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Review article

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Irritable bowel syndrome and mental health comorbidity — approach to multidisciplinary management

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Abstract

Irritable bowel syndrome (IBS) affects 5–10% of the global population. Up to one-third of people with IBS also experience anxiety or depression. Gastrointestinal and psychological symptoms both drive health-care use in people with IBS, but psychological comorbidity seems to be more important for long-term quality of life. An integrated care approach that addresses gastrointestinal symptoms with nutrition and brain–gut behaviour therapies is considered the gold standard. However, best practice for the treatment of individuals with IBS who have a comorbid psychological condition is unclear. Given the rising prevalence of mental health disorders, discussion of the challenges of implementing therapy for people with IBS and anxiety and depression is critical. In this Review, we draw upon our expertise in gastroenterology, nutrition science and psychology to highlight common challenges that arise when managing patients with IBS and co-occurring anxiety and depression, and provide recommendations for tailoring clinical assessment and treatment. We provide best practice recommendations, including dietary and behavioural interventions that could be applied by non-specialists and clinicians working outside an integrated care model.

Sections

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Introduction

Irritable bowel syndrome (IBS) is a common disorder of gut–brain interaction (DGBI)[1] in which individuals experience recurrent symptoms of abdominal pain, altered bowel habits and often bloating. Medical management of IBS has historically focused on treating the most bothersome of these gastrointestinal symptoms. However, evidence has shown that dietary modification and psychological therapies can improve global symptoms, and an integrated care model that includes medical management, dietary modifications and psychological therapy delivered by a multidisciplinary team is currently considered best practice for management of IBS[2], and should empower patients to self-manage their condition over time[3].

Common disorders of mental health, such as anxiety and depression, are highly prevalent globally and are a leading cause of disability and suicide[4]. IBS is frequently associated with these disorders, and evidence suggests that people with IBS are at increased risk of anxiety and depression[5]. The prevalence of anxiety and depression has increased over the past several decades[6]. The COVID-19 pandemic has accelerated this increase — the global prevalence of major depressive disorder and anxiety disorders increased by an estimated 28% and 26%, respectively, in 2020 (ref. 7). The prevalence of IBS also seems to be rising over time as a result of increasing recognition of the condition by physicians, westernization, and diet and lifestyle changes[8]. IBS is also one of several gastrointestinal manifestations of post-acute COVID-19 syndrome[9]. In the context of this potential increase in the prevalence of IBS and the increasing burden of mental health disorders globally, there is a critical need to discuss how to tailor existing therapies to meet the needs of people in which these conditions coexist.

In this Review, we first review the epidemiology and impact of IBS, depression and anxiety, and consider the shared pathophysiology between these conditions. We then discuss the challenges in and best practices for assessing and managing IBS when it co-occurs with a mood or anxiety disorder from the perspective of the gastroenterologist, the dietitian and the gastropsychologist, including guidelines for the use of digital tools. Finally, we provide practical, evidence-based dietary interventions and behavioural enhancement techniques that could be applied by non-specialists or clinicians working outside an integrated care model.

Epidemiology, impact and shared pathophysiology

Epidemiology

IBS affects 5–10% of the global population at any one time[10,11] and is more common among females than males. However, prevalence rates vary considerably between countries and cultures[12]. IBS is, like many other health conditions, frequently associated with anxiety and depression, either as diagnosed psychiatric disorders or as subclinical symptoms (throughout this Review, we refer primarily to symptoms of anxiety and depression, as very few studies specifically examine physician-confirmed diagnoses). Overall, people with IBS have a threefold higher risk of anxiety and depression than do healthy controls[5]. In one meta-analysis, the prevalence of symptoms of anxiety and depression among people with IBS was 39% and 29%, respectively, and the prevalence of co-occurring anxiety and depressive disorders was 23%[5].

Evidence from animals and humans suggests a bidirectional link between gastrointestinal symptoms and psychological comorbidity. A study in rats demonstrated that features of IBS occurred in a model of depression but not in healthy animals or rats with post-traumatic stress disorder[13]. Longitudinal studies in humans have shown that people who report symptoms of anxiety and/or depression with no comorbid IBS do develop gastrointestinal symptoms over time, whereas those with a diagnosis of IBS but no anxiety or depressive symptoms at baseline report anxiety or depressive symptoms at follow-up[14,15]. In a systematic review of 11 studies, people with depression had a twofold higher risk of comorbid IBS and a nearly twofold higher risk of developing new-onset IBS than people without depression[16]. A substantial body of evidence indicates a causal link between psychological factors and gastrointestinal symptoms, at least in subgroups of people with IBS. The strength of association in cohort studies, the fact that greater psychological distress is associated with more severe IBS, and the consistency of such findings across studies indicates a causal link between psychological factors and gastrointestinal symptoms. This link could be mediated via various mechanisms, such as dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis, immune activation and genetic mechanisms[17].

Impact

The impact of IBS is substantial but is compounded by psychological comorbidities. The total direct, annual cost of care for people with IBS is estimated at £1.3–2 billion in the UK[18], 3–4 billion euros in Germany[19] and US$2 billion in China[20]. Mean annual costs are substantially higher for individuals with severe gastrointestinal symptoms and for individuals with comorbid depression[18]. Indeed, the severity of IBS symptoms increases considerably as the number of co-occurring psychological comorbidities increases[21,22]. People with a greater number of co-occurring psychological comorbidities are also more likely to visit a doctor and to report that their IBS symptoms affect their activities of daily living[21]. Similarly, studies indicate that 5–50% of people with IBS need time off work because of symptoms[23,24], and that 82% experience overall work impairment due to IBS[25]. Impairment in work and activities of daily living are more likely in those with higher levels of anxiety and depression[25].

In addition, IBS has a considerable impact on quality of life owing to negative effects on the ability to socialize and travel[26,27]. Patients with IBS can experience stigma from friends, family and health-care professionals who do not fully understand or acknowledge these experiences[28]. Delays in diagnosis and commencement of effective treatment can lead to the onset of, or an increase in, symptoms of anxiety and depression[29]. Furthermore, observational data suggest that reduced quality of life in IBS is mainly driven by concurrent psychological comorbidity rather than gastrointestinal symptoms[30], reinforcing the need for an integrated approach to care.

Shared pathophysiology

Genetic susceptibility has been identified for IBS and for mood and anxiety disorders, and a genome-wide analysis of >250,000 people with IBS identified shared genetic risk factors across these conditions, indicating that they share pathophysiological mechanisms, rather than one condition causing the other[31]. Reduced brain volume and changes in resting brain functional connectivity across brain regions have also been implicated as shared pathophysiological mechanisms that could explain the link between IBS, depression and anxiety[32,33].

The primary physiological link between IBS and depression and anxiety is the gut–brain axis[34] — the bidirectional, neurohumoral communication system that connects the gut and brain through interactions between the autonomic nervous system, the HPA axis and the microbiome.

Dysregulation of the autonomic nervous system and the HPA axis. Even among healthy individuals, acute or chronic stress causes the autonomic nervous system to produce corticotrophin-releasing factor, which is known to impair gut function[35], and could therefore lead to gastrointestinal symptoms. In IBS, the HPA axis — the system that harnesses metabolism, immunity and the autonomic nervous system to buffer the physiological effects of stress — becomes dysregulated[36]. High activity in the amygdala also seems to contribute to this dysregulation[37]. This dysregulation means that the gut of an individual with IBS or another DGBI is more susceptible to, and less able to recover from, stressful events[38]. Psychological and physiological resilience to stress seem to be reduced in IBS and could underlie this susceptibility and impaired recovery[39,40]. Resilience has been identified as a protective factor in the development of psychological distress in the setting of gastrointestinal disorders[39,41,42] and has recently been assessed as a novel therapeutic target in brain–gut behaviour therapy (BGBT)[43,44]. HPA axis dysregulation is also a key pathophysiological mechanism of depression[45], so could explain the frequent co-existence of depression with IBS.

The microbiome. The microbiome is an important regulator of gastrointestinal function and has emerged as an integral component of gut–brain communication through its influence on endocrine, neural and immune pathways[34]. Microbiome composition differs between people with and without depression[46]. Among people with IBS, microbiome composition also differs between people with and without psychological comorbidity[47,48]. Some evidence suggests that probiotic supplementation could have beneficial effects in mood disorders[49] and in IBS[50], and one small trial has demonstrated that probiotics can improve mood and gastrointestinal symptoms in individuals with IBS[51].

Findings in animal models also indicate that the microbiome influences the interaction between the brain and the gut. Transplantation of stool samples from humans with symptoms of depression into mice induces inflammation and anxiety, whereas transplantation of stool samples from healthy volunteers does not[52]. Similarly, transplantation of stool samples from humans with anxiety and IBS into mice induces behavioural and gastrointestinal motility abnormalities accompanied by immune activation and gut barrier dysfunction[53].

Assessment and management

Complex, co-occurring conditions are best understood by recognizing that multiple factors affect the development of physical symptoms and one's behavioural response to them. For example, IBS pathophysiology involves disordered motility, visceral hypersensitivity and altered mucosal, immune and microbial integrity, these mechanisms can be triggered and perpetuated by psychological factors[54]. Indeed, some evidence suggests that anxiety related to gastrointestinal symptoms[25,26] can be a key driver of gastrointestinal symptom severity and impaired quality of life in IBS[27]. Importantly, the relative contribution of the gut and brain to the dysregulated gut–brain interaction as a whole is likely to be unique to each patient — cluster-based modelling in IBS has identified subgroups of patients with varying degrees of gastrointestinal symptoms, extra-intestinal symptoms and psychological comorbidity[55]. As a result, the optimal treatment approach will also be unique to each individual.

In the following sections, we consider how to approach the assessment and management of IBS with co-occurring depression or anxiety with various levels of integrated care. We divide this approach into three domains: medical, dietary and behavioural. Regardless of the resources available, considering each of the three domains for each patient is critical for developing and personalizing a treatment plan.

Medical domain

Assessment. A diagnosis of IBS is based on the presence of gastrointestinal symptoms that meet the latest Rome criteria[1]. Taking a careful history to identify the cardinal symptoms of IBS is, therefore, key. Exhaustive investigation is unnecessary, but limited testing to exclude some common organic disorders that can mimic IBS, such as coeliac disease, is important[56]. Good communication with the patient is vital, and physicians should take time to provide a clear explanation of IBS and the current understanding of its pathophysiology with respect to the gut–brain axis. They must also emphasize that IBS is not a psychological disorder and that the physical gastrointestinal symptoms are real.

Overall, discussion of mental health in IBS can be difficult in a medical consultation, not least because patients are likely to have consulted to discuss their gastrointestinal symptoms, and discussion of mental health requires sufficient time and sensitivity. Nevertheless, identification of co-occurring psychological disorders as early as possible is important for directing the choice of drug treatments and for an early referral for psychological and behavioural therapies. Guidelines typically recommend psychological and behavioural therapies for patients whose symptoms have not responded to multiple drug treatments[57]. However, these interventions have a low risk of harm and build lifelong management skills, so we recommend that they are adopted early in the treatment journey if patients are willing.

General approach to medical treatment. Overall, the aim of medical treatment for IBS is to relieve symptoms and lessen their impact on quality of life (Table 1). Medications are available for abdominal pain, diarrhoea and constipation; success is assessed on the basis of patient-reported symptom responses[58–60]. Anti-diarrhoeals, such as loperamide, are often prescribed first-line for the treatment of loose stools, but if this treatment is ineffective, second-line drugs, such as alosetron, ramosetron, rifaximin and eluxadoline, can be used where available[57,61]. Osmotic laxatives, such as polyethylene glycol, and stimulant laxatives, such as senna, are often used as first-line treatment of constipation in IBS[57] and are effective for treatment of chronic idiopathic constipation[62]. However, besides two trials of polyethylene glycol in IBS, only one of which demonstrated an improvement in stool frequency[63,64], evidence for the efficacy of laxatives in IBS with constipation is very limited. Nevertheless, use of laxatives as first-line therapy for IBS with constipation is reasonable on the basis that they are effective for constipation generally[62] and they are inexpensive, widely available and well-tolerated[63,64]. Secretagogues, such as linaclotide or plecanatide, have been developed as second-line treatments for constipation[57,61]. These drugs soften stools and accelerate gut transit by activating ion channels on the luminal surface of enterocytes resulting in the movement of ions and water into the intestinal lumen[65,66]. Abdominal pain is initially treated with antispasmodics, such as hyoscine, or peppermint oil, but if this approach is unsuccessful, neuromodulator drugs, such as amitriptyline, can be used[57,61].

Unfortunately, complete symptom resolution is often not achievable, and this must be made clear to patients to ensure that expectations are managed. Overall, the efficacy of all drugs for the treatment of IBS is modest[58], including newer drugs that have been developed specifically for the treatment of IBS[58,59]. For these reasons, drug treatment is not a panacea, but just one component of a multimodal approach to IBS management. Also important to take into account is that, despite the prevalence of psychological comorbidities in IBS, the role of drug

Table 1 | Current evidence-based interventions for irritable bowel syndrome with or without common psychological disorders

Specialty	Treatment	Treatment targets	Administration	Duration
Medical	First-line treatment (laxatives, anti-diarrhoeals, antispasmodics)	Predominant gastrointestinal symptoms (constipation, diarrhoea and pain)	Usually initiated by primary care clinician	4+ weeks, continued depending on symptomatic response
	Second-line treatment (secretagogues for constipation, pharmacological treatments for diarrhoea)	Predominant stool pattern abnormality (constipation or diarrhoea)	Initiated by clinician in secondary care where available	4+ weeks, continued depending on symptomatic response
	Neuromodulators	Gastrointestinal symptoms (particularly pain)	Initiated by clinician in primary or secondary care Low-dose TCAs first choice, but SSRIs preferred with concurrent mood disorder Neuromodulators can be combined for refractory symptoms under specialist guidance	At least 6 months in those who respond to treatment
Dietary	Standard diet	Global IBS symptoms	Dietetic counselling (1:1 or group); delivery by non-diet clinicians possible but not yet evaluated	4+ weeks
	Low FODMAP diet	Global gastrointestinal symptoms, abdominal pain, bloating or distension, stool output, quality of life	Dietetic counselling (1:1 or group)	10+ weeks for restriction and reintroduction phases (at least two sessions)
	Mediterranean diet	Symptoms of depression	Dietetic counselling (1:1 or group); delivery by non-diet clinicians possible but not yet evaluated	12+ weeks
Psychological	Cognitive behavioural therapy	Psychological stress, negative emotion, maladaptive cognitive processes, avoidance, psychological comorbidity, somatization, abuse and adverse early-life experiences	1:1 or group with mental health clinician, self-help or internet-based	4–12 sessions
	Gut-directed hypnotherapy	Psychological stress, maladaptive cognitive processes, somatization	1:1 or group with trained (non-mental-health) clinician or internet-based	7–12 sessions
	Mindfulness-based stress reduction	Psychological stress, negative emotion	1:1 or group with trained (non-mental-health) clinician or online	8–12 sessions
	Psychodynamic interpersonal psychotherapy	Negative emotion, abuse and adverse early-life experiences, versions available for common psychological disorders	1:1 or online with trained mental health clinician	Variable
	Self-management	Stress, sleep, self-efficacy	1:1 or group with non-mental-health clinician, self-help, phone-based or internet-based	4–8 sessions

IBS, irritable bowel syndrome; FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides and polyols; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

therapy is usually centred on the treatment of gastrointestinal symptoms, and the influence of psychological factors on drug efficacy is not generally accounted for in drug trials in IBS.

Owing to the difficulties in treating IBS, patients might be dissatisfied with outcomes or mistrustful of the diagnosis. This dissatisfaction can lead some — particularly those with more severe or refractory symptoms, which are often accompanied by higher levels of psychological comorbidity — to seek alternative therapies for which robust evidence is lacking, thereby increasing the risk of harm[67]. Adopting an evidence-based approach to IBS treatment and communicating this accurately to patients is therefore vital.

Central neuromodulation. Conventional analgesia, including the use of opiates, is not a successful strategy for treatment of pain in IBS. As mentioned above, first-line treatment of abdominal pain is with anti-spasmodics or peppermint oil, both of which have been shown to be safe and effective for the relief of abdominal pain and global IBS symptoms[68,69]. Second-line treatment of pain is with neuromodulators such as tricyclic antidepressants (TCAs) or selective serotonin reuptake inhibitors (SSRIs) (Fig. 1). The precise mechanism of action of these neuromodulators in IBS is unclear, but it seems likely that these drugs can act on pathways between the gut and the brain to improve symptoms (Fig. 2). For example, most neuromodulators are primarily antidepressants, so their effects in IBS could be a result of alterations in pain perception and central processing. These effects might be partly mediated by improvements in psychological symptoms and mood[70]. Neuromodulators could also act peripherally to reduce visceral hypersensitivity and pain response at the gut level, but evidence for this action in IBS is very limited[71,72].

A meta-analysis of studies in which TCAs or SSRIs were compared with placebo in the treatment of IBS demonstrated a significant benefit of TCAs for abdominal pain compared with placebo[73]. Therefore, for abdominal pain, TCAs should be the first choice, initiated at low doses and titrated according to symptomatic response. SSRIs offer

an alternative option if symptoms do not respond to TCAs. The effects of these drugs on bowel habits are unclear, but they could have serendipitous additional effects. For example, TCAs can cause constipation by prolonging whole-gut transit time[74,75], which might be helpful in diarrhoea-predominant IBS.

If a mood disorder is suspected, then an SSRI at a therapeutic dose might be a better initial choice than low-dose TCAs for managing gastrointestinal symptoms alongside psychological symptoms because low doses of TCAs are unlikely to be adequate to treat a mood disorder. Indeed, SSRIs are recommended as first-line treatment of mood disorders in general by the UK National Institute for Health and Care Excellence[76]. Selective noradrenaline reuptake inhibitors (SNRIs) could also be useful in IBS. No evidence from randomized controlled trials is available on their use in IBS, but they are beneficial in other chronic painful disorders[77], and they are used to treat depression and anxiety. Some evidence does suggest that SNRIs are helpful for managing gastrointestinal symptoms in some patients with IBS, particularly individuals with psychological comorbidity[78].

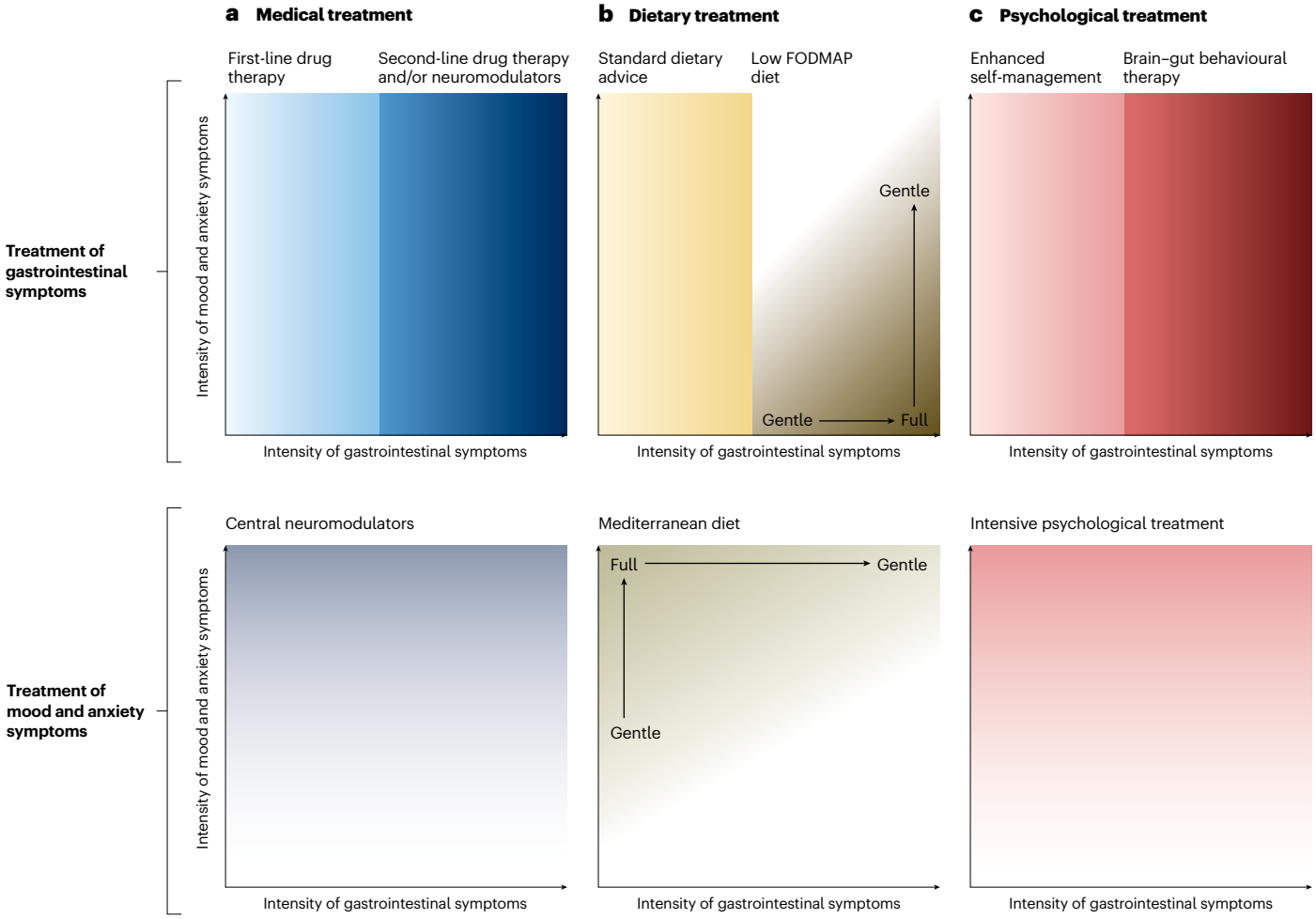

Fig. 1 | Guidelines for the treatment of individuals with IBS based on the severity of symptoms. These are general guidelines. Treatments within and across specialties can be combined, and selection of treatment is necessary on a case-by-case basis, and depends on the severity of gastrointestinal and mood or anxiety symptoms, the presence of other psychological and physical comorbidities, psychosocial history and patient preference. **a**, Medical treatment. Patients with predominantly gastrointestinal symptoms (top) should be treated with first-line medical therapy, then second-line therapy if their symptoms do not respond. If patients have a co-occurring mood disorder (bottom), use of central neuromodulators — particularly selective serotonin reuptake inhibitors — should be considered alongside treatment of gastrointestinal symptoms. Central neuromodulators, such as low-dose tricyclic antidepressants can also be used for abdominal pain and global symptoms. **b**, Dietary treatment. Patients with mild gastrointestinal symptoms should be provided standard dietary advice. If symptoms persist, or a patient has moderate to severe gastrointestinal symptoms, then the low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diet should be used (top). Elements of both approaches might be appropriate in some patients. In patients with substantial coexisting psychological symptoms, the gentle FODMAP diet approach is recommended. In patients in whom psychological symptoms predominate (bottom), the Mediterranean diet can be considered, and can also be modified for FODMAP content if necessary in those with moderate to severe gastrointestinal symptoms. **c**, Psychological treatment. Patients with a low severity of psychological symptoms and/or gastrointestinal symptoms should be counselled to self-manage symptoms via education and lifestyle. Brain–gut behaviour therapy, such as cognitive behavioural therapy and hypnotherapy, can be used in those with moderate to severe gastrointestinal symptoms (top). In patients with substantial psychological symptoms, this therapy could be complemented with traditional psychological treatment (bottom). IBS, irritable bowel syndrome.

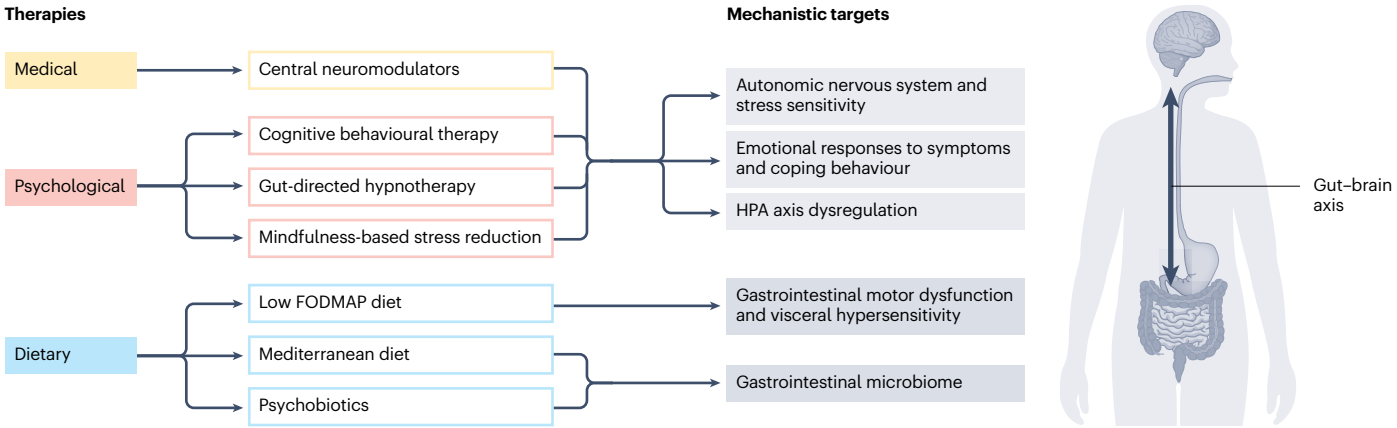

Fig. 2 | Key mechanistic targets and interventions that improve IBS and depression via the gut–brain axis. Various biological aberrations are present in the gut–brain axis in patients with irritable bowel syndrome (IBS), depression and anxiety. Medical, dietary and psychological therapies (right) can each theoretically target one or more of these aberrations, and when used in combination, they could work synergistically. Although only one key mechanisms or set of mechanisms is presented here for each therapy, some of these therapies might target more than one mechanism. For example, central neuromodulators and hypnotherapy might also target visceral hypersensitivity, the low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diet might influence symptoms via the microbiome, and the Mediterranean diet might target the hypothalamic–pituitary–adrenal (HPA) axis.

Finally, the concept of augmentation — the use of different neuromodulators in combination — is important in IBS. For example, when treating IBS and co-occurring depression with an SSRI, a low-dose TCA could be added for the treatment of persistent gastrointestinal symptoms, such as abdominal pain. This approach is supported by expert consensus[70], but many physicians might feel uncomfortable implementing this approach; indeed, gastroenterologists who are not experts in IBS and prescribing of central neuromodulators are altogether less likely to use neuromodulators in IBS[79]. Their reluctance could be, in part, due to the elevated risks of adverse events when combining antidepressants; however, the administered dose of each drug is usually lower when used in combination than when used alone, thereby attenuating these risks[80]. Augmentation can be useful in patients with severe or refractory symptoms of IBS irrespective of psychological comorbidity. Neuromodulators can also be used to augment the effectiveness of behavioural therapies, particularly when anxiety or pain are present[81].

Dietary domain

Dietary modification is a fundamental component of IBS treatment and features in US[61], UK[57], Canadian[82] and Japanese[83] clinical guidelines. It is also an integral component of the integrated care model[2]. Dietary interventions are predominantly administered by dietitians and can enable the discharge of many patients without the need for input from a gastroenterologist[84]. Research has shown that a clinical model in which patients see a gastroenterology-specialist dietitian first reduces general practitioner referrals to gastroenterologists by >30%, with subsequent savings to the health-care system[85]. Quality dietetic care of individuals with IBS incorporates comprehensive assessment, implementation of the nutrition care plan and monitoring as necessary.

Assessment. A detailed review of general clinical and dietary assessment is provided elsewhere[86], but we discuss here the key elements of a dietetic assessment for individuals with IBS. The onset, severity and frequency of symptoms should be recorded, ideally using validated tools, such as the gastrointestinal symptom rating scale[87], and stool frequency and consistency should be assessed with the Bristol Stool Form Scale[88]. Assessment of lifestyle, such as exercise and social factors (for example, employment and social support), will facilitate the identification of non-dietary factors that contribute to symptomatic burden. Comprehensive dietary assessment includes not only quantification of current dietary intake, but also identification of an individual's perceived dietary triggers, the sources of previous dietary advice, and the extent and nature of current and previous dietary restrictions. These aspects are critical given that >35% of individuals with IBS implement multiple concurrent diets[89] and the reported rate of disordered eating among people with IBS is as high as 25%[90].

When IBS co-occurs with anxiety or depression, the assessment should encompass additional considerations. Anxiety and depression symptomatology should be recorded, as this could affect engagement with and adoption of recommended treatments. Clinicians need to be able to bridge the gap between their own expectations and those of the patient if treatment is to be effective, and achieving this might require adjustments such as longer assessment appointments or assessment over more than one appointment. Other factors such as food insecurity, nutrient deficiencies, alcohol use, eating pathology and physical comorbidities should also be assessed, as they all affect nutrition status, the ability to meet nutrition goals and gastrointestinal symptoms (Table 2).

General approach to dietary treatment. In patients with recent unintentional weight loss, unnecessary dietary restrictions or disordered eating, the focus of management should be to improve nutrition status rather than management of gastrointestinal symptoms. Dietitians should use clinical judgement to facilitate such improvement without exacerbating gastrointestinal symptoms through a person-centred, trauma-informed and recovery-oriented approach. In individuals with adequate nutrition status, strategies for managing symptoms of IBS and co-occurring anxiety and depression are considered in the

following sections (Table 1). Diet-related anxiety might also need to be addressed (Box 1).

Standard diet. Standard dietary advice, based on empirical recommendations from the British Dietetic Association and the UK National Institute for Health and Care Excellence[91], is a reasonable first-line approach to improving symptoms of IBS. Such advice includes general and symptom-directed dietary recommendations, such as modification of fibre intake and restriction of caffeine and alcohol. Although this approach was not superior to any other control diet in a network meta-analysis[92], specific trials have demonstrated that it has an equivalent efficacy to that of a diet low in fermentable oligosaccharides,

Table 2 | Considerations in the biopsychosocial assessment of people with irritable bowel syndrome and symptoms of anxiety or depression

Consideration	Rationale for considering	Recommended actions		
		Medical	Dietary	Psychological
Physical health comorbidities	Health conditions such as diabetes mellitus, heart disease and metabolic syndrome are more common among people with mental illness than among people without mental illness[140] Psychotropic medications often have cardiometabolic effects Individuals with mental illness are less likely than those without to participate in routine health screening	Encourage screening of physical health (e.g. cardiometabolic biochemistry) On referral, detail comorbidities and current medications, as these could influence dietary or psychological priorities	Use clinical judgement to determine priority target of dietary changes (physical comorbidity, gastrointestinal or psychological symptoms)	Consider impact of physical comorbidities on choice of brain–gut behaviour therapy (e.g. multiple somatic comorbidities lend themselves to gut-directed hypnotherapy)
Co-occurring mental health conditions	Depression and anxiety often co-occur with other mental illness and alcohol use[121,122,141]; the latter can affect irritable bowel syndrome symptoms and/or nutrition status	Detail comorbidities and alcohol use on referral to other clinicians, as these can influence treatment goals Refer to specialist services where appropriate		
Co-occurring disordered eating or eating disorder	Disordered eating has a bidirectional relationship with common mental illnesses[142] Eating pathology might be central to the mental illness[143]	Detail established comorbidities on referral to other clinicians	Screen for detrimental eating behaviours and beliefs Tailor intervention to include strategies for disordered eating or eating disorders and avoid restrictive approaches Prioritize management of disordered eating or eating disorders over that of gastrointestinal symptoms when severity is high Refer to specialist eating disorder dietitian where necessary	Prioritize eating disorder behaviours; refer to specialty centre if unable to provide sufficient care Exposure-based interventions to increase tolerance of restricted foods
Medications	Commonly used physical health medications can have unintended gastrointestinal effects	Encourage medication to be taken with food where appropriate	None	None
Nutritional deficiency	Depression is associated with an increased risk of vitamin D, folate and zinc deficiency[144–146]	Review biochemical measures for deficiencies and assess nutritional adequacy of diet		None
History of sexual, physical or emotional abuse	Adverse experiences can affect symptom perception, treatment response and the patient–provider relationship[128]	Screen for adverse experience and practice trauma-informed care		
Insight into contribution of gut–brain axis	Insight facilitates readiness for treatments such as neuromodulators and psychological therapy	Master patient-friendly language to discuss gut–brain axis dysregulation and why behavioural therapies are part of integrated care; provide psychoeducation materials if necessary		
Patient perspective on goals of treatment	Patient goals of treatment might differ from clinician goals	Use patient perspectives to formulate a person-centred care plan		
Fatigue and cognitive factors	Fatigue, low motivation, impaired concentration and impaired memory are common in individuals with depression	Longer assessments or assessments over multiple appointments Formulate a care plan based on the patient's cognitive factors and readiness to change		
Food insecurity	Food insecurity is more common among individuals with depression than among people without a mental illness[147]	Assess the risk of food insecurity by using brief screening tools[148] or questions about food availability		

disaccharides, monosaccharides and polyols (low FODMAP) diet[93–96]. Whether this effect is the same among individuals with co-occurring psychological disorders is unknown. Dietary restrictions can be modified on the basis of individuals' needs.

Low FODMAP dietary advice. The most convincing evidence for dietary treatment of IBS supports the use of a low FODMAP diet. This intervention involves three phases: FODMAP restriction (4–8 weeks), FODMAP reintroduction (6–10 weeks) and FODMAP personalization. The restriction phase of the diet has the unwanted consequence of altering the microbiome, specifically bifidobacteria abundance[97], and can affect indices of diet quality (metrics that attempt to describe the 'healthiness' of the diet)[98]. Phases two and three are, therefore, critical for diet liberalization and for attenuating the effects on the microbiome[99]. Practice recommendations for the FODMAP diet have been published[100]. The mechanisms through which FODMAPs induce IBS symptoms are largely gut-specific (Fig. 2) and are reviewed in detail elsewhere[101]. In a network meta-analysis, the low FODMAP diet was ranked as superior to all control diets in IBS for reducing abdominal pain severity and bloating and increasing satisfaction with bowel habits[92].

Some evidence suggests that a low FODMAP diet can have some benefit on anxiety[102] and depression[96] in patients with IBS. In some trials, within-group improvements in symptoms of anxiety and depression have been observed but these improvements were not significantly greater than in controls[95,96]. To date, no trials of a low FODMAP diet have incorporated a threshold of psychological symptoms as a basis for enrolment.

Considering the limited evidence for efficacy of a low FODMAP diet on psychological symptoms together with the complexity of the diet, this approach should be avoided in individuals with moderate to severe symptoms of anxiety or depression. However, a gentle FODMAP diet might be appropriate, particularly in people with mild to moderate gastrointestinal symptoms (Fig. 1). Also known as the 'bottom-up' low FODMAP diet, this gentle approach involves restriction of selected FODMAPs. Although this approach has not yet been tested in trials, anecdotally it is routinely used in practice and described in detail elsewhere[103]. As an example of this approach, patients could be counselled to avoid selected foods that are high in fructans and/or galacto-oligosaccharides, as these are most abundant FODMAPs in many people's diets. The degree of restriction should be agreed upon, guided by baseline diet and the patient's ability to process and retain information.

Mediterranean diet. Accumulating evidence indicates that diet has a critical role in the treatment of depression; the most compelling evidence comes from trials of the Mediterranean diet. This traditional diet is rich in vegetables, fruit, legumes, wholegrains, nuts, seeds and olive oil (the principal source of added fat), and is low in red meat, and is the most studied dietary pattern globally[104]. In three randomized controlled trials, a Mediterranean diet delivered via dietary counselling significantly improved symptoms of depression[105–107]. In the landmark, 12-week SMILES trial of the Mediterranean diet for individuals with major depressive disorder, 32% of the group who received the intervention achieved remission compared with just 8% of controls who received a social befriending intervention[105]. The Mediterranean diet intervention was also associated with lower anxiety scores. These findings demonstrate the potential for diet to alleviate symptoms of depression[105]. The mechanisms underlying the effect of the Mediterranean diet on the brain are unclear but are likely to at least partially involve the microbiome[108] (Fig. 2).

To date, only one non-randomized, three-arm trial has compared the low FODMAP diet head-to-head with the Mediterranean diet in IBS[109]. This study demonstrated some benefit of the Mediterranean diet for gastrointestinal symptoms, although it was not randomized and the methodology used limits the interpretation of the data produced. Randomized controlled trials are needed to establish whether a Mediterranean diet, which is inherently moderately high in FODMAPs, can be used to improve psychological symptoms in IBS without exacerbating gastrointestinal symptoms. Until this evidence is available, a full Mediterranean diet is probably best reserved for individuals with a low severity of gastrointestinal symptoms. For people with moderate or severe gastrointestinal symptoms, a gentle Mediterranean diet (for example, initially incorporating legumes that are low in FODMAPs and only small amounts of vegetables that are high in FODMAPS, such as onions and garlic) might be more appropriate (Fig. 1).

Psychobiotics and other emerging treatments. Psychobiotics are substances that influence gut–brain signalling via the gut microbiome, and include probiotics, prebiotics, synbiotics, postbiotics and fermented food[110]. They can be administered as supplements, introduction of specific foods or whole-diet changes. Most evidence for a benefit of psychobiotics in depression comes from probiotic supplementation trials, and the largest systematic review and meta-analysis of these trials identified small effects on depression overall, but greater effects in populations with a formal diagnosis of depression[49]. With increasing interest in whole-diet interventions that can influence psychiatric outcomes[111], a 'psychobiotic' diet that is rich in prebiotics and fermented foods has been developed and had some impact on perceived stress in healthy individuals[112]. On the basis of work in preclinical models, various pathways have been proposed to underlie the

Box 1

Diet-related anxiety

Individuals with irritable bowel syndrome (IBS) and co-occurring anxiety or depression can present with food-related distress. This distress can manifest as longstanding, unnecessary dietary restrictions, strongly held beliefs around food and reluctance to divert from these beliefs, and fear of eating out or in settings in which total dietary control is not possible. Patients with such anxieties should be provided with evidence-based advice on appropriate dietary restrictions and with information that debunks dietary myths. Dietitians can also work with individuals to set realistic expectations (for example, explaining that dietary restriction is not a panacea for improving gastrointestinal symptoms), educate them about worst case scenarios if a 'forbidden' food is eaten, help them focus on what they can eat rather than what they cannot, and improve overall dietary diversity. Importantly, addressing diet-related anxiety can also have beneficial downstream effects on gastrointestinal symptoms. Referral to a specialist eating disorder dietitian is recommended for patients in whom food-related fear is pathological.

psychobiotic effect on microbiome–gut–brain communication, including an influence on the HPA axis[113], but much more work is necessary to decipher the mechanistic pathways for each individual psychobiotic substance in humans and whether they also have therapeutic effects on gastrointestinal symptoms.

Dietary exclusion of antigens has also been suggested as an approach to management of gastrointestinal symptoms in IBS. Use of confocal laser endomicroscopy, which enables visualization of the gut mucosa in real time, has indicated the potential for immune activation in response to dietary antigens, such as wheat, soy and milk, in IBS[114]. However, only one randomized controlled trial has tested this hypothesis, and assessment with dietary challenge and confocal laser endomicroscopy indicated that testing for immune activation has a low diagnostic accuracy[115]. Future research is required to confirm whether dietary components are triggers of immune activation and symptoms in IBS.

Psychological domain

Assessment. Psychological assessment can take many forms. Standard assessment tools include screening tools such as the Patient Health Questionnaire-9 (PHQ-9)[116], the Generalised Anxiety Disorder-7 (GAD-7)[117] and items from the National Institutes of Health Patient-Reported Outcomes Measurement Information System (PROMIS) toolbox[118]. Most of these have not been specifically validated in IBS[119] but can help to determine the need for further assessment by a psychologist. Some questionnaires, such as the Hospital Anxiety and Depression Scale (HADS)[120], incorporate diagnostic thresholds, above which scores indicate the likely presence of a mental health condition. The most rigorous screening is an interview with a psychologist or other mental health clinician. This interview enables a patient to be considered in the appropriate context, which is important because many symptoms of common psychological disorders, and particularly depression, overlap with symptoms of IBS; for example, changes in appetite, sleep and motivation. Also, important to consider is that the anxiety questionnaires that are often used in practice are validated to identify worry, not necessarily screen for other common anxiety disorders, such as panic disorder[121], post-traumatic stress[122] and obsessive–compulsive disorder[123]. Given that the incidence of eating disorders, including avoidant-restrictive food intake disorder, is increasing among patients with gastroenterological conditions, and particularly among individuals with IBS[124], patients with IBS should be assessed for this disorder because it is a contraindication for restrictive dietary therapy[125] (Table 2).

Although assessment tools might vary between providers and practice settings, several core principles can be helpful for assessing psychological comorbidity in a patient with IBS. First, recognize that the factors that triggered the patient's IBS (for example, infection, diet or stress) might not be the factors that keep it going. Second, identify the presence of symptom-specific anxiety and other cognitive factors that influence symptom perception, such as pain catastrophizing. Third, assure the patient that their psychological response is expected and modifiable, so questions are asked about stress, anxiety and other psychological concerns, because it is normal for IBS to affect mental health (instead of vice versa)[126].

Another important aspect of psychological assessment in IBS, particularly in patients with psychological comorbidity, is to identify any past or ongoing sexual, physical or emotional abuse (Table 2). These adverse experiences not only increase the risk of developing IBS[127] but can affect symptom perception, treatment response and the patient–provider relationship[128]. Patient-friendly language around this issue is important; for example, "It is very common for people with your history to have experienced trauma in their lives — have you had any experiences that you consider traumatic, such as physical or sexual abuse, a natural disaster or medical trauma?"[129].

General approach to psychological treatment. Psychological therapies, and sometimes psychotropic medications such as antidepressants and anxiolytics, are often indicated for mental health conditions, such as depression, anxiety, post-traumatic stress and substance abuse, and can be administered as an adjunct to IBS care by mental health providers in the community. These therapies can be augmented with IBS-specific behavioural interventions that are recommended in IBS clinical guidelines globally[57,61,82,83], as part of integrated care (Fig. 1).

Brain–gut behaviour therapy. BGBT (Table 1) focuses on the remediation of psychological and cognitive factors that impact gastrointestinal symptom perception; for example, anxiety when not close to toilets and the belief that only weak people cannot control their bowels. The scientific premise of these interventions is that they influence the gut–brain axis (Fig. 2), and this premise is supported by their ability to mitigate abdominal pain and other gastrointestinal symptoms and to improve gastrointestinal-specific quality of life[130]. BGBTs that have been tested the most in the context of IBS include cognitive behavioural therapy (CBT), gut-directed hypnotherapy, interpersonal psychodynamic therapy, and various forms of relaxation[73,131]. In a systematic review and meta-analysis of randomized controlled trials of these therapies in IBS that included a total of 4,072 participants, CBT (whether self-directed, minimal contact or face-to-face) and gut-directed hypnotherapy were the most effective in the long term[132].

Although the evidence base for CBT and interpersonal psychodynamic therapy is strong, these therapies require trained mental health providers for their delivery. In addition, although these brief, gastrointestinally focused interventions can improve symptoms of anxiety and depression, psychological symptoms are not the primary focus of treatment. Rather, the focus of treatment is on remediating the thoughts, feelings and behaviours that led to symptom-specific anxiety and avoidance. In fact, some evidence suggests that patients with IBS and mental health comorbidity respond less well to BGBTs than to community-based psychotherapy, and a referral to a general psychologist may need to be offered before a course of BGBT or concomitantly[69] (Fig. 1). The efficacy and mechanisms of BGBT are reviewed in detail elsewhere[81].

Guidelines for use of digital tools

Digital methods of treatment delivery, such as websites and mobile phone apps, could be powerful tools for treatment of gastrointestinal and psychological symptoms in people with IBS[133]. They can also be leveraged to offset limited access to integrated services. However, gastroenterology clinicians (gastroenterologists, dietitians and/or psychologists) should be gatekeepers for access to these methods, and should recommend specific tools only after a patient has been assessed in the appropriate context (medical, dietary and psychosocial). For example, with regard to dietetic interventions, apps are available that guide implementation of the low FODMAP diet but should only be used in association with existing dietetic support. This precaution safeguards against long-term and/or excessive restriction or implementation of the low FODMAP diet when it is contraindicated.

With regard to psychological interventions, clinicians must be attuned to the patient characteristics that lend themselves to

low-intensity interventions: mild (to moderate) disease severity; high insight into the gut–brain axis and the multifactorial aspect of IBS (for example, the clinician has credibly conveyed the role of BGBT); the absence of severe comorbid depression or anxiety disorder, as this scenario requires an individualized approach under the supervision of a mental health practitioner; the presence of a specific gastrointestinal symptom (for example, chronic pain or vomiting) or comorbidity (for example, fibromyalgia or chronic fatigue syndrome); and an understanding that if a digital therapy does not reduce the patient's symptoms, the class of therapy has not failed but more personalized intervention is needed. In addition, the risk associated with some therapies is higher when they are not delivered by a qualified clinician[133]. For example, hypnotherapy is not safe for all patients, and a qualified clinician would not offer it if screening identified risks, such as history of dissociation or substantial trauma. A self-help hypnotherapy resource would not ensure that a patient could receive the therapy safely, but might be prescribed by a clinician in some situations.

Guidelines for non-specialists and practice outside an integrated care model

The biopsychosocial model of care is possible only with a collaborative approach that involves a gastroenterologist, dietitian and gastropsychologist. Ideally, an integrated care model, in which dietitians and gastropsychologists are co-located within gastroenterology services, would be available to all patients with IBS. After initial consultation with a gastroenterologist, all patients would undertake dietetic and psychological screening to determine their need for input from each specialty. Access to these specialties would continue for weeks or months, depending on when the patient is confident to self-manage their DGBI independently. However, this ideal approach is not feasible in all settings, so in the following sections, we provide guidance for non-specialists or clinicians who are working outside an integrated care model to facilitate effective screening and treatment for patients with IBS and psychological comorbidity.

Dietary screening and treatment

Gastroenterologists and psychologists can undertake broad dietary assessments in people with IBS by comparing intake to national dietary guidelines. Diet monitoring via food records is not routinely recommended outside dietetic consultation. However, asking patients to recall their intake in the past 24 h can enable recent dietary intake to be compared with daily food recommendations for age and gender to identify excess or inadequacy. If the diet seems adequate, then dietary intervention could be explored.

Standard dietary advice can be provided in patients with mild to moderate gastrointestinal symptoms, ensuring that supporting written information is provided[134]. A Mediterranean diet can be introduced in individuals with mild gastrointestinal symptoms who are interested in dietary approaches for psychological symptoms[135]. The low FODMAP diet should be reserved for patients with access to a specialist dietitian, but knowledge of the specific foods that are high in FODMAPs might be useful for psychologists in some scenarios; for example, this knowledge could inform exposure therapy when a patient fears specific foods.

Psychological screening and treatment

Although gastroenterologists and dietitians do not typically perform mental health screening in their usual practice, they might be the first health-care providers to observe emotional difficulties in patients with IBS. These difficulties could be discussed with the patient and a referral provided back to the patient's general practitioner or directly to a psychologist or social worker. A direct referral might only be possible if the patient can cover the cost or is privately insured because psychologists operate in the private health-care system in many countries.

When a non-mental-health provider becomes aware of a diagnosed co-occurring psychological disorder, such as anxiety or depression, the patient's clinical response to treatment of that disorder must be assessed regardless of whether its onset was before or after diagnosis of IBS. Under-managed anxiety and depression are common and can negatively affect responses to the treatment of IBS[136,137]. When assessing responses to psychological treatment of IBS, progress must be measured in the physical and psychological domains. Similarly, deterioration in the mental health of patients with IBS should be addressed by any health professional. The patient's referring doctor, general practitioner or mental health provider should be informed about any changes in the patient's wellbeing, particularly if there is the risk of self-harm or harm to others. Dietitians can use mindfulness strategies (Box 2) and acquire training in gut-directed hypnotherapy to augment their dietary

Box 2

Mindfulness-based stress reduction

A promising, evidence-based mind–body approach for the management of irritable bowel syndrome (IBS) that does not require gastropsychology specialization is mindfulness-based stress reduction (MBSR). Mindfulness is the practice of purposefully paying attention to the present moment in a non-judgemental way[149]. Mindfulness enables detached self-observation and teaches to reflect on situations rather than to react in an automatic way. MBSR programmes are usually short — for example, 45 min of practice daily for 8 weeks — and are often delivered in groups[150]. Mindfulness practice can be combined with therapies derived from cognitive behavioural therapy, such as mindfulness-based cognitive therapy[151].

Trials of mindfulness in IBS have so far been uncontrolled or waiting list-controlled (and therefore not blinded), but the available evidence suggests that it can reduce IBS symptoms by replacing maladaptive thinking (for example, around the fear of symptoms) with non-judgemental observations, acting with awareness, and the ability to focus on the present moment[151,152]. Mindfulness is also an element of other newer therapies for IBS and other chronic pain conditions, including acceptance and commitment therapy[153].

Although mindfulness strategies have not been tested in randomized controlled trials, simple mindfulness strategies could be safely incorporated into practice by non-mental-health professionals. For example, dietitians can teach patients mindful eating with exercises that involve looking at, smelling, touching and tasting foods, promoting attentive and slow consumption (for example, to avoid swallowing large quantities of air associated with fast eating). A variety of digital apps that include mindfulness exercises are also available and could be recommended by a non-mental-health professional, assuming the patient is aware of the limitations of digital behavioural therapeutics.

Box 3

Top ten recommendations for managing individuals with irritable bowel syndrome and co-occurring symptoms of anxiety or depression

1 Master patient-friendly language for discussion of the gut–brain axis, its dysregulation, and how depression or anxiety can lead to the onset, perpetuation and/or maintenance of irritable bowel syndrome (IBS), and vice versa. Convey empathy and validation that gastrointestinal and psychological symptoms are real and taken seriously.

2 Adjust the duration and/or frequency of assessment and treatment visits to accommodate mental health needs and ongoing monitoring. Elongate an assessment over multiple visits if necessary to build a relationship and determine the context of symptoms, especially if the patient has a history of abuse.

3 Be familiar with the threshold for referral to specialist clinicians, especially if they are not already integrated into your care setting:
- Gastroenterologist: if the diagnosis of IBS is in doubt and symptoms have proven refractory to treatment in primary care.
- Specialist gastroenterology dietitian: if the patient is consuming a diet high in foods that trigger IBS symptoms, shows a clear dietary deficit or nutritional deficiency, shows recent unintended weight loss, or requests or is receptive to dietary modification advice.
- Gastropsychologist: if the patient shows moderate to severe symptoms of depression or anxiety, suicidal ideation and hopelessness, has a low social support system, has impaired quality of life or avoidance behaviour, or shows motivational deficiencies that affect ability to self-manage or adhere to treatment recommendations.
- Psychiatry or specialist psychologist (community): if the patient shows severe psychiatric illness and/or psychiatric medication use, there is concern about the use or misuse of anxiety medication or opiates, or if the patient has an eating disorder.

4 Limited investigations (for example, coeliac serology) are needed in all patients with suspected IBS, but exhaustive investigation should be avoided. The focus should be on making an early diagnosis of IBS to facilitate early initiation of treatment and access to integrated management.

5 Neuromodulators should be used as second-line treatment for IBS. Low-dose tricyclic antidepressants (TCAs) are preferred for gastrointestinal symptoms, particularly pain, but a selective serotonin reuptake inhibitor is preferred if there is a concurrent mood disorder because low-dose TCAs are unlikely to address psychological symptoms.

6 Dietary counselling should be patient-centred and tailored to the individual, taking into consideration nutrition status, the presence and severity of physical and mental comorbidities, and psychosocial factors.

7 A low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diet can be considered for individuals with moderate to severe gastrointestinal symptoms in the absence of red flags (for example, eating pathology or severe mental illness) and should be delivered by a dietitian. For people with co-occurring moderate-to-severe symptoms of anxiety or depression, a gentle FODMAP diet or standard diet might be appropriate. In patients with psychological-predominant symptoms, a Mediterranean diet should be considered.

8 Become familiar with the indications for brain–gut behaviour therapies (BGBTs) such as cognitive behavioural therapy, gut-directed hypnotherapy and mindfulness-based stress reduction. Also become familiar with the differences between BGBTs and psychological therapies that are specifically for depression and anxiety.

9 When possible, seek out training in other disciplines to be able to offer patients additional strategies to enhance self-management. For example, gastroenterologists and dietitians can be trained in mindfulness approaches and gut-directed hypnotherapy.

10 Assure patients that you will remain involved in their care and work with their other practitioners to ensure they are treated holistically.

interventions. Similarly, dietitians can readily acquire skills to offer exposure-based behavioural techniques to patients with excessive fear of re-emerging symptoms during FODMAP reintroduction.

Enhancing patient self-management

All clinicians, regardless of specialization, can improve care of patients with IBS by promoting patient empowerment and self-management skills. Self-management and lifestyle approaches include education and psychoeducation in the form of handouts, self-help books, websites and apps. These resources can provide strategies to modify aspects of lifestyle that are known to contribute to IBS symptomatology. For example, self-help resources can provide simple steps to increase physical activity, which is known to be beneficial for IBS symptoms[138]. Other commonly targeted issues are sleep hygiene, mindful eating and assertive communication with important others and health professionals. Self-management approaches are intended to engage patients in care while increasing their self-efficacy. A systematic review of studies in which self-management techniques were used confirmed that these techniques improve IBS symptoms and quality of life in the short term, although evidence for long-term efficacy is less robust[139].

Thresholds for referral

Where an integrated care approach is not possible, gastroenterologists should aim to build collaborative links with gastroenterology dietitians and gastropsychologists to coordinate high-quality multidisciplinary care. Referral to a dietitian should be made if the patient

reports considerable intake of foods that can trigger IBS symptoms, the patient requests or is receptive to receiving advice on dietary modification, dietary deficits or nutrition red flags are present (for example, avoidance of multiple food groups, unintentional weight loss of ≥5% in the previous 6 months or nutrient deficiency), and/or food-related fear is pathological. Referral to a gastropsychologist should be made if IBS symptoms or their impact are moderate to severe, the patient accepts that symptoms are related to gut–brain dysregulation, and the patient has time to devote to learning new coping strategies.

Future research

We previously outlined recommendations for future research into treatments for IBS with common psychological disorders[119]. Here, we summarize the research priorities specifically for dietary and psychological interventions and integrated models of care.

We encourage IBS guideline groups to re-evaluate their approach to assessing the quality of evidence behind non-pharmacological intervention trials. Trials of dietary and psychological or behavioural interventions involve unique methodological complexities that do not apply to trials of pharmaceuticals; examples include difficulties with blinding and standardization of delivery. As a result, these trials are often excluded from or minimized in treatment algorithms because they score low on quality criteria. Furthermore, in non-pharmacological trials, participants with psychological comorbidity are often excluded to reduce heterogeneity of the population, but this exclusion contributes to the gap in knowledge of how best to treat these patients.

Randomized controlled trials are needed to determine the efficacy of simple dietary approaches (such as the gentle FODMAP diet or standard diet) to improve gastrointestinal symptoms in people with IBS and psychological comorbidity, and to determine the efficacy and tolerability of the Mediterranean diet in this group. Psychological interventions that involve personalized cognitive and behavioural approaches and make use of technology (for example, approaches that combine therapist-led sessions with self-directed resources) are needed to address limited access to gastropsychologists worldwide and to increase the precision of care while reducing the cost. High-quality randomized controlled trials of integrated models of care are required, as are trials of combination therapies that target the gut and brain (for example, a neuromodulator or BGBT combined with the low FODMAP diet, or gut-directed pharmacotherapy combined with the Mediterranean diet). Trial designs that include active control interventions might help to offset the challenges associated with expectation bias and blinding that are inherent in trials of dietary and behavioural interventions, but these types of trials require large numbers of patients to achieve sufficient statistical power.

Studies to determine the efficacy of self-management techniques are needed. Predictors of response to these treatments are also required; such predictors could ultimately improve access to specialty services for patients who need in-person care. Measurement of biological end points, such as the microbiome and microbiome metabolites, will help to advance our understanding of the mechanisms of action of dietary and psychobiotic therapy. Collaboration with patients in the design, methodology and implementation of treatment trials is fundamental for identifying treatments that are effective and meet the needs of patients.

Conclusions

As the burden of psychological disorders within gastroenterology practice increases, new approaches are urgently needed to optimize the care of patients with IBS. The suboptimal efficacy of many therapies for IBS, including pharmacotherapy, dietary interventions and even brain–gut behavioural therapies, could be due to their focus on gut dysfunction in isolation, rather than on the contribution of the gut and the brain to symptoms. Development of well-defined clinical algorithms for the treatment of individuals with IBS and co-occurring anxiety or depression might be difficult given the complex interplay between many biopsychosocial factors that creates the clinical picture. However, we present key best-practice recommendations to support the tailoring of clinical assessment and treatment delivery for patients with IBS and co-occurring depression or anxiety, based on current evidence (Box 3). To build on these guidelines and improve care further, we need a better understanding of effective pharmacotherapies and dietary and psychological interventions, how they can be implemented in combination, and to what degree non-specialists can safely and effectively deliver these therapies.

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Author contributions

The authors contributed equally to all aspects of the article.

Competing interests

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