pain or discomfort relieved with defecation, associated with change in frequency or consistency of stool; two or more of the following: altered stool frequency, form, or passage or passage of mucous or bloating or abdominal distention
Rome II	At least 12 weeks, which need not be consecutive, in preceding 12 months of abdominal discomfort or pain associated with two of three features: relieved by defecation and/or change in frequency of stool and/or change in form (appearance of stool)
Rome III	Recurrent abdominal pain or discomfort at least 3 days a month in past 3 months associated with two of three of the following: improvement with defecation and/or change in frequency of stool and/or change in form (appearance of stool)

Table 2

Symptoms Concerning for Structural Cause of Abdominal Symptoms in Patients with IBS

Symptom of Potential Concern	Frequency*	Sensitivity (%)†
Blood in stool	210/1425 (14.7)	22.0
Awakened by gastrointestinal symptoms	565/1431 (39.5)	52.4
Unintended weight loss	325/1420 (22.9)	36.6
Antibiotic use	476/1411 (33.7)	40.7
Colon cancer family history	250/1426 (17.5)	26.8
Symptom onset after age 50	506/1411 (35.9)	47.6

Source.—Reference 8.

* Data are ratios of patients, with percentages in parentheses.

† Reported sensitivity is for the detection of gastrointestinal cancer, inflammatory bowel disease, or malabsorption.

instruction in evidence-based medicine. The second reviewer (M.M.M.) had 15 years of radiology experience and was an instructor in evidence-based practice with 10 years of experience in evidence-based medicine. Discrepancies were reviewed and resolved by a third reviewer (E.M.M.Q., with 30 years of experience in internal medicine) who coauthored several consensus statements and SRs of IBS. Twenty-five articles were reviewed by the third reviewer. The literature search was commenced in 2008 and was repeated on several occasions until January 2011. This SR was performed by posing an answerable question, searching and appraising the available evidence and applying the findings, and using evidence-based medicine practices as described previously in radiology literature (11–13).

Focused Clinical Question

The PICO (patient, intervention, comparison intervention, and outcomes of interest) format of evidence-based question formulation was used. The PICO question utilized for this SR was written in text form as follows: "In patients with IBS, how does radiological imaging compare with symptom-based diagnosis for the detection of structural pathology or an alternative diagnosis." To answer this question, an evidence-based practice paradigm was followed; the literature was viewed as an evidence pyramid consisting of four levels: secondary evidence composed of syntheses, synopses, and information systems and the primary literature (journals), which were examined from the top down (11).

Secondary Literature Search

The search that formed the basis of this SR initially focused on the secondary literature (evidence-based reviews, syntheses, or guidelines that follow evidence-based practice methods) (11). Initially, the broad search term "irritable bowel syndrome" was deliberately chosen to achieve a high sensitivity in the search for relevant SRs. Databases considered to be at the top of the evidence pyramid, namely Clinical Evidence and UpToDate, were initially searched (11). The next level searched included the Cochrane Library, the TRIP database, and the National Institute for Health and Clinical Excellence databases. After this, a search of the *American College of Physicians Journal Club* and *Evidence-Based Medicine* online was performed.

Primary Literature Search

Finally, a primary literature search by using the United States National Library of Medicine's PubMed *(www.pubmed.gov)* search engine was performed. Search terms were chosen on the basis of the PICO question and prior SRs of IBS (10,14–18). Medical subject headings (MeSH) and free text terms were searched for the terms "irritable bowel syndrome"[MeSH] OR "colonic diseases, functional"[MeSH] AND "diagnosis"[MeSH]. Subsequently, a separate PubMed search using the terms "irritable bowel syndrome"[MeSH] AND "colonography, computed tomographic (CT)"[MeSH] was performed to identify articles that investigated the role of CT colonography in patients with IBS. The search was limited to "1985/01/01"[PDAT] to "2010/07/01"[PDAT] AND English [language] AND humans.

Appraisal

Abstracts of articles retrieved from the primary and secondary literature were reviewed to identify articles that reported *(a)* current recommendations guiding radiologic imaging in IBS and

(b) radiologic imaging in patients with IBS with and without concerning symptoms. Full-text versions of the highest level articles (graded by following evidence-based practice diagnosis and SR criteria described by the Oxford Centre for Evidence Based Medicine *[http://www.cebm.net/index.aspx?o=1157]*) were reviewed to select those that were the most specific and comprehensive and used the best methods available with homogeneous disease classification and terminology.

Data Extraction and Analysis

For studies that investigated radiologic imaging in patients with IBS symptoms, data extracted included *(a)* the population studied, including the proportion of female patients, *(b)* the type of symptom-based criteria used (Manning [3], Rome I, II, or III [4–6], American College of Gastroenterology [10], World Gastroenterology Organization [12]), *(c)* the type of intervention (diagnostic evaluation performed and reference standard comparison, if applied), *(d)* outcomes (prevalence of confirmed structural gastrointestinal disease, resulting in an alternative diagnosis), and *(e)* statistical analyses pertaining to the accuracy of radiologic imaging tests, including sensitivity, specificity, positive predictive and negative predictive values, confidence intervals, positive likelihood ratio, and negative likelihood ratio (2,7,12,13,19,20). These statistical analyses were performed by using the online KT Clearinghouse Statistics Calculator funded by the Canadian Institute for Health Research (21).

Results

Secondary Literature Search

No SR focused solely on the use of radiologic imaging in IBS was found. The highest level of evidence in the secondary literature (UpToDate) contained one article; that article did not focus solely on the role of radiologic imaging in IBS but discussed imaging among other issues in IBS (22). Searches of lower levels of evidence in the secondary literature yielded four additional relevant articles (one SR [2] from the TRIP database and three evidence-based guidelines from the National Institute for Health and Clinical Excellence database [23,24] and from the TRIP database [25]). These reviews or guidelines comprehensively investigated many aspects of diagnosis and management of IBS including some analysis of radiologic imaging, although their primary focus was not imaging. These five articles were selected as representing the current best evidence regarding radiologic imaging in IBS.

Primary Literature Search

The PubMed search yielded 1451 studies, 111 of which were potentially relevant after abstract review (26). The 1340 articles excluded referred to some aspect of IBS, but on review of the article's abstract, there was no reference to the issue of radiologic imaging in IBS. Review of the short-listed articles (n = 111), supplemented, where necessary, by review of full-text versions, identified two additional SRs (10,27), both of which included Brandt as an author; the second SR published in 2009 was considered more valid to the current SR. In addition, five valid primary research articles (28–32) were identified, in which there was some focus on the issue of radiologic imaging in IBS. IBS was diagnosed by using symptom-based criteria in all but one article (Manning, Rome, or modified Rome criteria). These articles studied radiologic investigation of patients with IBS to a variable extent (Table 3). Five articles at least partially studied radiologic investigations in IBS (barium enema examination, US). Only two studies specifically addressed the role of radiologic imaging in IBS (31,32): barium enema examination exclusively in one (31) and US in another (32).

Grading of the levels of evidence and recommendation of these studies by using evidence-based practice criteria is summarized in Table 4. The quality of the methods of the retrieved studies was either moderate or low (grade 2B–4). Unfortunately, the articles with moderate quality evidence-based practice grading (retrospective cohort studies) only partially examined radiologic imaging in IBS, and the two studies that focused solely (31,32) on radiologic imaging were lower quality case series (grade 4) and studied either barium enema or US. One study included incomplete radiologic imaging data in the setting of IBS (28). Unfortunately, the diagnostic yield of radiologic imaging was not detailed by Vanner et al (28) for the 11 of 30 patients with IBS who underwent barium enema prior to enrollment. In addition, 24% (23 of 95) of patients underwent US prior to referral to a gastroenterology clinic; presumably, these investigations would have excluded a number of other patients from the study. Fifty-eight of 95 patients fulfilling the Rome criteria and lacking concerning symptoms for structural disease underwent either barium enema or colonoscopy; however, the proportion of barium enema examinations performed and the findings of these studies were not reported (28). The yield of radiologic imaging in patients who were subsequently found not to have IBS was not provided. Treacher et al (31), which was published in 1986, exclusively studied radiologic imaging (barium enema) in IBS and did not use any specific criteria for the diagnosis of IBS. In this retrospective study, patients had a clinical diagnosis of IBS at a first clinic visit after review by a physician in training or an attending gastroenterologist. Patients were excluded if there was a history of weight loss or blood per rectum; there was no control group, and all patients underwent sigmoidoscopy. An article by Francis et al (32) investigated radiologic imaging (US) in IBS and studied patients who fulfilled the Rome criteria for IBS, after excluding those with abnormal hematologic and biochemistry findings or who had frank or occult blood detected at stool examination. Because US was used for radiologic imaging, the bowel could not be examined, and all patients required sigmoidoscopy (32). On the other hand, an article by Tolliver et al (30) studied the yield of biochemical, hematologic, and lactose hydrogen breath testing and structural imaging in patients meeting the clinical criteria for

Table 3

Summary of Research Articles Found in Primary Literature

Diagnostic Test and Author	No. of Patients	No. of Control Subjects	Age (y)*	Female Patients (%)	Prevalence of Structural Disease†	Prevalence of Structural Disease in Control Subjects
Colonic‡						
Vanner et al (28)	193	0	17–89	86	NA	NA
Hamm et al (29)	1452	0	45	71	2 (7/306)	NA
Tolliver et al (30)	196	0	44	81	21.9 (43/196)	NA
Treacher et al (31)	114	0	48	70	23 (26/114)	NA
Francis et al (32)	125	0	39	80	18 (23/125)	NA
US						
Vanner et al (28)	193	0	17–89	86	NA	NA
Francis et al (32)	125	0	39	80	18 (23/125)	NA

Note.—NA = not available.

* Data are means or ranges.

† Data are percentages, with numbers used to calculate percentages in parentheses.

‡ Colonic investigations included conventional colonoscopy, sigmoidoscopy, and barium enema examination.

Table 4

Levels of Evidence and Focus on Diagnostic Imaging in Primary Literature

Author	Evidence-based Medicine Grade	Includes Data Specific to Diagnostic Imaging	Focused on Diagnostic Imaging
Vanner et al (28)	2B	No	No
Hamm et al (29)	2B	No	No
Tolliver et al (30)	2B	No	No
Treacher et al (31)	4	Yes	Yes
Francis et al (32)	4	Yes	Yes

Table 5

Statistical Analysis of Results in One Article on the Use of US in Patients with Clinical Diagnosis of IBS

Parameter	Datum	Confidence Interval
Sensitivity (%)	96	72, 99
Specificity (%)	95	88, 98
Positive predictive value (%)	78	54, 92
Negative predictive value (%)	99	94, 99
Positive likelihood ratio	20.33	7.3, 56.9
Negative likelihood ratio	0.04	0.003, 0.612

Source.—Reference 31.

IBS. The selection criteria used in this article therefore would suggest that a different patient cohort was examined than that in the article by Francis et al (32). Only one article quantified the effect of concerning symptoms on the diagnosis of disease in patients with IBS-type symptoms, but the proportion of patients who required imaging, the type of imaging, and their results were not documented (29). Treacher et al (31) noted that 27% (nine of 34) of patients with structural disease had an indicator of underlying disease and that only 27% (seven of 26) of patients with indicators of structural disease actually had a structural abnormality identified. Again, although imaging was used to evaluate some patients, no data were presented specifically referring to radiologic imaging. Four of the articles in the primary literature (28,30–32) examined 200 or fewer patients with IBS, which is a relatively small number for a common disorder of considerable heterogeneity. Only one article reported sufficient data pertaining to radiologic imaging to allow statistical analysis (Table 5). The results reported by Treacher et al (31) suggest that US has a sensitivity of 96% and specificity of 95% for the detection of a structural abnormality in patients with IBS. No primary literature article studied CT, which would be most likely to offer the best one-stop imaging examination of the abdomen. The flaws, listed previously, which affect all of the articles in different ways, detracted from the strength of the conclusions or recommendations that could be drawn in this review.

Current recommendations guiding radiologic imaging in IBS.—Radiologic imaging in patients with IBS was discussed in part by guidelines written by the American College of Gastroenterology task force (27). This task force recommended that for diarrhea-predominant IBS, "it is appealing to suggest that

diarrhea-predominant symptoms undergo colonoscopy with inspection of the distal ileum to exclude colon cancer and IBD [inflammatory bowel disease], respectively." It was noted that lymphocytic or microcytic colitis (2.3% [five of 216]) and nonspecific inflammation (1.9% [four of 216]) only occurred in patients with diarrhea-predominant IBS, and hence it was recommended that colonoscopy, when required, should include random colonic biopsies (27). Therefore, according to these guidelines, colonic investigation of diarrhea-predominant IBS and mixed diarrhea and constipation–type IBS subgroups with barium enema or CT colonography is not appropriate because of inability to perform random biopsies. However, in patients with constipation-predominant IBS, the task force did not recommend any one colonic investigation over another (colonoscopy, CT colonography, or barium studies) to exclude causes of mechanical obstruction (27).

SR-based guidelines addressed the use of colonic imaging, abdominal US, and CT in IBS (2). These guidelines suggested performance of these investigations should be influenced by the likely underlying disease (2). The American College of Gastroenterology SR emphasized that physicians experienced in IBS are less likely to order diagnostic tests than physicians with less experience, many of whom view IBS as a diagnosis of exclusion (27,32). One primary literature article (28) reported that the positive predictive value of the Rome I criteria for the diagnosis of IBS in patients without concerning symptoms was 100% and 98%, in retrospective and prospective patient groups, respectively. Nevertheless, 66% (41 of 62) of these patients with IBS younger than 45 years who did not have concerning symptoms had at least a partial investigation of the colon performed (28).

Another primary literature article (31) concluded that further investigation of patients younger than 50 years who fulfilled symptomatic criteria for IBS is not warranted on the basis of a retrospective review of 114 patients with IBS attending a gastroenterology clinic with new symptoms, not necessarily symptoms concerning for underlying structural disease. Structural disease was found in 12 patients (84 underwent barium enema), including uncomplicated diverticular disease and polyps but no cancer or inflammatory bowel disease (31). Patients with positive findings had biochemical or hematologic abnormalities that would have merited further examination. A prospective study of 1452 patients with IBS, irrespective of the presence of symptoms concerning for underlying structural disease, identified colonic disease in 2% (seven of 306) after colonoscopy or sigmoidoscopy with barium enema (29). Diagnostic imaging depicted an alternative cause for abdominal pain in four of these seven patients. Therefore, it was concluded that the low yield, cost, and inconvenience of diagnostic investigations should precipitate reevaluation of investigation patterns (29).

Routine US in patients with IBS is currently not indicated on the basis of the only primary literature article on this topic (32). Pathologic findings were found by using US in 22 of 125 patients (20 of 100 female patients and two of 25 male patients) with a diagnosis of IBS by using Rome I criteria (32). Gallstones, benign liver abnormalities, uterine fibroids, and adnexal cysts were found in female patients, and gallstones and hepatic steatosis were found in male patients. None of these abnormalities resulted in additional therapy. Hepatobiliary abnormalities were found in similar proportions of male and female patients (10% [10 of 100] vs 8% [two of 25]). Although gallstones were the most common abnormal hepatobiliary finding, they were not considered to entirely account for the presenting symptoms in any patient. Both this study and another, which evaluated diagnostic tests in IBS (including US) (28), suggested that routine US was not necessary and may be counterproductive because of incidental findings, which could lead to further diagnostic and therapeutic dilemmas, investigations, and interventions, with potential for distress for the patient (28,32). No specific guidelines for CT, MR imaging, fluoroscopy, or conventional film radiography in IBS were found.

Radiologic imaging in patients with IBS without symptoms concerning for underlying structural disease.—The American College of Gastroenterology task force analyzed the performance of colonic imaging in patients with IBS without symptoms to suggest underlying structural disease and referenced a SR that included three studies incorporating 636 patients with IBS who underwent colonoscopy or barium enema, with or without flexible sigmoidoscopy (27). Structural disease was found in only 1.3% (eight of 636) of patients (95% confidence interval: 0.06%, 2.3%) (Table 6) (27). The incidence of many structural diseases, such as inflammatory bowel disease, colorectal cancer, and gastrointestinal infection, was very low in patients with IBS and comparable with that of the general population; the prevalence of celiac disease and lactose intolerance, in contrast, seemed to be slightly higher in the IBS population (27). The American College of Gastroenterology task force also referenced an interim analysis of a prospective controlled multicenter trial conducted in the United States that compared colonoscopy in 216 patients with diarrhea-predominant IBS or mixed diarrhea and constipation–type IBS with 416 control subjects undergoing screening for colorectal cancer and found no difference in the prevalence of colorectal cancer between patients with IBS and control subjects (IBS, 0% [0 of 216]; control subjects, 0.2% [one of 416]) or that of inflammatory bowel disease (IBS, 0.46% [one of 216]; control subjects, 0% [0 of 416]) (17). Interestingly, the prevalence of adenomatous polyps (14% [30 of 216] vs 26% [109 of 416], $P = .0004$) and diverticulosis (13% [28 of 216] vs 21% [88 of 416], $P = .01$) were lower in the IBS cohort than in the patients undergoing screening investigations for colorectal cancer (27). Therefore, the American College of Gastroenterology SR concluded that colonic imaging was not required routinely in patients with IBS who were younger than 50 years in the absence of symptoms suggestive of underlying structural disease.

Table 6

Prevalence of Structural Disease in Patients Meeting Symptom-based Criteria for IBS

Structural Gastrointestinal Disease	Prevalence among Patients with IBS (%)	Prevalence among General Population (%)
Colitis or inflammatory bowel disease	0.51–0.98	0.3–1.2
Colorectal cancer	0–0.51	0–6
Gastrointestinal infection	0–1.7	5.1 (2695/52 840)*
Lactose malabsorption	22–26	25
Celiac disease	4.7	0.25–0.5%

Note.—Data are derived from SR of six articles that included performance of 6619 diagnostic studies including colonoscopy, rectal biopsy, hematology profile, thyroid function, biochemical test, fecal occult blood test, breath test, and US in patients with IBS (2).

* Data in parentheses are numbers used to calculate percentage. Prevalence of acute gastrointestinal illness in the general population was determined by Jones et al (33).

Table 7

Utility of Symptoms of Concern to Diagnose Colorectal Cancer

Symptom	Pooled Sensitivity (%)	Pooled Specificity (%)
Rectal bleeding	64 (55, 73)	52 (42, 63)
Anemia	19 (5.5, 33)	90 (87, 92)
Weight loss	22 (14, 31)	89 (81, 95)

Source.—Reference 22.

Note.—Data in parentheses are 95% confidence intervals.

Radiologic imaging in patients with IBS with symptoms concerning for underlying structural disease.—The American College of Gastroenterology review of the utility of symptoms of concern for the presence of underlying colorectal cancer diagnosis is summarized in Table 7 (27). There is evidence that patients presenting with IBS who have a family history of colorectal cancer, inflammatory bowel disease, and celiac disease are at higher risk for structural disease (27). Overall, the American College of Gastroenterology suggested "that the accuracy of alarm symptoms for identifying patients with underlying structural disease is disappointing" (27). It also suggested that rectal bleeding and nocturnal pain offer little discriminative value in separating patients with IBS from those with structural diseases and stated that "whereas anemia and weight loss have poor sensitivity for structural diseases, they offer good specificity" (27). The American College of Gastroenterology concluded that "in patients who fulfill the symptom-based criteria of IBS, the absence of selected alarm features, including anemia, weight loss, and a family history of colorectal cancer, IBD [inflammatory bowel disease] or celiac sprue, should re-assure physicians that the diagnosis of IBS is correct" (27).

Discussion

IBS is one of the most common disorders encountered in modern medicine; community surveys in western Europe and North America suggest a prevalence of around 11.5% (4828 of 41 984) in the adult population (34). While many of those affected do not seek medical attention and manage their symptoms by dietary changes and the use of a variety of remedies, a substantial minority have frequent and disabling symptoms that may incur a substantial effect on quality of life. Although the precise cause of IBS is not known, both psychologic and emotional factors and chronic stress have been regarded as important precipitating factors in the induction of IBS symptoms. While, more recently, enteric infection, food intolerance, and immune activation and disturbances in the colonic and small intestinal microflora have been proposed as playing a role in the pathophysiology of IBS (35), disordered intestinal motility and visceral hypersensitivity have long been regarded to be of primary importance (36). However, the precise nature of the relationship between any one of these factors and the clinical presentation and/or natural history of IBS has yet to be elucidated. The diagnosis of IBS currently rests, therefore, on symptoms alone or, more precisely, on an aggregation of clinical symptoms.

Imaging in patients with IBS has serious implications for health care resources; IBS accounts for 1.7–10 billion U.S. dollars in direct medical costs in the United States without substantial supportive evidence for their value (11,37–41). A Canadian study of patients with IBS-type symptoms found that 75% (1123 of 1497) fulfilled the Rome II criteria and that 69.2% (1075 of 1553) underwent diagnostic investigations (42). Widespread imaging in patients with IBS-type symptoms possibly stems from a persisting perception that it constitutes a diagnosis of exclusion (43). Symptoms can mimic other conditions, and physicians often fear missing structural disease (17,44). These concerns can precipitate overinvestigation, increased health care costs, exposure to ionizing radiation, and adverse events (45). For example, 23.8% (7084 of 29 710) of colonoscopies in the United States in patients younger than 50 years are for IBS symptoms (46). The perforation rate is 0.07% (343 of 491 311) for colonoscopy, 0.004% (30 of 738 216) for barium enema, and 0.02% (one of 5306) for CT colonography (47–49).

One SR demonstrated that the prevalence of structural disease in patients meeting symptom-based criteria for IBS was comparable with that of the general population (2). The exclusion of structural disease does not appear to be a valid justification for indiscriminate radiologic imaging in IBS. In the absence of worrisome symptoms, current advice on colon cancer screening in patients with IBS should be no different than in the normal population (50). It appears that early referral to a physician expert in IBS may be preferable to embarking on radiologic imaging, with a very low pretest probability of yielding structural disease. Physicians with expertise in IBS are less likely to order diagnostic tests than those without such a background (51). A study

of diagnostic costs in children with IBS found that pediatricians use imaging even less frequently than gastroenterologists (52). Gastroenterologists ordered abdominal US examinations, conventional radiography, and upper gastrointestinal series in 23.9% (11 of 46), 4.4% (two of 46), and 17.4% (eight of 46) of patients, compared with 4.7% (two of 43), 14% (six of 43), and 0%, respectively, among pediatricians. The cost of medical evaluation, including colonoscopy, but excluding upper gastrointestinal endoscopy, was five times greater in children seen by a gastroenterologist than a pediatrician, even though there was no difference in symptoms between the groups. It was concluded that parent perception of the child's symptoms could be the primary factor driving investigations (52).

The question of whether radiologic imaging is required for patients with IBS with symptoms that are potentially suggestive of underlying structural disease is a complex one, because their presence may, on the one hand, be deemed suggestive of underlying structural disease but, on the other hand, they by no means exclude the diagnosis of IBS (6). In patients with concerning symptoms, or in patients with IBS in whom initial treatment has failed to control symptoms, the choice of imaging modality should be influenced by likely underlying disease. Therefore, we suggest that radiologic imaging in patients with IBS should be guided by the American College of Radiology Appropriateness Criteria (gastrointestinal imaging) and that the choice of imaging investigation should be influenced by the likely differential diagnoses or typical symptom (53). For example, in a patient with right upper quadrant pain with biliary features, American College of Radiology Appropriateness Criteria recommend abdominal US first (53). Spiller suggests that only rarely should sphincter of Oddi dysfunction be considered, such as when pain is associated with a rise in liver enzymes or serum amylase level (9,53). However, the referring physician should exert caution in the interpretation of gallbladder US findings in IBS, and these investigations should be restricted to patients with typical meal-provoked symptoms, because patients with IBS with asymptomatic gallstones are in danger of being subjected to unnecessary cholecystectomy, without benefit to their pain (9).

With regard to the use of barium enema or CT colonography in IBS, there is little evidence in the literature. The American College of Gastroenterology guidelines suggest that where further investigation is required, diarrhea-predominant IBS and mixed diarrhea and constipation–type IBS should have colonoscopy supplemented by colonic biopsy, rather than barium enema or CT colonography (27). The additional yield of colonoscopy may still be limited even in these groups, given the results of a recent study of patients with nonconstipation IBS. It was found that there was no increased incidence of structural abnormalities in 466 patients with IBS and 451 control subjects after colonoscopy (54). The American College of Gastroenterology task force does not recommend any one colonic investigation in particular (colonoscopy, CT colonography, or barium studies) for the investigation of patients with constipation–type IBS to exclude mechanical obstruction (27). The American College of Radiology Appropriateness guidelines for colorectal cancer screening would suggest, however, that CT colonography and double-contrast barium enema examination are not appropriate in high-risk patients, but that CT colonography is appropriate for middle- and low-risk patients and double-contrast barium enema should be considered when CT colonography is unavailable (50,53). It must also be conceded that the use of treatment failure as a criterion for further assessment has not been studied in IBS and could well prove unhelpful given the poor record of available therapies in the management of IBS.

There are a number of potential methods of improving the evidence base relating to the use of radiologic imaging in IBS. As a starting point, a retrospective study could document factors that precipitate imaging in a well-defined cohort of patients with IBS and calculate the diagnostic yield of these investigations. Ultimately, it would be of the most interest to know if radiologic imaging affects patient outcome. This can be best achieved in a prospective study that adheres to strict guidelines for the performance of specific imaging modalities and then carefully follows clinical outcomes. Another approach could be a randomized control trial comparing the relative diagnostic yields with clinical effect of CT colonography and colonoscopy in a defined group of patients presenting with IBS-type symptoms. Outcomes such as cost, the frequency of clinically important extracolonic diagnoses, and the need for further optical colonoscopy could be assessed. A major limitation of all such studies is the relative infrequency of alternative diagnoses in subjects with IBS, in general; study population numbers could be reduced by selecting subpopulations with a likelihood of higher diagnostic yield, such as the elderly, for example.

The heterogeneity of the IBS cohorts affects the strength of the articles we analyzed and, therefore, that of our findings and conclusions. Some studies investigated diagnostic imaging in patients with IBS regardless of the presence or absence of symptoms of concern, whereas others only included patients with IBS with worrisome symptoms. There were additional potential limitations in the five primary literature articles. Four articles examined 200 patients with IBS or fewer, which represents a relatively small number and limits the recommendations that can be drawn (28,30–32). In addition, the IBS populations investigated did not always exclude patients who had already undergone diagnostic tests prior to referral to a specialist center. Thus, it is possible that some patients with IBS may have had structural disease already diagnosed or excluded prior to specialist referral, because those with abnormal biochemical or hematologic findings were excluded (32). These factors represent a possible explanation for the large range (2% [seven of 306]–23% [26 of 114]) in the prevalence of structural disease in the studies where

colonic investigations were performed. Restriction of our search to English language literature represented one of the potential weaknesses of this review. We did search for unpublished data, although we did not encounter any relevant unpublished data from scientific meetings. Our conclusions were limited by the lack of good evidence, but this also helps to highlight the need for further investigation in this area.

The main finding of this review was that there is a paucity of rigorously designed trials that address the use of diagnostic imaging in IBS. This lack of adequate information also precludes the conduction of a meta-analysis, which is one of the best ways of providing data to guide one's practice. There is no doubt that there is a need for a well-designed evaluation of imaging in IBS. The current evidence is weak but suggests that diverticulosis, colorectal cancer, structural small bowel disease (celiac disease, Crohn disease, and tumors), inflammatory bowel disease, and ovarian cancer are the most common mimics of IBS. The effectiveness of using concerning symptoms to identify patients with underlying structural disease is disappointing (27). Overall, in the absence of a better discriminator, concerning symptoms must still play a role in separating those patients with IBS symptoms, who require further evaluation to exclude structural disease, from those who do not. Further investigations, including diagnostic imaging, are not required in patients with IBS without alarm symptoms (27).

In conclusion, despite the proliferation of guidelines that comment on the issue, this article demonstrates that there is a striking dearth of robust evidence and prospective studies, in particular, regarding the appropriate use of radiologic imaging in patients with IBS.

Disclosures of Potential Conflicts of Interest: **O.J.O.** No potential conflicts of interest to disclose. **S.E.M.** No potential conflicts of interest to disclose. **S.M.** No potential conflicts of interest to disclose. **S.O.** No potential conflicts of interest to disclose. **F.S.** No potential conflicts of interest to disclose. **E.M.M.Q.** No potential conflicts of interest to disclose. **M.M.M.** No potential conflicts of interest to disclose.

References

1. Quigley EM. Impact of bloating and distention in irritable bowel syndrome: have we wandered too far from the Manning creed? Clin Gastroenterol Hepatol 2009;7(1):7–8.
2. Cash BD, Schoenfeld P, Chey WD. The utility of diagnostic tests in irritable bowel syndrome patients: a systematic review. Am J Gastroenterol 2002;97(11):2812–2819.
3. Manning AP, Thompson WG, Heaton KW, Morris AF. Towards positive diagnosis of the irritable bowel. BMJ 1978;2(6138):653–654.
4. Drossman DA, Richter JE, Talley NJ. The functional gastrointestinal disorders and their diagnosis: a coming of age. In: Drossman DA, Richter JE, Talley NJ, eds. The functional gastrointestinal disorders: diagnosis, pathophysiology and treatment. McLean, Va: Degnon Associates, 1994; 1–23.
5. Thompson WG, Longstreth GF, Drossman DA, Heaton KW, Irvine EJ, Müller-Lissner SA. Functional bowel disorders and functional abdominal pain. Gut 1999;45(suppl 2):II43–II47.
6. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. Gastroenterology 2006;130(5):1480–1491.
7. Whitehead WE. Development and validation of the ROME III diagnostic questionaire. In: Drossman DA, Corazziar E, Delvaux M, et al, eds. Rome III: the functional gastrointestinal disorders. Durham, NC: Degnon, 2006; 835–853.
8. Whitehead WE, Palsson OS, Feld AD, et al. Utility of red flag symptom exclusions in the diagnosis of irritable bowel syndrome. Aliment Pharmacol Ther 2006;24(1):137–146.
9. Spiller R. Clinical update: irritable bowel syndrome. Lancet 2007;369(9573):1586–1588.
10. Brandt LJ, Bjorkman D, Fennerty MB, et al. Systematic review on the management of irritable bowel syndrome in North America. Am J Gastroenterol 2002;97(11 suppl):S7–S26.
11. Staunton M. Evidence-based radiology: steps 1 and 2—asking answerable questions and searching for evidence. Radiology 2007;242(1):23–31.
12. Quigley EM, Fried M, Gwee KA, et al. Irritable bowel syndrome: a global perspective. http://www.worldgastroenterology.org/irritable-bowel-syndrome.html. Accessed June 18, 2010.
13. Dodd JD. Evidence-based practice in radiology: steps 3 and 4—appraise and apply diagnostic radiology literature. Radiology 2007;242(2):342–354.
14. Ford AC, Brandt LJ, Young C, Chey WD, Foxx-Orenstein AE, Moayyedi P. Efficacy of 5-HT3 antagonists and 5-HT4 agonists in irritable bowel syndrome: systematic review and meta-analysis. Am J Gastroenterol 2009;104(7):1831–1843.
15. Ford AC, Chey WD, Talley NJ, Malhotra A, Spiegel BM, Moayyedi P. Yield of diagnostic tests for celiac disease in individuals with symptoms suggestive of irritable bowel syndrome: systematic review and meta-analysis. Arch Intern Med 2009;169(7):651–658.
16. Moayyedi P, Ford AC, Talley NJ, et al. The efficacy of probiotics in the treatment of irritable bowel syndrome: a systematic review. Gut 2010;59(3):325–332.
17. Ford AC, Talley NJ, Spiegel BM, et al. Effect of fibre, antispasmodics, and peppermint oil in the treatment of irritable bowel syndrome: systematic review and meta-analysis. BMJ 2008;337:a2313. [Published correction appears in BMJ 2009;338:b1881.]
18. Ford AC, Talley NJ, Schoenfeld PS, Quigley EM, Moayyedi P. Efficacy of antidepressants and psychological therapies in irritable bowel syndrome: systematic review and meta-analysis. Gut 2009;58(3):367–378.
19. Maher MM, Hodnett PA, Kalra MK. Evidence-based practice in radiology: steps 3 and 4—appraise and apply interventional radiology literature. Radiology 2007;242(3):658–670.
20. Maher MM, McNamara AM, MacEneaney PM, Sheehan SJ, Malone DE. Abdominal aortic aneurysms: elective endovascular repair versus conventional surgery—evaluation with evidence-based medicine techniques. Radiology 2003;228(3):647–658.
21. KT Clearinghouse. Stats Calculator. Centre for Evidence-Based Medicine, Toronto. Funded by the Canadian Institute for Health Research. http://ktclearinghouse.ca/cebm/practise/ca/calculators/statscalc. Accessed July 12, 2011.
22. Wald A. Clinical manifestations and diagnosis of irritable bowel syndrome. http://www.uptodate.com/contents/topic.do?topicKey=GAST/2630. Accessed June 2, 2010.
23. National Institute for Health and Clinical Excellence. Irritable bowel syndrome in adults. Diagnosis and management of irritable bowel syndrome in primary care. http://www.nice.org.uk/CG061. Published 2008. Accessed October 2, 2010.
24. National Guideline Clearinghouse. Irritable bowel syndrome in adults. Diagnosis and

management of irritable bowel syndrome in primary care. http://www.guideline.gov/summary/summary.aspx?doc_id=13703. Accessed October 2, 2010.

25. van der Horst HE, Meijer JS, Muris JW, et al. NHG-Standaard prikkelbare darm syndroom (irritable bowel syndrome). Dutch College of General Practitioners (NHG) Practice Guidelines on IBS. Huisarts Wet 2001;44:58–65.
26. U.S. National Library of Medicine. NCBI PubMed Web site. http:/www.ncbi.nlm.nih.gov/sites/entrez/. Accessed March 13, 2011.
27. American College of Gastroenterology Task Force on Irritable Bowel Syndrome, Brandt LJ, Chey WD, et al. An evidence-based position statement on the management of irritable bowel syndrome. Am J Gastroenterol 2009;104(suppl 1):S1–S35.
28. Vanner SJ, Depew WT, Paterson WG, et al. Predictive value of the Rome criteria for diagnosing the irritable bowel syndrome. Am J Gastroenterol 1999;94(10):2912–2917.
29. Hamm LR, Sorrells SC, Harding JP, et al. Additional investigations fail to alter the diagnosis of irritable bowel syndrome in subjects fulfilling the Rome criteria. Am J Gastroenterol 1999;94(5):1279–1282.
30. Tolliver BA, Herrera JL, DiPalma JA. Evaluation of patients who meet clinical criteria for irritable bowel syndrome. Am J Gastroenterol 1994;89(2):176–178.
31. Treacher DF, Chapman JR, Nolan DJ, Jewell DP. Irritable bowel syndrome: is a barium enema necessary? Clin Radiol 1986;37(1):87–88.
32. Francis CY, Duffy JN, Whorwell PJ, Martin DF. Does routine abdominal ultrasound enhance diagnostic accuracy in irritable bowel syndrome? Am J Gastroenterol 1996;91(7):1348–1350.
33. Jones TF, McMillian MB, Scallan E, et al. A population-based estimate of the substantial burden of diarrhoeal disease in the United States; FoodNet, 1996-2003. Epidemiol Infect 2007;135(2):293–301.
34. Hungin AP, Whorwell PJ, Tack J, Mearin F. The prevalence, patterns and impact of irritable bowel syndrome: an international survey of 40,000 subjects. Aliment Pharmacol Ther 2003;17(5):643–650.
35. Quigley EM. Bacteria: a new player in gastrointestinal motility disorders—infections, bacterial overgrowth, and probiotics. Gastroenterol Clin North Am 2007;36(3):735–748.
36. Quigley EM. Disturbances of motility and visceral hypersensitivity in irritable bowel syndrome: biological markers or epiphenomenon. Gastroenterol Clin North Am 2005;34(2):221–233.
37. Olden KW. Diagnosis of irritable bowel syndrome. Gastroenterology 2002;122(6):1701–1714.
38. Dapoigny M, Bellanger J, Bonaz B, et al. Irritable bowel syndrome in France: a common, debilitating and costly disorder. Eur J Gastroenterol Hepatol 2004;16(10):995–1001.
39. Talley NJ, Gabriel SE, Harmsen WS, Zinsmeister AR, Evans RW. Medical costs in community subjects with irritable bowel syndrome. Gastroenterology 1995;109(6):1736–1741.
40. Goodman C, Cronin K, Gemmen E, et al. Chronic intestinal disorders. In: The burden of gastrointestinal diseases. Bethesda, Md: American Gastroenterological Association, 2001; 2–65.
41. Quigley EM, Bytzer P, Jones R, Mearin F. Irritable bowel syndrome: the burden and unmet needs in Europe. Dig Liver Dis 2006;38(10):717–723.
42. Paré P, Gray J, Lam S, et al. Health-related quality of life, work productivity, and health care resource utilization of subjects with irritable bowel syndrome: baseline results from LOGIC (Longitudinal Outcomes Study of Gastrointestinal Symptoms in Canada), a naturalistic study. Clin Ther 2006;28(10):1726–1735.
43. Spiegel BM. Do physicians follow evidence-based guidelines in the diagnostic work-up of IBS? Nat Clin Pract Gastroenterol Hepatol 2007;4(6):296–297.
44. Cash BD, Chey WD. Irritable bowel syndrome: an evidence-based approach to diagnosis. Aliment Pharmacol Ther 2004;19(12):1235–1245.
45. Wildi SM, Gubler C, Fried M, Bauerfeind P, Hahnloser D. Chronic abdominal pain: not always irritable bowel syndrome. Dig Dis Sci 2006;51(6):1049–1051.
46. Lieberman DA, Holub J, Eisen G, Kraemer D, Morris CD. Utilization of colonoscopy in the United States: results from a national consortium. Gastrointest Endosc 2005;62(6):875–883.
47. Panteris V, Haringsma J, Kuipers EJ. Colonoscopy perforation rate, mechanisms and outcome: from diagnostic to therapeutic colonoscopy. Endoscopy 2009;41(11):941–951.
48. Blakeborough A, Sheridan MB, Chapman AH. Complications of barium enema examinations: a survey of UK Consultant Radiologists 1992 to 1994. Clin Radiol 1997;52(2):142–148.
49. Bassett JT, Liotta RA, Barlow D, Lee D, Jensen D. Colonic perforation during screening CT colonography using automated CO2 insufflation in an asymptomatic adult. Abdom Imaging 2008;33(5):598–600.
50. Rex DK, Johnson DA, Anderson JC, et al. American College of Gastroenterology guidelines for colorectal cancer screening 2009 [corrected]. Am J Gastroenterol 2009;104(3):739–750.
51. Spiegel BM, Farid M, Esrailian E, Talley J, Chang L. Is irritable bowel syndrome a diagnosis of exclusion? a survey of primary care providers, gastroenterologists, and IBS experts. Am J Gastroenterol 2010;105(4):848–858.
52. Lane MM, Weidler EM, Czyzewski DI, Shulman RJ. Pain symptoms and stooling patterns do not drive diagnostic costs for children with functional abdominal pain and irritable bowel syndrome in primary or tertiary care. Pediatrics 2009;123(3):758–764.
53. ACR appropriateness criteria. http://www.acr.org/secondarymainmenucategories/quality_safety/app_criteria.aspx. Accessed October 2, 2010.
54. Chey WD, Nojkov B, Rubenstein JH, Dobhan RR, Greenson JK, Cash BD. The yield of colonoscopy in patients with non-constipated irritable bowel syndrome: results from a prospective, controlled US trial. Am J Gastroenterol 2010;105(4):859–865.