

## SPECIAL ARTICLE

**Asian consensus on irritable bowel syndrome**

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**Key words**

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**Abstract**

**Background and Aims:** Many of the ideas on irritable bowel syndrome (IBS) are derived from studies conducted in Western societies. Their relevance to Asian societies has not been critically examined. Our objectives were to bring to attention important data from Asian studies, articulate the experience and views of our Asian experts, and provide a relevant guide on this poorly understood condition for doctors and scientists working in Asia.

**Methods:** A multinational group of physicians from Asia with special interest in IBS raised statements on IBS pertaining to symptoms, diagnosis, epidemiology, infection, pathophysiology, motility, management, and diet. A modified Delphi approach was employed to present and grade the quality of evidence, and determine the level of agreement.

**Results:** We observed that bloating and symptoms associated with meals were prominent complaints among our IBS patients. In the majority of our countries, we did not observe a female predominance. In some Asian populations, the intestinal transit times in healthy and IBS patients appear to be faster than those reported in the West. High consultation rates were observed, particularly in the more affluent countries. There was only weak evidence to support the perception that psychological distress determines health-care seeking. Dietary factors, in particular, chili consumption and the high prevalence of lactose malabsorption, were perceived to be aggravating factors, but the evidence was weak.

**Conclusions:** This detailed compilation of studies from different parts of Asia, draws attention to Asian patients' experiences of IBS.

**Introduction**

On 15 October 2007, 18 active researchers in the field of gastrointestinal (GI) functional and motility disorders from different Asian countries met on the sidelines of the Asia-Pacific Digestive Disease Week held in Kobe, Japan. The formation of the Asian Neurogastroenterology and Motility Association (ANMA) was proposed to promote research into, exchange knowledge of, and

disseminate information pertaining to GI functional and motility disorders in Asia, with the ultimate aim of improving the care of those suffering from these highly-prevalent conditions. On 21 March 2008, ANMA was officially launched in Bangkok, Thailand, and the development of an Asian Consensus on irritable bowel syndrome (IBS) was initiated.

While IBS is one of the most common conditions encountered in gastroenterology and primary care practices, we believe that it

represents one of the least understood conditions for medical doctors in Asia. The reason for this could be partly attributed to the nature of IBS as a condition defined only by its symptoms in the absence of an objective marker, and partly because of the dominance of Western studies and ideas in the available scientific literature. As the perception of symptoms (such as abdominal pain and discomfort) and bowel function is inevitably influenced by the individual's psychosocial background, there is a need to question the relevance of the commonly perpetuated ideas of IBS based predominantly on studies from Western societies, and their socio-cultural expectations, to Asian patients. To address this, we felt it was important to review in detail the available Asian literature on IBS, bring the data from these studies to attention, and where data are lacking, to articulate the collective experience of our expert members practicing in different parts of Asia.

## Methods

A multinational group of physicians from Asia was selected based on the strength of their interests in the study of IBS. Participants were organized into four groups and tasked with raising statements on IBS pertaining to symptoms and diagnosis, epidemiology and infection, pathophysiology and motility, and management and diet. The consensus development process was carried out in a modified Delphi method.<sup>1</sup> Each team collected reference papers on IBS, published not only from Asia, but also from rest of the world through online literature searching systems. Papers in English and local languages not available online were searched manually. Each team had to present evidence in support of their statements. Through a series of intrateam and interteam discussions, email voting, and round table discussions held between 3 September 2008 and 10–11 January 2009, the statements were debated and modified to achieve consensus. The grade of the evidence and the level of agreement were based on the method of the GRADE Working Group (see Table 1).<sup>2</sup> When the proportion of those who voted either to accept completely or with minor reservation was 80% or higher, the statement was regarded as acceptable and a consensus as being reached. Finally consensus was achieved on the following 37 statements.

## Consensus statements

For each grade of evidence, high indicates that further research is unlikely to change our confidence in the estimate of effect, moderate indicates that further research is likely to have an important impact on our confidence in the estimate of effect and might change the estimate, and low indicates that further research is very unlikely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. For each level of agreement, a represents accept completely, b represents accept with minor reservation, c represents accept with major reservation, d represents reject with major reservation, e represents reject with minor reservation, and f represents reject completely.

## Symptoms and diagnosis

**Statement 1: IBS is a condition characterized by abdominal pain, bloating or other discomfort occurring in association**

**Table 1** Grade of evidence and level of agreement

Category	Description
Grade of evidence	
High	Further research is unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and might change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain
Level of agreement <sup>†</sup>	
a	Accept completely
b	Accept with minor reservation
c	Accept with major reservation
d	Reject with major reservation
e	Reject with minor reservation
f	Reject completely

<sup>†</sup>Statements were accepted when 80% or more of participants voted a or b.

### with disturbed bowel pattern in the absence of organic causes that can be detected by routine medical tests.

Grade of evidence: high.

Agreement: a. 11 (68.8%), b. 4 (25%), c. 1 (6.2%).

In this definition, we have intentionally qualified the term 'organic causes' as those that can be detected by routine medical tests. This is to take into account recent research employing more sensitive methods that have demonstrated differences in inflammatory markers, gut microbial flora, and genotypic expressions of inflammatory and neurotransmitter receptor molecules between IBS patients and controls.<sup>3–8</sup> Thus, the traditionally accepted markers of an organic disease—inflammation, infection and biochemical alterations—might not be strictly applied to the current understanding of IBS.

This definition also presents bloating as a key symptom among IBS patients in Asia. In our review of Asian IBS series, we have found that bloating occurs almost as commonly as abdominal pain, and is an important reason for patient consultation.<sup>9–16</sup> There is a common perception among clinicians that bloating is a symptom of an upper GI disorder. However, bloating is experienced more frequently in IBS patients than dyspeptic patients, and in recognition of this, the current Rome III guidelines no longer consider bloating as a symptom of dyspepsia.<sup>17–20</sup>

### Statement 2: Early and confident diagnosis of IBS is important to minimize excessive investigations, inappropriate treatment, and unnecessary surgery.

Grade of evidence: moderate.

Agreement: a. 16 (100%).

Among some Chinese communities, IBS appears to be underdiagnosed and underestimated. In Hong Kong, it was reported that only 21% of patients with IBS criteria seen by their medical practitioners had received this diagnosis.<sup>14</sup> In a study from Taipei, more than half of the 481 patients who were initially classified as having

functional dyspepsia were found to have IBS.<sup>21</sup> An interesting observation in this study was that women who had consulted for dyspepsia had a threefold greater risk of hysterectomy than non-consulters. In another study from Taipei, IBS patients were two times more likely to have had cholecystectomy.<sup>22</sup> In a study from Singapore, 28% of patients referred by their general practitioners for upper GI endoscopy were found to have IBS.<sup>23</sup>

Similar excess rates of abdominal surgery, in particular, cholecystectomy and hysterectomy, have been reported in the West.<sup>24–26</sup> It has been estimated that in the USA, 8% of IBS patients will undergo unnecessary cholecystectomy in their lifetime.<sup>27</sup> One study from the UK showed that over half of women who had gone to see their gynecologists for abdominal pain actually had symptoms of IBS, and yet, the gynecologist only diagnosed IBS in 16% of them.<sup>28</sup>

**Statement 3: It is recommended that all patients presenting with recurrent abdominal pain, bloating, or other discomfort of 3 months or longer duration should be screened for possible IBS by asking for bowel-related symptoms and checking for alarm features.**

Grade of evidence: low.

Agreement: a. 15 (93.8%), b. 1 (6.2%).

To promote an earlier diagnosis of IBS, we are introducing a broader entry portal. We wish to encourage doctors, in particular, primary care physicians, to consider the possibility of an IBS diagnosis early in their assessment of patients presenting with abdominal pain, bloating, or other abdominal discomfort. All patients with these symptoms should be asked specifically whether these symptoms are relieved with defecation, or associated with a change in stool consistency or frequency. In addition, patients should be asked about the presence of the alarm features listed in the statement.<sup>7</sup> Those who are possible IBS patients should be worked up according to the algorithm in the statement<sup>8</sup> (Fig. 1). The 3 months' duration of symptoms is applied to permit differentiation from acute causes. For clinical practice, we would recommend this practice-oriented approach over the use of the Rome criteria. Experience suggests that few clinicians are familiar with the Rome criteria, and few, if any, apply it in their clinical practice.<sup>29–31</sup> Furthermore, our recent review suggests that rigid application of the Rome II criteria could have led to misclassification of IBS patients as suffering from dyspepsia, and contributed to inappropriate treatment with proton pump inhibitors, and to the excess surgery that was reported in a number of centers.<sup>9</sup> However, for the purpose of standardization in clinical trials, we recommend that the current Rome criteria are applied, as well as the requirements set out in statement 9.

**Statement 4: Bowel-related symptoms consist of abdominal pain, bloating, or other discomfort that is either improved by passing stool or flatus, or associated with any change in stool form or frequency.**

Grade of evidence: low.

Agreement: a. 15 (93.8%), b. 1 (6.2%).

These characteristics are derived from the original studies by Manning and by Thompson.<sup>32,33</sup> In these pivotal studies, patients with IBS were compared with those who had peptic ulcer disease and inflammatory bowel disease (IBD). Bloating, abdominal pain relieved with defecation, looser stools with pain onset, and more

frequent stools with pain onset all discriminated best between IBS and peptic ulcer. In fact, of the four symptoms, bloating was the most commonly occurring, and only bloating occurred more frequently in IBS than IBD.<sup>32,33</sup> However, despite their inclusion in the Rome criteria, harder stools and less frequent stools with pain onset did not discriminate between IBS and organic disease in the original Manning study.<sup>32</sup>

**Statement 5: The patient's bowel pattern should not be described only by the stool frequency alone, but should include the stool type, according to the Bristol Stool Form Scale, and the specific defecation symptoms of straining at stool, feeling of incomplete defecation, and urgency.**

Grade of evidence: high

Agreement: a. 16 (100%).

Doctors should not simply ask whether a patient has constipation or diarrhea, but should enquire about specific defecation symptoms as recommended above. If the patient is not asked about their specific defecation symptoms or to identify their stool form, he or she might not recognize the association with abdominal pain, bloating, or discomfort. In Asia, the constipation and diarrhea symptoms of IBS can be mild, and IBS patients might appear to have normal bowel habits by Western definitions. In the Indian community, less than 1% of patients had stool frequencies of fewer than three per week, while among IBS patients, the median stool frequency was twice a day, regardless of whether they had constipation or diarrhea.<sup>10</sup> In a community study from Singapore, 77% of patients with IBS thought they had normal bowel habits, and yet when they were asked specific questions relating to defecation symptoms, 50% had criteria for constipation, 25% for diarrhea, and 4% for an alternating habit.<sup>13</sup> We would suggest that change in stool frequency as a symptom of IBS should be de-emphasized. Consistently across all Asian studies, a change in stool frequency was only a minor complaint, whereas difficulty with evacuation and passage of mucus were common reasons for consultation.<sup>9,11–14,22</sup>

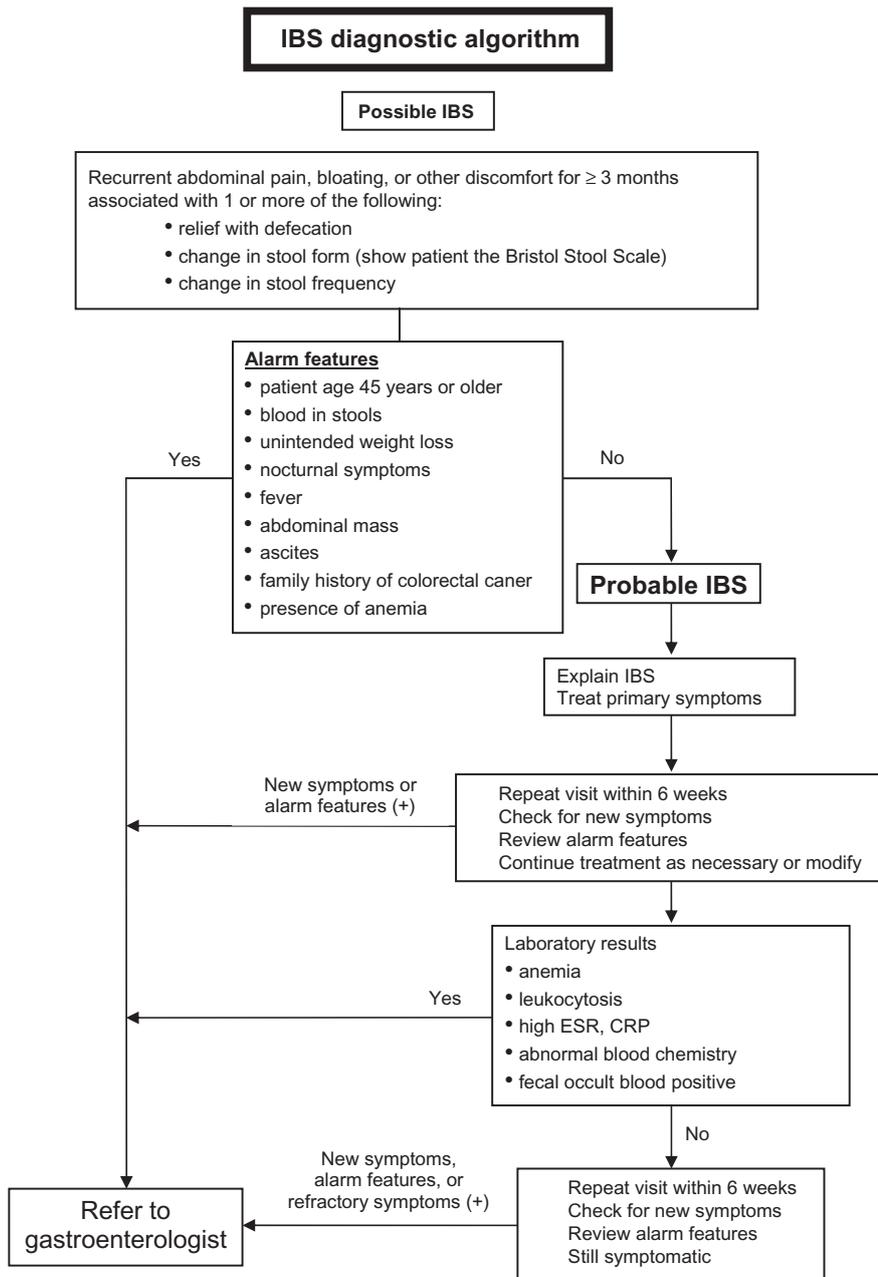
**Statement 6: IBS patients may complain of meal-related symptoms, which include abdominal pain, bloating, sensations of fullness or gas, and desire to defecate.**

Grade of evidence: high.

Agreement: a. 12 (75%), b. 3 (18.8%), c. 1 (6.2%).

Studies analyzing the relationship of IBS symptoms to meals, and studies of sensorimotor physiological responses to meals, provide strong evidence that eating a meal is an important trigger for symptoms in IBS.<sup>34–41</sup> One study from Sweden required IBS patients to chart in detail the timing of symptoms throughout the day for up to 6 weeks; this revealed that pain was relieved with defecation on only 10% of occasions, whereas 50% of pain episodes were brought on within 90 min of eating.<sup>42</sup> This suggests that the pain experienced by IBS patients might actually bear a stronger temporal relationship to eating than to defecation.

We believe that it is important to highlight the relationship of symptoms to meals in IBS. Mistaking meal-related IBS symptoms as dyspepsia could lead to excessive investigation with tests, such as upper GI endoscopy and ultrasound scans, inappropriate treatments, such as acid suppression, and unnecessary surgery, such as cholecystectomy.<sup>22,23</sup> This could be a particular problem in Asia because our patients appear to present more frequently with upper



**Figure 1** Diagnostic algorithm for irritable bowel syndrome (IBS). CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

abdominal pain than in Western series.<sup>10,11,13,43</sup> In a number of studies from Asia, it appeared that patients with IBS might have been misclassified as suffering from dyspepsia.<sup>9,12,21,44</sup> In a study from Taiwan, more than half of patients initially classified as suffering from dyspepsia were reclassified as having IBS when it was clarified that their upper abdominal pain was exclusively relieved with defecation.<sup>21</sup>

**Statement 7: Alarm features to check for in IBS include age 45 years or older, presence of anemia, blood in the stools, unintended weight loss, nocturnal symptoms, fever, abdominal mass, ascites, and a family history of colorectal cancer (see Fig. 1).**

Grade of evidence: moderate.

Agreement: a. 11 (68.8%), b. 4 (25%), c. 1 (6.2%).

We propose age of 45 years as a cut-off for ethnic groups who are more susceptible to colorectal cancer (Japanese, Koreans, Chinese), while other ethnic groups (Indians, Thais) can opt for a cut-off of 50 years. This is a modification of the recent Asia-Pacific consensus recommendations for colorectal cancer screening.<sup>45</sup> We have set a younger cut-off age because IBS patients are symptomatic and would not qualify for screening guidelines, which are intended for asymptomatic individuals.

A recent study from Australia has provided data on the diagnostic yield of alarm features in IBS.<sup>46</sup> Age over 45 years, blood coating stools, blood mixed with stools, and blood on toilet paper

were found to discriminate significantly between IBS and patients with organic bowel disease. However, weight loss and nocturnal pain did not significantly discriminate between IBS and organic disease. It should be noted that this study was based on an Australian population, and patients in the organic disease group consisted predominantly of those with IBD or diverticular disease, both of which are currently uncommon in many Asian countries.

**Statement 8: At the primary care level, use of a screening algorithm, comprising symptom criteria, a checklist of alarm features, and guidelines on monitoring procedure, is recommended (see Fig. 1).**

Grade of evidence: low.

Agreement: a. 13 (81.3%), b. 3 (18.7%).

We believe that it is important for doctors to move away from seeing IBS as a last resort diagnosis. This algorithm is meant to help the primary care physician make an early diagnosis of IBS (Fig. 1). In this algorithm, doctors are expected to consider a possible diagnosis of IBS the moment a patient presents with the main complaint of abdominal pain, or other discomfort. The next step is to ask the patient whether the main complaint is associated with relief upon defecation, or with a change in stool consistency or frequency. We feel it is important to qualify the symptom with a minimum of 3 months' or 12 weeks' duration of onset, and to exclude all the alarm features. Once this has been achieved, the patient should then be given the diagnosis of probable IBS. If the primary care physician suspects that a patient has lactose intolerance, then the patient could undertake either a trial of lactose exclusion or a lactose hydrogen breath test, and if this diagnosis is confirmed, then it should be managed accordingly. In patients with diarrhea, stool samples should be sent for microscopic examination to exclude parasitic infection.

We would emphasize that the diagnosis of IBS should also be put to the test of time, that is, a patient with a diagnosis of probable IBS should be encouraged to return for two consecutive reviews each to be carried out within 6 weeks of each other. At each visit, the patient should be assessed for their response to treatment, new symptoms, and alarm features. At any stage during this algorithm, if the patient is found to have any of the alarm features listed or any of the abnormal laboratory results, a gastroenterology consult should be sought. A gastroenterology consult should also be sought if the patient is still symptomatic at the end of the 12-week monitoring period.

**Statement 9: For clinical trials, all patients should have at least full blood counts, erythrocyte sedimentation rate, C-reactive protein, and colonoscopy, and other investigations, if indicated.**

Grade of evidence: moderate.

Agreement: a. 10 (62.4%), b. 3 (18.8%), c. 3 (18.8%).

A number of members expressed reservations because of cost considerations. However, we wish to emphasize that this recommendation is specific to clinical trials and is not applied to clinical practice. The main aim of this statement is to protect our patients from being entered inappropriately into clinical trials. For example, an ultrasound scan is recommended if patients present with symptoms of biliary colic, so that patients who might be harboring symptomatic gallstones are not treated as having IBS. Patients with upper abdominal symptoms should also undergo an

upper GI endoscopy, in view of the high prevalence of severe gastritis, peptic ulcer disease, and gastric cancer in many parts of Asia. The underlying motivation is also based on the expectation that these studies will be funded by either national research agencies or pharmaceutical companies. Thus, the costs involved will not impact on the cost-effectiveness of the day-to-day management of IBS.

**Statement 10: The subclassification of IBS, according to the bowel pattern, can be based on a modification of the Rome III criteria, but this needs validation.**

Grade of evidence: low.

Agreement: a. 10 (50%), b. 10 (50%).

In the Rome III classification, IBS is subtyped based on stool consistency alone. We believe that this approach is appropriate for Asia, given our observations that changes in stool frequency were only a minor complaint among our patients. In line with this, we recommend that patients with types 1–3 stools on the Bristol Stool Scale are classified as IBS with constipation (IBS-C), and those with type 5–7 stools are classified as IBS with diarrhea (IBS-D). Patients with both hard and soft stools over periods of hours or days are classified as IBS mixed type, while patients whose stools change from hard to soft, or vice versa, over weeks or months, are classified as IBS alternating type. This subclassification is presently adopted because good correlation has been demonstrated between stool form and colonic transit times, and this can be used as a guide to selection of treatments according to their effects on colonic transit. However, the impact of this on treatment response remains to be validated. Furthermore, this approach does not take into account other important pathophysiological disturbances, in particular, visceral sensitivity.

## Epidemiology and infection

**Statement 11: The reported prevalence of IBS in Asian countries varies from 2.9% to 15.6%, but the study population and diagnostic criteria have not been consistent.**

Grade of evidence: high.

Agreement: a. 14 (87.5%), b. 2 (12.5%).

It has been suggested that the prevalence of IBS is lower among Asian than Caucasian communities. Early studies employing the same questionnaire reported a lower prevalence of spastic irritable colon in the Thai community (4.4%) compared with British (13.6%) and US (22.3%) patients.<sup>47</sup> In a study applying the Manning criteria to different ethnic communities in California, USA, Asians had a lower prevalence compared with other racial groups.<sup>48</sup> In contrast, the prevalence appeared to be higher in Japan than in the Netherlands (25% vs 9%).<sup>49</sup> Recent studies applying the Rome II criteria also suggest that the prevalence in Japan (9.8%) and Singapore (8.6%) is comparable to Europe (9.6%) and Australia (6.9%), although not as high as in Canada and the UK (12%).<sup>9</sup>

Variation in the prevalence of IBS in different studies might be related to several factors, such as demographic characteristics of the population, willingness to respond to questionnaires, geographical location, and the criteria used to define IBS. For example, Manning criteria appears to yield higher values compared to either the Rome I or II criteria.<sup>50</sup> When Kang compared the prevalence of IBS in the East to that in the West, he reported

respective median values of 12% versus 17% by Manning criteria, 9.2% versus 10.4% by the Rome I criteria, and 7.6% versus 6% by the Rome II criteria.<sup>50</sup> Furthermore, it is possible that the prevalence of IBS in Asian countries has increased over time, accounting for the higher median value of more recent studies from Asia employing the Rome II criteria when compared with that from Western studies.<sup>43,50</sup>

**Statement 12: IBS is as prevalent in men as in women in some Asian countries.**

Grade of evidence: moderate.

Agreement: a. 10 (62.5%), b. 5 (31.3%), c. 1 (6.2%).

Most studies from the West reported two to three times higher prevalence of IBS in women than in men.<sup>9</sup> However, several recent studies from Asia have reported an as high, if not higher, prevalence of IBS in men than in women; (in India 7.9% vs 6.9% in one study, 4.3% vs 4% in another study; in Korea 7.1% vs 6%; in Hong Kong 6.6% vs 6.5%; in Pakistan 13.1% vs 13.4%).<sup>9</sup> Several other studies from Asian countries have reported non-significant differences in prevalence between men and women (in Taiwan 21.8% vs 22.8%; in Singapore 7.8% vs 9.4%).<sup>9</sup> Only studies from two Asian countries have reported a convincingly higher prevalence of IBS in women than in men (in Bangladesh 15% vs 9.4%; in Japan 15.5% vs 10.7%).<sup>9</sup>

**Statement 13: Dyspepsia is not uncommon in patients with IBS in Asia.**

Grade of evidence: high.

Agreement: a. 13 (81.3%), b. 2 (12.5%), c. 1 (6.2%).

The frequency of dyspeptic symptoms reported among patients with IBS in various Asian studies was as follows: India (58%), China (25–64%), and South Korea (14%).<sup>15,51–53</sup> Misclassification of IBS as dyspepsia could be a particular problem in Asia because our patients appear to present more frequently with upper abdominal pain than in Western series.<sup>9–11</sup> In a study from Singapore, Ho *et al.* classified all patients with upper abdominal symptoms as having dyspepsia; in an earlier study from the same institution, 44% of patients with a functional cause of chronic upper abdominal pain had IBS, and in a later study, it was reported that more than 50% of IBS patients localized their pain to the upper abdomen.<sup>12,13,54</sup> In a study from Taiwan, more than half of patients who were initially classified as suffering from dyspepsia were reclassified as having IBS when it was clarified that their upper abdominal pain was exclusively relieved with defecation.<sup>21</sup>

**Statement 14: In the population of some south Asian countries, stool frequency is higher than that in the West.**

Grade of evidence: moderate.

Agreement: a. 10 (62.5%), b. 6 (37.5%).

In the West, the normal stool frequency range is from three per week to three per day.<sup>55,56</sup> However, several studies from India have reported a higher stool frequency.<sup>10,57</sup> In a recent study from India involving 4500 patients drawn from the community, defecation frequency was on average greater than three stools per day in 167 (3.7%), three per day in 242 (5.4%), two per day in 1535 (34%), one per day in 2520 (56%), and less than three per week in 43 (1%).<sup>10</sup> In addition to higher stool frequency, the average stool weight also appears to be greater in the Indian adult population,

where it is 311 g per day, compared to less than 200 g per day in the West.<sup>11,12,57</sup> However, the normal stool frequency reported from other parts of Asia appears to be similar to that in the West; over 97% of people in Singapore and Thailand report stool frequency between three per day and three per week; 41% and 84% of people in Korea and China, respectively, report once daily bowel movement.<sup>47,58–60</sup> These differences should be taken into account when defining bowel habits in various populations.

**Statement 15: IBS can follow bacterial GI infections, although data are available only from a few Asian countries.**

Grade of evidence: high.

Agreement: a. 13 (81.3%), b. 3 (18.7%).

Studies from the West suggest that an acute GI infection is an important trigger for the development of IBS.<sup>61,62</sup> In Asia, there are two prospective studies documenting the development of IBS following Shigella infection. In a cohort study from Beijing, the incidence of functional bowel disorders and IBS by Rome II criteria among 295 patients recovering from dysentery was 22.4% and 8.1%, respectively, compared with an incidence of 7.4% and 0.8%, respectively, in the control cohort.<sup>63</sup> In a study from Seoul involving an outbreak of Shigella infection among 181 health-care workers, the odds ratio of developing IBS was calculated to be 2.9 at 12 months.<sup>64</sup>

**Statement 16: IBS in a proportion of patients can be associated with small intestinal bacterial overgrowth.**

Grade of evidence: moderate.

Agreement: a. 13 (81.3%), b. 3 (18.7%).

One center from the USA has reported a prevalence of small intestinal bacterial overgrowth (SIBO) in their IBS patients of 84% compared with 20% in healthy controls.<sup>65</sup> The definition of SIBO in that study was based on a rise in breath hydrogen concentration by 20 ppm above basal levels within 90 min following ingestion of a lactulose load (lactulose hydrogen breath test; LHBT). Using the same criterion, a study from Korea reported a SIBO prevalence of 48.7% in IBS and 26.5% in controls.<sup>66</sup> There are issues with the use of this definition in diagnosing SIBO. First, there is no validation of this criterion against quantitative jejunal aspirate culture, by which the prevalence of SIBO (defined as  $> 10^5$  bacteria/mL) in IBS was reported to be only 4%.<sup>67</sup> Another method of identifying SIBO employs the glucose hydrogen breath test (GHBT), which is less influenced by the orocecal transit time (OCTT). Using the GHBT, the prevalence of SIBO in IBS patients was reported to be 31% in a US study, 46% in a European study, and 8.5–13% in Indian studies.<sup>68–72</sup> It is important to take into account the relatively shorter OCTT that have been reported in Asian patients compared with the West.<sup>73–76</sup> The implication of this is that patients and healthy patients who have short transit times might give a false positive LHBT.

**Statement 17: In some endemic countries, a mild form of tropical sprue and Giardia infection can mimic IBS.**

Grade of evidence: low.

Agreement: a. 12 (75%), b. 4 (25%).

In some Asian populations, parasitic infestation, SIBO, and tropical sprue are common causes of malabsorption syndrome.<sup>77</sup> Such conditions, when mild, might not present with weight loss or nutritional deficiency, and could thus mimic IBS. In fact, there are

several reasons to suspect that there might be considerable overlap between post-infectious IBS and post-infectious malabsorption syndrome.<sup>78</sup>

**Statement 18: Perception of symptoms of IBS can vary in Asia; thus, a questionnaire including relevant socioeconomic and cultural factors in Asia should be developed and validated for future studies.**

Grade of evidence: low.

Agreement: a. 8 (50%), b. 6 (37.5%), c. 2 (12.5%).

Several lines of evidence suggest that the perception of symptoms by IBS patients in Asia could be different from those in the West. Patients in Asia appear to be bothered more by upper abdominal symptoms and bloating, and it appears that IBS could be misdiagnosed as dyspepsia.<sup>9</sup> Many IBS patients in Asia might not perceive their bowel pattern to be abnormal; in one study, 58% of patients who had criteria for constipation, diarrhea, or alternating pattern, perceived their bowel habit to be normal.<sup>13</sup> In India, the median stool frequency was twice a day, whether the patients considered themselves to have diarrhea or constipation.<sup>10</sup> Asian patients appear to be bothered less by the frequency of their stools and bothered more by the feeling of incomplete defecation.<sup>9</sup> A high rate of consultation for IBS has been reported from many Asian communities (Singapore, 84%; Japan, 59%; Taiwan, 55%; Hong Kong, 47–57%).<sup>9</sup> With such a high rate, the role of psychological disturbance in driving consultation behavior is questioned.

## Pathophysiology and motility

**Statement 19: IBS is a multifactorial disorder where a variable combination of genetic factors, gut infections, brain–gut interactions, and psychological disturbance can interact in the pathophysiology.**

Grade of evidence: low.

Agreement: a. 11 (64.71%), b. 6 (35.29%).

The factors listed above have been implicated in the pathophysiology of IBS. In any given patient, it is likely that more than one factor might be present. For example, in post-infectious IBS, stress from major life events predicts the development of IBS in patients with higher anxiety levels who also demonstrate more severe inflammatory changes and greater immune activation during the infection.<sup>3,62,79</sup> However, the type of factors present can vary from one patient to another. Although studies are more limited in non-post-infectious IBS, other factors, such as genotypic variations, differences in gut microbial flora, and altered brain activation patterns, have been implicated.<sup>7,80–85</sup>

**Statement 20: Altered GI motility can be found in IBS patients, although it does not always correlate with IBS symptoms.**

Grade of evidence: low.

Agreement: a. 15 (88.24%), b. 1 (5.88%), c. 1 (5.88%).

Differences between IBS patients and healthy controls have been reported when motility measurements have been studied in every region of the GI tract.<sup>36,86–91</sup> One study from Korea reported that gastric emptying time in patients with IBS was delayed compared to that of controls, but there was no difference in gastric emptying

time according to dyspeptic symptoms.<sup>92</sup> Studies from Taiwan and India recorded slower orocecal transit times in constipation-predominant IBS patients compared with healthy controls, while diarrhea-predominant IBS patients recorded faster times than healthy controls.<sup>73,74</sup> Enhanced colonic motility response to injection with corticotropin-releasing hormone (CRH) has been reported in a Japanese study.<sup>93</sup> Studies from Korea have reported that diarrhea-predominant IBS patients demonstrate differences in anorectal manometry findings from constipation-predominant IBS patients, as well as showing a significant post-prandial decrease in rectal compliance.<sup>94,95</sup> However, the association of motility disturbances with specific symptoms has been inconsistent, and differences in motility measurements between IBS and healthy controls appear to be quantitative rather than qualitative.<sup>96,97</sup>

**Statement 21: GI motility disturbances in IBS patients can arise from an exaggerated physiological response to environmental stimuli, such as meals and stressors.**

Grade of evidence: moderate.

Agreement: a. 11 (64.71%), b. 5 (29.41%), c. 1 (5.88%).

When IBS patients were compared with healthy controls, meal ingestion produced a greater increase in the pressure amplitude generated in the sigmoid colon, and also a longer increase in colonic motility.<sup>37,38,98</sup> The response to meals can vary depending on the bowel habit. In one study from Korea, diarrhea-predominant IBS patients demonstrated a greater increase in colonic motor activity than constipation-predominant IBS.<sup>99</sup> In examining the effects of stress, studies have employed experimentally-induced stressors, such as criticism, hypnotically-induced anger, dichotomous listening, and cold water hand immersion.<sup>100,101</sup> These studies reported differences between IBS and non-IBS patients in motor and sensory responses, such as increased colon motor activity and pressure wave amplitudes, as well as decreased antral motor activity, more intense and unpleasant sensation, and decreased rectal perception and pain thresholds.<sup>100,101</sup> A series of studies from a center in Japan has demonstrated that IBS patients have a greater colonic motor response than healthy patients to experimentally-induced stress, and suggests that CRH is a possible mediator of this response.<sup>102,103</sup> Furthermore, in these studies, CRH infusion produced abdominal pain or discomfort that lasted longer in IBS patients than in healthy controls, as well as higher plasma adrenocorticotrophic hormone levels in IBS patients than in controls.<sup>104</sup>

**Statement 22: Some diarrhea-predominant IBS patients have been shown to have rapid GI transit, while some constipation-predominant IBS patients have slow GI transit.**

Grade of evidence: low.

Agreement: a. 14 (82.35%), b. 3 (17.65%).

In general, Asian studies have reported similar observations as those from the West, where IBS patients with diarrhea have relatively shorter orocecal and colonic transit times, while those with constipation have relatively longer transit times. However, these differences in intestinal transit times are not invariable. Furthermore, studies from the West suggest that intestinal transit times demonstrate a closer correlation with stool form than with stool frequency.<sup>105</sup> The colonic transit times reported both for healthy volunteers and IBS patients from studies in India and Hong Kong appear to be faster than those reported from the West.<sup>57,106</sup>

**Statement 23: Visceral hypersensitivity plays an important role in the development of symptoms in IBS patients.**

Grade of evidence: high.

Agreement: a. 15 (88.24%), b. 2 (11.76%).

Studies employing distension of the colon to the study sensory threshold have demonstrated enhanced visceral sensitivity in IBS patients compared with controls.<sup>107,108</sup> Furthermore, using this paradigm, it is possible to reproduce the patient's usual abdominal pain.<sup>109,110</sup> It has also been suggested that visceral hypersensitivity could be a marker of IBS.<sup>107</sup> In one study, nearly all patients (94%) with IBS had altered rectal perception, and there was a correlation between this altered perception and lower abdominal pain, rectal fullness, and urgency.<sup>107</sup> It also appears that visceral hypersensitivity in IBS patients is not confined to the colon, but has also been reported in the esophagus, stomach, duodenum, and ileum, correlating with symptoms arising from these anatomical regions.<sup>36,111–113</sup>

As with Western studies, several studies from Korea, Japan, and China support the presence of enhanced visceral perception in IBS patients.<sup>95,114–119</sup> One study from Korea has shown that patients with constipation-predominant IBS show more rectal hypersensitivity than patients with functional (painless) constipation.<sup>118</sup> One study from China demonstrated that cold water intake lowered the visceral perception threshold.<sup>117</sup> In one study from Singapore, it was possible to reproduce the usual abdominal pain in up to 78% of IBS patients when air was insufflated into the rectum.<sup>120</sup> In one study from Korea, lower abdominal pain, rectal fullness, and urgency were reproduced by rectal balloon distension in 69% of IBS patients.<sup>107</sup> In another study, there was a significant correlation of post-prandial rectal hypersensitivity with a sense of incomplete evacuation and increased bowel movements.<sup>95</sup>

However, enhanced visceral perception was not observed in all IBS patients, and as many as one-third of IBS patients do not demonstrate a lower threshold to bowel distension.<sup>95,107</sup> One study from Korea has reported that the visceral sensory threshold in response to rectal balloon distension did not correlate with the reported severity of symptoms, such as bloating, straining, mucus, incomplete evacuation, urgency, stool form, and defecation frequency.<sup>119</sup>

**Statement 24: Certain foods can aggravate symptoms in some IBS patients.**

Grade of evidence: low.

Agreement: a. 13 (76.47%), b. 4 (23.53%).

Studies from the West suggest that the two main food groups that can aggravate symptoms in IBS are dairy products and cereals.<sup>121,122</sup> Studies from Asia suggest chili and curry are possible food triggers for dyspepsia-like upper abdominal pain in IBS patients.<sup>54,123</sup> Lactose intolerance is common in Asia, and it could be a contributing factor for symptoms, such as bloating, flatulence, and diarrhea. However, studies from both the West and Asia generally report similar prevalence of lactose malabsorption between controls and IBS patients, and the avoidance of lactose has yielded mixed results in studies from the West.<sup>72,99–101,124</sup> Fructose malabsorption has also been implicated in IBS.<sup>125</sup> However, the effect of fructose on IBS patients without fructose malabsorption is uncertain. Fructose tolerance has been less well studied in Asia, but limited studies suggests that this might be more prevalent in Asian women than men.<sup>126</sup>

Recent studies suggest that the measurement of serum immunoglobulin (Ig)G antibodies to food can help to identify specific food intolerance.<sup>127–131</sup> Zuo *et al.*, from Shandong province in China, examined food antigen-specific serum IgG and IgE antibodies in IBS patients.<sup>127</sup> Similar to the data from Western countries, Zuo *et al.* found no increase in IgE levels to various foods, but found increased IgG levels to wheat (but not to rice), and in addition, reported increased IgG levels to egg, soybean, shrimp, and crab. One Korean study reported higher rates of positive skin prick tests to certain food antigens.<sup>132</sup>

**Statement 25: IBS patients can show altered brain activations in specific regions, which might be involved in the perception of pain or discomfort.**

Grade of evidence: moderate.

Agreement: a. 13 (76.47%), b. 4 (23.53%).

Advanced brain imaging techniques, such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), have made it possible to study brain–gut interactions. Functional brain imaging studies have shown how the brain processes visceral sensation. Like somatic sensation, visceral sensation is presented to somatosensory cortices, and also to the limbic system and paralimbic structures, which modulate emotional changes via the autonomic nervous system. Only a few signals delivered to the brainstem and thalamus from visceral organs are consciously perceived in the cortex. Several brain imaging studies using PET and fMRI have demonstrated that experimental rectal pain produced altered or greater activation of pain processing regions in the brain, such as the anterior cingulate cortex, thalamus, insula, and prefrontal cortex.<sup>133–137</sup>

Asian studies showed good agreement with Western studies, regarding the activated cerebral regions during colon distension. One Japanese study using PET has reported that colonic distension, especially descending colon distension, produced enhanced visceral perception and activation of specific regions in the brain, including the limbic system and prefrontal cortex.<sup>135</sup> Another Chinese study using fMRI has reported that in most cases, rectal distension increased the activity of the anterior cingulate cortex, insula, prefrontal cortex, and thalamus in most cases.<sup>138</sup> In addition, they have demonstrated that the activated areas at the insular, prefrontal cortex, and thalamus regions were significantly greater in patients with IBS than that in control patients during rectal balloon distension. A study from Singapore indicated that there was abnormal activation of the brain areas observed in fMRI associated with the anticipation of rectal pain in IBS patients during rectal stimulation.<sup>139</sup>

**Statement 26: Psychological disturbances occur commonly in IBS patients.**

Grade of evidence: high.

Agreement: a. 11 (64.71%), b. 4 (23.53%), c. 2 (11.76%).

Psychiatric diagnoses, such as anxiety, depression, neuroticism, hypochondriasis, and abnormal illness behavior were commonly reported in studies from tertiary centers in the West.<sup>140,141</sup> Studies from Hong Kong, Japan, and India have reported higher anxiety and depression scores in IBS patients compared to non-IBS patients.<sup>15,142–147</sup> However, a psychological basis should not be generalized to all IBS patients. It is difficult to determine the cause and effect relationship of psychological disturbance with IBS. As

IBS is a chronic disease, the possibility remains that the poor quality of life, reduced productivity, and work absenteeism arising from symptoms could result in secondary anxiety, depression, and disturbed sleep.

Lifetime and daily stressful events were also reported to be more common in IBS patients than non-IBS patients and healthy controls.<sup>148–153</sup> Adverse lifetime stressors include physical, emotional, or sexual abuse. Several studies from Japan have sought to ascertain the contribution of stress and other psychological factors to the development of IBS. In one study, significantly more IBS than non-IBS patients met the criteria for agoraphobia and panic disorder.<sup>154</sup> In another study, IBS patients reported more perceived stress than asymptomatic controls.<sup>143</sup> In another study, perceived stress was reported in 55% of patients with IBS by Rome II criteria.<sup>155</sup> However, the role of perceived stress could have been overestimated in these Japanese studies because of a selection bias arising from the recruitment of these patients from psychosomatic medicine clinics rather than from general gastroenterology clinics.<sup>155</sup>

**Statement 27: Psychosocial factors have significant role in the development and aggravation of IBS symptoms.**

Grade of evidence: moderate.

Agreement: a. 12 (70.59%), b. 5 (29.41%).

Prospective studies in post-infectious IBS have clearly demonstrated that psychosocial stress factors, such as major life events, anxiety, neuroticism, and somatization, predict the development of IBS following an episode of acute gastroenteritis.<sup>3,62,79</sup> Furthermore, stress can provoke GI symptoms and exacerbate symptoms in IBS patients.<sup>150,152,156,157</sup> Although these phenomena are also observed in healthy patients, the response to stress was reported to be far greater and more persistent in IBS patients.<sup>158</sup>

One study from Korea has shown that depressed women complained of GI symptoms more frequently according to the severity of depression.<sup>146</sup> Two Japanese studies suggest that psychosocial stress can aggravate GI symptoms in IBS.<sup>155,159</sup>

**Statement 28: Psychosocial factors are important determinants of health-care seeking in those with moderate to severe IBS.**

Grade of evidence: low.

Agreement: a. 11 (64.71%), b. 6 (35.29%).

It has been suggested that psychosocial factors are important determinants of consultation behavior in IBS.<sup>160</sup> In one study from Hong Kong, anxiety proved to be the only independent predictor for health-care seeking.<sup>142</sup> In Pakistan, a high psychological distress score was a strong predictor of IBS in men, but not in women, while in India, there appeared to be more consulters in the higher socioeconomic classes.<sup>10,161</sup> However, in Japan and Korea, psychological distress did not appear to predict consultation for IBS.<sup>155,162</sup> Thus, there is only weak evidence to support the consensus group's perception that psychological distress is an important determinant of health-care seeking. Furthermore, consultation rates were reported to be as high as 84%, 57%, and 55% in Singapore, Hong Kong, and Taipei, respectively, and were generally higher than reported in certain Western countries.<sup>9,12,22,142,163,164</sup> Taking into account the high medical consultation rates, sociocultural factors might prove to be more important determinants of health-care seeking than psychological factors.

**Statement 29: Genetic factors can contribute to the development of IBS, and gene–environmental interactions need to be further investigated.**

Grade of evidence: low.

Agreement: a. 12 (70.59%), b. 4 (23.53%), c. 1 (5.88%).

It has been suggested that genetic factors can predispose to the development of IBS. This hypothesis has been based largely on findings of a higher prevalence of family history of IBS in patients than in non-IBS controls, and a higher concordance rate of monozygotic twins for IBS than that of dizygotic twins. However, familial aggregations can be due to both similar environments in families and genetic influences. The contributions of these factors have not clearly been distinguished by studies evaluating genetic influence, such as twin studies. Studies from Asia are limited and have produced conflicting results. One study from China reported that the 5-HTTLPR allele L/L genotype occurred with greater frequency in constipation-predominant IBS, although this could not be confirmed in another Chinese study.<sup>165,166</sup> One study from Korea reported that there was no relationship between serotonin transporter gene polymorphisms and IBS, but in another Korean study, which had a larger sample size, a significant association was observed between the serotonin transporter (SERT) polymorphisms and IBS, and in particular with diarrhea-predominant IBS.<sup>167,168</sup>

**Management and diet**

**Statement 30: The aims of IBS management are symptom relief and improvement in quality of life.**

Grade of evidence: high.

Agreement: a. 16 (94.12%), b. 1 (5.88%).

As IBS is a chronic, non-life-threatening disorder, its largest impact is expected to be on quality of life.<sup>169–174</sup> Studies from both the East and the West suggest that regardless of whether they seek professional medical advice or not, individuals with IBS report poorer quality of life than controls.<sup>143,175,176</sup> A number of studies from Asia provide additional evidence that quality-of-life scores in IBS patients are lower than in controls.<sup>143,161,175,177–179</sup> We recommend that the aims of IBS management should be to relieve symptoms as much as possible and to improve quality of life.

**Statement 31: A good doctor–patient relationship is important in the management of IBS. Physicians should try to identify contributing factors and address the patient's concerns.**

Grade of evidence: moderate.

Agreement: a. 16 (94.12%), b. 1 (5.88%).

Several studies support the notion that a strong doctor–patient relationship can produce a favorable response to treatment.<sup>169,171,180,181</sup> Based on an analysis of these studies, we recommend that the physician should strive to achieve the following: (i) identify, as far as possible, contributing factors, including GI infections, psychosocial stressors, use of medications (especially antibiotics and analgesics), previous abdominal or pelvic surgery, and recent dietary changes; (ii) develop appropriate analogies to help the patient understand the pathophysiological disturbances associated with IBS symptoms; (iii) provide reasonable evidence to reassure the patient that he or she does not have a life-threatening condition; and (iv) involve the patient in setting reasonable lifestyle, drug treatment, and behavioral goals. One of the anticipated outcomes of this approach is that if they can be confidently

reassured, it might be possible to manage patients with minimal symptoms (i.e. symptoms that are not bothersome), who might be consulting a doctor because of anxiety as an implication of their symptoms, without medications.

**Statement 32: Management of IBS should be individualized and should target all bothersome symptoms, while taking into account specific IBS subtypes, symptom severity, and contributing factors (including psychosocial issues).**

Grade of evidence: moderate.

Level of agreement: a. 13 (76.47%), b. 3 (17.65%), c. 1 (5.88%). The management approach propounded within statements 32–35 is based on a model proposed by Thompson and Drossman, which predicts that the majority of patients (estimated to account for 95% of all IBS patients) who are seen in primary and secondary care settings, will present with mild to moderate symptoms, for which physiological disturbances play an important role, and in whom psychological factors are not thought to be dominant.<sup>182</sup> The experience reviewed in statement 31 provides support that this approach can be reasonably expected to produce a favorable outcome. This approach is also consistent with the guidelines from other major professional organizations.<sup>97,183</sup> This statement is qualified by the premise that for patients with a major psychiatric diagnosis, it is important that the patient is co-managed by a psychiatrist (see statement 36).

**Statement 33: The taking of dietary history and dietary modification could be helpful in the management of some IBS patients.**

Grade of evidence: low.

Level of agreement: a. 5 (31.25%), b. 9 (56.25%), c. 2 (12.50%). Addressing the dietary aspects of IBS is important, as many IBS patients experience symptoms in relation to meals, and many are interested to know what foods to avoid.<sup>184,185</sup> Studies suggest that 20–67% of IBS patients might have dietary triggers, and a substantial number report improvement upon dietary management.<sup>185</sup> However, as a very large number (60 or more) of foods have been implicated in IBS, and many patients report intolerance to a large number of foods (40% of patients in one study had intolerance to six or more foods; in another study the mean number of foods patients were sensitive to was six), it is not possible to recommend a standard diet for all IBS patients.<sup>121,128</sup> Therefore, we suggest, as a first step, taking a detailed dietary history and the use of a food diary. Dietary modifications can then be suggested if this assessment identifies potential dietary factors. Based on our analysis of various food intolerance studies (discussed in statement 24), we suggest that doctors should look out for excessive consumption of dairy- and lactose-rich products, dietary fiber (especially in the form of bran or other cereals), and fructose- or fructan-rich foods. While we believe that this approach could contribute to building the doctor–patient relationship, there is limited information regarding the effects of dietary treatment on quality of life in IBS.<sup>150</sup>

The doctor should take care that dietary modification does not lead to an inadequate diet.<sup>186</sup> The tendency to an eating disorder might be present, particularly among female IBS patients.<sup>187–189</sup> It is possible that the improvement in IBS from dietary restriction stems from an overall reduction in food intake with reduced stimulation of post-prandial motility activity. In a recent study from

Japan, marked improvement in IBS symptoms was reported after 10 days of fasting with only water intake.<sup>190</sup> Many suspected food intolerances might not be substantiated when subjected to a double-blind food challenge.<sup>122,185,191</sup> In many instances, psychological factors appear to be important. There is very little evidence to support IgE food allergy testing in IBS.<sup>186</sup> Tests which employ electrodermal devices or a hair analysis to identify food allergy and intolerance are unproven, and consumer advocacy testing has shown several commercial allergy tests to be unreliable.<sup>192</sup> A small number of recent studies suggests a potential role for food-specific IgG antibody testing, but the clinical benefits are inconclusive.<sup>128,130,193</sup>

**Statement 34: Suggested initial treatments for patients with IBS include various combinations of antispasmodic, laxative, prokinetic, antidiarrheal, and probiotic agents.**

Grade of evidence: moderate.

Agreement: a. 6 (37.50%), b. 8 (50%), c. 1 (6.25%), d. 1 (6.25%).

In line with statement 32, we suggest the use of combination treatment to target all bothersome symptoms, as well as contributing factors. This suggestion is supported by a number of studies that have reported good treatment outcomes in as many as 90% of patients in response to a holistic approach (as outlined in statement 31) together with a combination of pharmacological treatments comprising antispasmodic agents, laxatives, and anxiolytic or antidepressant agents.<sup>169,180,194,195</sup> A critique published in 1988 of 43 controlled clinical trials, of which 39 involved only single agents, concluded that there was no convincing evidence that any therapy was effective in treating the IBS symptom complex. One study which compared the response to variable combinations of antispasmodic, anxiolytic, bulking agents, and placebo reported that the percentage of patients who achieved sustained improvement over 3 months rose with the number of active agents prescribed, with the highest response (recorded at 58%) observed in patients receiving three drugs.<sup>195</sup> However, in one recent study, only 31% of patients achieved satisfactory relief in a treatment protocol comprising only reassurance, explanation of IBS, and counseling, without receiving pharmacotherapy.<sup>196</sup>

Combinations of antispasmodic, laxative, antidiarrheal, and probiotic agents are suggested as first-line therapy, as they are generally safe and inexpensive. In various meta-analyses and systematic reviews, antispasmodics as a class of medications have been shown to improve abdominal pain and global symptoms in IBS.<sup>197–199</sup> Bulking agents were frequently promoted for IBS in the past, but recent careful re-evaluation has drawn attention to significant limitations. While ispaghula could have some benefit for treating mild constipation in IBS, dietary fiber, especially in the form of bran cereals, could aggravate abdominal pain and bloating.<sup>197,199–201</sup> While there are no placebo-controlled, randomized studies of commonly-available over-the-counter laxatives, these can be tried for patients with constipation in IBS-C, bearing in mind that lactulose could increase flatulence, and stimulant laxatives, like senna and bisacodyl, can cause abdominal cramps.<sup>202–204</sup> For the control of diarrhea symptoms, like frequency, consistency and incontinence, loperamide has the best quality of evidence, but has not been shown to improve abdominal pain or distension.<sup>205–209</sup>

Probiotics are defined as live microorganisms, which provide health benefits to the host. A recent meta-analysis suggested that

they are effective for improving abdominal pain and flatulence, with a trend for bloating, in IBS.<sup>210</sup> However, the magnitude of the benefits and the most effective species and strains of probiotic remain to be defined.<sup>210</sup> In general, they appear to be safe, but there have been rare reports of opportunistic infections with the use of probiotic bacteria.<sup>211</sup>

Currently, we see a limited role for prokinetic agents, as there are no convincing data for domperidone, mosapride, and itopride. While there are high-quality data that suggest that tegaserod, a 5-HT<sub>4</sub> partial agonist, is efficacious for IBS with constipation, its role is limited by a controversial withdrawal by the US Food and Drug Administration for suspected cardiovascular side-effects.<sup>212</sup> Non-absorbable antibiotics, including neomycin and rifaximin, provide reductions in global and bloating symptoms in IBS.<sup>213,214</sup> However, the effects of long-term, intermittent, non-absorbable antibiotic use in IBS are not known.

**Statement 35: Low-dose antidepressants, such as tricyclic antidepressants and selective serotonin reuptake inhibitor (SSRI), can be considered in patients who fail to respond to initial treatment, even in the absence of any overt psychological disorders.**

Grade of evidence: high.

Agreement: a. 13 (81.25%), b. 3 (18.75%).

A recent meta-analysis demonstrated that low-dose antidepressants (tricyclic anti-depressants (TCA) and SSRI) can be effective in the treatment of IBS, even in patients without concomitant psychiatric diagnoses.<sup>215–217</sup> As TCA, such as amitriptyline, have anticholinergic effects and can cause constipation, they are best used for the treatment of IBS-D patients, where they are effective in reducing the symptoms of incomplete defecation and loose stool, and in improving abdominal pain.<sup>218–220</sup> However, it might be more appropriate to use SSRI in IBS-C as they can shorten intestinal transit times. SSRI are effective in reducing global symptoms, bloating, and problematic bowel movements.<sup>215,216,221</sup> As patients frequently have reservations with regards to the stigma, as well as to the possible side-effects associated with their use, antidepressant agents are expected to be used for IBS patients with moderate to severe symptoms who have failed to respond favorably to other conventional treatments.

**Statement 36: Patients with IBS and co-morbid psychological disorders should be told that their psychiatric symptoms could modify the severity of their bowel symptoms and that adequate treatment of co-morbid psychological disorders is strongly suggested.**

Grade of evidence: high.

Agreement: a. 11 (68.75%), b. 5 (31.25%).

Several studies suggest that psychological conditions, such as high stress levels, can enhance visceral hypersensitivity and aggravate symptoms of IBS.<sup>222–224</sup> A study from Korea reported the presence of major depression in 72% of IBS patients with symptoms of severe bloating.<sup>225</sup> Additionally, a study conducted in Hong Kong reported increased health-care-seeking behavior associated with anxiety in IBS patients.<sup>142</sup> For IBS patients with co-morbid psychiatric illnesses, psychiatric medications can be superior to conventional medications for improving quality of life.<sup>226</sup> Therefore, if the patients have co-morbid psychiatric disorders, adequate treatment of these conditions should be required.

**Statement 37: In specialist centers, psychotherapy can be effective for IBS patients and considered as a treatment for refractory patients who fail medical treatments.**

Grade of evidence: moderate.

Agreement: a. 8 (50%), b. 5 (31.25%), c. 1 (6.25%), d. 2 (12.5%).

Several studies, most of which are of poor quality and have been conducted in tertiary centers, have demonstrated the effectiveness of psychotherapies, such as hypnotherapy and cognitive-behavioral therapy, for patients with IBS.<sup>215,227–230</sup> Psychotherapy can be useful in IBS patients, both with and without psychiatric disorders.<sup>229,231</sup> However, these psychiatric treatments, including hypnotherapy and cognitive-behavioral therapy, require the presence of well-trained mental health professionals and are not available in most centers.

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