Supplementary Table. Data Extraction Tables

Colonoscopy		Conclusion	Supporting evidence						
Source	[Reference]		SR/MA	NR	RCT	NRCS	OS	CS	G
G1 (ACG, 2014)[15]	None	None							
G2 (AGA, 2015)[16]	None	None							
G3 (NICE, 2015)[18]	The following tests are not necessary to confirm the diagnosis in people who meet the IBS diagnostic criteria: -Ultrasound -Rigid or flexible sigmoidoscopy -Colonoscopy, barium enema -Thyroid function test -Fecal ova and parasite test -Fecal occult blood -Hydrogen breath test (for lactose intolerance and bacterial overgrowth). [*All based on moderate and low quality evidence from RCTs and controlled trials.*]	None							
G7 (Europe, 2007)[17]	3.8 Alarm features While IBS should and can be diagnosed by its characteristic features, recognising when a patient does not have IBS is equally important. Several studies suggest that alarm features (box 5) improve the predictive value of the Rome criteria substantially in the outpatient setting.	Positive					2		

Reference	Study design	Participants	Intervention and comparator	Outcomes reported	Primary outcome
Vanner et al,[28] 1999	Observational study	N = 196 IBS without red flag sign (n = 98, retrospectively data collected) IBS with red flag sign (n = 98, prospectively collected)		Absence of alarm features and after a full history, examination, and investigation	The predictive value of the Rome criteria and absence of so-called "red flags" of clinical practice for diagnosing irritable bowel syndrome.
Hammer et al,[27] 2004	Observational study	N = 568 IBS (n = 214), FD (n = 70), organic diseases of the upper gastrointestinal tract (n = 66), or organic diseases of the lower gastrointestinal tract (n = 250)		Symptom questionnaire, alarm symptom, GI risk factors (pain, radiating pain, looser bowel movement, diarrhea, reflux)	The value of alarm features in differentiating between organic disease and IBS and FD
Whitehead et al,[31] 2006	Retrospective study	1434 patients with clinical diagnoses of irritable bowel syndrome, abdominal pain, diarrhea or constipation, who also completed questionnaires to identify Rome II criteria for irritable bowel syndrome and red flag symptoms.		Rome II symptom, red flag sign	The positive predictive value of the Rome II criteria for diagnosing irritable bowel syndrome can be enhanced by excluding red flag symptoms suggestive of organic diseases.
Black et al,[32] 2012	Observational study	IBS (n = 200) : red flag sign (+)		Rome III symptom questionnaire, red flag sign	To examine the yield of testing for "red flags"

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Source	Low FODMAP diet [Reference]	Conclusion	Supporting evidence						
			SR/MA	NR	RCT	NRCS	OS	CS	G
G1 (ACG, 2014)[15]	The third study examined the role of FODMAPs. Forty-one IBS patients were randomized to a low-FODMAP diet or their regular (habitual) diet for 4 weeks.[1] Of those randomized to the low-FODMAP diet, 68% (13/19) reported adequate control of their symptoms compared with 5/22 (23%) of the habitual diet group ($P = 0.005$). Stool consistency did not differ between groups; stool frequency was less in the low-FODMAP diet group. A significant limitation of this study was the lack of blinding regarding the dietary intervention.	Positive			1				
G2 (AGA, 2015)[16]	None	None			3				
G3 (NICE, 2015)[18]	If a person's IBS symptoms persist while following general lifestyle and dietary advice offer advice on further dietary management. Such advice should: - Include single food avoidance and exclusion diets—for example, a low FODMAP diet (updated recommendation.) -Be given only by a healthcare professional with expertise in dietary management. (New recommendation.) [Based on very low quality RCTs and controlled trials.]	Positive							
G7 (Europe, 2007)[17]	None	None							

Reference	Study design	Participants	Intervention and comparator	Outcomes reported	Primary outcome
Halmos et al,[34] 2014	RCT, crossover	N = 30 Australia, white people, control 8, IBS 30	Low FODMAP diet (< 0.5 g) for 21 days compared with typical Australian diet	Overall symptoms (low FODMAP diet 22.8, control 44.9, $P < 0.001$)	IBS symptom reduction, 100 mm visual analogue scale
Staudacher et al,[39] 2011	RCT	N = 43 IBS patents with diarrhea/bloating symptoms 82 using NICE criteria, stand diet (n = 38), low FODMAP diet (n = 43)	Low FODMAP diet (dietary advice, dietitian) for 4 weeks compared with habitual diet	Symptom response (low FODMAP diet 76%, control 54%, $P = 0.038$) Overall symptom response (low FODMAP diet 86%, control 49%, $P < 0.001$) Bloating improvement (low FODMAP diet 82%, control 49%, $P = 0.002$) Abdominal pain improvement (low FODMAP diet 85%, control 61%, $P = 0.023$)	IBS symptom improvemnt, questionnaires
Staudacher et al,[38] 2012	Controlled trial	N = 41 18-65 yr old with IBS symptoms, Rome III, GI symptom scale (4 point scale)	4 weeks, habitual diet (n = 22), low FODMAP diet (n = 19)	Overall symptoms (low FODMAP diet 75%, control 36%, $P = 0.006$) Bloating (low FODMAP diet 70%, control 31%, $P = 0.007$) Abdominal pain (low FODMAP diet 68%, control 49%, $P = 0.070$)	Daily symptom score improvement after 4 weeks

FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; SR, systemic review; MA, meta-analysis; NR, nonsystematic, narrative review; RCT, randomized controlled trial; NRCS, non-randomized comparative study; OS, observational study; CS, case series; G, guidelines; ACG, American College of Gastroenterology; AGA, American Gastroenterological Association; NICE, National Institute for Health and Care Excellence; IBS, irritable bowel syndrome.

Rifaximin		Supporting Evidence						
Source	[Reference]	SR/MA	NR	RCT	NRCS	OS	CS	G
G1 (ACG, 2014)[15]	Antibiotics in IBS: The poorly absorbable antibiotic rifaximin is effective at reducing total IBS symptoms and bloating in diarrhea predominant IBS. Recommendation: weak. Quality of evidence: moderate.	0	0	5	0	0	0	0
G2 (AGA, 2014)[16]	The overall quality of evidence across all critical outcomes for rifaximin was moderate.	0	0	4	0	0	0	0
G3 (NICE, 2015)[18]	Not described	0	0	0	0	0	0	0
G4 (Europe, 2007)[17]	A similar result has been seen in an RCT of rifamixin which showed benefit lasting up to 10 weeks after treatment.	0	0	2	0	0	0	0

Reference	Study design	Participants	Intervention and comparator	Outcomes reported	Primary outcome
Pimentel et al,[93] 2006	RCT	87 patients who met Rome I criteria for IBS and were enrolled from December 2003 to March 2005.	Participants who met enrollment criteria were randomly assigned to receive 400 mg of rifaximin 3 times daily for 10 days (n = 43) or placebo (n = 44). Eighty participants completed rifaximin therapy or placebo, and follow-up data were available for at least 34 participants per study group at any time point thereafter.	Over the 10 weeks of follow-up, rifaximin resulted in greater improvement in IBS symptoms ($P = 0.02$). In addition, rifaximin recipients had a lower bloating score after treatment.	Rifaximin improves IBS symptoms for up to 10 weeks after the discontinuation of therapy.
Pimentel et al,[94] 2011	RCT	A total of 1260 patients who had IBS without constipation were enrolled in the studies (623 patients in TARGET 1 and 637 in TARGET 2) and underwent randomization at one of 179 investigative sites in the United States (1217 patients) and Canada (43 patients).	In 2 identically designed, phase 3, double-blind, placebo-controlled trials (TARGET 1 and TARGET 2), patients who had IBS without constipation were randomly assigned to either rifaximin at a dose of 550 mg or placebo, 3 times daily for 2 weeks, and were followed for an additional 10 weeks.	Significantly more patients in the rifaximin group than in the placebo group had adequate relief of global IBS symptoms during the first 4 weeks after treatment (40.8% vs 31.2%, $P = 0.01$, in TARGET 1; 40.6% vs 32.2%, $P = 0.03$, in TARGET 2; 40.7% vs 31.7%, $P < 0.001$, in the 2 studies combined). Similarly, more patients in the rifaximin group than in the placebo group had adequate relief of bloating (39.5% vs 28.7%, $P = 0.005$, in TARGET 1; 41.0% vs 31.9%, $P = 0.02$, in TARGET 2; 40.2% vs 30.3%, $P < 0.001$, in the 2 studies combined). In addition, significantly more patients in the rifaximin group had a response to treatment as assessed by daily ratings of IBS symptoms, bloating, abdominal pain, and stool consistency. The incidence of adverse events was similar in the 2 groups.	Among patients who had IBS without constipation, treatment with rifaximin for 2 weeks provided significant relief of IBS symptoms, bloating, abdominal pain, and loose or watery stools.

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Reference	Study design	Participants	Intervention and comparator	Outcomes reported	Primary outcome
Sharara et al,[92] 2006	RCT	One hundred and twenty-four patients were enrolled (63 rifaximin and 61 placebo).	Randomized double-blind placebo-controlled trial consisting of three 10-day phases: baseline (phase 1), treatment with rifaximin 400 mg b.i.d. or placebo (phase 2), and post-treatment period (phase 3).	At the end of phase 2, there was a significant difference in global symptom relief with rifaximin versus placebo (41.3% vs 22.9%, $P = 0.03$). This improvement was maintained at the end of phase 3 (28.6% vs 11.5%, $P = 0.02$). Mean cumulative and bloating-specific scores dropped significantly in the rifaximin group ($P < 0.05$). Among patients with IBS, a favorable response to rifaximin was noted (40.5% vs 18.2%; $P = 0.04$) persisting by the end of phase 3 (27% vs 9.1%; $P = 0.05$). H_2-breath excretion dropped significantly among rifaximin responders and correlated with improvement in bloating and overall symptom scores ($P = 0.01$).	Rifaximin is a safe and effective treatment for abdominal bloating and flatulence, including in IBS patients. Symptom improvement correlates with reduction in H_2-breath excretion.
Lembo et al,[135] 2008	RCT	Baseline demographics were similar between the RFX (n = 191) and PBO (n = 197) groups.	The primary comparison consisted of 2 groups of adult patients with IBS-D (Rome II) that received RFX 550 mg twice daily or PBO for 14 days, followed by an additional 14 days of PBO in both groups and a 12-week follow-up phase. The follow-up phase included only patients who had adequate relief by week 4.	During the treatment period, a significantly larger portion of patients in the RFX versus PBO group reported successful relief in SGA (52% vs 44%, respectively; $P = 0.03$) and BL (46% vs 40%, respectively; $P = 0.04$). RFX also significantly improved both SGA and BL in ≥ 2 of 4 weeks ($P < 0.05$); during all 4 weeks ($P = 0.02$); and at week 3 ($P < 0.02$) and week 4 ($P < 0.02$). At the end of the treatment phase (week 4), more patients in the RFX group achieved relief of SGA (53%) and BL (50%) versus the PBO group (43% and 42%, respectively; $P = 0.01$). The beneficial effects of RFX versus PBO was maintained during the 12 weeks of follow-up. At the end of follow-up, RFX improved SGA versus PBO (62% vs 49%, respectively; $P < 0.05$) and BL versus PBO (59% vs 51%, respectively; $P < 0.05$). The safety profiles were similar between RFX and PBO.	In patients with IBS-D, rifaximin 1100 mg/d for 14 days significantly improved SGA and BL with sustained response throughout the 12 weeks of follow-up. This study supports the important role of RFX in the treatment of patients with IBS-D.

RCT, randomized controlled trial; IBS, irritable bowel syndrome; RFX, rifaximin; PBO, placebo; IBS-D, diarrhea-dominant IBS; SGA, global IBS symptoms; BL, IBS-associated bloating.

Source	Probiotics [Reference]	Conclusion	Supporting Evidence						
			SR/MA	NR	RCT	NRCS	OS	CS	G
G1 (ACG, 2014)[15]	Probiotics in IBS: Taken as a whole, probiotics improve global symptoms, bloating, and flatulence in IBS. Recommendations regarding individual species, preparations, or strains cannot be made at this time because of insufficient and conflicting data. Recommendation: weak. Quality of evidence: low.	Positive	2		23				
G2 (AGA, 2015)[16]	None								
G3 (NICE, 2015)[18]	*Only remarks*: "Advise people who choose to try probiotics to take the product for at least 4 weeks, at the dose recommended by the manufacturer, while monitoring the effect."								
G7 (Europe, 2007)[17]	Five randomised placebo controlled trials of probiotics have shown benefit for some symptoms, notably bloating and flatulence, using a variety of probiotic agents including *Lactobacillus rhamnosus* plantarum and VSL#3, a mixture of lactobacilli, bifidobacteria, and a *streptococcus*.	Positive			5				

Reference	Study design	Participants	Intervention and comparator	Outcomes reported	Primary outcome
Moayyedi et al,[136] 2010	systemic review	19 RCTs (18 papers) in 1650 patients with IBS There were 10 RCTs involving 918 patients Fifteen trials assessing 1351 patients	probiotics with placebo or no treatment	Probiotics were statistically significantly better than placebo (RR of IBS not improving = 0.71; 95% CI 0.57 to 0.88) with a NNT = 4 (95% CI 3 to 12.5).	IBS symptoms
Ford et al,[137] 2014	systemic review	3216 citations	Compared prebiotics, probiotics, or synbiotics with placebo or no therapy	The RR of IBS symptoms persisting with probiotics vs placebo was 0.79 (95% CI 0.70-0.89). Probiotics had beneficial effects on global IBS, abdominal pain, bloating, and flatulence scores.	IBS symptoms
Enck et al,[138] 2008	RCT	297 patients with lower abdominal symptoms diagnosed as IBS	Treated for 8 weeks by the compound ProSymbioflor ([R]) (Symbiopharm GmbH, Herborn, Germany)/ assessed the presence of core IBS symptoms	The responder rate in GSS to the drug was 102/149 (68.5%) in comparison to placebo with 56/148 (37.8%) ($P < 0.001$), the improvement in APS was 108/149 (72.5%) and 66/148 (44.6%) respectively. The NNT was 3.27 for GSS and 3.59 for the APS report.	Responders had at least a 50% decrease in GSS and in APS reports at ≥ 1 visit during treatment

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Reference	Study design	Participants	Intervention and comparator	Outcomes reported	Primary outcome
Cha et al,[107] 2012	RCT	Fifty patients with IBS-D	Treatment by placebo or probiotic mixture was taken daily for 8 weeks.	The proportion of adequate relief was consistently higher in the probiotics group than in the placebo group throughout the 10-week period ($P < 0.05$). The proportion of responders was significantly higher in the probiotics group than in the placebo group (48% vs. 12%, $P = 0.01$).	Adequate relief of overall IBS symptoms, effects on individual symptoms, stool parameters, and quality of life.
Ringel-Kulka et al,[139] 2011	A double-blind, placebo-control clinical trial	Sixty patients (probiotic, n = 31; placebo, n = 29	Probiotic bacteria L-NCFM and B-LBi07 twice a day (2×10^{11} CFU/day) versus placebo over 8 weeks	Abdominal bloating improved in the probiotics compared with the placebo group at 4 weeks (4.10 vs 6.17, $P = 0.009$; change in bloating severity $P = 0.02$) and 8 weeks (4.26 vs 5.84, $P = 0.06$; change in bloating severity $P < 0.01$).	Global relief of gastrointestinal symptoms and satisfaction with treatment
Niedzielin, et al,[101] 2001	RCT	Forty patients	LP299V in liquid suspension (n = 20)/placebo (n = 20)	With regards to all IBS symptoms an improvement was noted in 95% of patients in the LP299V group vs 15% of patients in the placebo group ($P < 0.0001$)	Clinical examination, GI symptoms by applying a scoring system.
Agrawal et al,[140] 2009	A single center, randomized, double-blind, controlled, parallel group study	Population of 34 patients	Patients consumed the test product or control product for 4 weeks/ patients consumed the test product or control product for 4 weeks	Compared with control product, the test product resulted in a significant reduction in the percentage change in maximal distension (median difference -39%, 95% CI [-78, -5]; $P = 0.02$) and a trend towards reduced mean distension during the day (-1.52 cm [-3.33, 0.39]; $P = 0.096$). An acceleration of orocaecal (-1.2 hr [-2.3,0]; $P = 0.049$) as well as colonic (-12.2 hr [-22.8, -1.6]; $P = 0.026$) transit was observed and overall symptom severity (-0.5 [-1.0, -0.05]; $P = 0.032$) also improved.	Abdominal distension, orocaecal and colonic transit time.
Nobaek et al,[102] 2000	RCT	Patients fulfilling the Rome criteria, without a history of malabsorption, and with normal blood tests underwent a sigmoidoscopy with biopsy	Receiving 400 mL per day of a rosehip drink containing 5 x 10^7 CFU/mL of *Lactobacillus plantarum* (DSM 9843) and 0.009 g/mL oat flour weeks/placebo	Flatulence was rapidly and significantly reduced in the test group compared with the placebo group (number of days with abundant gas production, test group 6.5 before, 3.1 after vs 7.4 before and 5.6 after for the placebo group). Abdominal pain was reduced in both groups. At the 12-month follow-up, patients in the test group maintained a better overall GI function than control patients.	IBS symptoms

RCT, radomized controlled trial; IBS-D, diarrhea-dominant irritable bowel syndrome; GI, gastrointestinal.