Do you manage patients with irritable bowel syndrome?

Need a practical tool to guide you through best patient care and management?

If so, this is the book for you. Highly practical, expertly-written, and packed with handy text tools like case histories, pitfall boxes and management algorithms, this attractive and convenient manual provides you with complete clinical guidance to irritable bowel syndrome (IBS), one of the most common GI conditions that doctors face daily.

With contributions from the world's leading experts in IBS and edited by a stellar editor team, inside you'll find:

- A comprehensive symptom-specific approach to treatment options
- Strong emphasis on the clinical care and management of patients
- Exploration of the interface between primary and secondary care for IBS sufferers
- Self-assessment MCQs to improve clinical skills
- Examination of the overlap and difference between the USA and Europe in the management of IBS

Perfect for doctors in primary care as well as gastroenterologists of all levels, *Irritable Bowel Syndrome: Diagnosis and Clinical Management* is the ideal consultation tool for the management of this extremely prevalent condition.

**Titles of Related Interest**

- *Clinical Dilemmas in Inflammatory Bowel Disease*, Second Edition

- *Practical Manual of Gastroesophageal Reflux Disease*
Irritable Bowel Syndrome
Irritable Bowel Syndrome
Diagnosis and Clinical Management

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Foreword

One of the last great medical mysteries waiting to be unravelled is MUPS, or so-called medically unexplained physical symptoms. Examples include the irritable bowel syndrome (IBS), functional (or non-ulcer) dyspepsia (FD), fibromyalgia and chronic fatigue syndrome. Disorders such as IBS and FD are remarkably common, impact on quality of life, often overlap and share a number of features in common including co-morbid anxiety or depression. Some attribute MUPS to somatoform disorder, itself a controversial entity. Yet is IBS really unexplained, or are gut biological markers emerging? Is it a psychological disorder? Is a positive diagnosis of IBS possible or is the disorder still a diagnosis of exclusion? And, most importantly, what should you do when faced with a patient with this diagnosis? What treatments really work and what should you do first? Is a pathophysiologically tailored approach now the way to go? If initial therapy for IBS fails, what’s next?

It is with great pleasure that I introduce this excellent new book on IBS. Dr Emmanuel and Professor Quigley are international authorities in the field. As editors they have brought together the cream of the crop in IBS, a veritable who’s who in neurogastroenterology worldwide. The editorial team and authors have developed a refreshingly readable book; it presents a practical management approach. Impressively, in a relatively brief space the book summarizes the current state-of-the-art. The text is evidence-based and contains illustrative case histories, potential pitfall boxes, key points, management algorithms and useful web links that will guide you undertake best practice.

In my opinion, IBS has evolved into a particularly exciting field and translational research has exploded in this area in recent years. You will read about new hints in terms of the aetiopathogenesis (including genes, inflammation, infections and the gut microbiome). I predict the pathophysiological advances are so major that this is likely to translate into objective diagnostic testing and possibly curative rather than suppressive therapies. The role of diet has dramatically changed and increasingly fibre is now recognized to be far from the only option. I am impressed that new dietary approaches can provide striking relief for some sufferers. You will see why the mind–body connection is so important, with neurological
signalling going in both the up and down directions; this may explain the overlap of IBS with other disorders, and why psychological treatments such as cognitive behavioural therapy are so valuable.

I commend the editors and authors for crafting this new book on IBS; its creation signals an approaching maturity in the field. Despite all the inherent difficulties studying a condition based on a characteristic symptom profile, translational research in IBS represents a triumph starting to bear fruit. While IBS has a bright future as evidenced by this book, I remain doubtful that the concept of MUPS will survive long term!

Nicholas J. Talley, MD, PhD
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Preface

Patients with irritable bowel syndrome frequently report unhappiness with their care and the manner in which their disorder is approached by healthcare professionals. These clinical experiences contrast sharply with the research arena, where our understanding of the condition is increasing rapidly based on findings in both laboratory and clinical studies. There is a need and an opportunity to bridge this clinical–research divide; thus the motivation to write this book. We consider ourselves immensely fortunate to have been able to recruit enthusiastic support for this project from what is truly an ‘A-team’ of IBS experts who have generously contributed to this book.

The book is intended to be of direct assistance in clinical practice. Each chapter includes information, tips and techniques that will help in your next clinic with an IBS patient. The book is structured to match this aim. There are four sections, the first of which is a necessary and complete introduction to the condition. Section two focuses on assessment – the importance of making a positive diagnosis, a practical approach to quantifying the condition and the increasingly important topic of the care pathway between general practitioner and specialist. The next section comprises a range of chapters focusing on state-of-the-art advice regarding treatment of specific symptoms and treatment modalities – it offers a review of established and more recent therapies. This segues into the final section, which addresses emerging areas of therapy in IBS.

We wish to express our deep appreciation to our colleagues in Wiley-Blackwell. From the initiation of the project through to the review of proofs we have been met with outstanding speed, clarity and vision from every member of an excellent team. The quality of presentation of this book owes as much to them as the content does to the authors.

Anton Emmanuel and Eamonn Quigley
London and Cork, December 2012
PART 1
Overview of Irritable Bowel Syndrome
CHAPTER 1
Definitions and Classifications of Irritable Bowel Syndrome

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Key points
• Irritable bowel syndrome is common.
• The condition can be difficult to diagnose.
• Physicians should try to make a positive diagnosis, without need for extensive investigation.
• Existing symptom-based diagnostic criteria for the diagnosis of IBS perform modestly.
• The Rome criteria have not been extensively validated.

Background

Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder characterized by abdominal pain or discomfort, in association with altered bowel habit. The natural history of the condition is a relapsing and remitting one [1–4], with most sufferers experiencing episodes of exacerbation of symptoms and other periods where symptoms are less troublesome, or even quiescent. The prevalence of IBS in the general population varies between 5 and 20% in cross-sectional surveys [5–7], and may be influenced by the demographics of the population under study. For example, IBS is commoner in females [8, 9] and younger individuals [7, 10, 11], although evidence for any effect of socioeconomic status is conflicting [12–14]. The prevalence of IBS appears to be comparable among Western nations and those of the developing world and the Far East [7, 10, 15, 16], although there are fewer data available from the latter regions. Prevalence is also higher in those with coexisting functional gastrointestinal diseases [17], particularly dyspepsia and gastro-oesophageal reflux disease [18, 19], and other functional disorders, such as fibromyalgia and chronic fatigue [20].

At the time of writing, there is no known structural, anatomical, or physiological abnormality that accounts for the symptoms that IBS sufferers
Part 1: Overview of Irritable Bowel Syndrome

experience, and it seems unlikely that there is a single unifying explanation for them. It is more plausible that a combination of factors contributes to the abdominal pain and disturbance in bowel habit. Proposed etiological mechanisms that may be involved in the disorder include altered gastrointestinal motility [21, 22], visceral hypersensitivity [23, 24], abnormal pain processing in the central nervous system [25, 26], dysregulated intestinal immunity [27], low-grade inflammation and altered gastrointestinal permeability following enteric infection [28, 29], imbalances in intestinal flora [30] and altered psychological state [31]. Irritable bowel syndrome also aggregates in families [32] but whether this is due to genetic factors, shared upbringing, or both is unclear.

Individuals with IBS are more likely to consume healthcare resources than those without gastrointestinal symptoms [33]. Up to 80% of sufferers may consult their primary care physician as a result of symptoms [34, 35], and the condition accounts for approximately 25% of a gastroenterologist’s time in the outpatient department [36]. Diagnosing IBS can be challenging for the physician, due to the potential for overlap between the symptoms that sufferers report and those of organic gastrointestinal conditions such as coeliac disease, small intestinal bacterial overgrowth, bile acid diarrhoea, exocrine pancreatic insufficiency, inflammatory bowel disease and even colorectal cancer. Several studies have examined the yield of diagnostic testing for these conditions in individuals with symptoms suggestive of IBS [37–41], but clear evidence for the routine exclusion of any of these disorders, with the exception of coeliac disease, is lacking. Attempts to identify a biomarker for the condition have, to date, been unsuccessful [42].

As a result of this uncertainty, and despite recommendations made by various medical organizations for a diagnosis of IBS to be made on clinical grounds alone [43–46], many patients with symptoms suggestive of IBS will undergo investigation, in an attempt to reassure both the patient and the physician that there is no organic explanation for the symptoms [47]. However, once a diagnosis of IBS is reached it is unlikely to be revised following further investigations of the gastrointestinal tract for the same symptoms in the future [48], and the subsequent detection of a ‘missed’ diagnosis of organic disease, which may have been the underlying explanation for the patient’s original presentation with symptoms, is unlikely [49].

Medical treatment for IBS is considered to be unsatisfactory, with patients representing a significant financial burden to health services. The annual cost of drug therapy for IBS has been estimated at $80 million in the US [50]. Placebo response rates in treatment trials for IBS are high [51], perhaps because there is no structural abnormality that can be corrected by successful therapy, and therefore any benefit following treatment is often assessed by an improvement in global symptoms, an endpoint that may be less objective than those used in trials conducted for organic diseases.
Despite this, there is evidence that fibre, antispasmodic drugs, antidepressants and probiotics are all more effective than placebo in the short-term therapy of IBS [52–54], although no single medical treatment has been demonstrated to alter the long-term natural history of the disorder.

The definition and classification of IBS are both of paramount importance to the management of sufferers. Accurate definitions allow physicians to diagnose IBS with confidence, hence reducing the costs of managing the condition to the health service. Whether or not this approach is cost effective is uncertain [55], but it should discourage physicians from over-investigating young patients who are otherwise well and clearly meet these criteria, and in whom the diagnostic yield of such investigations is likely to be low. It may also avoid unnecessary surgery in patients with IBS. Cholecystectomy, appendectomy and hysterectomy rates in IBS patients have been shown to be two to threefold higher than those observed in controls without IBS [56]. Classification of IBS according to symptoms allows the tailoring of therapy according to the predominant symptom reported by the patient, as well as the assessment of which of the existing, as well as novel, treatments are effective in particular subgroups of patients.

**Definitions of irritable bowel syndrome**

Functional bowel disorders were described in the medical literature as early as the nineteenth century, but it was not until 1950 that the term irritable bowel syndrome was first coined [57], eventually replacing spastic colon or irritable colon syndrome as the accepted nomenclature. There were descriptions of case series of patients in the 1960s that studied the clinical features of the condition as well as reporting the prognosis [58, 59], but it was not until the 1970s that attempts were made to define the condition using the symptoms reported by sufferers.

**Individual symptoms in irritable bowel syndrome**

Medical students are taught that up to 90% of diagnoses are made through obtaining a thorough symptom history from the patient. Subjects with IBS often report abdominal pain or discomfort that is relieved by defaecation, altered stool form (looser or harder), altered stool frequency (more or less frequent), a sensation of bloating or visible abdominal distension, a sensation of incomplete evacuation and the passage of mucus per rectum. The presence of these symptoms suggests a diagnosis of IBS and it has often been assumed that the more of them that are present, the higher the likelihood of the patient having IBS. However, there have been few studies that have examined the diagnostic utility of individual symptoms in predicting a diagnosis of IBS.
A recent systematic review and meta-analysis examined the accuracy of these individual symptoms in discriminating IBS from organic lower gastrointestinal diseases [60]. Four studies reported on the presence of passage of mucus per rectum, tenesmus, looser stools at onset of abdominal pain, more frequent stools at onset of abdominal pain and abdominal pain relieved by defaecation [61–64], and three collected data on patient-reported visible abdominal distension [62–64]. Pooled sensitivity of these individual symptom items ranged from 39 to 74%, and pooled specificity from 45 to 77%.

This suggests that individual symptoms are only modestly accurate, at best, in terms of reaching a diagnosis of IBS. This may be due to differences in the perceived connotation of individual symptom items between patients, such that standardizing the meanings of these from one patient to another is difficult. In addition, it is rare that a physician uses only one item from the clinical history in reaching a diagnosis; more often, individual items are combined with other symptoms, as well as patient characteristics, such as age and gender. It is therefore not surprising that diagnostic criteria, consisting of a combination of symptoms, were developed; these are discussed in the following sections.

The Manning criteria
In a now seminal paper published in the British Medical Journal in 1978 [63], Adrian Manning and colleagues collected symptom data from 65 unselected outpatients presenting to a gastroenterology clinic with gastrointestinal symptoms and followed these individuals up in order to record the ultimate diagnosis. They reported that four symptoms: distension, relief of abdominal pain with a bowel movement, looser bowel movements with the onset of abdominal pain and more frequent bowel movements with the onset of abdominal pain were all significantly more common in patients with an ultimate diagnosis of IBS. Another two symptoms: tenesmus and passage of mucus per rectum, were also more common in those with IBS, but the difference in frequency in individuals with and without IBS for these was not statistically significant.

These symptoms became known as the Manning criteria; they are detailed in Table 1.1. As a result of their findings, the authors speculated that the use of these symptoms to positively diagnose IBS may reduce the need for investigations to reach a diagnosis. As the total number of individual symptom items reported by the patient increased, the probability of the patient being diagnosed with IBS also increased. Despite this finding, the authors did not recommend, or validate, what specific number of these criteria should be used as a cut off to diagnose IBS, although three or more are most often used in clinical practice.

The utility of the Manning criteria in diagnosing IBS has been assessed in a recent systematic review and meta-analysis [60]. This identified three
Chapter 1: Definitions and Classifications of IBS

In total, therefore, four studies containing over 500 patients have assessed the accuracy of these criteria in reaching a diagnosis of IBS. When three or more of the Manning criteria were used they performed modestly, with a pooled sensitivity for the diagnosis of IBS of 78% (Figure 1.1) and a pooled specificity of 72% (Figure 1.2). In terms of the individual studies identified, they performed best in the original report by Manning and colleagues [63], with a sensitivity of 84% and a specificity of 76%, and in a subsequent validation study conducted among 347 Turkish outpatients consulting with gastrointestinal symptoms [65], with a sensitivity of 90% and a specificity of 87%. Despite the continuing evolution of symptom-based diagnostic criteria for IBS, the Manning criteria are still in frequent use, both in clinical practice and research, more than 30 years after their original description.

**Table 1.1** The Manning Criteria.

<table>
<thead>
<tr>
<th>Year described</th>
<th>Symptom items included</th>
<th>Minimum symptom duration required</th>
</tr>
</thead>
</table>
| 1978           | Abdominal pain relieved by defaecation  
More frequent stools with onset of pain  
Looser stools with onset of pain  
Mucus per rectum  
Feeling of incomplete emptying  
Patient-reported visible abdominal distension | No |

![Sensitivity of the Manning criteria in the diagnosis of IBS.](Image)

**Figure 1.1** Sensitivity of the Manning criteria in the diagnosis of IBS.
Part 1: Overview of Irritable Bowel Syndrome

The Kruis statistical model

In 1984, Kruis and colleagues validated a statistical model to predict the likelihood of a patient having IBS [66]. The model used a combination of symptoms reported by the patient, signs recorded by the physician and laboratory tests (full blood count and erythrocyte sedimentation rate), with a score of 44 or more used as the cut off to define the presence of IBS. The individual items that are included in the model are detailed in Table 1.2. This model was applied to 317 consecutive outpatients seen in

Figure 1.2 Specificity of the Manning criteria in the diagnosis of IBS.

Table 1.2 The Kruis statistical model.

<table>
<thead>
<tr>
<th>Year described</th>
<th>Symptom items, signs, and laboratory investigations included</th>
<th>Minimum symptom duration required</th>
</tr>
</thead>
<tbody>
<tr>
<td>1984</td>
<td><strong>Symptom items (reported by the patient using a form)</strong></td>
<td>&gt; 2 years</td>
</tr>
<tr>
<td></td>
<td>Abdominal pain, flatulence, or bowel irregularity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Description of abdominal pain as “burning, cutting, very strong, terrible, feeling of pressure, dull, boring, or ‘not so bad’”</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Alternating constipation and diarrhoea</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Signs (each determined by the physician)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Abnormal physical findings and / or history pathognomonic for any diagnosis other than IBS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Impression by the physician that the patient’s history suggests blood in the stools</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Laboratory investigations</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Erythrocyte sedimentation rate &gt; 20 mm/2 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Leucocytosis &gt; 10,000/μL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anaemia (Haemoglobin &lt; 12 g/dL for females or &lt; 14 g/dL for males)</td>
<td></td>
</tr>
</tbody>
</table>
a gastroenterology clinic. The authors reported that the sensitivity of their model was as high as 83% and that specificity was between 97 and 99%. Organic diseases were well-discriminated by the application of the score.

The aforementioned systematic review and meta-analysis of symptom-based definitions of IBS [60] identified a further three subsequent studies that had applied the model described by Kruis et al. to patients consulting with gastrointestinal symptoms [65, 67, 68]. This means that the accuracy of the Kruis model has been studied in a total of 1171 patients. The pooled sensitivity of the model in diagnosing IBS was 77% (Figure 1.3), with a pooled specificity of 89% (Figure 1.4). As with the Manning criteria, the Kruis model performed best in the original validation study [66]. The variables collected by
the physician were more important than those reported by the patient, strengthening the argument for obtaining blood tests in patients consulting with suspected IBS. Combining four items self-reported by the patient with a basic history, physical examination and simple laboratory tests may hold significant appeal, as this mirrors routine clinical practice to some extent.

This greater accuracy compared with the Manning criteria may be because statistical models, such as that developed by Kruis and colleagues, reflect usual clinical practice more accurately, by combining several features from the clinical history. However, this finding could also be the result of the fact that the items in the model 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 – hence the need for prospective validation studies of symptom-based diagnostic criteria. Certainly in two of the three subsequent studies conducted, the Kruis model performed with similar accuracy to that reported in the original study.

One of the variables in the Kruis statistical model, symptom duration of more than two years, probably explains some of its accuracy, as this is likely to be a highly efficient way of ruling out serious underlying pathology. It would be self-evident to most physicians that any process that has been of this duration, with no organic cause detected previously, is likely to be functional in origin. Other limitations of the model include the fact that several of the symptom items were not clearly defined, such as ‘irregularities of bowel habit’ and ‘alternating constipation and diarrhoea’, whilst others are open to numerous interpretations, including the descriptions of abdominal pain and stool properties provided. In addition, despite its improved accuracy, the Kruis model seems rather unwieldy for routine clinical use.

The Rome criteria
The groups of symptoms that, together, are thought to make up IBS tend to cluster together and have demonstrated statistically significant associations with each other in community-based factor analysis studies [69–71], lending weight to the biological plausibility of IBS as a distinct clinical entity. It was these observations that first led to a group of multinational experts convening to produce a consensus document on all of the functional gastrointestinal disorders [72]. This led to the development of the Rome process, and the first iteration of a set of new diagnostic criteria for IBS, dubbed the Rome I criteria (Table 1.3), were born. These criteria have been revised on two subsequent occasions, to produce the Rome II and Rome III criteria (Table 1.3) [73, 74].

The Rome I criteria have some similarities to those described by Manning et al., although it was acknowledged that the change in stool frequency or
form could be in either direction, rather than just more frequent and/or looser. Subsequent refinements to the Rome criteria have retained the three pain-related features originally described by Manning, but the presence of bloating or visible abdominal distension, tenesmus and passage of mucus per rectum are now no longer considered to be essential to, but may be supportive of, the diagnosis of IBS. Despite this modification, bloating is reported by up to 80% of IBS sufferers in cross-sectional surveys [75, 76]. Another difference between the various iterations of the Rome criteria and those of Manning is the requirement for a minimum duration and frequency of symptoms. This has become increasingly complex, with the Rome I criteria requiring a minimum symptom duration of at least three months, but the Rome III criteria requiring symptoms to have been present for at least six months and for the individual to have experienced symptoms on three or more days per month during the previous three months.

A recent systematic review and meta-analysis searched for studies that had attempted to validate the Rome criteria [60]. The authors identified only one study, published almost 10 years ago [77], which studied the Rome I criteria in 602 consecutive new referrals to a gastroenterology outpatient department in the United Kingdom. There were no studies identified that

<table>
<thead>
<tr>
<th>Iteration and year described</th>
<th>Symptom items included</th>
<th>Minimum symptom duration required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rome I, 1990</td>
<td>Abdominal pain or discomfort relieved with defaecation, or associated with a change in stool frequency or consistency, PLUS two or more of the following on at least 25% of occasions or days: Altered stool frequency Altered stool form Altered stool passage Passage of mucus Bloating or distension</td>
<td>≥ 3 months</td>
</tr>
<tr>
<td>Rome II, 1999</td>
<td>Abdominal discomfort or pain that has 2 of 3 features: Relieved with defaecation Onset associated with a change in frequency of stool Onset associated with a change in form of stool</td>
<td>≥ 12 weeks (need not be consecutive) in last 1 year</td>
</tr>
<tr>
<td>Rome III (2006)</td>
<td>Recurrent abdominal pain or discomfort ≥ 3 days per month in the last 3 months associated with 2 or more of: Improvement with defaecation Onset associated with a change in frequency of stool Onset associated with a change in form of stool</td>
<td>Symptom onset ≥ 6 months prior to diagnosis</td>
</tr>
</tbody>
</table>
assessed the accuracy of either the Rome II or Rome III criteria for the
diagnosis of IBS prospectively, despite the fact that the former had been
published for eight years at the time this systematic review was conducted.
In the study conducted by Tibble et al. [77], the Rome I criteria also
performed only modestly, with a sensitivity of 71% and a specificity of
85% for the diagnosis of IBS.

The Rome Foundation has made great advances in our understanding of
the functional gastrointestinal disorders. From a research perspective, the
Rome criteria have become increasingly important over the last 20 years
and have become the accepted gold-standard for diagnosing IBS. They
have also been used to standardize the type of patients recruited into treat-
ment trials for the disorder, and thereby reduce heterogeneity between
study participants. This has led to an expectation that investigators con-
ducting research in to any other aspect of IBS will use these criteria, or risk
criticism of their study methodology. However, with only one published
study validating any of the available iterations, this reflects poorly on the
gastroenterology research community as a whole. Further validation studies
assessing the accuracy of the more recent Rome III criteria are, therefore,
urgently required.

A further issue that limits the usefulness of the Rome process is its rigidity.
Its symptom-based classification of functional gastrointestinal disorders has
become increasingly complex and the majority of these conditions are now
mutually exclusive. This ignores evidence that there is considerable overlap
among these various disorders. A meta-analysis demonstrated that the prev-
ance of IBS in individuals with functional dyspepsia was eightfold that in
those without [19], and there was considerable overlap between the two
conditions, no matter which of the various available symptom-based diag-
nostic criteria for each were used to define their presence. Another recent
study examined the issue of overlap between IBS and chronic idiopathic con-
stipation, evaluating the ability of the Rome II criteria to distinguish between
the two disorders [78]. The authors suspended the mutual exclusivity of
the two sets of diagnostic criteria and reported that this led to significant
overlap between them, implying that IBS and chronic idiopathic constipation
may be different subgroups within the same disorder. This calls into question
potentially artificial divisions between the functional gastrointestinal disor-
ders based on symptom reporting.

A physician’s opinion
It is argued that the Manning and Rome criteria are less relevant to physicians
in primary care, as they have been developed primarily by gastroenterolo-
gists in secondary or tertiary care. One Scandinavian study that compared
the degree of agreement between a general practitioner’s diagnosis of IBS
and that using the Rome II criteria reported only 58% concordance between
Chapter 1: Definitions and Classifications of IBS

A consensus panel suggested that existing diagnostic criteria were not sufficiently broad for use in primary care [80], and surveys demonstrate that few primary care physicians are aware of, or use, any of the existing diagnostic criteria to diagnose IBS, yet can still diagnose the condition with confidence using a pragmatic approach [81]. In a study conducted among Dutch general practitioners more than half thought that the cardinal feature of the condition was recurrent attacks of abdominal pain [82]. As primary care is the setting where the majority of IBS patients will present initially with symptoms, and be diagnosed and treated, this calls into question the ethos behind the use of such criteria to make the diagnosis of IBS. Unfortunately, there were no published studies reporting on the utility of a physician’s opinion in making a diagnosis of IBS identified in a recent systematic review and meta-analysis [60], and guidelines for the management of IBS in primary care still advocate the use of available symptom-based diagnostic criteria [45, 83].

Agreement between various definitions of IBS

Even though the Rome I and II criteria were derived from the Manning criteria, there are some differences between them that have already been discussed. In addition, the Rome I criteria only require the presence of one of the pain-related symptoms that make up the Manning criteria, whereas the Rome II criteria require at least two. Given the continuing evolution of definitions of IBS, it is important to assess the reproducibility of a diagnosis of IBS with one set of symptom-based diagnostic criteria compared with another. There have been several published studies that have examined this issue, with conflicting results. Overall, the prevalence of IBS appears generally higher when the Manning criteria are used to define its presence, perhaps because there is no minimum symptom duration required in order to meet diagnostic criteria [84–86]. There was generally good agreement between the Manning and Rome I criteria in two studies [85, 86], which is perhaps not surprising given the similarity of the definitions used in each. However, a third study that examined this issue reported a lower degree of concordance [84].

Agreement between Rome II criteria and those of Manning was less impressive [84, 85], and that for Rome I and Rome II criteria was of a similar magnitude [84, 85, 87]. These studies highlight that the continued refinement of the definitions of IBS reduces the overall prevalence of the disorder. This may lead to a proportion of individuals, who undoubtedly have gastrointestinal symptoms, no longer meeting diagnostic criteria for IBS when the more recent iterations of the Rome criteria are used. Instead these individuals have symptoms that are not able to be classified. This is probably not an ideal situation for either the physician or the sufferer and has led to some researchers to hypothesize that the later revisions of the
Rome criteria are too restrictive for clinical practice, and that perhaps those of Manning *et al.* should be preferred in this setting [84].

**Classification of irritable bowel syndrome**

As has been discussed, when the Rome criteria were first proposed the pain-related symptoms required to fulfil a diagnosis of IBS were modified slightly from those of Manning *et al.*, to allow the change in stool form or frequency to include harder or less frequent stools, rather than only looser or more frequent stools as had originally been proposed. This adjustment has allowed the classification of IBS into subgroups based on the predominant stool pattern experienced by the patient. As a result, in the latest Rome III definition it is possible to classify IBS into diarrhoea-predominant (IBS-D), constipation-predominant (IBS-C), or those who fluctuate between the two, so-called mixed IBS (IBS-M). This is a useful approach for several reasons. Firstly, it allows the targeting of therapies by the physician towards the most troublesome symptom reported by the patient. Secondly, it aids the development of new pharmaceutical agents to treat these symptom subgroups discretely. Thirdly, it allows the investigation of patients according to these subcategories in order to explore possible underlying pathophysiological mechanisms, towards which future therapies may be directed.

From the year 2000 onwards there were a succession of randomized controlled trials of therapies for IBS that recruited patients according to the predominant stool pattern experienced [88–93]. These trials used agents acting on the 5-hydroxytryptamine receptor, which is thought to play an important role in gastrointestinal motility and sensation. Unfortunately, the drugs that were used in these trials, alosetron in IBS-D and tegaserod in IBS-C, have been withdrawn due to serious concerns about their safety. However, the principle of testing drugs in patients according to their predominant symptom has continued ever since, with drugs such as lubiprostone and linaclotide being tested in IBS-C [94, 95], the glucagon-like peptide analogue ROSE-010 being used in IBS patients with recurrent attacks of abdominal pain [96] and the efficacy of rifaximin, a non-absorbable antibiotic, being studied in patients with non-constipated IBS, but who reported troublesome bloating [97].

Whilst the classification of IBS according to stool pattern or the predominant symptom reported by the patient would seem a sensible approach, there are several potential limitations. Firstly, it has been shown that there may be a poor correlation between the stool frequency classification of the Rome criteria and diarrhoea or constipation as reported by the patient with IBS [98], leading to particular problems with the mixed stool pattern subgroup. Secondly, community-based cross-sectional surveys and
case series of gastroenterology clinic patients with IBS consistently demonstrate that a significant minority of subjects with IBS, between 20 and 35%, will change their predominant stool pattern during extended follow-up [99–101]. Thirdly, in some sufferers gastrointestinal symptoms may either disappear altogether, or the symptoms alter to such an extent that the individual no longer meets diagnostic criteria for IBS, but does meet criteria for one of the other functional gastrointestinal disorders, such as dyspepsia, gastro-oesophageal reflux disease or chronic idiopathic constipation [2, 4, 101, 102]. Finally, terms such as constipation or diarrhoea are highly subjective. More objective measures such as stool weight have rarely been studied in IBS, and whether this is altered in patients with IBS-D or IBS-C is unclear [103, 104].

As a result of all this, it is therefore important that the patient with IBS is reassessed at regular intervals to ensure that they still meet criteria for IBS. If IBS criteria are still met, the physician should check whether the predominant symptom or stool pattern has changed. The inherent instability of bowel habit and of the most troublesome symptom reported that is part of the relapsing and remitting natural history of the condition suggests that relatively few patients will experience sustained relief of their symptoms with a single treatment regimen in the longer term. Despite these limitations of current classification systems for IBS, this approach remains a useful strategy for directing therapy, as well as for the testing of novel treatment agents in order to identify subgroups of patients which are likely to derive the most benefit.

Conclusions

Irritable bowel syndrome is a highly prevalent condition in the community. Defining the condition using symptom-based criteria, in order to encourage physicians to make a positive diagnosis of IBS, thereby reducing inappropriate invasive investigation in patients who clearly meet these criteria, remains an important part of the management process. However, available symptom-based criteria perform only modestly in most cases. In addition, the current gold-standard for defining IBS, the Rome criteria, has not been extensively validated in prospective studies. This is concerning and needs to be addressed. In the absence of an accurate biomarker for the condition, we require either more studies recruiting groups of patients with gastrointestinal symptoms undergoing lower gastrointestinal investigation that apply the current diagnostic criteria to assess their accuracy in making a diagnosis of IBS, or studies that assess newer and potentially more accurate ways of detecting the condition. Ideally, any novel definitions that are developed should be equally applicable to physicians in primary and secondary care settings.
In terms of the classification of IBS, establishing the patient’s predominant or most troublesome symptom is an important part of the effective management of the condition, and therapy should be tailored accordingly. However, the fluctuating nature of IBS should be borne in mind. Patients should be reassessed at regular intervals to ensure that they have not become asymptomatic, changed their predominant symptom or developed an alternative functional gastrointestinal disorder, and hence that the treatment that is being delivered is still appropriate. Further research based on these subgroups of IBS patients may allow us to discover new pathophysiological mechanisms that underlie this heterogeneous disorder, as well as develop new and more effective therapies against it.

References