



Irritable Bowel Syndrome Guideline Update: January 11, 2012

The summary information from the following studies obtained from a search of the National Library of Medicine using PubMed search engine. Publications reviewed for inclusion were from January 2008 through 12/16/11. Studies were selected based on their relevancy for decision-making in patients with IBS. None of the studies are at low risk of bias but may be useful for informing clinical decisions by providing additional information about diagnostic and treatment options and about potential benefits and harms. Note—many of the included studies do not formally address potential harms of therapies.

Definitions

NNT = Number-needed-to-treat to benefit 1 person

Diagnostic Interventions

PubMed search date: 12/16/11

Search terms: "diagnosis"[MeSH Major Topic] AND "irritable bowel syndrome"

Limits: Dates 1/1/2008 to 12/16/11

REFERENCE; STUDY CHARACTERISTICS	SUMMARY
<p>O'Connor OJ, McSweeney SE, McWilliams S, O'Neill S, Shanahan F, Quigley EM, Maher MM. Role of Radiologic Imaging in Irritable Bowel Syndrome: Evidence-based Review. <i>Radiology</i>. 2011 Dec 9. [Epub ahead of print] PubMed PMID: 22156992; 7SRs and 5 research articles.</p>	<p>ABSTRACT Purpose: To critically evaluate the current literature in an effort to establish the current role of radiologic imaging (computed tomography, magnetic resonance imaging, ultrasonography [US], fluoroscopy, conventional film radiography) in irritable bowel syndrome (IBS).</p> <p>Materials and Methods: The term "irritable bowel syndrome" was used to search Clinical Evidence, UpToDate, Cochrane Library, TRIP, and National Institute for Health and Clinical Excellence databases and the American College of Physicians Journal Club and Evidence-Based Medicine online. PubMed was searched by using medical subject headings ("irritable bowel syndrome;" "colonic diseases, functional;" "diagnosis;" "colonography;" "computed tomographic (CT)") and the dates January 1, 1985 to July 1, 2010. Appraisal was independently performed by two reviewers who followed the Oxford Centre for Evidence Based Medicine practice criteria.</p> <p>Results: No systematic review (SR) specifically examined radiologic imaging in IBS; however, in the secondary literature, five relevant SRs or guidelines partially addressed this topic. A PubMed search identified 1451 articles, 111 of which at least partially addressed radiologic imaging. Of these, seven valid articles (two SRs and five primary research articles) were identified. The five primary research articles</p>

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	<p>examined either colonic investigations (colonoscopy and barium enema examination) (n = 5) or US (n = 2) or both (n = 2). Structural disease found infrequently in patients with IBS-type symptoms included diverticulosis, colorectal cancer, celiac disease, inflammatory bowel disease, and ovarian cancer. The incidence of structural disease in patients with concerning symptoms was low.</p> <p>Conclusion: Although widely used, there is a surprising paucity of evidence guiding radiologic imaging in IBS. Radiologic imaging may not be required in patients with IBS without potentially concerning symptoms but should be considered where such symptoms exist, and choice of imaging study should be influenced by predominant symptoms. Definitive recommendations must await further research</p>
<p>Kunkel D, Basseri RJ, Makhani MD, Chong K, Chang C, Pimentel M. Methane on breath testing is associated with constipation: a systematic review and meta-analysis. <i>Dig Dis Sci.</i> 2011 Jun;56(6):1612-8. Epub 2011 Feb 1. Review. PubMed PMID: 21286935; Study Characteristics: SR of 21 case control studies.</p>	<p>Breath tests</p> <ul style="list-style-type: none"> • IBS patients were more likely to have abnormal breath testing (predominantly lactulose but also included glucose, fructose, sucrose, xylose) compared with age- and sex-matched healthy controls (odds ratio [OR] 9.94, 95% CI 4.26 to 21.82)—all trials. • Sensitivity and specificity: 43.6% sensitivity and 83.6%.
<p>Bratten JR, Spanier J, Jones MP. Lactulose breath testing does not discriminate patients with irritable bowel syndrome from healthy controls. <i>Am J Gastroenterol.</i> 2008 Apr;103(4):958-63. Epub 2008 Mar 26. PubMed PMID: 18371134; 224 patients with IBS and 40 controls were studied.</p>	<p>ABSTRACT</p> <p>INTRODUCTION Recent reports suggest that abnormalities of lactulose breath testing (LBT) are common in patients with irritable bowel syndrome (IBS), although the criteria for abnormal studies are poorly validated, and controlled comparisons are limited. The goal of this study was to determine the prevalence of abnormal LBT using the previously published criteria in both IBS patients and healthy controls, as well as to determine the prevalence and symptom association with methane (CH₄) and hydrogen (H₂) productions during LBT.</p> <p>METHODS Consecutive LBT from patients meeting Rome II criteria for IBS and healthy control subjects were examined. Patients listed their most bothersome digestive symptom at the start of the test. LBT was performed using 10 g of lactulose mixed in 240 mL of water, and breath samples collected every 20 min for a 180-min period. Both breath H₂ and CH₄ were measured. LBT was considered positive if it met any of the previously published criteria: (a) breath H₂ of > 20 parts per million (ppm), (b) increase in breath H₂ in < 90 min, (c) dual H₂ peaks (12-ppm increase over baseline with a decrease of > or = 5 ppm before 2nd peak), and (d) breath CH₄ of > 1 ppm.</p> <p>RESULTS In total, 224 patients with IBS and 40 controls were studied. Twenty percent of IBS patients were CH₄(+) compared with 15% of controls.</p>



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	<p>CH(4)(+) IBS patients were significantly more likely than CH(4)(-) IBS patients to have constipation, and significantly less likely to have diarrhea; however, the association did not hold for symptoms of bloating or pain. Patients and controls did not differ significantly with respect to the frequency of a positive study defined by increase in breath H(2) in < 90 min (121 per 180 vs 26 per 40, P = 0.79), increase in breath H(2) of > 20 ppm (92 per 180 vs 24 per 40, P= 0.31), or dual peaks (25 per 180 vs 9 per 40, P = 0.17).</p> <p>CONCLUSIONS</p> <p>The majority of patients with IBS and healthy subjects meet criteria for an "abnormal" LBT using previously published test criteria, and groups are not discriminated using this diagnostic method. Similarly, while CH(4) production was associated with constipation among IBS patients, the prevalence of CH(4)-positive subjects did not significantly differ between IBS patients and controls. The utility of LBT, in its current form as a diagnostic tool in IBS requires critical reappraisal.</p>
<p>Suares NC, Ford AC. Prevalence of, and risk factors for, chronic idiopathic constipation in the community: systematic review and meta-analysis. <i>Am J Gastroenterol.</i> 2011 Sep;106(9):1582-91; quiz 1581, 1592. doi:10.1038/ajg.2011.164. Epub 2011 May 24. Review. PubMed PMID: 21606976; 45 observational studies.</p>	<p>IBS patients had greater risk of chronic idiopathic constipation compared to patients without IBS (odds ratio 7.98, 95% CI 4.58 to 13.92)</p>
<p>Chey WD, Nojkov B, Rubenstein JH, Dobhan RR, Greenson JK, Cash BD. The yield of colonoscopy in patients with non-constipated irritable bowel syndrome: results from a prospective, controlled US trial. <i>Am J Gastroenterol.</i> 2010 Apr;105(4):859-65. Epub 2010 Feb 23. PubMed PMID: 20179696; PubMed Central PMCID: PMC2887227.</p>	<p>Investigators found no increased prevalence of structural abnormalities, including polyps, diverticulosis, and angiodysplasia at colonoscopy in cases with IBS compared with controls. The prevalence of inflammatory bowel disease and microscopic colitis following colonic biopsy was 0.4 and 1.5%, respectively. Colonoscopy is unlikely to detect any significant underlying organic condition in individuals with IBS.</p>

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Therapeutic Interventions

Search date: 12/16/11

Search terms: "irritable bowel syndrome, treatment, therapy"

Limits: systematic reviews; randomized controlled trials

The following studies from January 2008 to search date are relevant. None are at low risk of bias but may be useful for informing clinical decisions.

REFERENCE; STUDY CHARACTERISTICS	SUMMARY
<p>Menees SB, Maneerattannaporn M, Kim HM, Chey WD. The Efficacy and Safety of Rifaximin for the Irritable Bowel Syndrome: A Systematic Review and Meta-Analysis. <i>Am J Gastroenterol</i>. 2011 Nov 1. doi: 10.1038/ajg.2011.355. [Epub ahead of print] PubMed PMID: 22045120.</p>	<p>ABSTRACT</p> <p>OBJECTIVES Irritable bowel syndrome (IBS) affects 10-15% of the population, and treatment options are limited. Rifaximin is a minimally absorbed antibiotic that has shown efficacy in IBS patients. The objective of our study was to perform a meta-analysis and systematic review of available randomized, placebo controlled trials evaluating the efficacy and tolerability of rifaximin in patients with IBS.</p> <p>METHODS We performed a systematic literature search of multiple online electronic databases regardless of language. Inclusion criteria entailed randomized, placebo controlled trials and IBS defined by accepted symptom-based criteria. Meta-analysis was conducted to evaluate the summary odds ratios (ORs) and 95% confidence intervals (CIs) of combined studies for the primary and secondary outcomes using a random-effects model based on the Der Simonian and Laird method to reflect both within- and between study variability. We assessed heterogeneity using χ^2 test and the inconsistency index statistic (I²). Significant heterogeneity was defined as I² ≥25%. Meta-regression was performed using generalized linear mixed-effects model and study as random effects to estimate the summary OR adjusting for covariate differences across studies and treatment group. Publication bias was assessed by funnel plot analysis.</p> <p>RESULTS Systematic review identified 13,700 citations. Eighteen were deemed to be potentially relevant, of which five articles met eligibility. Meta-analysis found rifaximin to be more efficacious than placebo for global IBS symptom improvement (OR=1.57; 95% CI=1.22, 2.01; therapeutic gain=9.8%; number needed to treat (NNT)=10.2), with mild heterogeneity (P=0.25, I²=26%). For the key secondary outcome of bloating, raw data were available for four studies. Rifaximin was significantly more likely to improve bloating than placebo (OR=1.55; 95% CI=1.23-1.96; therapeutic gain=9.9%; NNT=10.1), with no significant heterogeneity (P=0.27, I²=23%). We found that studies with older patients and more females demonstrated higher response rates, which was consistent regardless of treatment group. In addition, studies with higher cumulative dose tended to report a higher response rate. Of the covariates evaluated, we found age to be most predictive of</p>

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	<p>response, with a correlation coefficient of 0.97 between aggregate response rate and mean age in the placebo groups. Although studies with higher cumulative dose tended to show increased response rates, this was also seen consistently in both the treated and placebo groups. Adverse effects were similar among patients receiving rifaximin or placebo in all studies. The most common adverse events (AEs) ($\leq 10\%$) with rifaximin were headache, upper respiratory infection, nausea, nasopharyngitis, diarrhea, and abdominal pain. Serious AEs were rare ($< 1\%$) and similar with rifaximin and placebo.</p> <p>CONCLUSIONS Rifaximin proved more effective than placebo for global symptoms and bloating in IBS patients. The modest therapeutic gain was similar to that yielded by other currently available therapies for IBS. AEs were similar between rifaximin and placebo.</p>
<p>Ruepert L, Quartero AO, de Wit NJ, van der Heijden GJ, Rubin G, Muris JW. Bulking agents, antispasmodics and antidepressants for the treatment of irritable bowel syndrome. Cochrane Database Syst Rev. 2011 Aug 10;(8):CD003460. Review. PubMed PMID: 21833945; 56 trials— 12 studies of bulking agents (621 patients), 29 of antispasmodics (2333 patients), and 15 of antidepressants (922 patients).</p>	<ul style="list-style-type: none"> • Soluble fibers (e.g., ispaghula) might improve global symptoms of IBS. • Insoluble fibers (e.g., wheat) might improve IBS-related constipation. • Antispasmodics were associated with improvement in abdominal pain in analysis of 13 trials with 1,392 patients; NNT 4-19 with 46% abdominal pain in placebo group. <ul style="list-style-type: none"> ○ Significant improvement was reported with cimetropium/dicyclomine, peppermint oil, pinaverium, and trimebutine. ○ No significant differences reported with alverine, mebeverine, otilonium, pirenzepine, propinox, and scopolamine derivatives • Antidepressants: There was a beneficial effect for antidepressants over placebo for improvement of abdominal pain (54% of antidepressants patients improved compared to 37% of placebo; 8 studies; 517 patients; RR 1.49; 95% CI 1.05 to 2.12; P = 0.03; NNT = 5), global assessment (59% of antidepressants patients improved compared to 39% of placebo; 11 studies; 750 patients; RR 1.57; 95% CI 1.23 to 2.00; P < 0.001; NNT = 4) and symptom score (53% of antidepressants patients improved compared to 26% of placebo; 3 studies; 159 patients; RR 1.99; 95% CI 1.32 to 2.99; P = 0.001; NNT = 4). Subgroup analyses showed a statistically significant benefit for selective serotonin releasing inhibitors (SSRIs) for improvement of global assessment and for tricyclic antidepressants (TCAs) for improvement of abdominal pain and symptom score. Separate analysis of studies with adequate allocation concealment found a significant benefit for improvement of symptom score and global assessment. Adverse events were not assessed as an outcome in this review.
<p>Johannesson E, Simrén M, Strid H, Bajor A, Sadik R. Physical activity improves symptoms in irritable bowel syndrome: a randomized controlled trial. Am J Gastroenterol. 2011 May;106(5):915-22. Epub 2011 Jan 4. PubMed PMID: 21206488; RCT, N=102.</p>	<p>Authors report that physical activity associated with significantly greater improvement in IBS Severity Scoring System (IBS-SSS) scores (p = 0.003).</p>
<p>Enck P, Junne F, Klosterhalfen S, Zipfel S, Martens U. Therapy options in irritable bowel syndrome. Eur J Gastroenterol Hepatol. 2010 Dec;22(12):1402-11. Review. PubMed PMID: 21389791; 121 trials (used Jadad scale for quality assessment).</p>	<p>ABSTRACT</p> <p>Background Numerous meta-analyses have recently assessed the overall clinical benefit of single therapy options and groups of therapies in the irritable bowel syndrome (IBS). By large, this should enable physicians to select from a number of therapy options available.</p>

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	<p>Methods</p> <p>We entered dichotomous outcome data from 121 IBS trials published over the last 35 years with different groups and subgroups of drugs (antispasmodics, motility affecting agents, antidepressants, peppermint oil), dietary interventions (bran, probiotics), and psychotherapy (cognitive behavioral, psychodynamic, hypnotherapy, relaxation techniques) into meta-analytic tools and estimate the overall efficacy (odds ratio, number needed to treat).</p> <p>Results</p> <p>Highest efficacy is currently found for peppermint oil, followed by psychotherapeutic and psychopharmacological interventions and probiotics. Traditional antispasmodic therapy has a moderate efficacy, whereas the list of (partially failed or cancelled) motility affecting drugs yielded weak clinical results, and therapies by bran and fibers are of no value in IBS.</p> <p>See Review for endpoints:</p> <ul style="list-style-type: none"> • Peppermint oil NNT 2-3 • Psychotherapy NNT 4-5 • Probiotics NNT 7-8 • TCA NNT 5-6 • SSRI NNT 8-9 • Cilansetron NNT 6-7 • Spasmolytics NNT 5-6 • Alosetron NNT 6-7 • Domperidone NNT 9-10 • Tegaserod NNT14-15 • Renzapride NNT 22 • Cisapride NNT 28 • Fibres, Bran NNT30
<p>Hoveyda N, Heneghan C, Mahtani KR, Perera R, Roberts N, Glasziou P. A systematic review and meta-analysis: probiotics in the treatment of irritable bowel syndrome. <i>BMC Gastroenterol.</i> 2009 Feb 16;9:15. Review. PubMed PMID: 19220890; PubMed Central;14 RCTs.</p>	<p>ABSTRACT</p> <p>BACKGROUND</p> <p>Irritable Bowel Syndrome (IBS) is a common chronic gastrointestinal disorder and the evidence for efficacy of most drug therapies in the treatment of IBS is weak. A popular alternative is probiotics, which have been used in several conditions including IBS. Probiotics are live microbial food supplements. The aim of this systematic review and meta-analysis of randomized trials study was to evaluate the efficacy of probiotics in alleviating symptoms in patients with irritable bowel syndrome. We searched Ovid versions of MEDLINE (1950-2007), EMBASE (1980-2007), CINAHL (1982-2007), AMED (1985-2007), the Cochrane library and hand searched retrieved papers.</p> <p>RESULTS</p> <p>We identified 14 randomized placebo controlled trials. Combined data suggested a modest improvement in overall symptoms after several weeks of treatment: for dichotomous data from seven trials the overall Odds Ratio (OR) was 1.6 (95% CI, 1.2 to 2.2); for continuous data from six trials the standardised mean difference (SMD) was 0.23 (95% CI, 0.07 to 0.38).For individual symptoms the results differed between the pooled dichotomous and</p>

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	<p>pooled continuous data. Trials varied in relation to the length of treatment (4-26 weeks), dose, organisms and strengths of probiotics used.</p> <p>CONCLUSION Probiotics may have a role in alleviating some of the symptoms of IBS, a condition for which currently evidence of efficacy of drug therapies is weak. However, as IBS is a condition that is chronic and usually intermittent longer term trials are recommended. Such research should focus on the type, optimal dose of probiotics and the subgroups of patients who are likely to benefit the most.</p>
<p>Zijdenbos IL, de Wit NJ, van der Heijden GJ, Rubin G, Quartero AO. Psychological treatments for the management of irritable bowel syndrome. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD006442. Review. PubMed PMID: 19160286.</p>	<p>ABSTRACT</p> <p>BACKGROUND No consensus exists on the optimal treatment for irritable bowel syndrome (IBS). Psychological treatments are increasingly advocated but their effectiveness is unclear.</p> <p>OBJECTIVES To evaluate the efficacy of psychological interventions for the treatment of irritable bowel syndrome.</p> <p>SEARCH STRATEGY A computer assisted search of MEDLINE, EMBASE, PsychInfo, CINAHL, Web of Science, The Cochrane Library and Google Scholar was performed for the years 1966-2008. Local databases were searched in Europe.</p> <p>SELECTION CRITERIA Randomised trials comparing single psychological interventions with either usual care or mock interventions in patients over 16 years of age. No language criterion was applied.</p> <p>DATA COLLECTION AND ANALYSIS The search identified 25 studies that fulfilled the inclusion criteria. The relative risk (RR), risk difference (RD), number needed to treat (NNT) and standardized mean difference (SMD) along with 95% confidence intervals were calculated using a random effects model for each outcome.</p> <p>MAIN RESULTS Psychological interventions as a group The SMD for symptom score improvement at 2 and 3 months was 0.97 (95% CI 0.29 to 1.65) and 0.62 (95% CI 0.45 to 0.79) respectively compared to usual care. Against placebo, the SMDs were 0.71 (95% CI 0.08 to 1.33) and -0.17 (95% CI -0.45 to 0.11) respectively. For improvement of abdominal pain, the SMDs at 2 and 3 months were 0.54 (95%CI 0.10 to 0.98) and 0.26 (95% CI 0.07 to 0.45) compared to usual care. The SMD from placebo at 3 months was 0.31 (95% CI -0.16 to 0.79). For improvement in quality of life, the SMD from usual care at 2 and 3 months was 0.47 (95%CI 0.11 to 0.84) and 0.31 (95%CI -0.16 to 0.77) respectively.</p> <p>Cognitive behavioural therapy The SMD for symptom score improvement at 2 and 3 months was 0.75 (95% CI -0.20 to</p>

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1.70) and 0.58 (95% CI 0.36 to 0.79) respectively compared to usual care. Against placebo, the SMDs were 0.68 (95% CI -0.01 to 1.36) and -0.17 (95% CI -0.45 to 0.11) respectively. For improvement of abdominal pain, the SMDs at 2 and 3 months were 0.45 (95% CI 0.00 to 0.91) and 0.22 (95% CI -0.04 to -0.49) compared to usual care. Against placebo the SMD at 3 months was 0.33 (95% CI -0.16 to 0.82). For improvement in quality of life, the SMDs at 2 and 3 months compared to usual care were 0.44 (95% CI 0.04 to 0.85) and 0.92 (95% CI 0.07 to 1.77) respectively.

Interpersonal psychotherapy

The RR for adequate relief of symptoms was 2.02 (95% CI 1.13 to 3.62), RD 0.30 (95% CI 0.13 to 0.46), NNT 4 for comparison with care as usual. The SMD for improvement of symptom score was 0.35 (95% CI -0.75 to 0.05) compared with usual care.

Relaxation/Stress management

The SMD in symptom score improvement at 2 months was 0.50 (95%CI 0.02 to 0.98) compared with usual care. The SMD in improvement of abdominal pain at 3 months was 0.02 (95%CI -0.56 to 0.61) compared with usual care.

Long term results

Very few long term follow-up results were available. There was no convincing evidence that treatment effects were sustained following completion of treatment for any treatment modality.

AUTHORS' CONCLUSIONS

Psychological interventions may be slightly superior to usual care or waiting list control conditions at the end of treatment although the clinical significance of this is debatable. Except for a single study, these therapies are not superior to placebo and the sustainability of their effect is questionable. The meta-analysis was significantly limited by issues of validity, heterogeneity, small sample size and outcome definition. Future research should adhere to current recommendations for IBS treatment trials and should focus on the long-term effects of treatment.