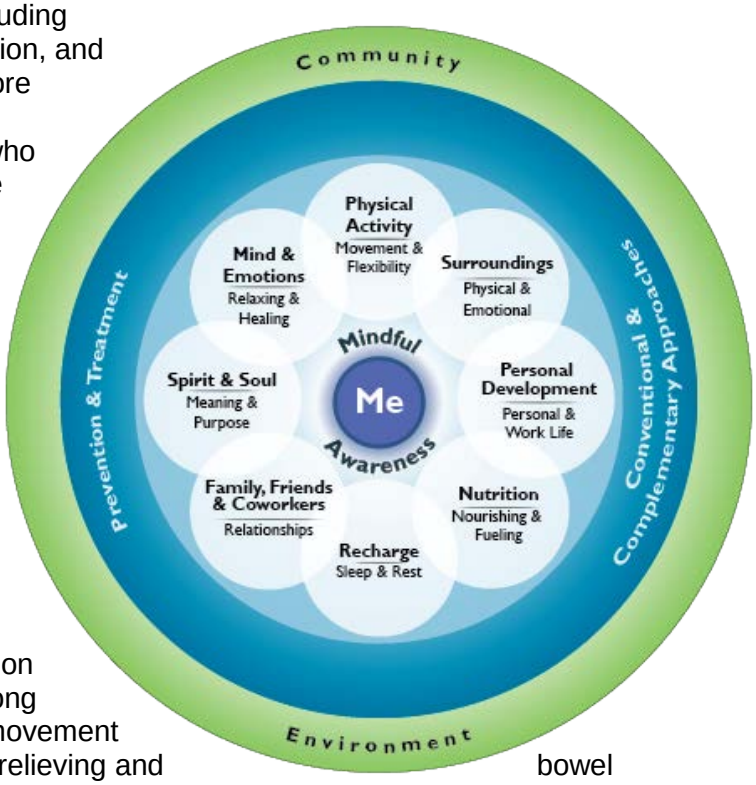
Irritable Bowel Syndrome (IBS)

Irritable bowel syndrome (IBS) is influenced by many factors—neurological, immunological, psychological, and likely others. The following offers evidence-based suggestions for an Integrative Health approach to IBS, recognizing that no one intervention is effective or curative for everyone; pharmaceuticals are no exception. Successfully treating IBS requires one to approach this complex and dynamic interplay on a *case-by-case* basis. A continuous therapeutic relationship is essential. Because of the lack of consistent effectiveness of pharmaceuticals, nearly 40% of those with IBS turn to other therapeutic options.[1] These are discussed below.

IBS is often associated with comorbidities, including posttraumatic stress disorder (PTSD), depression, and anxiety.[2] A history of sexual trauma is even more strongly associated with IBS than any mood disorder.[3] IBS is also more common in those who have suffered some sort of "hit" that throws the ecosystem of their GI tract out of balance. Examples include infections (e.g., traveler's diarrhea), medication use (antibiotics, steroids, chemotherapy), and significant emotional stressors. A clinician should address potential chronic sequelae of these "hits" to determine how best to bring this dynamic ecosystem back into balance.[4]



Research for the Circle of Health items as they relate to IBS is summarized below.

Physical Activity

Regular physical activity has a positive impact on nearly all diseases, especially those with a strong mind-body component. The positive effect of movement on IBS symptoms likely stems from the stress-relieving and bowel motility benefits it confers. Mild physical exercise has been found to increase gas clearance and reduce bloating.[5] Women who are more

physically active tend to have fewer and less severe IBS symptoms.[6] One small randomized controlled trial showed that increasing physical activity had symptomatic benefits in those with constipation-predominant IBS.[7] Despite these demonstrated benefits of exercise on IBS symptoms, research does not support alternative exercise recommendations for those with IBS versus the general population.

Yoga

Several studies have shown positive results with various types of yoga, particularly pranayama, a form of yoga that focuses on the breath. Pranayama breathing stimulates the parasympathetic autonomic system, which mediates relaxation of intestinal spasm through the vagus nerve. A 2-month study showed that twice-daily yoga was equivalent to loperamide in those with diarrhea-predominant IBS symptoms.[8] A systematic review supports increases in quality of life, improved anxiety, and decreased symptoms, but it was no more effective than daily walking to meet general exercise recommendations. [9]

Nutrition

The first-line approach to diet should not differ between those with or without IBS. Given that most Americans do not adhere to general dietary guidelines, these recommendations should serve as a starting point. Further, those with IBS may be particularly sensitive to excessive consumption of alcohol, spicy foods, caffeine, and dietary fat, and inadequate consumption of hydrating fluids.[10]

Elimination diets

Individuals with IBS may be particularly sensitive to intestinal gas accumulation triggered by fermentation of specific types of carbohydrates. For this reason, the "Low FODMaP Diet" (fermentable oligo-, di, and monosaccharides and polyols) has been developed, and this dietary approach is increasingly becoming a second-line recommendation (after general dietary guidance, above). Check out "The Low FODMaP Diet" tool, and consider incorporating a simple list of common FODMaP foods.

FODMaP foods all contain short-chain carbohydrates of varying lengths that are often incompletely absorbed by the GI tract. By remaining present in the GI tract rather than being absorbed, these carbohydrates are vulnerable to fermentation by enteric bacteria, producing gas and abdominal distention. Gibson and colleagues found that avoiding foods containing these carbohydrates led to relief in 75% of those with IBS.[11] Newer studies support this dietary approach for only those with *diarrhea* or *mixed* IBS subtypes (not constipation), and only when *led by a dietician*; giving brief instruction and handouts have proved less effective[10] and possibly less safe.

A third-line dietary approach is a more targeted and personalized elimination diet. This may include selecting a few or more foods that are high in FODMaPs or as guided by an individual's experiences and intuition. (To learn more, review the "Elimination Diets" tool.) Several controlled studies have shown that people who based an elimination diet on IgG results improved more than those who eliminated random foods.[12, 13] However, IgG testing (as opposed to IgE) is not widely available, and studies have been small and of low quality; therefore, incorporating IgG testing should be reserved as a fourth-line option if a more personalized elimination diet is not

effective. More about various GI tests is available in the "Testing to Assess the Gastrointestinal Ecosystem" Integrative Health tool.

It is worth noting that many individuals consider eliminating gluten to improve their symptoms as a part of an elimination diet. While a review of gluten intolerance is beyond the scope of this resource, wheat, barley, and rye make up about 50% of the FODMaPs in the average Americans' diet. Several well-controlled studies have shown that people who based an elimination diet on IgG results improved more than those who eliminated random foods.[12, 13] Therefore, eliminating these common grains may well provide benefits, regardless of a possible mechanism related to gluten.

Fiber

Fiber maintains a healthy intestinal mucous layer, acts as a prebiotic (a "food" for probiotic bacteria), and lowers cholesterol. It undergoes fermentation in the colon, leading to gas and short-chain fatty acid production. These characteristics likely improve stool frequency and consistency in those with IBS, but overall, results of studies focused on fiber and IBS are quite mixed.[14] Whether fiber is insoluble or soluble, however, seems to make a difference. Several studies have shown that insoluble fiber (i.e., bran) often worsens symptoms, though this may be due in part to inadequate increases in fluid intake. Other studies show that soluble fiber, at least for those with constipation-type IBD, is likely effective.[8, 15-20] Good examples of soluble fiber include guar gum (5-10 gm per day), ground flaxseed (1 tbsp once or twice per day), and psyllium husk (1 tbsp in 8 oz of water twice per day). As a general principle, start fiber at low doses, increase slowly, and allow time for an adequate trial (1-2 months).

Mind and Emotions

Our GI system, often is referred to as our "second brain," rivals the brain in terms of numbers of neural connections and volume of neurotransmitters. However, it may be most useful to consider the brain and GI nervous system as a *single* unit, given how entwined they are. Their relationship is mediated by the autonomic nervous system, hypothalamic-pituitary axis, and the immune system. Problematic thoughts and emotions can manifest as abdominal pain, bloating, and spasms. This interplay has given rise to many common metaphors, such as "I have butterflies in my stomach." It is worth listening for such statements as clues to how best to work with people with IBS.

Individuals with IBS have increased perception of stress, and this can chronically affect their symptoms. Furthermore, IBS sufferers are hyper-vigilant regarding body sensations.[21] The power of the mind can have a powerful effect on IBS in the following ways:

Cognitive behavioral therapy

Cognitive Behavioral Therapy (CBT) focuses on identifying behaviors and thought patterns, as well as negative emotions that hinder progress toward one's self-defined goals. [21, 22] This mind-body modality has the most robust evidence base for improvements in function.[23, 24] Some data suggests that online delivery may be as effective as live delivery, which may allow systems to greatly expand this underutilized service. [23]

Hypnotherapy

Hypnotherapy is a method of deliberately using verbal cues to induce an altered state of awareness for a targeted therapeutic indication. These verbal cues can enhance relaxation, the ability to generate imagery, and focus. Evidence supports the use of either Gut-Directed Hypnotherapy (GDH) or audiotape hypnotherapy, and one trial found these equally effective for IBS with response rates of 50%-75%.[25] GDH is more resource intensive than a self-directed audiotape, requiring 8-12 sessions that are one-half to 1 hour long. Several studies showed that hypnotherapy seems to have consistent positive effects on IBS, with an estimated 25-73% improvement in bowel symptoms, psychological distress, and quality of life that lasted over a year after treatment was completed.[26-28] In refractory cases referred to a GI clinic, an uncontrolled prospective study of 204 individuals found that 81% received benefit; 71% of these continued to have benefits 5 years later.[29] Although larger randomized trials are needed to verify the effectiveness of hypnotherapy, its safety and potential benefit makes it a worthwhile therapeutic option. It also remains unclear how this intervention compares to others.

For self-guided hypnosis audio resources, visit Health Journeys website. For a copy of a script you can use for yourself or with patients to ease abdominal pain, see "Balloon Self-Hypnosis Technique for IBS and Abdominal Pain—A Guide for Clinicians."

Brief Psychodynamic Psychotherapy

This insight-oriented talk therapy focuses on discussions of symptoms, emotions, and the mind-body connection. It is used extensively in the United Kingdom. Two large studies have yielded positive results. The largest of these included 257 individuals and had control groups that included paroxetine as well as standard medical care. Both the psychotherapy group and the paroxetine group had similar improvements in quality of life, but the psychotherapy group had lower health care costs.[22]

Meditation

Meditation can be done in many ways, and the goal of all of them is to focus one's attention. Given the role of maladaptive stress in those with IBS, it makes sense that altering one's stress response through meditation can be beneficial. However, to date, no controlled studies have been done. Research does suggest that people with GI symptoms who attend a Mindfulness-Based Stress Reduction (MBSR) course have a reduction of symptoms.[21, 30, 31] Given the multitude of confirmed and suspected health benefits of meditation, this very safe intervention should be considered for those with IBS.

A note on the placebo response: Placebos can be viewed as proactive healing mechanisms that are stimulated through social support, positive expectation, and hope. One meta-analysis estimates a 40%-50% response rate to these important elements of an Integrative Health approach.[32, 33] Factors associated with higher placebo response rates include longer treatment duration, more office visits, and the overall treatment effect of the agent with which the placebo is being compared.[34] Placebo responses derive from malleable expectations and are not necessarily related to the specific type of treatment; placebo response rates in trials for IBS across modalities show no consistent trends, whether studying a medication, mind-body intervention, or supplement.[35] Given that positive expectations about treatments can be greatly

enhanced by therapeutic patient-practitioner relationships, building trust and instilling hope should be key ingredients in any Personal Health Plan (PHP) for someone with IBS.

Dietary Supplements

Note: Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

Peppermint oil

Peppermint is one of the most commonly used supplements for IBS. Its main active ingredient is menthol, an antispasmodic. It works best to treat spasms that lead to abdominal pain as opposed to treating distention and flatulence. It has also been shown to improve diarrhea, constipation, urgency, and incomplete defecation.[36] One systemic review showed response rates in those using peppermint oil of 79% for abdominal pain, 83% for abdominal distention, and 73% for flatulence.[37] These findings are as good as those for pharmaceuticals—if not better—and peppermint oil has fewer side effects. In fact, the number needed to treat (NNT) is 2-3, making this possibly the single, most-effective intervention for IBS.[38]

One common side effect of peppermint is heartburn because it also relaxes the lower esophageal sphincter. Use Peppermint with caution for those with gastroesophageal reflux disease (GERD). An enteric-coated preparation may allow release of the peppermint more distally in the GI tract. Most quality products have at least 44% menthol and less than 1% pulegone (a neuro- and hepatotoxin).[39] A common dose is 0.2 to 0.4 mL three times daily of enteric-coated capsules. Adverse effects are rare.

Probiotics

Increased intestinal permeability and intestinal dybiosis seem to be a part of IBS pathogenesis. Those with IBS have differences in their microbiomes than those without this condition, particularly in those with the diarrhea subtype.[40] Intestinal bacteria directly interact with the intestinal wall to influence how easy or difficult it is for larger molecules to be absorbed from the gut into the bloodstream. An intestine that is too permeable allows macromolecules into the bloodstream, where they are more likely to trigger an immune response than smaller compounds. As macrophages, antibodies, and cytokines mobilize, food intolerances and IBS symptoms can develop.

Probiotics may offer benefit in many ways, including healing the gut mucosal barrier, improving intestinal flora, altering one's immune response, decreasing inflammation, and/or altering fermentation in the intestinal tract. Many studies investigating a wide range of bacterial strains have been performed, and the most positive single-species studies have shown the specific strain *Bifidobacterium infantis* (*B. infantis*) 35624 at a dose of 10^8 colony-forming units (CFUs) to be the most effective.[41, 42] However, multi-species probiotics seem to provide superior relief when used for at least eight weeks; these should contain *Lactobacillus* and at least one of either Streptomyces or *Bifidobacterium* species.[43]

In one meta-analysis, the number of people who needed to be treated (NNT) with probiotics, to have one individual experience improvement, was found to be as low as four.[44] Probiotics have significant favorable effects on abdominal pain, bloating, and bowel movement difficulty, especially in those with the diarrhea subtype.[14, 45]

While using probiotics can be helpful, it remains unclear if they provide long-term benefits beyond several months. Some studies suggest that they do not, and other studies suggest that they may possibly *worsen* symptoms after 3-4 months.[46] Therefore, using probiotics mainly during times of worsening symptoms, while incorporating other modalities, may be the best approach.

Iberogast (STW 5)

Iberogast (STW 5), originally from Germany, is a combination of extracts from nine different herbs. It has been studied for several functional GI disorders. Its contents include the following:

- Bitter candytuft (*Iberis amara*) also known as clown's mustard
- Angelica root (*Angelica archangelica*)
- Milk thistle fruit (*Silybum marianum*)
- Celandine aerial parts (*Chelidonium majus*)
- Caraway fruit (*Carum carvi*)
- Licorice root (*Glycyrrhiza glabra*)
- Peppermint leaf (*Menthae piperitae*)
- Lemon balm leaf (*Melissae officinalis*)
- Chamomile flower (*Matricaria recutita*)

Several studies have shown a benefit over placebo for abdominal pain.[47] The constituents of Iberogast (STW 5) have properties that alter GI motility; many also have anti-inflammatory properties. Its varied mechanisms of action likely explain its wide-ranging effectiveness.[48]

Other Healing Systems

Acupuncture

Randomized controlled studies have not shown a clear benefit of acupuncture in reducing symptoms or severity or in improving quality of life. However, a few Chinese trials have shown that acupuncture may be more beneficial than antispasmodic medications. It may be that individuals who prefer acupuncture as a treatment modality, or have greater expectations of improvement with acupuncture, will benefit more from acupuncture than medications.[49, 50] In many studies, quality of life improves in both treatment and sham acupuncture groups. Given that acupuncture has a favorable benefit-to-risk ratio, it may be worth considering, though cost and accessibility must also be taken into account.[51]

Summary of NonPharmaceutical Options for iBS

To receive an "A" rating, based on the Strength of Recommendation Taxonomy (SORT) criteria, a therapy needs to be supported by a systematic review or meta-analysis showing benefit, a Cochrane review with clear recommendation, or a high-quality, patient-oriented randomized controlled trial.

The following therapies are supported by consistent, good-quality, and patient-oriented evidence and would receive an “A” rating:

- **Cognitive Behavioral Therapy** through health psychology referral; consider other mind-body modalities if not available
- **Probiotics:** *B. infantis* 35624 (brand name: Align); if not available, consider other *Bifidobacterium* and/or *Lactobacillus* species
- **Soluble fiber**: psyllium husk, 1 tbsp in 8 oz water twice daily (best evidence); ground flaxseed, 1 tbsp twice daily; guar gum, 5 gm daily
- **FODMaP Diet:** should be dietician-guided
- **Peppermint**: 0.2-0.4 mL enteric-coated capsules three or four times daily

The following therapies, supported by inconsistent or limited-quality patient-oriented evidence, receive a “B” rating:

- **Elimination diet**: if different from FODMaP; can be empiric or individualized
- **Clinical Hypnosis: GDH** by a certified practitioner; if not available, self-hypnosis techniques may be an option
- **Iberogast (STW 5)**: 20 drops three times daily (before/with meals)
- **Brief Psychodynamic Psychotherapy** through a health psychology referral

The following therapies are supported by consensus, usual practice, opinion, disease-oriented evidence or case series and would receive a “C” rating:

- **Meditation/relaxation:** MBSR course; consider other forms of relaxation therapies as available (Guided Imagery, progressive muscle relaxation, breathing exercises)
- **Acupuncture:** certified practitioner; consider only recommending to those with positive expectations
- **Physical activity:** vigorous activity 30 minutes or more on most days of the week; consider yoga

Resource Links

- Balloon Self-Hypnosis Technique for IBS and Abdominal Pain—A Guide for Clinicians: https://www.fammed.wisc.edu/files/webfm-uploads/documents/outreach/im/tool-balloon-self-hypnosis.pdf
- Circle of Health: https://www.fammed.wisc.edu/files/webfm-uploads/documents/outreach/im/handout-Whole-Health-it-starts-with-me-Final.pdf
- Elimination Diets: https://www.fammed.wisc.edu/files/webfm-uploads/documents/outreach/im/tool-elimination-diets.pdf
- Health Journeys website: http://www.healthjourneys.com/
- Low FODMaP Diet: https://www.fammed.wisc.edu/files/webfm-uploads/documents/outreach/im/tool-low-fodmap-diet
- Passport to Whole Health: https://wholehealth.wiscweb.wisc.edu/wp-content/uploads/sites/414/2018/09/Passport-to-Whole-Health-3rd-Edition-2018.pdf

- Testing to Assess the Gatrointestinal Ecosystem: https://www.fammed.wisc.edu/files/webfm-uploads/documents/outreach/im/tool-testing-to-assess-GI.pdf

Author(s)

"Irritable Bowel Syndrome" was adapted for the University of Wisconsin Integrative Health Program from the original written by David Lessens, MD, MPH (2014, updated 2020). Sections of this document were adapted from "An Integrative Approach for Treating Irritable Bowel Syndrome" by David Rakel, MD.

This Integrative Health tool was made possible through a collaborative effort between the University of Wisconsin Integrative Health Program, VA Office of Patient Centered Care and Cultural Transformation, and Pacific Institute for Research and Evaluation.

References

1. Langmead L, Rampton DS. Review article: herbal treatment in gastrointestinal and liver disease--benefits and dangers. *Aliment Pharmacol Ther*. Sep 2001;15(9):1239-52.
2. Savas LS, White DL, Wieman M, et al. Irritable bowel syndrome and dyspepsia among women veterans: prevalence and association with psychological distress. *Aliment Pharmacol Ther*. Jan 2009;29(1):115-25. doi:10.1111/j.1365-2036.2008.03847.x
3. White DL, Savas LS, Daci K, et al. Trauma history and risk of the irritable bowel syndrome in women veterans. *Aliment Pharmacol Ther*. Aug 2010;32(4):551-61. doi:10.1111/j.1365-2036.2010.04387.x
4. Porter CK, Gloor K, Cash BD, Riddle MS. Risk of functional gastrointestinal disorders in U.S. military following self-reported diarrhea and vomiting during deployment. *Dig Dis Sci*. Nov 2011;56(11):3262-9. doi:10.1007/s10620-011-1762-3
5. Villoria A, Serra J, Azpiroz F, Malagelada JR. Physical activity and intestinal gas clearance in patients with bloating. *Am J Gastroenterol*. Nov 2006;101(11):2552-7. doi:10.1111/j.1572-0241.2006.00873.x
6. Lustyk MK, Jarrett ME, Bennett JC, Heitkemper MM. Does a physically active lifestyle improve symptoms in women with irritable bowel syndrome? *Gastroenterol Nurs*. May-Jun 2001;24(3):129-37.
7. Daley AJ, Grimmett C, Roberts L, et al. The effects of exercise upon symptoms and quality of life in patients diagnosed with irritable bowel syndrome: a randomised controlled trial. *Int J Sports Med*. Sep 2008;29(9):778-82. doi:10.1055/s-2008-1038600
8. Yoon JS, Sohn W, Lee OY, et al. Effect of multispecies probiotics on irritable bowel syndrome: a randomized, double-blind, placebo-controlled trial. *J Gastroenterol Hepatol*. Jan 2014;29(1):52-9. doi:10.1111/jgh.12322
9. Schumann D, Anheyer D, Lauche R, Dobos G, Langhorst J, Cramer H. Effect of yoga in the therapy of irritable bowel syndrome: a systematic review. *Clin Gastroenterol Hepatol*. Dec 2016;14(12):1720-1731. doi:10.1016/j.cgh.2016.04.026
10. McKenzie YA, Bowyer RK, Leach H, et al. British Dietetic Association systematic review and evidence-based practice guidelines for the dietary management of irritable bowel syndrome in adults (2016 update). *J Hum Nutr Diet*. Oct 2016;29(5):549-75. doi:10.1111/jhn.12385
11. Gibson PR. Food intolerance in functional bowel disorders. *J Gastroenterol Hepatol*. Apr 2011;26 Suppl 3:128-31. doi:10.1111/j.1440-1746.2011.06650.x
12. Atkinson W, Sheldon TA, Shaath N, Whorwell PJ. Food elimination based on IgG antibodies in irritable bowel syndrome: a randomised controlled trial. *Gut*. Oct 2004;53(10):1459-64. doi:10.1136/gut.2003.037697
13. Drisko J, Bischoff B, Hall M, McCallum R. Treating irritable bowel syndrome with a food elimination diet followed by food challenge and probiotics. *J Am Coll Nutr*. Dec 2006;25(6):514-22.

14. Chey WD, Maneerattaporn M, Saad R. Pharmacologic and complementary and alternative medicine therapies for irritable bowel syndrome. *Gut Liver*. Sep 2011;5(3):253-66. doi:10.5009/gnl.2011.5.3.253
15. Bijkerk CJ, de Wit NJ, Muris JW, Whorwell PJ, Knottnerus JA, Hoes AW. Soluble or insoluble fibre in irritable bowel syndrome in primary care? Randomised placebo controlled trial. *BMJ*. 2009;339:b3154. doi:10.1136/bmj.b3154
16. Jenkins DJ, Kendall CW, Marchie A, et al. Direct comparison of a dietary portfolio of cholesterol-lowering foods with a statin in hypercholesterolemic participants. *Am J Clin Nutr*. Feb 2005;81(2):380-7.
17. Giannini EG, Mansi C, Dulbecco P, Savarino V. Role of partially hydrolyzed guar gum in the treatment of irritable bowel syndrome. *Nutrition*. Mar 2006;22(3):334-42. doi:10.1016/j.nut.2005.10.003
18. Eswaran S, Muir J, Chey WD. Fiber and functional gastrointestinal disorders. *Am J Gastroenterol*. May 2013;108(5):718-27. doi:10.1038/ajg.2013.63
19. Ford AC, Talley NJ, Spiegel BM, et al. Effect of fibre, antispasmodics, and peppermint oil in the treatment of irritable bowel syndrome: systematic review and meta-analysis. *BMJ*. 2008;337:a2313. doi:10.1136/bmj.a2313
20. Singh R, Salem A, Nanavati J, Mullin GE. The role of diet in the treatment of rrritable bowel syndrome: a sytematic review. *Gastroenterol Clin North Am*. Mar 2018;47(1):107-137. doi:10.1016/j.gtc.2017.10.003
21. Kearney DJ, Brown-Chang J. Complementary and alternative medicine for IBS in adults: mind-body interventions. *Nat Clin Pract Gastroenterol Hepatol*. Nov 2008;5(11):624-36. doi:10.1038/ncpgasthep1257
22. Naliboff BD, Frese MP, Rapgay L. Mind/Body psychological treatments for irritable bowel syndrome. *Evid Based Complement Alternat Med*. Mar 2008;5(1):41-50. doi:10.1093/ecam/nem046
23. Laird KT, Tanner-Smith EE, Russell AC, Hollon SD, Walker LS. Comparative efficacy of psychological therapies for improving mental health and daily functioning in irritable bowel syndrome: A systematic review and meta-analysis. *Clin Psychol Rev*. Feb 2017;51:142-152. doi:10.1016/j.cpr.2016.11.001
24. Ford AC, Moayyedi P, Chey WD, et al. American College of Gastroenterology monograph on management of irritable bowel syndrome. *Am J Gastroenterol*. Jun 2018;113(Suppl 2):1-18. doi:10.1038/s41395-018-0084-x
25. Forbes A, MacAuley S, Chiotakakou-Faliakou E. Hypnotherapy and therapeutic audiotape: effective in previously unsuccessfully treated irritable bowel syndrome? *Int J Colorectal Dis*. Nov 2000;15(5-6):328-34.
26. Whitehead WE. Hypnosis for irritable bowel syndrome: the empirical evidence of therapeutic effects. *Int J Clin Exp Hypn*. Jan 2006;54(1):7-20. doi:10.1080/00207140500328708
27. Wilson S, Maddison T, Roberts L, Greenfield S, Singh S. Systematic review: the effectiveness of hypnotherapy in the management of irritable bowel syndrome. *Aliment Pharmacol Ther*. 2006;24(5):769-780.
28. Peters SL, Muir JG, Gibson PR. Review article: gut-directed hypnotherapy in the management of irritable bowel syndrome and inflammatory bowel disease. *Aliment Pharmacol Ther*. Jun 2015;41(11):1104-15. doi:10.1111/apt.13202
29. Gonsalkorale WM, Miller V, Afzal A, Whorwell PJ. Long term benefits of hypnotherapy for irritable bowel syndrome. *Gut*. Nov 2003;52(11):1623-9.
30. Kearney DJ, McDermott K, Martinez M, Simpson TL. Association of participation in a mindfulness programme with bowel symptoms, gastrointestinal symptom-specific anxiety and quality of life. *Aliment Pharmacol Ther*. Aug 2011;34(3):363-373. doi:10.1111/j.1365-2036.2011.04731.x
31. Thakur ER, Shapiro J, Chan J, et al. A systematic review of the effectiveness of psychological treatments for IBS in gastroenterology settings: promising but in need of further study. *Dig Dis Sci*. Sep 2018;63(9):2189-2201. doi:10.1007/s10620-018-5095-3

32. Dorn SD, Kaptchuk TJ, Park JB, et al. A meta-analysis of the placebo response in complementary and alternative medicine trials of irritable bowel syndrome. *Neurogastroenterol Motil*. Aug 2007;19(8):630-7. doi:10.1111/j.1365-2982.2007.00937.x
33. Patel SM, Stason WB, Legedza A, et al. The placebo effect in irritable bowel syndrome trials: a meta-analysis. *Neurogastroenterol Motil*. Jun 2005;17(3):332-40. doi:10.1111/j.1365-2982.2005.00650.x
34. Sands BE. The placebo response rate in irritable bowel syndrome and inflammatory bowel disease. *Dig Dis*. 2009;27 Suppl 1:68-75. doi:10.1159/000268123
35. Flik CE, Bakker L, Laan W, van Rood YR, Smout AJ, de Wit NJ. Systematic review: The placebo effect of psychological interventions in the treatment of irritable bowel syndrome. *World J Gastroenterol*. Mar 28 2017;23(12):2223-2233. doi:10.3748/wjg.v23.i12.2223
36. Chang FY, Lu CL. Treatment of irritable bowel syndrome using complementary and alternative medicine. *J Chin Med Assoc*. Jun 2009;72(6):294-300. doi:10.1016/s1726-4901(09)70375-2
37. Mann NS, KS S. Pepermint oil in irritable bowel syndrome: systematic evaluation of 1634 cases with meta-analysis. *J Integr Med*. 2012;19(1)
38. Hawrelak JA, Wohlmuth H, Pattinson M, et al. Western herbal medicines in the treatment of irritable bowel syndrome: A systematic review and meta-analysis. *Complement Ther Med*. Jan 2020;48:102233. doi:10.1016/j.ctim.2019.102233
39. Nair B. Final report on the safety assessment of mentha piperita (peppermint) oil, mentha piperita (peppermint) leaf extract, mentha piperita (peppermint) leaf, and mentha piperita (peppermint) leaf water. *Int J Toxicol*. 2001;20 Suppl 3:61-73.
40. Liu HN, Wu H, Chen YZ, Chen YJ, Shen XZ, Liu TT. Altered molecular signature of intestinal microbiota in irritable bowel syndrome patients compared with healthy controls: A systematic review and meta-analysis. *Dig Liver Dis*. Apr 2017;49(4):331-337. doi:10.1016/j.dld.2017.01.142
41. Brenner DM, Moeller MJ, Chey WD, Schoenfeld PS. The utility of probiotics in the treatment of irritable bowel syndrome: a systematic review. *Am J Gastroenterol*. Apr 2009;104(4):1033-49; quiz 1050. doi:10.1038/ajg.2009.25
42. Floch MH, Walker WA, Madsen K, et al. Recommendations for probiotic use-2011 update. *J Clin Gastroenterol*. Nov 2011;45 Suppl:S168-71. doi:10.1097/MCG.0b013e318230928b
43. Dale HF, Rasmussen SH, Asiller Ö, Lied GA. Probiotics in irritable bowel syndrome: an up-to-date systematic review. *Nutrients*. Sep 2 2019;11(9)doi:10.3390/nu11092048
44. Moayyedi P, Ford AC, Talley NJ, et al. The efficacy of probiotics in the treatment of irritable bowel syndrome: a systematic review. *Gut*. Mar 2010;59(3):325-32. doi:10.1136/gut.2008.167270
45. Liang D, Longgui N, Guoqiang X. Efficacy of different probiotic protocols in irritable bowel syndrome: A network meta-analysis. *Medicine (Baltimore)*. Jul 2019;98(27):e16068. doi:10.1097/md.0000000000016068
46. Didari T, Mozaffari S, Nikfar S, Abdollahi M. Effectiveness of probiotics in irritable bowel syndrome: Updated systematic review with meta-analysis. *World J Gastroenterol*. Mar 14 2015;21(10):3072-84. doi:10.3748/wjg.v21.i10.3072
47. Liu JP, Yang M, Liu YX, Wei M, Grimsgaard S. Herbal medicines for treatment of irritable bowel syndrome. *Cochrane Database Syst Rev*. 2006;(1):Cd004116. doi:10.1002/14651858.CD004116.pub2
48. Rahimi R, Abdollahi M. Herbal medicines for the management of irritable bowel syndrome: a comprehensive review. *World J Gastroenterol*. Feb 21 2012;18(7):589-600. doi:10.3748/wjg.v18.i7.589
49. Manheimer E, Cheng K, Wieland LS, et al. Acupuncture for treatment of irritable bowel syndrome. *Cochrane Database Syst Rev*. 2012;5
50. Sun JH, Wu XL, Xia C, et al. Clinical evaluation of Soothing Gan and invigorating Pi acupuncture treatment on diarrhea-predominant irritable bowel syndrome. *Chin J Integr Med*. Oct 2011;17(10):780-5. doi:10.1007/s11655-011-0875-z
51. Schneider A, Streitberger K, Joos S. Acupuncture treatment in gastrointestinal diseases: a systematic review. *World J Gastroenterol*. Jul 7 2007;13(25):3417-24.