

WJG 20<sup>th</sup> Anniversary Special Issues (4): Irritable bowel syndrome**Complementary and alternative medicines in irritable bowel syndrome: An integrative view**

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**Abstract**

Irritable bowel syndrome (IBS) is a common gastrointestinal disorder with a high incidence in the general population. The diagnosis of IBS is mainly based on exclusion of other intestinal conditions through the absence of inflammatory markers and specific antigens. The current pharmacological treatment approaches available focus on reducing symptom severity while often limiting quality of life because of significant side effects. This has led to an effectiveness gap for IBS patients that seek further relief to increase their quality of life. Complementary and alternative medicines (CAM) have been associated with a higher degree of symptom management and quality of life in IBS patients. Over the past decade, a number of important clinical trials have shown that specific herbal therapies (peppermint oil and Iberogast®), hypnotherapy, cognitive behavior therapy, acupuncture, and yoga present with improved treatment outcomes in IBS patients. We propose an integrative approach to treating the diverse symptoms of IBS by combining the benefits of and need for pharmacotherapy with known CAM therapies to provide IBS patients with the best treatment outcome achievable.

Initial steps in this direction are already being considered with an increasing number of practitioners recommending CAM therapies to their patients if pharmacotherapy alone does not alleviate symptoms sufficiently.

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**Key words:** Irritable bowel syndrome; Complementary and alternative medicine; Hypnotherapy; Cognitive behavioral therapy; Herbal therapy; Peppermint

**Core tip:** Irritable bowel syndrome is a prevalent gastrointestinal disorder that interferes with daily living in 5%-20% of the population. The current review summarizes the most widely used complementary and alternative medicine (CAM) approaches that have proven to be effective and have been endorsed by professional organizations. The review encourages the use of both pharmacotherapy and CAM approaches in an integrative setting to provide the best outcome and quality of life to patients.

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**INTRODUCTION**

Irritable bowel syndrome (IBS) is among the most common gastrointestinal disorders with a prevalence ranging from 5%-20% in the general population worldwide<sup>[1,2]</sup>. IBS is more commonly diagnosed in women than in men and in people younger than 50 years<sup>[1,3,4]</sup>. The high prevalence of diagnosis also results in a significant so-

cioeconomic burden through decreased work productivity, increased direct and indirect healthcare costs, and - depending on the severity - a reduction in quality of life for IBS patients and their caregivers<sup>[5-8]</sup>. The estimated indirect and direct healthcare costs related to IBS in the United States have been steadily increasing and amount to \$1.35 billion dollar as of 2003<sup>[9]</sup>. The worldwide health costs associated with IBS are estimated to exceed \$200 billion United States dollars<sup>[10]</sup>. The International Classification of Diseases (ICD) of the World Health Organization in its latest revision, ICD-10, classifies IBS as a functional digestive disorder with the ICD-10 classification 58.9 with sub-classifications as irritable colon or spastic colon<sup>[11]</sup>. This classification does not distinguish between the Rome-III criteria and the consensus of many professional medical organizations that have divided IBS into four different subgroups based on the primary symptom presentation as constipation-predominant IBS (IBS-C), diarrhea-predominant IBS (IBS-D), mixed or alternating IBS, and unspecified IBS<sup>[2,12]</sup>. The diagnosis of IBS is mainly dependent on the absence of pathophysiological and morphological indicators and therefore remains an exclusion diagnosis concentrated on symptom presentation<sup>[13]</sup>. There have been indications in recent research studies that IBS may be the result of a low-grade inflammatory process within the lower intestinal tract but definitive and validated biochemical markers have not emerged as of yet<sup>[14-17]</sup>. There also remains a gap in our understanding of the underlying pathophysiology and what causes IBS. A few hypotheses have linked genetic predisposition, post-infectious small bowel bacterial overgrowth, and certain diets with a higher incidence for developing IBS<sup>[18-20]</sup>. However, a unified understanding of the pathophysiology that may result in a feasible and causal treatment approach has not emerged. In defense of this deficit, similar knowledge gaps exist for a wide range of conditions for which symptomatic treatment to date provides the only therapeutic approach.

Because current pharmacological treatment approaches for IBS are solely based on symptom reduction, many patients remain undertreated and dissatisfied with their quality of life. In addition, many pharmacological treatment approaches are associated with side effects that result in a smaller benefit to the patient in terms of treatment outcomes<sup>[18,19]</sup>. The treatment also depends on the specific subtype of IBS. While IBS-C patients mainly suffer from abdominal pain because of slow bowel movement and less frequent bowel release, patients with IBS-D suffer from a social stigma due to the frequent bowel release that requires a bathroom in close proximity as well as bloating and increased flatulence<sup>[8,19,21,22]</sup>. Comorbidities between IBS with depressive and anxiety disorders have been well defined although it remains unknown which of these is the cause and the effect<sup>[23-26]</sup>. A common treatment for all subtypes of IBS are antidepressants which may indicate that certain depressive and anxiety disorders play a role in the pathophysiology of IBS<sup>[25,27-29]</sup>. Another emerging field of research is the

investigation of the gut-brain axis also referred to as the enteric nervous system (ENS). It has been established that interconnected sensing of afferent and efferent neurons in the ENS influences gut motility based mainly on serotonergic and cholinergic nerve innervations<sup>[30,31]</sup>. The 2 major serotonin receptors present in the intestinal tract, 5-HT<sub>3</sub> and 5-HT<sub>4</sub>, and a serotonin reuptake transporter are either differently expressed or even present with mutations in certain IBS populations<sup>[27,28,32-34]</sup>. This correlates well with the current pharmacological treatment approaches of using 5-HT<sub>3</sub> receptor antagonists and 5-HT<sub>4</sub> receptor agonists in IBS patients to reduce both visceral pain perception and regulate gastrointestinal motility<sup>[35-37]</sup>. Considering that the neurotransmitter and hormone serotonin is involved in both intestinal motility and mood regulation may serve as an indicator that changes in the ENS neurotransmission are involved in the comorbidity between IBS with depressive and anxiety disorders.

As mentioned, current pharmacological treatment approaches provide limited symptomatic relief to IBS patients. This has resulted in a significant increase in self-medication and the use of complementary and alternative medicines (CAM) by patients and even healthcare providers to bridge the gap and increase quality of life<sup>[38-42]</sup>. This review will summarize the current knowledge of CAM alone and in conjunction with pharmacological treatments as an integrative approach to manage patients with IBS and improve their quality of life. Although the review is not comprehensive in addressing all aspects of CAM and integrative medical approaches to treating IBS, it is intended to provide practitioners with the most commonly used and most widely recommended CAM approaches that have shown repeated success in clinical trials over the past decades. It is important to point out that pharmacological treatment should not be abandoned by patients and their providers in lieu of CAM approaches but rather an integrative approach considered that provides both maximum relief of symptoms and increased quality of life.

## LITERATURE SEARCH

This article reviews current research regarding the most commonly used CAM therapies for IBS in the United States, which are single or combination herbal products, acupuncture, yoga, hypnotherapy, and cognitive behavioral therapy. The literature search covered the period from January 1996 to June 2013 using Medline and PubMed with the search terms “irritable bowel syndrome” in combination with “yoga”, “hypnotherapy”, “cognitive behavioral therapy”, “CBT”, “CAM”, “acupuncture”, “herbal therapy”, and “integrative medicine”. Out of 714 total articles retrieved, 243 were excluded because they were reviews or protocols, 215 were not in English, and 102 were duplicates or did not relate to IBS. A total of 154 articles were selected for inclusion in this review (Figure 1).

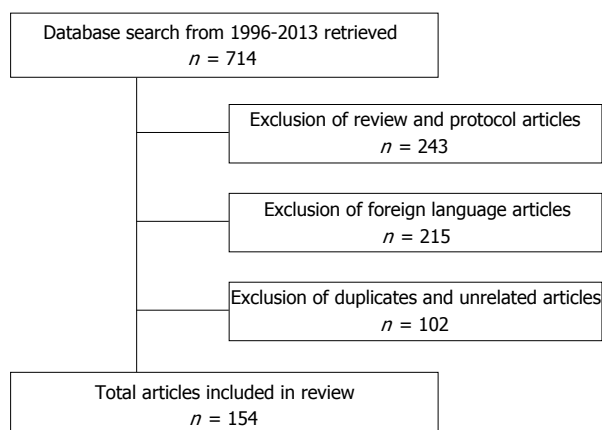


Figure 1 Flow chart illustrating the selection criteria for inclusion of articles.

## PHARMACOLOGICAL TREATMENT APPROACHES

The current approach to treating IBS is symptomatic and consists of a regimen of first line pharmacological treatment options often coupled with lifestyle adjustments followed by potential off-label use of a number of other medications that are not specifically indicated for IBS if symptom management is insufficient<sup>[2,20,43]</sup>. The current leading guidelines have been developed by the Task Force on Irritable Bowel Syndrome of the American College of Gastroenterology (ACG) and the British Society of Gastroenterology<sup>[2,12]</sup>. Both associations recognize that symptomatic treatment of IBS is associated with a significant placebo effect which has been confirmed in a number of studies as well as in a now well-known unblinded study where patients were told that they were receiving placebo and still showed significant improvements in symptoms<sup>[44]</sup>. These findings support the hypothesis of an underlying connection between the brain and the gut and the potential interplay of emotions and mood disorders affecting the severity of IBS symptoms.

Considering the increased incidence of comorbid depressive and anxiety disorders in patients with IBS, the use of antidepressants, mainly tricyclic (TCA) and selective serotonin reuptake inhibitor (SSRI) antidepressants, have shown improvements in IBS symptoms and there seems to be an indication that such medication may also provide symptom relief in IBS patients without comorbid psychiatric disorders<sup>[45-48]</sup>. The effectiveness of low dose TCA and SSRI antidepressants as well as benzodiazepines is yet another indication that the enteric nervous system is influenced by mood and that this in turn affects the innervation by serotonergic and cholinergic neurons in the gastrointestinal (GI) tract<sup>[49,50]</sup>.

The initial step in treating IBS is to consider supportive treatments that may help to alleviate mild gastrointestinal symptoms by increasing fiber and probiotics consumption, regular exercise regimens, and eliminating certain food items that may be linked to an allergic reaction (often lactose intolerance). These supportive treat-

ments can be considered integrative in nature since many IBS patients will remain on a specialized diet even after initiating pharmacotherapy if their symptoms are moderate to severe<sup>[40,51,52]</sup>. Patients with moderate IBS symptoms often require a first line treatment to reduce symptoms and may also benefit from CAM therapy, especially cognitive behavior therapy (CBT) or hypnotherapy<sup>[53-57]</sup>. A number of publications indicate that the patient-practitioner relationship can have a significant influence on treatment outcomes<sup>[58,59]</sup>. Practitioners should try to communicate clearly with patients about the diagnostic process, the potential treatment options, setting realistic goals for outcomes and improvement, and providing an atmosphere that is caring and supportive.

The most commonly used pharmacological interventions for symptomatic relief of moderate to severe IBS constitute prokinetics and antispasmodics for IBS-C patients and opioid agonists, anticholinergics, and 5-HT<sub>3</sub> antagonists for relieving IBS-D symptoms<sup>[19,20]</sup>. Prokinetics are not specific to IBS and increase gastrointestinal motility in general by acting *via* dopamine and 5-HT<sub>3</sub> receptors as antagonists or 5-HT<sub>4</sub> receptors as agonists<sup>[60,61]</sup>. Tegaserod is to date the only Food and Drug Administration approved prokinetic drug specific for the treatment of IBS-C but has been significantly limited in its use due to an increased cardiovascular risk<sup>[62,63]</sup>. Lubiprostone, a 5-HT<sub>4</sub> agonist, has been recently approved to treat IBS-C in women through activation of chlorine channels leading to increased water secretion into the lumen which decreased transit time and associated visceral pain in patients<sup>[61]</sup>. The common use of 5-HT<sub>3</sub> receptor antagonists such as ondansetron and granisetron to reduce visceral pain perception in IBS-D patients has shown some benefits but is also limited by side effects. The best risk-to-benefit ratio has been shown for the 5-HT<sub>3</sub> antagonist alosetron to date<sup>[36,64,65]</sup>.

The common use of antispasmodics in both IBS-C and IBS-D patients serves to reduce abdominal pain and cramping but requires close monitoring especially in IBS-C patients because of further slowing of GI motility<sup>[66-68]</sup>. All of the currently available antispasmodics are not specific to IBS and act as anticholinergics which are associated with a number of side effects including hyposalivation and cardiovascular events<sup>[20,69]</sup>.

The use of opioid agonists to reduce GI motility in IBS-D patients is another off-label use that can help to improve quality of life and reduce pain perception. The most commonly used opioid agonists are diphenoxylate and loperamide although there is a risk for dependence development which needs to be monitored<sup>[70,71]</sup>.

Low-grade inflammation has been observed in some IBS patients, especially those with post-infectious IBS and small intestinal bacterial overgrowth (SIBO) which has led to the use of antibiotics and glucocorticoids<sup>[72-74]</sup>. An important consideration in the treatment of low-grade inflammatory processes is the choice of agents since the anti-inflammatory effects should remain localized and not influence the systemic immune system.

So far, the salicylate derivative mesalazine which is also used to treat Crohn's disease with a known inflammatory component has shown an increase in quality of life and symptom reduction in IBS-D patients<sup>[75]</sup>. Glucocorticoids may provide benefits in IBS although this has only been shown in animal models to date and is based on the observation that patients on oral glucocorticoids show a lower incidence of IBS<sup>[76,77]</sup>. Rifaximin remains the only antibiotic that has been tested in IBS patients and has shown a moderate improvement in GI symptoms and quality of life whereas other anti-infectives such as nystatin and tetracyclines did present with unacceptable systemic side effects and a low responder rate<sup>[78-81]</sup>.

A number of new targets and accompanying drugs are being developed and tested which may provide additional benefits in the treatment of IBS<sup>[19,82]</sup>. The coming years will show if they are effective and associated with less side effects compared to the currently available pharmacological options.

Aside from the pharmacological treatments which are often limited by significant side effects, up to 50% of patients are self-medicating using herbals and dietary supplements or other CAM approaches to improve their quality of life and reduce IBS symptoms<sup>[38,83,84]</sup>. Further increases in the use of CAM are a result of underdiagnosed or misdiagnosed IBS since the differential diagnosis of IBS can be complicated and delayed<sup>[40,85,86]</sup>. This review addresses the current state of CAM use in IBS and how both CAM and conventional therapeutic treatment can be used in synergy as an integrative approach to treating IBS and providing patients with the best possible quality of life.

## COMPLEMENTARY AND ALTERNATIVE MEDICINES

The wide variety of CAM approaches includes basic changes in diet and lifestyle such as increased fiber intake or regular exercise as well as specific use of herbal medicines, combination products, mechanical interventions (acupuncture or massage), or behavioral therapy (cognitive behavioral therapy, relaxation techniques, and hypnotherapy)<sup>[43,84]</sup>. CAM is often used for chronic health conditions either alone or in conjunction with pharmacological treatment options. About half of IBS patients reported using at least one CAM treatment alone or in addition to their prescription medicine<sup>[42,87]</sup>. A lack of evidence-based clinical trials often limits the available knowledge about the efficacy of CAM in disease conditions, which is why the ACG Task force on IBS reports that CAM have not consistently demonstrated a strong positive outcome<sup>[2]</sup>. Recent systematic reviews, however, show indications that various CAM modalities may benefit IBS patients and increase their quality of life<sup>[42,43,84,88]</sup>. Since IBS can present with varying symptoms and severity even with daily or weekly fluctuations within the same patient, the effectiveness of CAM may at times appear inadequate or questionable by patients themselves. The most commonly used CAM interventions that have been evaluated in clin-

ical trials, are dietary changes, use of probiotics, exercise, single herbal extracts, herbal combination products, hypnotherapy, acupuncture, and relaxation techniques. All of these approaches are discussed in more detail.

### Diet and lifestyle modifications

Diet modifications are not generally considered CAM and usually are the first step in reducing IBS symptom severity even before pharmacotherapy is initiated (Table 1). However, exclusion diets can often be supplemented with CAM to reduce specific symptoms such as bloating and distension<sup>[2,89]</sup>. Exclusion diets may benefit patients with a known allergy and those in post-infectious IBS or SIBO<sup>[40,51,52]</sup> and consists of removing wheat, dairy products, eggs, coffee and caffeinated beverages, yeast, potatoes, and citrus fruits<sup>[52]</sup>. Despite the reported successes with exclusion diets, they may, at times, be hard to follow thereby resulting in bouts of increased IBS symptom severity. While dietary restrictions may benefit some IBS patients, entirely skipping meals actually has shown to worsen IBS symptoms<sup>[52,90]</sup>.

Some contribution to intestinal symptoms may come from a diet that is high in fat, carbohydrates, and sugar alcohols. It has been shown that increased fat consumption is linked to increased stool numbers and diarrhea and therefore should be considered as a factor in worsening IBS-D<sup>[90,91]</sup>. Fructose-rich food and beverage items (soft drinks, baked and packaged goods, cereals) can also aggravate flatulence, abdominal discomfort, and diarrhea and should therefore be monitored in IBS patients<sup>[51,52]</sup>. Especially poorly absorbed sugar alcohols that are present in diet soft drinks and low carbohydrate foods can exacerbate GI symptoms<sup>[51,92]</sup>. Together with general restrictions on carbohydrate intake, lactose intolerance and malabsorption appear to be more prevalent in IBS patients. If lactose is not absorbed from the GI tract it is metabolized *via* the gut bacteria and leads to increased bloating, distension, and diarrhea which can aggravate IBS symptoms<sup>[93-95]</sup>.

Fiber is often recommended as a dietary change to reduce global IBS symptoms but the clinical data to date are less clear. It has been shown that soluble fiber can lower GI symptoms in IBS-C although the data supporting it is highly variable both in the amount of fiber consumed (ranging from 5-30 g/d) and the duration of the trials (3-16 wk)<sup>[51,91,96,97]</sup>. Fiber, regardless soluble or insoluble, was not able to reduce pain perception in IBS patients and specifically insoluble fiber such as nuts and whole grains may exacerbate IBS symptoms overall<sup>[97]</sup>.

An important lifestyle adjustment that should be recommended to IBS patients is regular exercise. Mild exercise or physical activity has been shown to reduce IBS symptoms and alleviates bloating and gas production in several studies<sup>[98,99]</sup>. Since regular exercise also helps to increase gastrointestinal motility it is beneficial in IBS-C patients with primary low GI movement and hard stools<sup>[100]</sup>. As part of exercise, yoga has been investigated due to its low impact on joints and its relatively targeted postures

**Table 1 Clinical trials on diet and exercise interventions for irritable bowel syndrome**

Intervention	Study design	Sample size	Outcome	Ref.
Acceptability questionnaire	Anonymous survey	256	Most acceptable were tablets (84%), diet and lifestyle changes (82%), yoga (77%); less acceptable were acupuncture (59%) and suppositories (57%)	[40]
Food elimination	Open label pilot study	20	Significant improvements in stool frequency ( $P < 0.05$ ), pain ( $P < 0.05$ ), and IBS-QOL ( $P < 0.001$ )	[89]
Diet and lifestyle	Cross-sectional study	1717	Significant difference between IBS and non-IBS participants in regards to residential type (OR = 1.27) and frequency of meals (OR = 1.69)	[90]
Diet and lifestyle	Questionnaire	983	BMI was associated with abdominal pain and diarrhea, healthier diet and physical activity were associated with fewer GI symptoms	[91]
Diet	3-way cross-over study	22	IBS-D patients showed significant increase in small bowel and mucosal permeability for mannitol and lactulose sugars compared to healthy controls	[92]
Diet	Questionnaire	1978	Potential for higher lactose intolerance incidence in patients with IBS compared to healthy patients	[93]
Diet	Case-control study	177	Symptomatic lactose intolerance more frequent in patients with IBS than healthy subjects, but incidence of lactose intolerance not different between groups	[94]
Diet	Case-control study	120	Lactose intolerance resulted in more frequent self-reported symptoms in patients with IBS-D than controls ( $P < 0.001$ , OR = 6.25), IBS-D patients consumed significantly less dairy products ( $P = 0.04$ )	[95]
Exercise	Randomized, controlled trial	56	No difference in quality of life between exercise and usual care groups, exercise group presented with significant less symptoms of constipation after 12 wk intervention	[98]
Exercise	Cross-over study	8	Gas retention during rest was associated with significant abdominal symptoms in IBS patients ( $P < 0.01$ ), symptoms improved during exercise ( $P < 0.05$ ) compared to rest	[99]
Exercise	Descriptive comparative study	89	Women with IBS report less physical activity ( $P < 0.05$ ), women with IBS who were physical active reported significantly less symptoms of fatigue ( $P = 0.003$ ) compared with the ones with IBS who were physically inactive	[100]
Yoga	Randomized cross-over study	25	Lower functional disability ( $P = 0.073$ ) and anxiety levels ( $P = 0.09$ ) in the yoga group compared to the waitlist group, significantly lower GI symptoms ( $P < 0.01$ )	[101]
Yoga	Randomized parallel design	21	Similar reductions in symptoms after 2 mo for yoga and the group receiving loperamide in IBS-D patients	[102]

IBS: Irritable bowel syndrome; QOL: Quality of life; BMI: Body mass index; IBS-D: Diarrhea-predominant IBS; GI: Gastrointestinal.

that can help to reduce GI symptoms<sup>[101,102]</sup>. Pranayama yoga administered twice daily has been shown to increase sympathetic tone and may benefit IBS-D patients that present with decreased sympathetic activity to the same degree than daily loperamide administration in the control group<sup>[102]</sup>.

**Herbal medicines and supplements**

Aside from diet and lifestyle changes, another commonly used CAM intervention that is often self-administered is the use of herbal supplements either as single herbs or in combination products (Table 2). A few well-designed clinical studies have been performed on a number of such herbal supplements but in general the current knowledge remains limited to make a definitive judgment about their effectiveness in treating IBS symptoms. Many of the commonly used supplements have evolved from folk and traditional applications as remedies for gastrointestinal disorders.

The use of peppermint extracts has been studied in a number of clinical trials which evaluated the administration of enteric coated peppermint oil capsules to IBS patients<sup>[103-107]</sup>. The duration of the trials ranged from 4-8 wk and was not divided into specific IBS subtypes. The trials showed a significant reduction in abdominal pain and severity compared to placebo after 4 wk and a significant increase in quality of life although the effects did not last once peppermint was discontinued<sup>[108-110]</sup>. The spasmolytic effects of peppermint oil have been well known in

folk medicines and mainly been attributed to the presence of mono- and sesquiterpenes<sup>[110]</sup>. Peppermint oil has also been recommended by the American Academy of Pediatricians as well as received a positive evaluation from the Task force on IBS of the ACG<sup>[2,111]</sup> although caution is advised for its use in young children due to its side effects of causing respiratory depression and heartburn<sup>[111]</sup>. Peppermint oil appears to be more potent in exerting the spasmolytic effects than aqueous extractions such as teas since it allows for a more concentrated dose of the proposed active ingredients<sup>[112]</sup>.

Hydroalcoholic extracts from artichoke leaves have also been used to reduce IBS symptoms and evaluated in at least two clinical studies<sup>[113,114]</sup>. Artichoke has long been used as a digestive aid which aims to reduce bloating, abdominal pain and cramps, as well as reducing both diarrhea and constipation through normalization of GI motility<sup>[115]</sup>. Both studies were conducted as part of a post-marketing surveillance which may limit the credibility of the results due to limited influence on the study design (no double-blinding, no placebo control) and potential consumer bias. Both trials report a significant improvement in IBS symptoms, specifically in normalizing GI motility and reducing bloating as well as relieving distension and abdominal pain and cramps<sup>[113]</sup>. Since the change in IBS symptom severity was compared between baseline and follow-up, the results provide limited evidence of the effectiveness compared to placebo or standard pharmacological treatment. Given the high placebo responder rate,

**Table 2 Clinical trials on Herbal medicines and supplements for irritable bowel syndrome**

Intervention	Study design	Sample size	Outcome	Ref.
Peppermint oil	Randomized, double-blind, placebo-controlled study	99	Peppermint oil (Colpermin®) group showed significant symptom improvement ( $P < 0.05$ ) compared to placebo group after 1 mo	[104]
Peppermint oil	Randomized, placebo-controlled study	18	Peppermint oil significantly reduced GI symptoms ( $P < 0.01$ ) after 3 wk compared to placebo	[106]
Peppermint oil	Randomized, double-blind, Placebo-controlled study	57	Total IBS severity score was significantly decreased after 4 wk of treatment ( $P < 0.009$ ) and after 2 mo ( $P < 0.01$ ) in the peppermint oil group compared to placebo	[108]
Peppermint oil	Randomized, double-blind, placebo-controlled study	90	Significant reduction in IBS symptoms, no abdominal pain in more patients in the peppermint oil group compared to placebo ( $P < 0.001$ ), less severe abdominal pain in peppermint oil group ( $P < 0.05$ ) in peppermint oil group after 2 mo	[109]
Peppermint oil	Randomized, double-blind, placebo-controlled study	65	Significant reduction in abdominal pain in peppermint oil group compared to placebo group ( $P < 0.001$ ), but pain score increased 2 wk after completion of trial	[110]
Artichoke leaf	Post-marketing surveillance	279	Significant reduction ( $P < 0.05$ ) in overall IBS symptoms after 6 wk of treatment	[113]
Artichoke leaf	Post-marketing surveillance in IBS with concomitant dyspepsia	209	Significant reduction in Nepean Dyspepsia Index after 2 mo ( $P < 0.001$ ) and normalization of bowel pattern ( $P < 0.001$ )	[114]
Turmeric	Partially blinded, randomized, two-dose pilot study	207	Reduction in IBS prevalence in both treatment groups (1 or 2 tablets) compared to baseline ( $P < 0.001$ ) after 2 mo intervention, no significant differences between groups	[116]
Curcuma and fumitory	Randomized, double-blind, placebo-controlled study	106	No significant differences between curcuma, fumitory, and placebo groups in abdominal pain ( $P = 0.81$ ) and distension ( $P = 0.48$ ) after 3 mo	[117]
STW5	Randomized, double-blind, placebo-controlled study in patients with dyspepsia	137	Significant decrease in gastrointestinal symptom score between STW5 and placebo ( $P < 0.001$ )	[118]
STW5	Randomized, double-blind, placebo-controlled multicenter study in patients with functional dyspepsia	315	Significant decrease in gastrointestinal symptom score between STW5 and placebo ( $P < 0.05$ ) after 2 mo intervention	[119]
STW5	Randomized, double-blind, placebo-controlled multicenter study	203	Significant reduction in abdominal pain scores for STW5 ( $P = 0.009$ ) and STW5-II ( $P = 0.005$ ) and IBS-SSS ( $P = 0.001$ for STW5 and $P = 0.0003$ for STW5-II) compared to placebo after 4 wk intervention	[120]
Padma Lax	Randomized, double-blind, placebo-controlled pilot study	61	Significant improvement in global IBS symptom scores compared to placebo ( $P < 0.05$ ) following 3 mo intervention	[123]
TCM	Randomized, double-blind, placebo-controlled study	119	No significant improvements in IBS global symptom score between TCM and placebo group at week 8 ( $P = 0.38$ ) and week 16 ( $P = 0.62$ )	[129]

IBS: Irritable bowel syndrome; TCM: Traditional chinese medicine; SSS: Symptom severity scale.

artichoke leaf extracts will require additional trials that are more rigorous in terms of study design.

Turmeric, a spice traditionally used in Asian cuisine where it often provides both for taste and color improvement, was evaluated in IBS patients and indicated decreases in IBS symptoms and increased quality of life if given in two different doses of 72 and 144 mg per day over 8 wk<sup>[116]</sup>. However, this study again lacks a double-blinded and placebo-controlled design which reduces the strength of the presented data. Another double-blind placebo controlled study compared curcuma extract from which turmeric is derived with a placebo and a fumitory extract<sup>[117]</sup>. Both curcuma and fumitory extracts did not show any significant improvements in abdominal pain and distension compared to the placebo group.

All single herbal supplements discussed have a strong folkloric and traditional background as digestive aids and it is therefore not surprising that to date trials with such herbal supplements are focused on these single extracts.

Combination products of herbal extracts add to the wide range of available supplements used in the self-treat-

ment of IBS. The first combination product which has received some interest from patients and healthcare providers alike is Iberogast®, a mixture of nine herbal plant extracts that was originally mainly used for functional dyspepsia in Germany<sup>[118,119]</sup>. The product has been on the market for more than 30 years. Iberogast® for use in IBS symptoms was investigated in 208 patients with various IBS subtypes in the United States<sup>[120]</sup>. This study adheres to the clinical trial standards by utilizing a randomized, double-blind, placebo-controlled study protocol over a 4 wk period. The extract consists of liquid extracts from chamomile flowers, bitter candytuft, angelica root, caraway fruits, milk thistle, lemon balm leaves, greater celandine, licorice root, and peppermint leaves<sup>[121]</sup>; all of which have been used in folklore and traditional medicines to aid in digestive disorders. The study indicates that Iberogast® significantly improves quality of life and reduces abdominal pain in IBS patients<sup>[122]</sup> which appears to be mediated through influences on serotonin, acetylcholine, and opioid receptors in the GI tract<sup>[121]</sup>. Despite the positive outcome, further research is required to support the findings of this

**Table 3 Clinical trials on mechanical complementary and alternative medicines interventions for irritable bowel syndrome**

Intervention	Study design	Sample size	Outcome	Ref.
Physical activity	Randomized study	75	Significant decrease in IBS-SSS between physical activity and placebo group ( $P = 0.003$ )	[133]
Reflexology	Randomized, single-blind, placebo-controlled study	34	No significant difference between foot reflexology and non-reflexology massage group	[134]
Acupuncture	Randomized, single-blind, placebo-controlled study	230	Acupuncture and sham acupuncture significantly improved IBS-GIS scores compared to waitlist group ( $P = 0.001$ ), no difference between acupuncture and sham acupuncture during 3 wk intervention	[143]
Acupuncture	Randomized, single-blind, placebo-controlled study	43	Significant improvements ( $P = 0.022$ ) in quality of life for both acupuncture and sham acupuncture compared to baseline after 10 intervention sessions (5 wk), no differences between acupuncture and sham acupuncture	[144]
Acupuncture/ moxibustion	Randomized, single-blind, placebo-controlled study	29	Significant reduction in IBS-SSS in acupuncture/moxibustion group after 4 wk compared to sham acupuncture/moxibustion group ( $P = 0.01$ )	[146]
Yoga	Observational pilot study (adolescents)	20	Decrease in pain frequency ( $P = 0.031$ for 8-11 yr old and $P = 0.004$ for 12-18 yr old) and pain intensity ( $P = 0.015$ in 8-11 yr old) after 10 yoga sessions compared to baseline, decrease in pain frequency was maintained for 3 mo following intervention ( $P = 0.004$ for 8-11 yr old)	[149]

IBS: Irritable bowel syndrome; GIS: Global improvement scores; SSS: Symptom severity scale.

study and a few case reports from patients and healthcare providers alike. Iberogast® has been recognized by the ACG task force on IBS as a potential complementary treatment to reduce certain IBS symptoms<sup>[2]</sup>.

A Tibetan preparation of twelve different plant extracts, commonly referred to and marketed as Padma Lax, was tested in IBS-C patients over the course of three months in a randomized and double-blinded observational study and showed significant improvements over a placebo in reducing constipation, abdominal pain, and flatulence<sup>[123]</sup>. The dose had to be adjusted for some of the patients since they developed loose stools that bordered on diarrhea indicating that this combination herbal product may have significant potential as a laxative. The ingredient list includes the known laxatives rhubarb root, cascara bark, and nux vomica seeds which have been used as strong laxatives in severe constipation in traditional medicines across the world<sup>[124]</sup>. It has been proposed that some of the herbs exert the laxative effect through activity on cholinergic receptors as antagonists to reduce GI contractility<sup>[124,125]</sup>.

Traditional Chinese medicine (TCM) has provided a range of different treatment approaches over the centuries, among them a number of TCM herbal mixtures that are specifically formulated based on the patients' symptoms<sup>[126]</sup>. Such individualized medicine is not uncommon but has the obvious limitation of resisting standardization and fitting the rigorous clinical trial design that is used as a major determinant of effectiveness in Western medicine. *Tong Xie Yao Fang* (TXYF) is one such TCM that has been studied in a few clinical trials but often adjustments were made to the herbal combination based on the predominant IBS symptom presentation<sup>[127-129]</sup>. A review of 12 studies with modified TXYF preparations reached the general conclusion that the extracts improved IBS symptoms, in particular abdominal pain, distension, flatulence, and diarrhea<sup>[128]</sup>. However, the study design and end points were diverse between these studies complicating a

direct comparison of outcomes. A more streamlined and standardized approach to TXYF trials is warranted.

Overall, the use of single and combination herbal supplements appears promising but should be approached with caution given the lack of rigorous larger clinical trials. The strongest evidence for the use of herbal medicines is currently available for peppermint oil preparations and the herbal combination product Iberogast®.

### Mind-body therapies

Since there is evidence of the involvement of the enteric nervous system or brain-gut axis in the pathophysiology of IBS, the use of mind-body interventions as CAM treatments may provide benefits in relieving symptoms. Mind-body therapies are interventions that primarily "focus on the interactions among the brain, mind, body, and behavior with the intent to use the mind to affect physical functioning and promote health"<sup>[130]</sup>. Yoga, Tai-chi, meditation, hypnotherapy, deep-breathing exercises, relaxation techniques, and acupuncture all fall under this definition. While yoga, relaxation techniques, and acupuncture are commonly used as CAM therapies, they involve both a physical and psychological component with a focus on influencing physical functions through mechanical interventions. Meditation, hypnotherapy, and CBT do not involve a mechanical component but rather seek to change physiological function through psychological reprogramming entirely<sup>[131,132]</sup>. Mind-body therapies have been evaluated for their potential application as CAM in IBS. Clinical evidence supporting the use of yoga, relaxation, acupuncture, hypnotherapy, and cognitive behavior therapy is indicating that these CAM interventions show improvement in IBS symptoms and overall quality of life.

### Mechanical CAM interventions

Mechanical interventions are based on direct body interventions such as massage, acupuncture, yoga, and physical exercise (Table 3)<sup>[131]</sup>. While some interventions may

not benefit patients with IBS because of the significant physical involvement that may cause a temporary worsening of symptoms, low impact physical exercise such as aerobic training, bike riding, and muscle strengthening have shown benefits in maintaining GI function and reducing flatulence and gas production<sup>[90,99,100,133]</sup>. One study indicated that strenuous exercise shows an inverse relationship with IBS symptoms<sup>[91]</sup> while another study pointed to reduction of constipation in IBS-C patients with mild exercise levels<sup>[98]</sup>. Johannesson and colleagues evaluated the impact of regular exercise on IBS symptoms severity scores compared to a control group and found a significant reduction in symptoms over the course of 12 wk<sup>[133]</sup>. It is therefore important to emphasize that a patient should start off with low impact and light exercise regimens that are not exhausting or causing increases in abdominal pain or overall IBS symptoms. As such, mild physical exercise may be considered a lifestyle change rather than an actual CAM intervention, but guided assistance may benefit IBS patients who seek counseling and advice on respective exercise regimens for their condition.

To date there is little information about the potential impact of massage and reflexology treatments on IBS symptoms. One study compared the use of foot reflexology massage to non-reflexology foot massage and could not find any significant difference in the small study of 34 patients<sup>[134]</sup>. However, case reports have indicated that gut-directed massage may relieve specific symptoms such as bloating and chronic constipation although such reports were not specific to IBS patients<sup>[135-137]</sup>. It therefore remains unknown if reflexology or massage techniques can provide benefits to IBS patients.

A number of trials investigated the effect of gut-directed and general acupuncture on symptom relief in IBS patients. It is well known that acupuncture can affect physiological functions in a number of conditions through regulating various neurotransmitter systems. It has been shown that application of acupuncture in IBS patients targets serotonergic, cholinergic, and glutamatergic pathways, can lower blood cortisol levels related to stress, and can increase the concentration of endogenous opioids to reduce visceral and global pain perception<sup>[138-140]</sup>. A complicating factor in the study of acupuncture effects are adequate comparison groups. One commonly used comparison group is sham acupuncture which uses needles as well so to suggest to patients that they are being treated when the practitioner does not utilize the specific acupuncture points and only superficially applies needles<sup>[141,142]</sup>. What appears to be a contributing factor to the effectiveness of acupuncture is the patient-practitioner relationship, especially in IBS patients where an underlying psychological contribution to IBS symptoms can be suspected<sup>[58,59]</sup>. In one study, a sample of 230 IBS patients were randomly assigned to receive either acupuncture, sham acupuncture, or remain on a waitlist for the duration of the trial<sup>[143]</sup>. Initially both the true acupuncture and sham acupuncture groups received only sham acupuncture for 3 wk followed by 3

wk of true acupuncture in half of these patients while the other half continued receiving sham acupuncture. Both groups showed significant improvement in global IBS symptoms compared to the waitlist control group, but the patients receiving true acupuncture did not differ from the sham acupuncture group thus complicating interpretation of results related to the actual acupuncture points being used. Other studies using sham acupuncture as a comparator have also found that improvements in quality of life and IBS symptoms did not differ from true acupuncture points thus potentially indicating that acupuncture for IBS is primarily a placebo response<sup>[144,145]</sup>. When combined with moxibustion, acupuncture has shown significant improvements in IBS symptoms with reduced abdominal pain, gas and bloating being reported in one study including 29 subjects over a 4 wk, eight session intervention<sup>[146]</sup>. A Cochrane meta-analysis of studies including acupuncture suggests that further studies are warranted to confirm the beneficial effects of such treatments in IBS patients<sup>[147]</sup>.

A mechanical intervention that has been studied in IBS is yoga as a specific form of exercise and focused relaxation technique combined<sup>[148]</sup>. Yoga consists of different poses accompanied by a specific breathing pattern to focus attention on muscle contraction and relaxation. There are certain poses that can be utilized to focus on GI tract motility and abdominal pain perception. There are only few trials conducted with yoga as the intervention but a number of indicators suggest that yoga may provide relief of IBS symptoms. One study in 22 male patients with confirmed IBS-D compared yoga poses and breathing techniques to conventional treatment over the course of 8 wk<sup>[102]</sup>. Overall GI symptoms were reduced in both groups at the end of the study but the yogic intervention group showed a higher parasympathetic reactivity leading to improved IBS symptom outcomes whereas the control group presented with increased gastric activity. Another small clinical trial compared the use of yoga in adolescents to a wait list group over the course of 8 wk<sup>[101]</sup>. In the first 4 wk, the yoga intervention group received instructions on daily yoga practices and continued the poses after the first 4 wk. The control wait list group received yoga intervention after 4 wk for another month at which point both groups were compared. This preliminary study indicates that yoga intervention over the course of a 2 mo period improves GI symptoms in adolescent IBS patients and is well received by youth. Another small yoga intervention study conducted in 20 children aged 8-18 years with IBS or functional abdominal pain indicates that yoga does decrease both pain frequency and pain intensity at the end of intervention and that this effect also persisted for at least another 3 mo after the intervention has ended<sup>[149]</sup>. In addition, adolescents in this trial reported increased quality of life throughout the intervention and during follow-up. Although not many studies have been conducted using yoga as a CAM intervention, the current data suggests that it may provide benefits in IBS patients by alleviating both pain and GI symptoms.



**Table 4 Clinical trials on psychological complementary and alternative medicines interventions for irritable bowel syndrome**

Intervention	Study design	Sample size	Outcome	Ref.
Hypnotherapy	Pre- and post-assessment	23	Normalized hypersensitivity pain threshold in hypersensitive group ( $P = 0.04$ ) after 12 wk of treatment, no significant change in hyposensitive and normosensitive groups	[154]
Hypnotherapy	Randomized controlled trial in children with functional abdominal pain or IBS	53	Significant reduction in pain scores in hypnotherapy group ( $P < 0.001$ ) compared to standard medical therapy at 1-yr after intervention	[159]
Hypnotherapy	Questionnaire	83	69% of patients were either satisfied or very satisfied with hypnotherapy following 12 wk intervention, overall improvement in quality of life and GI symptoms	[160]
Hypnotherapy	Randomized, placebo-controlled study	138 in two studies (90 and 48)	Significant reduction in IBS symptoms in hypnotherapy groups ( $P < 0.05$ ) compared to supportive therapy after 3 mo of intervention	[161]
Hypnotherapy	Randomized, placebo-controlled study	90	Significant improvement in overall IBS symptoms in gut-directed hypnotherapy and medical treatment group compared to medical treatment group alone ( $P = 0.046$ ) after 12 wk; improvement remained up to 12 mo after intervention in hypnotherapy group ( $P = 0.004$ ) compared to medical treatment alone	[162]
Hypnotherapy	Pre- and post-assessment	75	Group hypnotherapy decreased symptom severity significantly ( $P < 0.01$ ) at 3, 6, and 12 mo post-intervention	[163]
Hypnotherapy	Retrospective analysis	208	Significantly higher use of hypnotherapy ( $P < 0.001$ ) by initial responders <i>vs</i> non-responders at 2-7 yr follow-up, in total 87% of participants reported hypnotherapy to be useful	[164]
Cognitive behavior therapy	Randomized-comparator-controlled study in patients with functional bowel disorders	431	CBT was more effective than education ( $P = 0.0001$ ) and desipramine was more effective than placebo ( $P = 0.01$ ) after 12 wk of treatment as assessed by treatment satisfaction	[170]
Cognitive behavior therapy	Randomized, placebo-controlled study in patients with functional bowel disorders	397	No significant differences between treatment arms for desipramine, cognitive behavior therapy, and placebo groups	[171]
Cognitive behavior therapy and mindfulness training	Randomized controlled trial	195	Internet-delivered cognitive behavior therapy resulted in adequate relief of IBS symptoms that was significant compared to internet-delivered stress management at 6 mo follow-up ( $P = 0.004$ )	[173]
Cognitive behavior therapy	Randomized controlled trial	149	Significant reduction in symptom severity scores in CBT plus mebeverine group compared to mebeverine alone at post-treatment and 3, 6, and 12 mo follow-up (regression $P = 0.001$ )	[174]
Psychotherapy [cognitive behavior therapy]	Randomized controlled trial	50	Rome-II scores significantly decreased ( $P = 0.001$ ) in patients receiving CBT in conjunction with standard medical care compared to standard medical care alone after 2 mo intervention	[175]
Cognitive behavior therapy	Randomized controlled trial	28	Psychosocial functioning was significantly improved ( $P = 0.004$ ) in patients receiving CBT in addition to standard medical care compare to standard medical care alone at 3 mo follow-up	[176]
Cognitive behavior therapy	Randomized controlled trial	76	Cognitive behavior therapy presented with significant improvements compared to stress management and attention control groups in reducing visceral sensitivity ( $P < 0.0001$ ) compared to baseline at 3 mo follow-up	[177]
Cognitive behavior therapy	Randomized, placebo-controlled study	85	Internet delivered CBT reduced several IBS symptom parameters (total pain, diarrhea, bloating primary symptoms all $P < 0.001$ ) after 10 wk of intervention compared to discussion board control group; quality of life and visceral sensitivity were also significantly improved ( $P < 0.001$ ) after 3 mo follow up	[179]
Mindfulness training	Randomized controlled trial	75	Women in mindfulness training group showed significant reduction ( $P = 0.006$ ) in IBS symptom severity compared to support control group after 8 wk of intervention which remained significant at 3 mo follow-up ( $P = 0.001$ )	[180]
Cognitive behavior therapy	Retrospective analysis	75	Long-term follow-up after 15-18 mo of original intervention resulted in lasting significant reductions in visceral sensitivity ( $P < 0.05$ ), increase in quality of life ( $P < 0.05$ ), and gastrointestinal symptoms ( $P < 0.05$ )	[181]

IBS: Irritable bowel syndrome; CBT: Cognitive behavior therapy; GI: Gastrointestinal.

**Psychological CAM interventions**

While mechanical interventions can provide IBS symptom relief, compliance can often be an issue as well as limited physical ability to follow the treatment (especially

with exercise and yoga). Other mind-body CAM approaches are solely based on psychological interventions with hypnotherapy and cognitive behavior therapy showing the most clinical evidence of effectiveness (Table 4).

Hypnotherapy is based on initiating a suggestive state for the patient similar to sedation but without loss of consciousness that allows for heightened senses and control over body functions affecting mood, pain perception, cardiovascular responses, and gastrointestinal motility<sup>[150,151]</sup>. Hypnosis and hypnotherapy have been used for various applications foremost for the treatment of acute and chronic pain conditions but also to improve mood or change certain undesirable behaviors<sup>[152,153]</sup>. It has been shown that gut-directed hypnotherapy can alleviate IBS symptoms comparable to current pharmacological treatment approaches<sup>[154-156]</sup>. Several clinical studies and meta-analysis indicate that 8-12 weekly hypnotherapy sessions can improve pain, GI motility, mood (improving depressive and anxiety disorders), and overall quality of life of IBS patients significantly even in the absence of pharmacological treatment<sup>[157-161]</sup>. Interestingly, in a number of studies during follow-up the beneficial effects of hypnotherapy remained for at least 10 mo even if patients did not continue therapy<sup>[155,155,162-164]</sup>. A Cochrane database review examined available studies and found a positive effect associated with hypnotherapy although the effect size could not be determined due to the heterogeneity of study designs and the relatively small sample sizes<sup>[54]</sup>. Although there is clinical evidence for the use of hypnotherapy in treating IBS symptoms, further research utilizing a homogenous study design needs to be emphasized to support its benefits.

In contrast to hypnosis where the patient is being influenced and subjected to a subconscious suggestive state that influences physiological processes, CBT takes a more direct approach in influencing the conscious awareness of IBS symptoms and attempts to enable the patient to overcome the negative attitudes they may have towards their chronic condition<sup>[165-167]</sup>. Similar to hypnosis, patients are enabled to change a negatively perceived situation into a positive outlook which then affects the actual symptoms. CBT has been shown to be effective in improving symptoms in a number of chronic disorders such as obesity, chronic pain, insomnia, or depressive disorders<sup>[166,168,169]</sup>. While hypnosis can be utilized to directly affect perception of symptoms, CBT is more geared towards enabling patients themselves to change their behavior and thought processes about their condition. In IBS patients, symptom aggravation may often occur when patients worry about the condition and focus their thoughts around them<sup>[170,171]</sup>. CBT has been shown to improve both the quality of life and reduce symptom severity in IBS patients, especially in regards to pain perception and comorbid depressive and anxiety disorders<sup>[170,172,173]</sup>. Comparing the use of CBT as a CAM approach to treating IBS with conventional pharmacological treatment indicates that it does not only improve the direct IBS symptoms such as pain and GI dysmotility, but in addition also benefits mood and coping with the condition<sup>[174-177]</sup>. Although the effects of CBT lasted past the intervention period in some of the trials, the beneficial effects seemed to wane over time which may indicate a long-term supportive treatment with CBT at least in frequent intervals

following the initial treatment period. Currently, an ongoing irritable bowel syndrome outcome study evaluates the long-term effects of self-versus clinician-administered CBT on IBS symptoms and the economic benefit of this intervention<sup>[178]</sup>.

Closely related to CBT as a CAM intervention is mindfulness exercises that promote acceptance instead of control of IBS symptoms<sup>[179,180]</sup>. This technique is often delivered in conjunction with CBT and is more patient-centered to increase quality of life through coping mechanisms. In conjunction with CBT, mindfulness exercises have shown a reduction in IBS symptoms beyond the intervention period up to 3 years<sup>[173,181]</sup>.

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## INTEGRATIVE APPROACHES AND CLINICAL IMPLICATIONS TO TREATING IBS

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Most of the clinical trials that have been discussed focus on the comparison between CAM approaches and standard care with pharmacological therapies in treating IBS symptoms. This separation often creates a painful choice for patients that need the immediate relief with medication but also seek long-term alleviation of the symptoms through a pro-active approach. Integrating both conventional pharmacological care and CAM treatments to provide the best symptom relief and highest quality of life to IBS patients should therefore be considered by health-care providers. A number of clinical trials - although small in sample sizes and number - have shown that a combination of pharmacotherapy with a CAM treatment is superior to either treatment alone. As long as the CAM treatment does not interfere or interact with the pharmacological treatment, both can coexist in the treatment of IBS symptoms.

A study evaluating the use and cost of CAM by patients with functional bowel disorders (including IBS patients) reported a number of interesting results<sup>[85]</sup>. The most common types of CAM were ginger, massage therapy, and yoga with a median yearly cost of \$200, which was considered significantly less compared to standard pharmacotherapy. Furthermore, the use of CAM was associated with female gender, higher education, and comorbid anxiety disorders. Although most of the patients using CAM (35% of 1012 participating patients) were not referred by their healthcare provider, those who received a recommendation from their primary care physician followed the advice. This indicates the important role of the healthcare provider as a mediator and facilitator for patients to seek CAM treatments. Several of the CAM approaches discussed in this review have been recommended or given at least positive consideration by current professional organizations (ACG and the British Society for Gastroenterology) to be considered in the treatment of IBS in addition to pharmacotherapy<sup>[2,12]</sup>. Another important point that the study reveals is that CAM use is not based on dissatisfaction with pharmacotherapy but seems to be rather linked to higher comorbidity with de-

pressive and anxiety disorders as well as somatization of their condition<sup>[85]</sup>. CAM users in this study also showed a higher symptom severity on the IBS-SSS as well as gastrointestinal distension. The authors of the study conclude that CAM use can benefit patients with various functional bowel disorders and should be made more widely available potentially through providing insurance coverage. Medical professionals should recommend CAM approaches such as hypnotherapy, yoga, cognitive behavior therapy, or herbal supplements that have shown benefits to IBS patients that do not experience adequate symptom relief with pharmacotherapy alone.

In a study that evaluated a gap in effectiveness between current treatment approaches and treatment outcomes conducted in the United Kingdom, 32% of general practitioners reported an effectiveness gap for IBS patients in their practice<sup>[86]</sup>. The most common reasons given for the effectiveness gap were lack of effective treatments, adverse effects of current treatments, and unacceptability of available treatments by patients. These findings are supported by other studies which indicate a lack of treatment effectiveness in a significant percentage of IBS patients<sup>[40,43,182]</sup>. The use of CAM has been shown in randomized controlled trials as well as in systematic reviews to decrease or close the effectiveness gap thereby increasing quality of life and treatment outcomes for IBS patients. The authors of this study conclude that there is a discrepancy between available evidence for the effectiveness of CAM in various chronic conditions and its recommendation by current practice guidelines which often omit such approaches. In addition, patients appear to be more favorable towards trying CAM approaches than practitioners thereby most referrals are initiated by patients themselves or without including the healthcare provider when considering CAM treatments in addition to conventional care<sup>[86,183,184]</sup>.

The integrative medical approach has gained significant traction in the last decade with the growth of the Consortium of Academic Health Centers for Integrative Medicine<sup>[185]</sup> to which many well respected United States institutions belong (Yale University, Stanford University, University of California, Johns Hopkins University, among others). Integrative medicine as a subdivision of medical practice is seeking to emphasize on patient-centered care and improve wellness and quality of life rather than limiting the treatment outcome to a specific disorder. The definition of integrative medicine remains somewhat elusive to date ranging from simply adding CAM treatments to conventional care to a more holistic healthcare approach overall. While the conventional approach to treating IBS is primarily founded on evidence-based clinical trials and extensive knowledge, the CAM approach to treating IBS also claims a long tradition of use and an increasing body of research supporting the benefits of CAM treatments in IBS. The debate over integrative medicine continues with defenders of conventional medicine indicating that such a definition should not exist because treatments with proven benefits will eventually become the standard of care no matter where they originated from. However, proponents of integra-

tive medicine argue that excluding CAM or preventing patients from seeking CAM treatments in addition to conventional care will result in reduced quality of life and worse treatment outcomes. As mentioned above, this has been supported by various studies. It has been argued that even if a CAM treatment is not supported by sufficient evidence-based clinical trials, as long as it does not cause adverse effects or interfere with conventional therapy it should not be denied to patients seeking such treatments. Instead, physicians and healthcare providers should seek training or knowledge in integrative medicine to best support their patients. This applies especially to chronic conditions such as IBS that present with a high placebo response and where a number of CAM treatments - herbal therapies, probiotics, dietary changes, acupuncture, yoga, hypnotherapy, and cognitive behavior therapy - have shown benefits.

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