

# **IRRITABLE BOWEL SYNDROME**

**in adults**

**Not just a gut feeling**

*Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterised by recurrent bouts of abdominal discomfort and pain, bloating and a changeable bowel habit. Generally a patient with IBS will have periods of time when they feel well, interspersed with acute bouts of their particular gastrointestinal symptoms. IBS is regarded as the most frequently encountered gastrointestinal diagnosis in primary care. In some patients, IBS can significantly affect quality of life, however, reassurance can be given that IBS itself does not predispose the patient to life-threatening disease. Patients with IBS tend to be high users of health care services and some patients invest a significant amount of time and money on dietary modification and over-the-counter remedies in an attempt to control or relieve their symptoms. Ongoing research is changing the way IBS is viewed and this is providing evidence for new treatment approaches.*

## **What is irritable bowel syndrome?**

People with irritable bowel syndrome (IBS) experience recurrent bouts of abdominal discomfort and pain, which may be accompanied by bloating, and a changeable bowel habit. Between bouts of symptoms, people with IBS usually feel well. However, some people may also have non-gastrointestinal symptoms such as fatigue, nausea and backache and feelings of anxiety or depression.<sup>1, 2</sup> IBS can contribute to a reduced quality of life for some people and may affect all aspects of day-to-day life including diet, education, work, travel, personal and social relationships, self-image and psychological well-being.<sup>3</sup> IBS is not, however, associated with structural damage to the bowel, as it is in people with inflammatory bowel disease, and weight loss is usually not a feature of IBS.<sup>2, 4</sup>

People with IBS are more likely to be:

- Female – approximately 70% of people with IBS are female<sup>5, 6</sup>
- Younger than age 50 years<sup>5, 6</sup>
- From a lower socioeconomic group<sup>5</sup>

## **IBS is the most common gastrointestinal diagnosis in primary care**

IBS affects an estimated 10 – 20% of people throughout the western world,<sup>1</sup> although the reported prevalence varies widely due to the use of different diagnostic criteria over time and between populations.<sup>7</sup> There have been no studies in New Zealand which have examined the prevalence of IBS by

ethnicity. IBS is reported to be one of the top ten reasons for visiting a General Practitioner, although it is thought that up to 50% of people with symptoms of IBS do not consult their General Practitioner.<sup>7</sup>

## **Pathophysiology of IBS**

The pathophysiology of IBS remains unclear, however, what is known is that it is a complex biopsychosocial illness.<sup>6, 8</sup> Psychological factors (e.g. stress and emotional state), social factors (e.g. upbringing and support systems) and biological factors (e.g. gut motility and visceral sensitivity) interact in a complex way to induce and exacerbate the symptoms of IBS.<sup>9, 10</sup>

Although traditionally referred to as a functional bowel disorder because there are no obvious structural or biochemical abnormalities that can explain the symptoms of IBS, ongoing research is changing the way IBS is viewed.<sup>11</sup> A number of mechanisms have been proposed to explain the symptoms experienced by people with IBS. These include food sensitivity, intestinal inflammation, altered gastrointestinal motility, hypersensitivity of the viscera, alterations in microflora, bacterial overgrowth, post-infectious reactivity, dysregulation of immune function, brain-gut interactions and genetic and environmental factors.<sup>6, 8, 12</sup> It is likely that there is a complex interplay between these factors that results in a characteristic array of gastrointestinal symptoms in people with IBS.<sup>11</sup> How this might occur remains a topic of ongoing research (see: “Emerging evidence on the role of gastrointestinal bacteria and the immune system in IBS”, over page).

## Emerging evidence on the role of gastrointestinal bacteria and the immune system in IBS

Gastrointestinal bacteria have an important role in the normal physiological and immunological function of the gastrointestinal tract. There is a growing body of evidence suggesting that they play a complex role in the pathogenesis of a number of gastrointestinal disorders including IBS, however, it is unclear whether the alterations in bacterial flora are a cause or a consequence of the disorder.<sup>11</sup> There is some evidence that low-grade inflammation and abnormalities of immune function may also have a role in the pathogenesis of IBS.<sup>11</sup>

Evidence has shown that:<sup>11</sup>

- Alterations in the gastrointestinal bacteria affect gastrointestinal function such as changes in intestinal motility and visceral hypersensitivity
- People with IBS appear to have an altered composition of gastrointestinal bacteria, specifically a reduction in diversity of bacterial species and an overabundance of some bacterial species
- Gastrointestinal bacteria responsible for fermentation of poorly absorbed fermentable carbohydrates may be altered in people with IBS resulting in looser stools and increased gas production
- There may be increased permeability of the gut in people with IBS due to alterations in the gastrointestinal bacteria and mucosal inflammation
- Gastrointestinal bacteria may also play a role in gut motility and the perception of pain due to factors such as stimulation of smooth muscle and bile acid malabsorption
- There is a similarity in symptoms between people with small-intestinal bacterial overgrowth and those with IBS
- Some people with IBS have increased levels of activated mast cells, histamine, intestinal epithelial lymphocytes, T cells and pro- and anti-inflammatory cytokines in the gastrointestinal tract

## Three key factors are responsible for the majority of symptoms of IBS

The three key factors that appear to most influence the symptoms of patients with IBS are:

- Altered gastrointestinal motility
- Altered sensation within the gastrointestinal tract
- Psychosocial factors, e.g. stress, upbringing, coping strategies

### Altered gastrointestinal motility

The traditional understanding of IBS centres around dysfunction of colonic motility with abnormalities that include luminal contractions that are increased in frequency and irregularity, a shorter or prolonged transit time depending on the subtype of IBS and an exaggerated motor response to ingestion of food.<sup>2</sup>

### Altered sensation within the gastrointestinal tract

People with IBS tend to experience increased sensations from the gastrointestinal tract in response to stimuli, such as distension. This visceral hypersensitivity occurs when there is selective hypersensitisation of various types of receptors in the gut wall. This has been demonstrated in studies involving balloon distension of the intestine where patients with IBS experience awareness and pain with a smaller balloon volume than patients without IBS.<sup>6</sup>

### Psychosocial factors

Psychosocial factors play a significant role in patients with IBS, tending to increase the frequency and severity of symptoms such as abdominal pain and diarrhoea. It also influences the way a patient views their problem, when they decide to present for a consultation and their beliefs and expectations regarding the illness and its treatment.<sup>12</sup>

## Making a diagnosis of IBS

IBS is diagnosed clinically from history and examination based on the Rome III diagnostic criteria (see: "Diagnostic criteria for IBS").<sup>13</sup> These criteria aim to encourage clinicians to make a positive diagnosis based on the patient's symptoms and to no longer regard IBS as a diagnosis of exclusion. The 2008 NICE guideline also recommends that a diagnosis be made based on the presence of symptoms.<sup>1</sup> A recent study in the UK, however, reports that many clinicians continue to use a diagnostic approach based primarily on the exclusion of sinister symptoms, rather than the presence of characteristic symptoms of IBS, because both clinicians and patients tend to have concerns that the symptoms could indicate a

more “serious” condition, e.g. inflammatory bowel disease or gastrointestinal cancer.<sup>3</sup> This represents a valid concern but, in the appropriate clinical context, e.g. a female aged under 50 years, provided red flag indicators are assessed and excluded, a positive clinical diagnosis of IBS can be made without subjecting the patient to multiple unnecessary investigations or health care consultations.

### Assess for the presence of symptoms

A diagnosis of IBS should be considered if a patient presents with a history of six months or more of any of the following symptoms:<sup>1</sup>

- Abdominal pain or discomfort
- Bloating
- Change in bowel habit

Ask the patient more detailed questions about these symptoms to assess whether they fulfil the Rome III criteria for a positive diagnosis of IBS (see: “Diagnostic criteria for IBS”).

**Abdominal pain** – The abdominal pain or discomfort experienced by people with IBS varies widely – not only between individuals but also for each person. Symptoms are often made worse by eating and the patient may already be aware of particular foods that aggravate their symptoms. In females, pain may be worse pre-menstrually.<sup>2</sup> Typically with each bout of symptoms, the pain will vary in intensity and site, often being reported anywhere in the abdomen. The location and timing of the pain may help differentiate IBS from other gastrointestinal conditions. Relief of pain or discomfort with defaecation is characteristic of IBS, but is not always reported by patients.

## Diagnostic criteria for IBS

The Rome III diagnostic criteria for IBS state that the patient has recurrent abdominal pain or discomfort\* for at least three days per month, in the last three months, associated with two or more of the following:<sup>13</sup>

- An improvement with defaecation
- The onset associated with a change in frequency of stool
- The onset associated with a change in form (appearance) of stool

\* “Discomfort” is defined as an uncomfortable sensation not described as pain.

There is debate within the literature regarding the validity of the Rome III criteria for use in primary care with a limited evidence base, and some authors still prefer older criteria such as the Manning criteria.<sup>15, 16, 17</sup> The Rome III criteria have also been criticised for not being useful in a practical clinic setting because it is felt that patients who seek medical advice with symptoms of IBS prefer to be

investigated, and can become rapidly dissatisfied if this does not occur.<sup>18</sup> However, a balance has to be sought between requesting sufficient investigations to check for other conditions, such as inflammatory bowel disease or coeliac disease, and over-investigation.

The Manning criteria, which date from 1978, includes six symptoms that were significantly more common amongst patients and felt to be characteristic of IBS:<sup>17, 19</sup>

- Looser stools at onset of pain
- More frequent bowel movements at onset of pain
- Pain eased after bowel movement (often)
- Visible distension
- Feeling of incomplete emptying
- Mucus per rectum

The Manning criteria have been criticised for a lack of specificity which led to the development of the Rome criteria.

**Bloating** – Abdominal bloating is more likely to be described by females with IBS than by males. Patients with IBS often have increased belching and flatus.<sup>2</sup>

**Change in bowel habit** – An altered bowel habit is the most consistent symptom for patients with IBS. The change in bowel habit may include altered stool consistency (either firm or loose), changes in frequency of bowel motions, urgency, straining, incomplete evacuation or faecal incontinence (usually as a result of urgency). Patients may also describe the passage of mucus with bowel motions.<sup>2</sup> Patients often report the need to urgently pass a bowel movement after eating a meal – referred to as an exaggerated gastric-colic reflex.<sup>12</sup> This can occur in response to specific trigger foods but it may be the act of eating itself which initiates the postprandial symptoms.<sup>12</sup> Diarrhoea or constipation may predominate, or the patient may alternate between symptoms.<sup>2</sup>

In addition, patients may have other symptoms including nausea, dyspepsia, early satiety, lethargy, low back ache and bladder symptoms such as frequency and urgency.<sup>1,2</sup>

IBS tends to be more common in people with a family history of IBS and people with IBS may have other co-morbidities, such as anxiety, depression, fibromyalgia or restless legs.<sup>2, 6</sup> Ask if the patient has had a recent bout of gastroenteritis as this can be a precipitating event, although reported incidence varies widely in the literature – from 5 – 32%.<sup>2, 14</sup> It is estimated that there is a six-fold increase in the risk of developing IBS after a significant episode of gastroenteritis and that this risk remains high for two to three years.<sup>14</sup>

Depending on the clinical context, consider the possibility that similar symptoms could be attributable to another condition such as:

- Coeliac disease
- Inflammatory bowel disease
- Lactose intolerance
- Colorectal cancer
- Small-intestinal bacterial overgrowth, microscopic colitis, diverticulitis and other gastrointestinal conditions
- Gynaecological conditions such as endometriosis, pelvic inflammatory disease, ovarian cancer

### 🚩 Check for red flags

The presence of red flag symptoms should raise the possibility of an alternative diagnosis and referral to secondary care is recommended.

Red flags from the history include:<sup>1, 2, 12</sup>

- Unintentional or unexplained weight loss
- Rectal bleeding that is not due to haemorrhoids
- Nocturnal symptoms, e.g. waking from sleep with pain or the need to defaecate
- Onset of symptoms in patients aged greater than 50 years (over 60 years in the NICE guideline)
- A family history of gastrointestinal cancer, inflammatory bowel disease or coeliac disease



Additional red flags may be detected on clinical assessment or with targeted laboratory testing (see below). These include:


- Abdominal mass
- Rectal mass
- Iron deficiency anaemia
- Raised inflammatory markers

### Laboratory investigations

There is no specific diagnostic test for IBS. The following initial tests are usually recommended, primarily to check for the possibility of conditions such as inflammatory bowel disease and coeliac disease:<sup>1</sup>

- Full blood count
- C-reactive protein
- Coeliac antibodies (IgA tissue transglutaminase – IgA TTG)

**Ferritin, liver function tests and renal function** may also be considered depending on the clinical situation. Additional investigations are generally only required if the patient presents with atypical or red-flag features. In older patients with a new onset of symptoms, gastrointestinal cancer must be considered as a diagnosis and appropriate investigations and referral arranged depending on the clinical circumstances. If the patient has clinical features on history or examination that indicate thyroid dysfunction, consider testing **thyroid stimulating hormone**. Patients with a shorter duration of symptoms, particularly diarrhoea and risk factors for infectious diarrhoea, e.g. recent overseas travel or immigration, or ingestion of contaminated food or fluid, should be assessed for infectious causes of diarrhoea.

 For further information on investigating patients with infectious diarrhoea see: “Making sense of testing for enteric pathogens”, Best Tests (Mar, 2008)

**Faecal calprotectin**, a marker of intestinal inflammation, is not routinely recommended but may have a limited role in selected patients where there is uncertainty about the diagnosis, e.g. younger patients who have presenting symptoms and signs that could indicate inflammatory bowel disease rather than IBS. A negative faecal calprotectin result (the suggested cut off value is 50 micrograms/g) effectively excludes a diagnosis of inflammatory bowel disease.<sup>4</sup> Levels of faecal calprotectin are typically seen to exceed 500 micrograms/g if there is mucosal inflammation, as in the case of patients with inflammatory bowel disease. The faecal calprotectin test is an expensive test and is not universally available. Knowledge and use of this test varies throughout New Zealand.

### Determine the subtype of IBS

Once a diagnosis is established, patients with IBS can be grouped into three main subtypes based on their predominant bowel symptoms – IBS with diarrhoea (IBS-D), IBS with constipation (IBS-C), and mixed IBS (IBS-M).<sup>8</sup> This approach is useful because it can help guide management of the patient’s symptoms, however, there can be considerable overlap between the subgroups and, for some people, abdominal pain may be the predominant symptom rather than altered stools (Page 24).

#### IBS-D

IBS with diarrhoea as the predominant symptom is the most common type of subgroup of people with IBS.<sup>5</sup> Patients tend to have frequent loose, often watery stools reflecting a shorter colonic transit time.<sup>8</sup> However, factors such as diet and stress also have a major influence on symptoms and this can result in a pronounced day to day variability of the patient’s bowel habits.<sup>8</sup>

#### IBS-C

People with IBS who have constipation as their predominant symptom tend to have less frequent, often irregular, firm stools reflecting a prolonged colonic transit time. IBS-C is more often present in females than males.<sup>4</sup>

#### IBS-M

Patients with IBS who have a mixed picture tend to have alternating episodes of diarrhoea and constipation.



## The concept of a low FODMAP diet

Researchers at Monash University in Australia are regarded as the pioneers of the low FODMAP diet.<sup>26, 27</sup> The acronym stands for **F**ermentable, **O**ligo-saccharides, **D**isaccharides, **M**ono-saccharides **A**nd **P**olyols. Their work began with observations of the role of fructose in producing symptoms in patients with IBS. From there, further work resulted in the development of the concept of a low FODMAP diet. It is thought that FODMAPs contribute to the symptoms of IBS by their rapid fermentation and an osmotic effect which results in distension of the lumen of the gut.<sup>20</sup>


Although there is evidence that individual components of the FODMAP group contribute to IBS symptoms, the new concept was to consider the collective role of these poorly absorbed short-chain carbohydrates and to show the benefits for patients of a diet low in FODMAPs.<sup>20</sup>

Major dietary FODMAPs include:

- Fructose found in fruits such as apples, pears and mango, honey and high fructose corn syrup. Concentrated sources of fructose, e.g. dried fruit, tomato paste and wine.
- Fructans found in food such as wheat, rye, onions, spring onions, leek, asparagus and artichokes
- Artificial sweeteners such as sorbitol, xylitol, mannitol (found in products such as sugar-free chewing gum, sweets and drinks)

There is increasing evidence that a low FODMAP diet can be of benefit for many patients with IBS, however, it is not a cure-all and as yet, there is little evidence regarding its use in the longer term.

N.B. Some patients may enquire about investigation of fructose malabsorption. This can be measured using a breath hydrogen test after a challenge with fructose, however, this test is not widely available in New Zealand.

 Further information on the FODMAP diet is available from: [www.med.monash.edu.au](http://www.med.monash.edu.au)



## Management of patients with IBS

IBS can be a difficult condition to manage and there is a potential for frustration and dissatisfaction for both patients and clinicians due to uncertainties surrounding the underlying aetiology of IBS and its diagnosis.<sup>3</sup> It is therefore important to listen to and address any concerns the patient may have. The major concern for most patients is that there is a “serious” organic cause for their symptoms. Ensuring the patient understands IBS and what it may mean for them is likely to be the key to helping the patient self-manage their condition. Aim to provide an explanation of the underlying cause of their symptoms – it may help to draw a parallel with colic in infants and to avoid statements such as “I don’t know what’s wrong...”, “There’s nothing wrong with you...” or “It’s all in your head...” Establishing a positive diagnosis and avoiding unnecessary investigations will help reduce anxiety and reassure the patient. Consider if there are stressors in the patient’s life that may be aggravating symptoms and offer strategies to help the patient manage these.

All patients with IBS are likely to benefit from dietary and lifestyle changes such as increasing exercise and reducing stress and for some, this approach may provide sufficient control over their symptoms.<sup>10</sup> Patients with persistent, often severe, symptoms that have not responded to initial dietary and lifestyle changes can be more challenging to treat.

### Dietary modifications can reduce symptoms

The majority of patients with IBS find that certain foods will trigger their symptoms, e.g. a high fat meal may result in abdominal pain followed by diarrhoea that begins relatively soon after eating. Often, patients will have already altered their diet to minimise or exclude foods that trigger their symptoms and some will report benefit from these changes. In the past, however, most guidelines for the management of IBS have not included consistent dietary advice as there has been a lack of evidence that excluding or restricting foods resulted in a significant improvement for patients.<sup>20, 21</sup>

The British Dietetic Association has recently released evidence-based guidelines for the dietary management of IBS in adults.<sup>21</sup> They have produced an algorithm which includes a three-tiered approach to dietary interventions and regular clinical review at each level.

#### First-line dietary advice

Once a diagnosis of IBS has been established, first-line dietary advice for all patients should be to encourage a diet that is healthy and nutritionally adequate. Assess the patient’s usual

eating pattern and dietary choices. Establish if the patient has any known or suspected allergies or intolerances to foods, e.g. to lactose, and how these affect their IBS symptoms. A food and symptoms diary can be a useful tool to establish the frequency and timing of symptoms and whether any patterns are present, e.g. symptoms provoked by meals, exercise, stress or menstrual cycle in females.

General dietary guidance should include advice about:

- Regular meals
- Good eating behaviour such as chewing food thoroughly, taking time over meals, not eating late at night
- Regular adequate fluid intake (aiming for 1.5 – 3.0 L/day), avoiding carbonated beverages, caffeine and alcohol

Common foods that can aggravate symptoms in people with IBS include caffeine, alcohol, fatty food, spicy food, wheat, cheese, milk, pure fruit juices, artificial sweeteners and vegetables that increase flatus, such as cabbage, Brussels sprouts, corn, onion and legumes (e.g. baked beans, lentils, chickpeas).<sup>21</sup>

The patient’s intake of fibre should be assessed. Many patients will have been advised in the past to increase their intake of fibre, particularly insoluble fibre such as wheat bran, however, there is now good evidence that this is unlikely to be beneficial for the majority of patients with IBS, particularly those with IBS-D, and may worsen symptoms.<sup>21</sup> Some patients may therefore need to be advised to reduce their fibre intake.

#### Second-line dietary advice

If the patient has not had an improvement in symptoms with first-line interventions the next steps are recommended.

**If constipation is the predominant symptom**, an increase in a form of soluble fibre may be beneficial. The patient should be advised this can be achieved by increasing their intake of foods that are high in soluble fibre such as oats,<sup>1</sup> or with a prescription product containing psyllium husk or sterculia.<sup>22</sup> There is some evidence that ground or whole linseeds (also called flax seeds – available from health food stores), which are a source of both soluble and insoluble fibre, may help to relieve symptoms,<sup>23, 24</sup> and their use is recommended in some guidelines.<sup>1, 21</sup>

**Consider a trial of a low FODMAP diet** which can significantly reduce gastrointestinal symptoms in patients with any of the subtypes of IBS (see: “The concept of a low FODMAP diet”).<sup>20</sup> Patients should be referred to a dietitian to ensure the diet is nutritionally adequate. Many patients will be aware of the low



FODMAP diet and may have trialled it before seeking advice about their IBS symptoms.

**A four week trial of probiotics** in the form of yogurts or other fermented milk products can be considered, however, some of these products also contain ingredients that may worsen IBS symptoms, such as fructans, fructose or lactose. A recent systematic review has concluded that there is some evidence that probiotics, e.g. *Lactobacillus*, may improve the overall symptoms, abdominal pain, bloating and distension in patients with IBS but little or no evidence that they will improve other symptoms such as diarrhoea, constipation and flatus.<sup>25</sup>

### Third-line dietary advice

If there has been no improvement in symptoms after second-line approaches have been trialled, consider an exclusion diet where one or two foods that appear to aggravate symptoms are excluded for two to four weeks and then re-introduced as a challenge. An elimination diet\* should only be considered if the patient suspects multiple food intolerances and trials of avoidance of single trigger foods have not been effective.<sup>21</sup> The advice of a dietitian is required to ensure that the elimination diet is nutritionally adequate. If there has been no improvement in symptoms after two to four weeks of an elimination or exclusion diet then it is usually accepted that those excluded foods are unlikely to be contributing to the patient's symptoms.<sup>21</sup>

\* An elimination diet generally includes a selection of low allergen foods, e.g. one meat, one cereal, two fruit and vegetables, a milk substitute and a fat source.

## Treatment should address the most troublesome symptom

Treatment for IBS is intended to relieve the patients' symptoms rather than to cure them. Treatment is likely to be of most benefit if it is tailored towards the patients' most troublesome symptom, e.g. diarrhoea, constipation or pain.<sup>6</sup> The pattern of symptoms in people with IBS varies widely, however, a combination of medicines may be required to achieve relief. Despite this, the use of multiple medicines for the control of symptoms is often reported as being of insufficient benefit and there is the potential for dissatisfaction with the treatments and for an increase in adverse effects. Medicines that have the potential to target more than one symptom of IBS, such as tricyclic antidepressants, are increasingly recommended. A significant placebo response rate, up to 70%, to all treatments in patients with IBS has been reported.<sup>6</sup>

### People with diarrhoea as their predominant symptom

Dietary advice should be given following the three-tiered plan

outlined above. Increasing dietary fibre is not recommended because this is likely to worsen symptoms in patients with diarrhoea as their main symptom. A Cochrane review found that the use of bulking agents (a fibre supplement) was not effective in the treatment of patients with IBS, particularly those with diarrhoea-predominant IBS.<sup>28</sup> An increase in fibre not only worsens diarrhoea but is also likely to aggravate abdominal discomfort and bloating.<sup>8, 28</sup>

The combination of a regular daily dose of loperamide and an antispasmodic, such as mebeverine, can help to increase stool firmness, decrease stool frequency and reduce urgency. Loperamide can be used as a regular daily medicine at a fixed daily dose (e.g. 2 mg once or twice a day) rather than the usual dosing regimen for acute self-limiting diarrhoea. Mebeverine (one 135 mg tablet) can be taken three times daily as required, 20 minutes prior to meals which may help postprandial symptoms.<sup>2, 22</sup>

An approach that has been suggested for patients who are fearful of the sudden and urgent need to defaecate that can occur with IBS, is for them to take 2 – 4 mg of loperamide approximately 45 minutes before leaving their house, particularly if access to a toilet is limited such as when shopping or exercising.<sup>8</sup>

There is some evidence that serotonin antagonists (5HT<sub>3</sub>-receptor antagonists) such as ondansetron may modulate the effect of stressors on gut function and reduce diarrhoea.<sup>8</sup> The dose of ondansetron that is recommended initially is 4 mg, once daily, increasing to a maximum of 8 mg, three times daily, depending on the patient's response.<sup>29</sup> This is, however, an unapproved indication for ondansetron.

### People with constipation as their predominant symptom

Some patients in whom constipation is the predominant symptom may find that an increase in either soluble dietary fibre, from foods such as oats or soluble fibre in the form of a bulk-forming laxative such as psyllium husk, and avoiding foods with insoluble fibre, e.g. wheat, bran, brown rice, can help achieve a softer stool and provide relief from constipation. People with IBS-C should avoid eating foods with carbohydrates that are poorly digested in the small intestine (regarded now as FODMAPs) and therefore reach the colon relatively intact to aggravate symptoms.<sup>4</sup>

Laxatives may be required; the dose is usually adjusted by the patient depending on the consistency of the stool. Lactulose should be avoided as it may aggravate bloating.<sup>1, 22</sup> Stimulant laxatives, e.g. bisacodyl, docusate sodium, docusate sodium with sennoside B, should be used intermittently or avoided

## Future directions in the management of IBS

New understanding of the underlying mechanisms that cause the symptoms of IBS has led to increased interest in treatments that target the gastrointestinal flora and the immune system. However, currently there is limited evidence and a lack of consistent guidance on the use of these treatments.<sup>11</sup>

**Antibiotics** – Due to the increasing evidence that intestinal bacterial may have a role in the pathophysiology of IBS, there has been research into the use of antibiotics (e.g. rifaximin\*) to normalise the bacterial flora of the gastrointestinal tract.<sup>30</sup> At this stage there is limited evidence regarding their effectiveness and much of the research has been industry sponsored.<sup>8</sup>

**Anti-inflammatory medicines** – there is currently no evidence to support the use of anti-inflammatory medicines in patients with IBS.<sup>11</sup>

**Linaclotide** – a synthetic 14-amino acid peptide, has recently been approved for use in Europe and the USA for patients with IBS-C and a clinical trial commenced in New Zealand at the end of 2013. It acts in the gastrointestinal tract to increase colonic transit, to stimulate the secretion of fluid and to reduce abdominal pain.<sup>31</sup>

**Lupiprostone** – a locally acting chloride channel activator, has approval for use in the USA for treatment of females aged 18 years and over with IBS-C, however, research is ongoing with regards to its effectiveness and safety.<sup>32</sup>

**Alosetron** – a serotonin antagonist (5-HT<sub>3</sub> receptor antagonist), is also available in the USA for the treatment of severe diarrhoea-predominant IBS in female patients only who have not responded to other conventional treatments.<sup>30</sup> This medicine has, however, been associated with ischaemic colitis and patient deaths.

\* In New Zealand rifaximin is not subsidised and although available, is indicated only to reduce the recurrence of hepatic encephalopathy.<sup>22</sup>



if possible.<sup>22</sup> The preferred option if a laxative is required is macrogol, an osmotic laxative, however, this is only fully subsidised under Special Authority. The Special Authority criteria are that *“the patient has problematic constipation requiring intervention with a per rectal preparation despite an adequate trial of other oral pharmacotherapies including lactulose where lactulose is not contraindicated.”*<sup>22</sup> Initial applications are valid for six months with renewals for 12 months, provided that the patient is compliant with treatment and continuing to gain benefit. The recommended dose is one sachet, once daily, dissolved in half a glass (approximately 125 mL) of water, although this can be increased to 2 – 3 sachets daily if required.<sup>22</sup> Some patients may find half a sachet daily sufficient to maintain a soft stool.

### **People with pain as their predominant symptom**

Antispasmodic medicines are likely to be effective for the relief of abdominal pain or discomfort. Mebeverine is the recommended first-line antispasmodic medicine (dosed the same as for patients with IBS-D).

Bloating may be relieved or reduced by the use of peppermint oil or tea. Peppermint oil capsules (0.2 mL) are available in New Zealand but are not subsidised. The recommended dose is one to two capsules taken 30 – 60 minutes before meals, three times daily, for up to three months if necessary.<sup>22</sup>

Opioid analgesics should be avoided as they are likely to worsen constipation which may in turn aggravate abdominal pain, however, low dose codeine, used cautiously, can be effective in firming the stool in patients with diarrhoea. “Narcotic bowel syndrome” is a complication of using opioid analgesia in patients with IBS. It is characterised by chronic or frequently recurrent abdominal pain that worsens with escalating or ongoing doses of opioids.

If patients experience nausea as part of their IBS symptoms, domperidone may be effective. Domperidone 10 – 20 mg can be taken up to four times daily if required, 15 – 20 minutes before meals.<sup>22</sup>

There is good evidence that tricyclic antidepressants (TCA) are effective in reducing abdominal pain in patients with IBS and that they can also have a global effect on a variety of other symptoms.<sup>2, 28, 30</sup> The use of a TCA may give relief from

abdominal pain by altering visceral sensation and increasing pain thresholds.<sup>30</sup> TCAs may also reduce diarrhoea by slowing colonic transit times and, although recommended doses are low, they may also provide relief from depression if this is present.<sup>30</sup> The main limitation to the use of TCAs is reported to be patient tolerance of the medicines.<sup>30</sup> They should be used with caution in patients who have constipation.<sup>2</sup>

The majority of the research has focused on the use of amitriptyline and imipramine, however, nortriptyline is also thought to be effective and is generally better tolerated by patients.<sup>8</sup> The usual starting dose is 5 – 10 mg of amitriptyline (or nortriptyline) at night with gradual increases in dose as required, e.g. by 10 mg increments every two weeks, to a maximum of 30 mg each night.<sup>22</sup> This is an unapproved indication for the use of TCAs.

There is less evidence that SSRIs are effective in patients with IBS, however, they appear to provide similar benefits to TCAs and can be considered in people who are unable to tolerate these.<sup>28</sup> This is an unapproved indication for the use of SSRI antidepressants.

### **Regular review is required**

Although self-management of IBS should be encouraged, patients should continue to be reviewed medically to assess how they are coping with the condition and to check for the emergence of any red flags or alarm symptoms. The NICE guideline suggests an annual review, although, how often the patient will be seen is likely to be determined by their need for medicines and their response to any interventions.<sup>1</sup> Some patients may improve with dietary and lifestyle changes while others will continue to have lifelong symptoms. Patients who develop any of the red flag or alarm symptoms should be referred for further investigation.

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## References

1. National Institute for Health Care Excellence (NICE). Irritable bowel syndrome in adults. Diagnosis and management of irritable bowel syndrome in primary care. NICE, UK; 2008. Available from: [www.nice.org.uk](http://www.nice.org.uk) (Accessed Jan, 2014).
2. Malone M. Irritable bowel syndrome. *Prim Care Clin Off Pr*. 2011;38:433–47.
3. Harkness E, Harrington V, Hinder S, et al. GP perspectives of irritable bowel syndrome - an accepted illness, but management deviates from guidelines: a qualitative study. *BMC Fam Pr*. 2013;14:92.
4. Waugh N, Cummins E, Royle P, et al. Faecal calprotectin testing for differentiating amongst inflammatory and non-inflammatory bowel diseases: systematic review and economic evaluation. *Health Technol Assess*. 2013;17(55):1–212.
5. Andrews E, Eaton S, Hollis K, et al. Prevalence and demographics of irritable bowel syndrome: results from a large web-based survey. *Aliment Pharmacol Ther*. 2005;22:935–42.
6. Ford A, Talley N. Irritable bowel syndrome. *BMJ* 2012;345:e5836.
7. Wilson S, Roberts L, Roalfe A, et al. Prevalence of irritable bowel syndrome: a community survey. *Br J Gen Pr*. 2004;54:495–502.
8. Wald A. Irritable bowel syndrome - diarrhoea. *Best Pract Res Clin Gastroenterol*. 2012;26:573–80.
9. Tanaka Y, Kanazawa M, Fukudo S, Drossman D. Biopsychosocial model of irritable bowel syndrome. *J Neurogastroenterol Motil*. 2011;17(2):131–9.
10. Fichna J, Storr M. Brain-gut interactions in IBS. *Front Pharmacol*. 2012;3:127.
11. Ringel Y, Maharshak N. Intestinal microbiota and immune function in the pathogenesis of irritable bowel syndrome. *Am J Physiol Gastrointest Liver Physiol*. 2013;305:G529–G541.
12. Occhipinti K, Smith J. Irritable bowel syndrome: A review and update. *Clin Colon Rectal Surg*. 2012;25:46–52.
13. Longstreth G, Thompson W, Chey W, et al. Functional bowel disorders. Available from: [www.romecriteria.org](http://www.romecriteria.org) (Accessed Jan, 2014).
14. Thabane M, Marshall J. Post-infectious irritable bowel syndrome. *World J Gastroenterol*. 2009;15(29):3591–6.
15. Whitehead W, Drossman D. Validation of symptom-based diagnostic criteria for irritable bowel syndrome: A critical review. *Am J Gastroenterol*. 2010;105:814–20.
16. Dang J, Ardila-Hani A, Amichai M. Systematic review of diagnostic criteria for IBS demonstrates poor validity and utilization of Rome III. *Neurogastroenterol Motil*. 24:853–60.
17. Engsbro A, Begtrup L, Kjeldsen J, et al. Patients suspected of irritable bowel syndrome - cross-sectional study exploring the sensitivity of Rome III criteria in primary care. *Am J Gastroenterol*. 2013;108:972–80.
18. El-Salhy M. Irritable bowel syndrome: diagnosis and pathogenesis. *World J Gastroenterol*. 2012;18(37):5151–63.
19. Manning A, Thompson W, Heaton K, Morris A. Towards positive diagnosis of the irritable bowel. *BMJ*. 1978;2:653–4.
20. Halmos E, Power V, Shepherd S, et al. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterol*. 2014;146(1):67–75.
21. McKenzie Y, Alder A, Anderson W, et al. British Dietetic Association evidence-based guidelines for the dietary management of irritable bowel syndrome in adults. *J Hum Nutr Diet*. 2012;25:260–74.
22. New Zealand Formulary (NZF). NZF v19. NZF; 2013. Available from: [www.nzf.org.nz](http://www.nzf.org.nz) (Accessed Jan, 2014).
23. Tarpila S, Tarpila A, Grohn P, et al. Efficacy of ground flaxseed on constipation in patients with irritable bowel syndrome. *Curr Top Nutraceut Res*. 2004;2:119–25.
24. Cockerell K, Watkins A, Reeves L, et al. Effects of linseeds on the symptoms of irritable bowel syndrome: a pilot randomised controlled trial. *J Hum Nutr Diet*. 2012;25:435–43.
25. Hungin A, Mulligan C, Whorwell P, et al. Systematic review: probiotics in the management of lower gastrointestinal symptoms in clinical practice - an evidence-based international guide. *Aliment Pharmacol Ther*. 2013;38:864–86.
26. Shepherd S, Gibson P. Fructose malabsorption and symptoms of irritable bowel syndrome: guidelines for effective dietary management. *J Am Diet Assoc*. 2006;106:1631–9.
27. Gibson P, Shepherd S. Evidence-based dietary management of functional gastrointestinal symptoms: the FODMAP approach. *J Gastroenterol Hepatol*. 2010;25:252–8.
28. Ruepert L, Quartero A, de Wit N, et al. Bulking agents, antispasmodics and antidepressants for the treatment of irritable bowel syndrome (Review). *Cochrane Database Syst Rev*. 2011;(8):CD003460.
29. Garsed K, Chernova J, Hastings M, et al. A randomised trial of ondansetron for the treatment of irritable bowel syndrome with diarrhoea. *Gut*. 2013;[epub ahead of print].
30. Olden K. Targeted therapies for diarrhea-predominant irritable bowel syndrome. *Clin Exp Gastroenterol*. 2012;5:69–100.
31. McCormack P. Linaclotide: A review of its use in the treatment of irritable bowel syndrome with constipation. *Drugs*. 2014;74:53–60.
32. Raschi E, De Ponti F. Lubiprostone: pharmacokinetic, pharmacodynamic, safety and regulatory aspects in the treatment of constipation-predominant irritable bowel syndrome. *Expert Opin Drug Metab Toxicol*. 2014;10(2):293–305.

