Web supplement

Table 1. Placebo-Controlled Trials of IBS Medications

Medication	Patients; IBS Subtype	Dose; Duration	Study Design	Clinical Efficacy Outcomes
Loperamide[7]	N=60; males and females; IBS-All	4 mg QHS; 3 wks	RCT double-blind	**Global Improvement:** Significant improvement **Abdominal Pain:** Significant decrease in days with colicky pain in subgroup of N=21 with IBS-A and abdominal pain **Stool Form/Consistency:** Significant improvement in stool in subgrps of N=16 IBS-painless diarrhea and N=21 with IBS-A and abdominal pain **Frequency:** Significant improvement in stool frequency in

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				subgrps of N=16 IBS-painless diarrhea and N=21 with IBS-A and abdominal pain
Loperamide[8]	N=28; males and females; IBS-All	2 mg BID, then titrate to max 12 mg; 5 wks (mean dose dose ~ 4.8 mg/d)	RCT double-blind crossover	**Stool Form/Consistency, Urgency, Frequency, Borborygmi:** Significant improvement
Loperamide[9]	N=90; males and females; IBS-All	2 mg QHS, then titrate to max 6 mg; 5 wks (mean dose dose ~ 3 mg/d)	RCT double-blind	**Stool Form/Consistency, Frequency:** Significant improvement
Loperamide[47]	N=25; males and females; IBS-D	2 mg QHS, titrated Qwk to max 8 mg	RCT double blind	**Global Improvement, Abdominal Pain, Stool Form/Consistency, Urgency :**

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		QHS; 13 wks		Significant improvement **Frequency, Flatulence, Borborygmi:** No Significant improvement
Ispaghula husk[10]	N=80; males and females; IBS-All	3.6 gm sachet TID; 12 wks	RCT double-blind	**Global Improvement:** Significant improvement **Frequency:** Significant decrease in days with no bowel movement
Ispaghula husk[11]	N=20; males and females; IBS-All	30 gm QD; 4 wks	RCT double-blind crossover; 7-10 d washout	**Global Improvement:** Significant improvement **Frequency:** No improvement
Ispaghula	N=80; males and	3 gm sachet BID; 4	RCT double-blind	**Global Improvement:**

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husk/poloxamer 188[12]	females; IBS-All	wks		No significant difference in resolution or improvement in symptoms
Ispaghula husk [13]	N=12; males and females; IBS-All	3.5 gm BID; 16 wks	RCT double-blind	**Global Improvement:** Significant improvement
Ispaghula husk[14]	N=77; males and females; IBS-All	6.4 gm TID; 8 wks	RCT double-blind	**Global Improvement, Abdominal Pain, or Stool Form/Consistency:** No significant improvement
Psyllium or Bran[15]	N=275; males and females; IBS-All	1) 10 gm psyllium, split BID, or 2) 10 gm bran split BID; 12 wks	RCT double-blind	**Global Improvement:** Psyllium-Significant improvement in symptom severity at month 3 only; Bran-No improvement **Abdominal Pain:** Psyllium-Significant relief at months 1 and 2 only, but no change in severity; Bran-Significant relief at month 3 only, but no

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				change in severity
Lubiprostone[45]	N=193; males and females; IBS-C	8, 16, or 24 mcg BID; 12 wks	RCT double-blind; dose ranging; 2 wk follow-up	**Global Improvement:** Significant improvement at 28 days with 24 mcg BID dose **Adominal Pain:** Significant trend for improvement in abdominal pain at 28 days; trend not significant at 3 mos **Bloating:** Significant trend for improvement; trend not significant at 3 mos **Stool Form/Consistency:** Significant improvement limited to 24 mcg BID after 1 mo

Medication	Patients; IBS Subtype	Dose; Duration	Study Design	Clinical Efficacy Outcomes
				Frequency: Significant improvement
Amitriptyline[16]	N=40; Males and females; IBS-All	25 mg x 1 wk titrated to 50 mg x 1 wk, then 75 mg QHS; 12 wks	RCT double-blind	**Global Improvement, Abdominal Pain:** Significant improvement **Frequency, Flatulence:** No significant improvement
Amitriptyline[17]	N=33 adolescents; males and females; IBS-All	30-50 kg:10 mg; 50-80kg:20 mg; >80kg 30 mg QHS; 8 wks	RCT double-blind; 3 wk follow-up	**Global Improvement:** Significant improvement **Abdominal Pain:** Significant improvement in pain relief isolated to periumbilical and right lower quadrant areas; No improvement in abdominal pain intensity and frequency
Amitriptyline[48]	N=54; Males and	10 mg QHS; 8 wks	RCT double-blind	**Global Improvement, Stool Form/Consistency,**

Medication	Patients; IBS Subtype	Dose; Duration	Study Design	Clinical Efficacy Outcomes
	females; IBS-D			**Incomplete Evacuation:** Significant improvement **Abdominal Pain, Flatulence, Mucus Passage:** No improvement
Trimipramine[18]	N=61; males and females; IBS-All	50 mg QD; 4 wks	RCT double-blind	**Mucus:** Significant improvement
Trimipramine[19]	N=428; males and females; IBS-All	50 mg QHS, 10 mg QAM plus 40 mg QPM, 35 mg QPM, 10 mg TID; $\geq$ 6wks	RCT double-blind	**Abdominal Pain:** Significant improvement limited to doses of 50 mg QHS and 10 mg QAM plus 40 mg QPM **Frequency:** No significant improvement
Imipramine[23]	N=51; males and females; IBS-All	25 mg x 2 weeks, then 50 mg QHS;	RCT double-blind	**Global Improvement, Abdominal Pain, Frequency:**

Medication	Patients; IBS Subtype	Dose; Duration	Study Design	Clinical Efficacy Outcomes
		12 weeks		No significant improvement
Desipramine[21]	N=28; males and females; IBS-All	50 mg a 1 wk, 100 mg x 1 wk, then 150 mg QHS; 6 wks	RCT double-blind crossover; 2 wk washout	**Global Improvement:** Improvement, significance not reported **Abdominal Pain:** Significant improvement in IBS-D subgroup **Frequency:** Significant improvement
Desipramine[22]	N=31; males and females; IBS-All depressed	150 mg QHS; 8 wks	RCT double-blind	**Abdominal Pain:** No significant improvement
Doxepin[20]	N=44; males and females; IBS-All	75 mg QHS; 6 wks	RCT double-blind; 4 wk follow-up	**Global Improvement, Abdominal Pain, Incomplete Evacuation:** Significant improvement

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Citalopram[23]	N=51; males and females; IBS-All	20 mg x 2 weeks, then 40 mg QAM; 12 weeks	RCT double-blind	**Global Improvement, Abdominal Pain, Frequency:** No significant improvement
Citalopram[24]	N=23; males and females; IBS-All non-depressed	20 mg x 3 wks, then 40 mg QD x 3 wks; 6 wks	RCT crossover; 3 wk washout	**Global Improvement, Bloating, Urgency, Incomplete Evacuation, Abdominal Pain:** Significant improvement
Fluoxetine[25]	N=40; males and females; IBS-All non-depressed	20 mg QHS; 6 wks	RCT double-blind	**Global Improvement, Abdominal Pain, Urgency, Incomplete Evacuation, Bloating, Flatulence:** No improvement
Fluoxetine[26]	N=44; males and females; IBS-C	20 mg QD; 12 wks	RCT double-blind; 4 wk follow-up	**Bloating, Stool Form/Consistency, Frequency:** Significant improvement
Paroxetine[27]	N=72; males and	12.5 mg titrated to	RCT double-blind	**Global Improvement:**

Medication	Patients; IBS Subtype	Dose; Duration	Study Design	Clinical Efficacy Outcomes
	females; IBS-All non-depressed	50 mg QD as tolerated; 12 weeks		Significant improvement **Abdominal Pain:** No improvement
Hyoscine butylbromide[13]	N=12; males and females; IBS-All	10 mg QID; 16 wks	RCT double-blind	**Global Improvement:** No significant improvement
Dicyclomine[46]	N=97; males and females; IBS-C	40 mg QID; 2 wks	RCT double-blind	**Global Improvement, Abdominal Pain:** Significant improvement
Peppermint Oil[28]	N=50; males and females; IBS-All	550 mg QD; 4 wks	RCT double-blind; 4 wk follow-up	**Global Improvement, Abdominal Pain, Bloating, Urgency, Incomplete Evacuation:** Significant improvement
Peppermint Oil[29]	N=110; males and females; IBS-All	187 mg TID or QID; 4 wks	RCT double-blind	**Abdominal Pain, Frequency, Flatulence, Borborygmi:** Significant improvement

Medication	Patients; IBS Subtype	Dose; Duration	Study Design	Clinical Efficacy Outcomes
Rifaximin[31]	N=87; males and females; IBS-All	400 mg TID x 10 days; 10 days	RCT double-blind placebo; 10 wk follow up	**Bloating:** Significant improvement
Rifaximin[49]	N=388; males and females; IBS-D	550 mg BID x 14 days; 14 days	RCT double-blind; 12 wk follow up	**Bloating:** Significant improvement in bloating during treatment and maintained for 12 weeks following treatment
Pregabalin[32]	N=26; males and females; IBS-All without psychiatric disorders	50 mg TID x 3 days titrated to 100 mg TID x 4 days, 150 mg TID x 4 days, then 200 mg TID; 3 wks	RCT double-blind	**Abdominal Pain:** Significant improvement in sensory threshold of abdominal pain; No difference in sensory threshold of moderate abdominal; **Urgency:** Significant improvement in sensory threshold

Medication	Patients; IBS Subtype	Dose; Duration	Study Design	Clinical Efficacy Outcomes
Gabapentin[30]	N=40; males and females IBS-D	100 mg TID x 3 days titrated to 200 mg TID x 2 days; 6 days	RCT double-blind	**Abdominal Pain, Bloating:** Significant improvement sensory threshold
Clonidine[50]	N=44; males and females; IBS-D	0.1 mg BID; 4 wks	RCT double-blind; dose-ranging; pilot study	**Global Improvement:** No significant improvement in wks with relief; Significant improvement in proportion of wks with relief **Stool Form/Consistency, Frequency:** No significant improvement
Octreotide[51]	N=46; males and females; IBS-D and A	20 mg IM q4wks; 8 wks	RCT double-blind	**Global Improvement, Abdominal Pain, Frequency, Bloating, Flatulence, Incomplete Evacuation:**

Medication	Patients; IBS Subtype	Dose; Duration	Study Design	Clinical Efficacy Outcomes
				No significant improvement **Stool Form/Consistency:** Significant improvement
Probiotics: L. acidophilus[15]	N=40; males and females; IBS-All	$2x10^9$ cfu BID; 4 wks	RCT double-blind	**Abdominal Pain, Incomplete Evacuation:** Significant improvement **Stool Form/Consistency, Frequency:** No significant improvement
Probiotics: B. infantis[33]	N=362; males and females; IBS-All	10^8 cfu QD; 4 wks	RCT double-blind; dose-ranging; 2 wk follow-up	**Global Improvement, Abdominal Pain, Bloating, Incomplete Evacuation, Flatulence:** Significant improvement **Urgency, Mucus:** No significant improvement

Medication	Patients; IBS Subtype	Dose; Duration	Study Design	Clinical Efficacy Outcomes
Probiotics: E. coli[34]	N=298; males and females; IBS-All	0.75 ml TID x 1 wk, then 1.5 ml TID ($1.5\text{-}4.5\text{x}10^7$ cfu/mL); 8 wks	RCT double-blind	**Global Improvement, Abdominal Pain, Stool Form/Consistency, Bloating:** Significant improvement **Frequency:** No significant improvement
Probiotics: E. coli and E. faecalis[35]	N=297; males and females; IBS-All	0.75 ml TID x 1 wk, 1.5 ml TID x 2 wks, then 2.25 ml TID ($3\text{-}9\text{x}10^7$ cfu/1.5 mL); 8 wks	RCT double-blind	**Global Improvement, Abdominal Pain:** Significant
Probiotics: L. plantarum[36]	N=40; males and females; IBS-All	$5\text{x}10^7$ cfu BID; 4 weeks	RCT double-blind	**Global Improvement, Abdominal Pain:** Significant improvement
Probiotics:BLLS***	N=100; males and	$1\text{x}10^{10}$ cfu QD; 4	RCT double-blind	**Global Improvement:**

Medication	Patients; IBS Subtype	Dose; Duration	Study Design	Clinical Efficacy Outcomes
[37]	females; IBS-All	wks		No significant improvement **Abdominal Pain:** Significant improvement between wks 1 and 4; No significant improvement in satisfactory relief **Flatulence:** Significant improvement **Frequency:** Significant improvement in the IBS-C subgroup
Probiotics: B. coagulans[38]	N=44; males and females; IBS-D	8 x 10^9 cfu QD; 8 wks	RCT double-blind	**Abdominal Pain, Bloating:** Significant improvement
Probiotics:LBP*[39]	N=86; males and females; IBS-All	1.2 dL QD (1.7 x 10^7 cfu of each strain/mL); 20 wks	RCT double-blind; 3 wk follow-up	**Abdominal Pain, Borborygmi:** Significant improvement **Flatulence:**

Medication	Patients; IBS Subtype	Dose; Duration	Study Design	Clinical Efficacy Outcomes
				No significant improvement
Probiotics: B. infantis[40]	N=75; males and females; IBS-All	10^{10} cfu QD; 8 wks; 4 wk follow up	RCT double-blind	**Abdominal Pain, Incomplete Evacuation:** Significant improvement **Bloating:** No significant improvement
Probiotics:LBP*[41]	N=81; males and females; IBS-All	8-9 x 10^{9} cfu QD; 24 wks	RCT double-blind	**Abdominal Pain:** No significant improvement; significant improvement in % of pts with dec abdominal pain **Urgency, Incomplete Evacuation, Borborygmi:** Significant improvement **Flatulence:** No significant improvement; significant improvement in % of pts with decreased flatulence
Probiotics:BLS**[42]	N=48; males and	4.5x10^{6} cfu QD; 4	RCT double-blind	**Abdominal Pain,**

Medication	Patients; IBS Subtype	Dose; Duration	Study Design	Clinical Efficacy Outcomes
	females; IBS-All	wks		**Bloating, Urgency:** No significant improvement **Flatulence:** Significant improvement
Probiotics: L. reuteri[43]	N=54; males and females; IBS-All	10^8 cfu, 4 tabs daily x 7 d, then 2 tabs QD; 22 wks	RCT double-blind	**Global Improvement, Abdominal Pain, Bloating, Incomplete Evacuation, Flatulence:** No significant improvement
Probiotics: L. GG[44]	N=50; males and females; IBS-All children	10^{10} cfu BID; 6 wks	RCT double-blind	**Global Improvement, Abdominal Pain:** No significant improvement

*LBP: L. rhamnosus, B. breve and P. freudenreichii

**BLS:Bifidobacterium, Lactobacillus, S. salivarius

***BLLS:B. longum, L. acidophilus, L. lactis, S. thermophilus