

## Complementary and alternative medicine for treatment of irritable bowel syndrome

Yi-Hao A. Shen Richard Nahas MD CCFP

**I**rritable bowel syndrome (IBS) is the most common functional gastrointestinal disorder. It is characterized by chronic abdominal pain or discomfort and altered bowel habits. The symptom-based Rome III criteria<sup>1,2</sup> for the diagnosis of IBS comprise recurrent abdominal pain or discomfort, at least 3 days per month in the past 3 months, and at least 2 of the following:

- improvement of pain with defecation,
- onset associated with a change in frequency of stool, or
- onset associated with a change in form (appearance) of stool.

With an estimated prevalence of 12% in Canada, IBS is a common reason for seeking medical care.<sup>2,3</sup>

Although current guidelines state that extensive diagnostic evaluation of suspected IBS is usually not routinely necessary, patients older than 50 with constipation should undergo screening colonoscopy, and parasitic infection, lactose intolerance, and celiac disease should be considered in all patients.<sup>2</sup> The approach to treatment emphasizes education, reassurance, dietary modification, and stress management.<sup>4</sup>

Current drug therapy is of limited benefit. Tricyclic antidepressants are supported by solid clinical evidence,<sup>5</sup> but there is less robust evidence supporting the use of antispasmodics<sup>6</sup> or selective serotonin reuptake inhibitor antidepressants.<sup>7</sup> Agents targeting serotonin subtypes are not widely used owing to potential risks. Alosetron is associated with ischemic colitis and tegaserod with cardiovascular events; neither is licensed for use in Canada.<sup>7</sup>

Based on low levels of satisfaction both with the treatment they receive<sup>8,9</sup> and their overall care,<sup>10-12</sup> it is not surprising that almost 50% of IBS patients turn to complementary and alternative medicine (CAM) therapies.<sup>8</sup> Here we present a review of

This article has been peer reviewed.

Cet article a fait l'objet d'une révision par des pairs.

*Can Fam Physician* 2009;55:143-8

### Abstract

**OBJECTIVE** To review the evidence supporting selected complementary and alternative medicine approaches used in the treatment of irritable bowel syndrome (IBS).

**QUALITY OF EVIDENCE** MEDLINE (from January 1966), EMBASE (from January 1980), and the Cochrane Database of Systematic Reviews were searched until March 2008, combining the terms *irritable bowel syndrome* or *irritable colon* with *complementary therapies, alternative medicine, acupuncture, fiber, peppermint oil, herbal, traditional, yoga, massage, meditation, mind, relaxation, probiotic, hypnotherapy, psychotherapy, cognitive therapy, or behavior therapy*. Results were screened to include only clinical trials, systematic reviews, and meta-analyses. Level I evidence was available for most interventions.

**MAIN MESSAGE** Soluble fibre improves constipation and global IBS symptoms. Peppermint oil alleviates IBS symptoms, including abdominal pain. Probiotic trials show overall benefit for IBS but there is little evidence supporting the use of any specific strain. Hypnotherapy and cognitive-behavioural therapy are also effective therapeutic options for appropriate patients. Certain herbal formulas are supported by limited evidence, but safety is a potential concern. All interventions are supported by systematic reviews or meta-analyses.

**CONCLUSION** Several complementary and alternative therapies can be recommended as part of an evidence-based approach to the treatment of IBS; these might provide patients with satisfactory relief and improve the therapeutic alliance.

### Résumé

**OBJECTIF** Examiner les preuves en faveur de l'utilisation de certaines thérapies complémentaires et alternatives dans le traitement du syndrome du côlon irritable (SCI).

**QUALITÉ DES PREUVES** On a fouillé MEDLINE (depuis janvier 1966), EMBASE (depuis janvier 1980) et la Cochrane Database of Systematic Reviews jusqu'en mars 2008, en combinant les termes *irritable bowel syndrome* ou *irritable colon* avec *complementary therapies, alternative medicine, acupuncture, fiber, peppermint oil, herbal, traditional, yoga, massage, meditation, probiotic, hypnotherapy, psychotherapy, cognitive therapy* ou *behavior therapy*. Parmi les résultats, seuls les essais cliniques, les revues systématiques et les méta-analyses ont été retenus. La plupart des interventions présentaient des preuves de niveau I.

**PRINCIPAL MESSAGE** Les fibres solubles soulagent la constipation et la plupart des symptômes du SCI. L'huile de menthe poivrée soulage les symptômes du SCI, incluant les douleurs abdominales. Les essais sur les probiotiques indiquent qu'ils sont généralement bénéfiques mais il y a peu de preuves en faveur d'une souche en particulier. L'hypnothérapie et la thérapie cognitivo-comportementale sont également des options valables pour certains patients. Un nombre limité de données appuient l'usage d'herbes médicinales, mais leur innocuité pourrait être source de préoccupations. Toutes les interventions s'appuient sur des revues systématiques ou des méta-analyses.

**CONCLUSION** Plusieurs thérapies complémentaires ou alternatives peuvent être recommandées comme partie intégrante d'une approche basée sur des données probantes pour le traitement du SCI; elles pourraient procurer un soulagement satisfaisant et améliorer la relation médecin-patient.

CAM interventions for which safety and efficacy are supported by clinical evidence.

## Quality of evidence

MEDLINE (from January 1966), EMBASE (from January 1980), and the Cochrane Database of Systematic Reviews were searched until March 2008, combining the terms *irritable bowel syndrome* or *irritable colon* with *complementary therapies, alternative medicine, acupuncture, fiber, peppermint oil, herbal, traditional, yoga, massage, meditation, mind, relaxation, probiotic, hypnotherapy, psychotherapy, cognitive therapy, or behavior therapy*. The interventions included in this review were selected by the authors based on literature reviews and clinical experience. We included clinical trials, systematic reviews, and meta-analyses in the review. Level I evidence was available for most interventions (Table 1<sup>13-26</sup>).

**Table 1. Summary of evidence for CAM treatments for IBS**

INTERVENTION	BODY OF EVIDENCE
Peppermint oil	2 meta-analyses of 5 and 4 RCTs <sup>13,14</sup>
Probiotics	Meta-analysis of 23 RCTs <sup>15</sup>
Soluble fibre	Meta-analysis of 9 RCTs <sup>16</sup>
Tong xie yao fang	Meta-analysis of 12 prospective trials <sup>17</sup>
Hypnotherapy	1 Cochrane and 3 other systematic reviews <sup>18-21</sup>
CBT	5 RCTs (3 individual CBT and 2 group CBT) <sup>22-26</sup>

CAM—complementary and alternative medicine, CBT—cognitive-behavioural therapy, IBS—irritable bowel syndrome, RCT—randomized controlled trial.

## Interventions

**Fibre.** Increasing fibre intake through diet or supplementation is often the first advice given to IBS patients.<sup>27</sup> This intervention was first proposed based on epidemiologic data and adopted based on a clinical trial that demonstrated benefits in 26 affected patients.<sup>28</sup> It seems that soluble but not insoluble fibre might be effective, but the evidence is problematic.

Soluble fibre is usually administered as psyllium, the ground seed coat of members of the genus *Plantago*. It is also found in whole grains, fruits, and vegetables. It forms a gel in water and is fermented by colonic

bacteria, yielding metabolites that might decrease gut transit time and intracolonic pressure. Insoluble fibre, found in wheat bran and corn bran, undergoes minimal change but it retains water to increase stool bulk and decrease transit time.

We found 2 systematic reviews that examined the role of fibre in treating IBS. A Cochrane review of 11 randomized controlled trials (RCTs) limited to bulking agents (4 trials using wheat bran and 7 trials using soluble fibre) failed to demonstrate any effect on abdominal pain (relative risk [RR] 1.22, 95% confidence interval [CI] 0.86 to 1.73), global assessment (RR 1.09, 95% CI 0.78 to 1.50), or symptom scores (RR 0.93, 95% CI 0.56 to 1.54).<sup>29</sup> An earlier systematic review examined soluble fibre (9 RCTs) and insoluble fibre (8 RCTs) separately.<sup>16</sup> Overall, the trials indicated improvement of global IBS symptoms (RR 1.33, 95% CI 1.19 to 1.50), especially in IBS-related constipation (RR 1.56, 95% CI 1.21 to 2.02), but no improvement in abdominal pain. When examined separately, soluble fibre—particularly from *Plantago isphagula*—fared better (RR 1.55, 95% CI 1.35 to 1.78) than insoluble fibre, which had no effect (RR 0.89, 95% CI 0.72 to 1.11). In summary, there is good evidence that soluble but not insoluble fibre improves constipation and global IBS symptoms. There is less evidence to support its effect on abdominal pain.

These findings are limited by several factors. Almost all of the trials were conducted in referral centres with populations that differed from those typical in primary care.<sup>30</sup> In addition, most investigators did not screen patients for small intestinal bacterial overgrowth (SIBO), lactose intolerance, or celiac disease (gluten sensitivity). The latter diagnosis is particularly relevant to trials of wheat bran, some of which have reported worsening symptoms.<sup>31,32</sup> This heterogeneity of study populations is a considerable limiting factor in many IBS clinical trials.

**Peppermint oil.** An oil extract of the peppermint plant (*Mentha piperita* Linnaeus) has been used to treat stomach upset for thousands of years. It appears to relax intestinal smooth muscle cells by interfering with calcium channels.<sup>33</sup> Short-term trials suggest that daily use of 3 to 6 enteric-coated capsules containing 0.2 to 0.4 mL of peppermint oil each improves IBS symptoms.<sup>34-38</sup>

These observations are supported by 2 meta-analyses. The first was based on 5 trials that suggested efficacy, but heterogeneous diagnostic criteria and symptom scores weakened the findings.<sup>13</sup> Another review of 4 small trials found overall symptom improvement with peppermint oil (odds ratio 2.7, 95% CI 1.6 to 4.8).<sup>14</sup> These results are strengthened by a recent trial of 110 patients who were screened for celiac disease, lactose intolerance, and SIBO.<sup>34</sup> After patients took 4 capsules daily for 4 weeks, symptoms improved in 75% of those taking peppermint oil compared with 38% of those taking placebo ( $P < .01$ ). The strict inclusion criteria limit the generalizability of

## Levels of evidence

**Level I:** At least one properly conducted randomized controlled trial, systematic review, or meta-analysis

**Level II:** Other comparison trials, non-randomized, cohort, case-control, or epidemiologic studies, and preferably more than one study

**Level III:** Expert opinion or consensus statements

the results, but peppermint oil could be considered for all patients with IBS symptoms.

Peppermint oil appears to alleviate IBS symptoms, including abdominal pain. Patients should be reminded not to chew the capsules, which are enteric coated to prevent gastroesophageal reflux from lower esophageal sphincter relaxation. Perianal burning and nausea are occasionally reported side effects.<sup>39,40</sup> The safety of peppermint oil during pregnancy has not been demonstrated.

**Herbal formulas.** The combination of several herbs to achieve a desired therapeutic effect is a common practice in traditional healing systems. Herbalists suggest that such approaches might offer superior efficacy to single-herb therapies while minimizing side effects.<sup>41</sup>

Tong xie yao fang (TXYF) is one such formula commonly used by traditional Chinese medicine (TCM) practitioners. A meta-analysis of different variations of this formula included 12 Chinese studies examining its use in IBS.<sup>17</sup> The authors found TXYF to be more effective than placebo (RR 1.35, 95% CI 1.21 to 1.50), but cautioned that the trials were heterogeneous and of poor quality and that the TXYF formula itself was inconsistent. Among 3 trials from the English-language literature employing different TCM herbal formulas containing the TXYF ingredients, 2 demonstrated efficacy<sup>42,43</sup> but the other did not.<sup>44</sup>

A Tibetan herbal digestive formula known as Padma Lax has been manufactured and used in Europe for several decades. One trial of 61 constipation-predominant IBS patients, screened for celiac disease or lactose intolerance, reported global improvement in 76% of those using Padma Lax versus 31% of those receiving placebo.<sup>45</sup>

Two herbal formulas known as STW 5 and STW 5-II contain several commonly used herbal digestive aids. In a recent trial, 208 patients with IBS received STW 5, STW 5-II, a single-plant extract, or placebo.<sup>46</sup> Pain and symptom scores were significantly improved among patients receiving the STW formulas ( $P < .001$ ). In a recent Cochrane systematic review of herbal medicines for the treatment of IBS, certain formulations of TXYF, Padma Lax, and STW 5 were determined to improve global IBS symptoms compared with placebo.<sup>47</sup>

Safety is a common concern with herbal medicines. A systematic review of 22 RCTs of herbal medicines for IBS symptoms reported that adverse events occurred in 2.97% of patients (95% CI 2.04% to 3.90%), none of which was considered serious.<sup>48</sup> The authors cautioned, however, that most of these trials were of poor quality and might have underreported adverse events. Clinicians should weigh the potential benefits and uncertainties of these therapies when advising patients about their use.

**Probiotics.** Probiotics are defined as live organisms that, when ingested in adequate amounts, exert a health benefit on the host.<sup>49</sup> Their therapeutic use was

popularized in the late 19th century by Nobel laureate Elie Metchnikoff, who linked the health of Balkan peasants to their consumption of kefir, a fermented milk drink with a thin yogurt-like consistency. Probiotic-rich fermented foods such as yogurt, kefir, miso, tempeh, and sauerkraut have been consumed for centuries.

Probiotics appear to act in several ways that are not yet completely understood. They alter the intraluminal milieu, producing beneficial short-chain fatty acids and deconjugating bile acids, and limit the growth of pathogenic bacteria by direct competition. They also exert potent anti-inflammatory effects, modulating cytokine expression by interacting with gut-associated lymphoid tissue. This immunomodulatory effect also attenuates the visceral hypersensitivity characteristic of IBS.<sup>49,50</sup>

A recent meta-analysis of 23 trials involving 1404 patients found improvement in global IBS symptoms (RR 0.77, 95% CI 0.62 to 0.94) and abdominal pain (RR 0.78, 95% CI 0.69 to 0.88) compared with placebo.<sup>15</sup> This encouraging finding is somewhat limited by the heterogeneous organisms, strains, and doses used. Strains of *Lactobacillus* or *Bifidobacterium* are more prevalent in research and in clinical practice, but there is insufficient evidence to support the use of one strain over another.

Patients should be encouraged to consume more of the probiotic-rich foods mentioned above. Supplementation with capsules or powders might be beneficial, and side effects such as gas and bloating are uncommon and usually transient. It is difficult to advise patients about specific products, as commercial probiotics vary widely in terms of strains used, quality, and the ability to deliver adequate numbers of live bacteria to the colon. Daily oral doses of 10 to 100 billion bacteria are most common.

**Mind-body therapies.** Brain-gut interactions are increasingly recognized in the pathogenesis of IBS, and almost half of IBS patients have comorbid psychiatric disorders.<sup>51</sup> This makes mind-body medicine an appealing approach to IBS treatment. A recent systematic review of psychological treatments included controlled trials of hypnotherapy, cognitive-behavioural therapy (CBT), biofeedback therapy, progressive muscle relaxation, relaxation, and stress management.<sup>52</sup> Of these, hypnotherapy and CBT are supported by the most robust evidence.

**Hypnotherapy:** Therapeutic suggestions have been given to patients in a state of deep relaxation and narrow focus since the 19th century.<sup>53</sup> Gut-directed hypnotherapy is a specific technique that combines suggestions related to emotional well-being and intestinal health. Its use in IBS was first reported in a small trial of 30 patients, in which improvements in symptoms were greater after 7 weekly sessions of hypnotherapy than they were with supportive psychotherapy.<sup>54</sup>

This was 1 of 4 trials identified in a Cochrane review of hypnotherapy in IBS.<sup>18</sup> The other 3 trials were also positive compared with wait-list or usual medical treatment

controls.<sup>55-57</sup> In the largest trial, 81 IBS patients in primary care received either 5 weekly sessions and a self-hypnosis audiotape to use daily or no treatment.<sup>57</sup> Patients receiving hypnotherapy had a greater decline in symptom scores at 3 months (mean change in score of 13.0 out of 100 points vs 4.5 points in the control group,  $P = .008$ ); improvements in quality of life did not reach statistical significance. One additional controlled trial demonstrated benefit in children with functional abdominal pain or IBS.<sup>58</sup> Other systematic reviews have yielded similar positive results,<sup>19-21</sup> with 1 review reporting an 87% median response rate to hypnosis treatment.<sup>21</sup>

There is strong evidence supporting the use of hypnotherapy for the treatment of IBS; safety and potential long-term benefits add to its appeal.<sup>59</sup> Clinical experience suggests that some patients are more "hypnotizable" than others,<sup>60</sup> but it is reasonable to advise patients to consider a trial with a therapist trained in gut-directed hypnotherapy.

*Cognitive-behavioural therapy:* Patients undergoing CBT are trained to recognize and correct thoughts and behaviours that amplify symptoms or undermine well-being. This is often combined with psychological strategies for coping with symptoms and illness.<sup>61,62</sup>

Five controlled trials have evaluated CBT in the treatment of IBS with mixed results.<sup>22-26</sup> Three trials used individual CBT, with the largest ( $N=431$ ) trial demonstrating that 12 weekly sessions improved symptoms more than education did (response rate to therapy 70% vs 37%,  $P = .0001$ ).<sup>22</sup> Of the 2 smaller trials, 1 found CBT to be equivalent to a relaxation technique<sup>23</sup> and the other was limited by a dropout rate of more than 50%.<sup>24</sup> The remaining 2 trials used group CBT; 1 ( $N=45$ ) found that symptoms and well-being improved more with CBT than a wait-list control,<sup>25</sup> but the other ( $N=188$ ) found that group CBT was not superior to psychoeducational support.<sup>26</sup>

Psychological interventions should be considered for most patients with IBS, but the specific intervention used can depend on many factors, including patient preference, cost, and the availability of trained providers. Clinicians trained in CBT can consider providing it to their IBS patients. Hypnotherapy should be recommended if it is available, but providers trained in other modalities should also be considered as part of an integrated approach to IBS treatment.

**Acupuncture.** Acupuncture is a therapeutic modality anchored in TCM. It has been used to treat several gastrointestinal symptoms in functional and organic diseases, and has been shown

### EDITOR'S KEY POINTS

- Irritable bowel syndrome (IBS) is a common reason for seeking medical care. Current drug therapy often provides inadequate relief of IBS symptoms, leading many patients to consider complementary and alternative medicine (CAM) therapies. This review examines the current evidence for CAM therapies in the treatment of IBS.
- Peppermint oil and probiotics are supported by enough evidence to recommend their use in the treatment of IBS. Similar evidence exists to consider hypnotherapy and cognitive-behavioural therapy in appropriate patients. Soluble fibre alleviates IBS-related constipation but not abdominal pain. Some herbal formulas are supported by limited evidence, but clinicians should consider issues of quality and purity before recommending them to patients.
- Most CAM studies for IBS have methodologic limitations. Many are limited by small sample sizes or inconsistencies in the preparations studied. In some, the study populations differed considerably from typical primary care populations, and participants were not always screened to rule out other possible causes of their symptoms (such as lactose intolerance or celiac disease). Some studies experienced difficulties finding appropriate placebo control strategies, and others might have underreported adverse events. The potential limitations of the data should be considered when recommending CAM therapies.

### POINTS DE REPÈRE DU RÉDACTEUR

- Le syndrome du côlon irritable (SCI) est une raison fréquente de consultation. Le traitement pharmacologique actuel est souvent incapable de soulager adéquatement les symptômes du SCI, ce qui amène plusieurs patients à considérer des thérapies complémentaires ou alternatives (TCA). Cette revue examine les données actuelles sur l'usage des TCA dans le traitement du SCI.
- Il existe suffisamment de preuves indiquant que l'huile de menthe poivrée et les probiotiques peuvent être utilisés dans le traitement du SCI. Des preuves analogues suggèrent que l'hypnothérapie et la thérapie cognitivo-comportementale peuvent être recommandées à certains patients. Les fibres solubles soulagent la constipation causée par le SCI mais non les douleurs abdominales. Un petit nombre de données soutiennent l'emploi d'herbes médicinales, mais le médecin devrait penser aux problèmes éventuels de qualité et de pureté avant de les recommander au patient.
- La plupart des études sur l'usage des TCA dans le SCI présentent des limitations méthodologiques. Plusieurs portent sur de petits échantillons ou sur des préparations non uniformes. Dans certaines, les populations étudiées diffèrent considérablement des clientèles typiques des soins primaires, et les participants n'avaient pas toujours été examinés pour éliminer d'autres causes de leurs symptômes (p. ex. intolérance au lactose ou maladie cœliaque). Certaines études ont eu des difficultés à trouver des stratégies appropriées pour les placebos, et d'autres pourraient ne pas avoir rapporté tous les effets indésirables. On devrait penser aux limitations potentielles des données avant de recommander les TCA.


to influence visceral reflex activity, gastric emptying, and acid secretion.<sup>63</sup> Brain-gut disturbances implicated in IBS make it reasonable to consider treating the disorder with acupuncture.<sup>63,64</sup>

Five controlled trials have evaluated standard acupuncture in the treatment of IBS. Three RCTs found it to be equivalent to sham acupuncture, which illustrates the challenges of acupuncture studies.<sup>65-67</sup> Some chose nonacupuncture points as a “sham control,” and others used telescopic needles that did not penetrate the skin. Some used a standard set of points for the intervention; others used different points for each patient that were selected after an assessment by a blinded acupuncturist. Interestingly, 1 trial (N=100) reported that acupuncture and psychotherapy were more effective than psychotherapy alone (RR 1.20, 95% CI 1.03 to 1.39),<sup>68</sup> and another (N=132) reported that it was superior to the herbal formula TXYF (RR 1.14, 95% CI 1.00 to 1.31).<sup>69</sup> The quality of these 2 trials is unknown because they were not published in English.

Two systematic reviews of acupuncture for IBS found insufficient evidence that real acupuncture offers any additional benefit to sham control (pooled RR 1.28, 95% CI 0.83 to 1.98; N=109).<sup>64,70</sup> Authors of both reviews pointed out the need for methodologic standards and suggested that sham acupuncture might not be an adequate placebo control. Acupuncture might be beneficial for some patients with IBS, but current evidence does not support its use.

## Conclusion

Current drug therapy often provides inadequate relief of IBS symptoms, leading many patients to consider CAM therapies. Peppermint oil and probiotics are supported by enough evidence to recommend their use. Hypnotherapy and CBT are also logical therapeutic choices, and enough evidence exists to consider their use in appropriate patients. Soluble fibre alleviates IBS-related constipation but not abdominal pain. Some herbal formulas are supported by limited evidence, but clinicians should consider issues of quality and purity before recommending them to patients.

Physicians should screen for parasitic infection, gluten sensitivity, SIBO, and lactose intolerance before making the diagnosis of IBS. They should inquire about current and past use of CAM therapies and encourage patients to communicate freely about the options they are considering. This has the potential to strengthen the therapeutic alliance, which might also improve IBS patient outcomes. 

**Dr Nahas** is a lecturer in the Department of Family and Community Medicine at the University of Ottawa in Ontario and Medical Director of Seekers Centre for Integrative Medicine. **Mr Shen** is a second-year medical student at the University of Ottawa.

### Contributors

**Dr Nahas** and **Mr Shen** contributed to the literature review, selection and review of studies, and preparation of the manuscript for publication.

### Competing interests

**Dr Nahas** is the founder and Medical Director of Seekers Centre for Integrative Medicine.

### Correspondence

**Dr Richard Nahas**, Seekers Centre for Integrative Medicine, 6 Deakin St, Ottawa, ON K2E 1B3; telephone 613 727-7246; e-mail [richard@seekerscentre.com](mailto:richard@seekerscentre.com)

### References

- Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology* 2006;130(5):1480-91.
- Vidlock EJ, Chang L. Irritable bowel syndrome: current approach to symptoms, evaluation, and treatment. *Gastroenterol Clin North Am* 2007;36(3):665-85, x.
- Pare P, Gray J, Lam S, Balshaw R, Khorasheh S, Barbeau M, et al. Health-related quality of life, work productivity, and health care resource utilization of subjects with irritable bowel syndrome: baseline results from LOGIC (Longitudinal Outcomes Study of Gastrointestinal Symptoms in Canada), a naturalistic study. *Clin Ther* 2006;28(10):1726-35; discussion 1710-1.
- Paterson WG, Thompson WG, Vanner SJ, Faloon TR, Rosser WW, Birtwhistle RW, et al. Recommendations for the management of irritable bowel syndrome in family practice. IBS consensus conference participants. *CMAJ* 1999;161(2):154-60.
- Jackson JL, O'Malley PG, Tomkins G, Balden E, Santoro J, Kroenke K. Treatment of functional gastrointestinal disorders with antidepressant medications: a meta-analysis. *Am J Med* 2000;108(1):65-72.
- Schoenfeld P. Efficacy of current drug therapies in irritable bowel syndrome: what works and does not work. *Gastroenterol Clin North Am* 2005;34(2):319-35, viii.
- McFarland LV. State-of-the-art of irritable bowel syndrome and inflammatory bowel disease research in 2008. *World J Gastroenterol* 2008;14(17):2625-9.
- Hussain Z, Quigley EM. Systematic review: complementary and alternative medicine in the irritable bowel syndrome. *Aliment Pharmacol Ther* 2006;23(4):465-71.
- Whitehead WE, Levy RL, Von Korff M, Feld AD, Palsson OS, Turner M, et al. The usual medical care for irritable bowel syndrome. *Aliment Pharmacol Ther* 2004;20(11-12):1305-15.
- Thompson WG, Heaton KW, Smyth GT, Smyth C. Irritable bowel syndrome in general practice: prevalence, characteristics, and referral. *Gut* 2000;46(1):78-82.
- Lacy BE, Weiser K, Noddin L, Robertson DJ, Crowell MD, Parratt-Engstrom C, et al. Irritable bowel syndrome: patients' attitudes, concerns and level of knowledge. *Aliment Pharmacol Ther* 2007;25(11):1329-41.
- Dhaliwal SK, Hunt RH. Doctor-patient interaction for irritable bowel syndrome in primary care: a systematic perspective. *Eur J Gastroenterol Hepatol* 2004;16(11):1161-6.
- Pittler MH, Ernst E. Peppermint oil for irritable bowel syndrome: a critical review and metaanalysis. *Am J Gastroenterol* 1998;93(7):1131-5.
- Spanier JA, Howden CW, Jones MP. A systematic review of alternative therapies in the irritable bowel syndrome. *Arch Intern Med* 2003;163(3):265-74.
- McFarland LV, Dublin S. Meta-analysis of probiotics for the treatment of irritable bowel syndrome. *World J Gastroenterol* 2008;14(17):2650-61.
- Bijkerk CJ, Muris JW, Knotnertus JA, Hoes AW, de Wit NJ. Systematic review: the role of different types of fibre in the treatment of irritable bowel syndrome. *Aliment Pharmacol Ther* 2004;19(3):245-51.
- Bian X, Wu T, Liu L, Miao J, Wong H, Song L, et al. Effectiveness of the chinese herbal formula TongXieYaoFang for irritable bowel syndrome: a systematic review. *J Altern Complement Med* 2006;12(4):401-7.
- Webb AN, Kukuruzovic RH, Catto-Smith AG, Sawyer SM. Hypnotherapy for treatment of irritable bowel syndrome. *Cochrane Database Syst Rev* 2007;4(4):CD005110.
- Gholamrezaei A, Ardestani SK, Emami MH. Where does hypnotherapy stand in the management of irritable bowel syndrome? A systematic review. *J Altern Complement Med* 2006;12(6):517-27.
- Wilson S, Maddison T, Roberts L, Greenfield S, Singh S; Birmingham IBS Research Group. Systematic review: the effectiveness of hypnotherapy in the management of irritable bowel syndrome. *Aliment Pharmacol Ther* 2006;24(5):769-80.
- Whitehead WE. Hypnosis for irritable bowel syndrome: the empirical evidence of therapeutic effects. *Int J Clin Exp Hypn* 2006;54(1):7-20.
- Drossman DA, Toner BB, Whitehead WE, Diamant NE, Dalton CB, Duncan S, et al. Cognitive-behavioral therapy versus education and desipramine versus placebo for moderate to severe functional bowel disorders. *Gastroenterology* 2003;125(1):19-31.
- Boyce PM, Talley NJ, Balaam B, Koloski NA, Truman G. A randomized controlled trial of cognitive behavior therapy, relaxation training, and routine clinical care for the irritable bowel syndrome. *Am J Gastroenterol* 2003;98(10):2209-18.
- Kennedy T, Jones R, Darnley S, Seed P, Wessely S, Chalder T. Cognitive behaviour therapy in addition to antispasmodic treatment for irritable bowel syndrome in primary care: randomised controlled trial. *BMJ* 2005;331(7514):435.
- Van Dulmen AM, Fennis JF, Bleijenbergh G. Cognitive-behavioral group therapy for irritable bowel syndrome: effects and long-term follow-up. *Psychosom Med* 1996;58(5):508-14.

26. Blanchard EB, Lackner JM, Sanders K, Krasner S, Keefer L, Payne A, et al. A controlled evaluation of group cognitive therapy in the treatment of irritable bowel syndrome. *Behav Res Ther* 2007;45(4):633-48.
27. Zuckerman MJ. The role of fiber in the treatment of irritable bowel syndrome: therapeutic recommendations. *J Clin Gastroenterol* 2006;40(2):104-8.
28. Manning AP, Heaton KW, Harvey RF. Wheat fibre and irritable bowel syndrome. A controlled trial. *Lancet* 1977;2(8035):417-8.
29. Quartero AO, Meineche-Schmidt V, Muris J, Rubin G, de Wit N. Bulking agents, antispasmodic and antidepressant medication for the treatment of irritable bowel syndrome. *Cochrane Database Syst Rev* 2005;2(2):CD003460.
30. Miller V, Lea R, Agrawal A, Whorwell PJ. Bran and irritable bowel syndrome: the primary-care perspective. *Dig Liver Dis* 2006;38(10):737-40.
31. Francis CY, Whorwell PJ. Bran and irritable bowel syndrome: time for reappraisal. *Lancet* 1994;344(8914):39-40.
32. Snook J, Shepherd HA. Bran supplementation in the treatment of irritable bowel syndrome. *Aliment Pharmacol Ther* 1994;8(5):511-4.
33. Kligler B, Chaudhary S. Peppermint oil. *Am Fam Physician* 2007;75(7):1027-30.
34. Cappello G, Spezzaferro M, Grossi L, Manzoli L, Marzio L. Peppermint oil (mintoil) in the treatment of irritable bowel syndrome: a prospective double blind placebo-controlled randomized trial. *Dig Liver Dis* 2007;39(6):530-6.
35. Kline RM, Kline JJ, Di Palma J, Barbero G. Enteric-coated, pH-dependent peppermint oil capsules for the treatment of irritable bowel syndrome in children. *J Pediatr* 2001;138(1):125-8.
36. Liu JH, Chen GH, Yeh HZ, Huang CK, Poon SK. Enteric-coated peppermint-oil capsules in the treatment of irritable bowel syndrome: a prospective, randomized trial. *J Gastroenterol* 1997;32(6):765-8.
37. Rees WD, Evans BK, Rhodes J. Treating irritable bowel syndrome with peppermint oil. *Br Med J* 1979;2(6194):835-6.
38. Dew MJ, Evans BK, Rhodes J. Peppermint oil for the irritable bowel syndrome: a multicentre trial. *Br J Clin Pract* 1984;38(11-12):394-8.
39. Lawson MJ, Knight RE, Tran K, Walker G, Roberts-Thomson IC. Failure of enteric-coated peppermint oil in the irritable bowel syndrome: a randomized, double-blind crossover study. *J Gastroenterol Hepatol* 1988;3(3):235-8.
40. Nash P, Gould SR, Bernardo DE. Peppermint oil does not relieve the pain of irritable bowel syndrome. *Br J Clin Pract* 1986;40(7):292-3.
41. Lu W, Kaptchuk TJ, Wong H, George C. Chinese herbal medicine for irritable bowel syndrome. *JAMA* 1999;282(11):1035-7.
42. Bensoussan A, Talley NJ, Hing M, Menzies R, Guo A, Ngu M. Treatment of irritable bowel syndrome with chinese herbal medicine: a randomized controlled trial. *JAMA* 1998;280(18):1585-9.
43. Wang G, Li TQ, Wang L, Xia Q, Chang J, Zhang Y, et al. Tong-xie-ning, a chinese herbal formula, in treatment of diarrhea-predominant irritable bowel syndrome: a prospective, randomized, double-blind, placebo-controlled trial. *Chin Med J (Engl)* 2006;119(24):2114-9.
44. Leung WK, Wu JC, Liang SM, Chan LS, Chan FK, Xie H, et al. Treatment of diarrhea-predominant irritable bowel syndrome with traditional chinese herbal medicine: a randomized placebo-controlled trial. *Am J Gastroenterol* 2006;101(7):1574-80.
45. Sallon S, Ben-Arye E, Davidson R, Shapiro H, Ginsberg G, Ligumsky M. A novel treatment for constipation-predominant irritable bowel syndrome using padma lax, a tibetan herbal formula. *Digestion* 2002;65(3):161-71.
46. Madisch A, Holtmann G, Plein K, Hotz J. Treatment of irritable bowel syndrome with herbal preparations: results of a double-blind, randomized, placebo-controlled, multi-centre trial. *Aliment Pharmacol Ther* 2004;19(3):271-9.
47. Liu JP, Yang M, Liu YX, Wei ML, Grimsgaard S. Herbal medicines for treatment of irritable bowel syndrome. *Cochrane Database Syst Rev* 2006;1(1):CD004116.
48. Shi J, Tong Y, Shen JG, Li HX. Effectiveness and safety of herbal medicines in the treatment of irritable bowel syndrome: a systematic review. *World J Gastroenterol* 2008;14(3):454-62.
49. Quigley EM, Flourie B. Probiotics and irritable bowel syndrome: a rationale for their use and an assessment of the evidence to date. *Neurogastroenterol Motil* 2007;19(3):166-72.
50. Camilleri M. Probiotics and irritable bowel syndrome: rationale, putative mechanisms, and evidence of clinical efficacy. *J Clin Gastroenterol* 2006;40(3):264-9.
51. Hayee B, Forgacs I. Psychological approach to managing irritable bowel syndrome. *BMJ* 2007;334(7603):1105-9.
52. Lackner JM, Mesmer C, Morley S, Dowzer C, Hamilton S. Psychological treatments for irritable bowel syndrome: a systematic review and meta-analysis. *J Consult Clin Psychol* 2004;72(6):1100-13.
53. Whorwell PJ. Review article: the history of hypnotherapy and its role in the irritable bowel syndrome. *Aliment Pharmacol Ther* 2005;22(11-12):1061-7.
54. Whorwell PJ, Prior A, Faragher EB. Controlled trial of hypnotherapy in the treatment of severe refractory irritable-bowel syndrome. *Lancet* 1984;2(8414):1232-4.
55. Galovski TE, Blanchard EB. The treatment of irritable bowel syndrome with hypnotherapy. *Appl Psychophysiol Biofeedback* 1998;23(4):219-32.
56. Palsos OS, Turner MJ, Johnson DA, Burnelt CK, Whitehead WE. Hypnosis treatment for severe irritable bowel syndrome: investigation of mechanism and effects on symptoms. *Dig Dis Sci* 2002;47(11):2605-14.
57. Roberts L, Wilson S, Singh S, Roalfe A, Greenfield S. Gut-directed hypnotherapy for irritable bowel syndrome: piloting a primary care-based randomised controlled trial. *Br J Gen Pract* 2006;56(523):115-21.
58. Vlieger AM, Menko-Frankenhuis C, Wolfkamp SC, Tromp E, Benninga MA. Hypnotherapy for children with functional abdominal pain or irritable bowel syndrome: a randomized controlled trial. *Gastroenterology* 2007;133(5):1430-6.
59. Gonsalkorale WM, Miller V, Afzal A, Whorwell PJ. Long term benefits of hypnotherapy for irritable bowel syndrome. *Gut* 2003;52(11):1623-9.
60. Gonsalkorale WM, Houghton LA, Whorwell PJ. Hypnotherapy in irritable bowel syndrome: a large-scale audit of a clinical service with examination of factors influencing responsiveness. *Am J Gastroenterol* 2002;97(4):954-61.
61. Hayee B, Forgacs I. Psychological approach to managing irritable bowel syndrome. *BMJ* 2007;334(7603):1105-9.
62. Palsos OS. Should we incorporate psychological care into the management of IBS? *Nat Clin Pract Gastroenterol Hepatol* 2006;3(9):474-5.
63. Enck P, Martens U, Klosterhalfen S. The psyche and the gut. *World J Gastroenterol* 2007;13(25):3405-8.
64. Lim B, Manheimer E, Lao L, Ziea E, Wisniewski J, Liu J, et al. Acupuncture for treatment of irritable bowel syndrome. *Cochrane Database Syst Rev* 2006;4(4):CD005111.
65. Schneider A, Enck P, Streitberger K, Weiland C, Bagheri S, Witte S, et al. Acupuncture treatment in irritable bowel syndrome. *Gut* 2006;55(5):649-54.
66. Forbes A, Jackson S, Walter C, Quraishi S, Jacyna M, Pitcher M. Acupuncture for irritable bowel syndrome: a blinded placebo-controlled trial. *World J Gastroenterol* 2005;11(26):4040-4.
67. Lowe C, Depew W, Vanner S. A placebo-controlled, double-blind trial of acupuncture in the treatment of irritable bowel syndrome (IBS). *Gastroenterology* 2000;118(4 Suppl 2):A3168.
68. Liu GZ. Treatment of acupuncture and moxibustion plus psychotherapy for irritable bowel syndrome [Chinese]. *Zhongguo Zhen Jiu* 1997;10:611-2.
69. Liao YC. Acupuncture treatment for 132 cases of irritable bowel syndrome. *Clin J Acupunct Moxibustion* 2000;16(6):13.
70. Schneider A, Streitberger K, Joos S. Acupuncture treatment in gastrointestinal diseases: a systematic review. *World J Gastroenterol* 2007;13(25):3417-24.

