TABULATED SUMMARY OF DOUBLE BLIND THERAPEUTIC TRIALS IN IBS

	Author year	Study design	Treatment population	Treatment	Results
Anti-spasmodics	Wheatley 1976	Crossover placebo-controlled	29 (no diagnostic criteria)	Dicyclomine 20mg tid	No change in pain symptoms - investigator assessed
	Ritchie 1979	Randomised placebo-controlled, multiple agents	96 (no diagnostic criteria)	Hyoscamine 10mg qid vs ispaghula vs lorazepam, 12 weeks	No change in global symptoms - investigator and patient assessed
	Fielding 1980	Randomised placebo-controlled	60	Trimebutine 200mg tid plus high fibre vs high fibre, 6 months	No advantage of trimebutine plus high fibre over placebo plus high fibre
	Luttecke 1980	Randomised placebo-controlled crossover; three trials -	Trial 1,2: 45 Trial 3: 40	Trial1: trimebutine 200mg tid, 3 days Trial2: trial 100mg tid, 3 days Trial3: trimebutine 200mg tid vs mebeverine 100mg qid, 2 week	High dose trimebutine improves pain and distension ($p<0.001$) – no significant effect with low dose. No difference between anti-spasmodics
	Page 1981	Randomised placebo-controlled	71 (no diagnostic criteria)	Dicyclomine 40mg qid, 2 weeks	Improved global and pain/bowel function
	Ferrari 1986	Randomised trial of two anti-	40	Cimetropium 50mg bid vs otilonium	Improved pain and global score vs baseline (both

		spasmodics		20mg bid, 6 weeks	p<0.05)
Anti-spasmodics	Ghidini 1986	Randomised placebo-controlled, multiple agents	90	Rociverine 20mg tid vs trimebutine 100mg tid, 60 days	Improved pain and bowel function both agents over placebo
	Kruis 1986	Randomised placebo-controlled, multiple agents	120	Mebeverine 135mg tid vs open label wheat bran 5gm tid vs placebo, 16 weeks	No advantage over placebo for mebeverine
	Tudor 1986	Crossover placebo-controlled trial of two anti-spasmodics	45	Mebeverine 135mg tid vs alverine 60mg tid,4 weeks	Improved pain for both drugs vs placebo (p<0.02 for both)
	Piai 1987	Randomised placebo-controlled	30 (all c-IBS)	Cimetropium 50mg tid, 12 weeks	Improved global score (p<0.01)
	Centonze 1988	Randomised placebo-controlled	48	Cimetropium 50mg tid, 6 months	Improved pain and global score (both p<0.01)
	Gilvarry 1989	Randomised placebo-controlled	24	Pirenzapine 50mg bid, 4 weeks	No advantage over placebo
	Dobrilla 1990	Randomised placebo-controlled	70	Cimetropium 50mg tid, 12 weeks	Improved pain (p=0.0005) and global score (p=0.039)
	Schaffstein 1990	Randomised placebo-controlled	199	Trimebutine 200mg tid vs mebeverine 135mg tid, 28 days	Improved pain with both agents (p=0.0001) compared to baseline
	Baldi 1991	Randomised placebo-controlled	72	Otilonium 40mg tid, 4 weeks	Improved pain and bloating (both p<0.02)
	Awad 1995	Randomised	40 (Rome I)	Pinaverium 50mg	Improved pain and bowel

		placebo-controlled		tid, 3 weeks	function (p<0.01)
Anti-spasmodics	Battaglia 1998	Randomised placebo-controlled	378	Otilonium 40mg tid, 15 weeks	Improved pain (p<0.01), distension (p<0.05) and global score (p<0.01)
	Glende 2002	Randomised placebo-controlled	378 (Rome I)	Otilonium 40mg tid, 15 weeks	No significant advantage over placebo
Antidepressants	Heefner 1978	Randomised placebo-controlled	44	Desipramine up to 150mg, 8 weeks	Improved QoL (92% vs 60%)
	Steinhart 1981	Crossover placebo-controlled	14	Amitriptyline up to 50mg, 4 weeks	“Improved” symptoms, p<0.08
	Myren 1982	Randomised placebo-controlled	61	Trimipramine up to 25mg, 4 weeks	Improved global symptoms 83% vs 68%
	Myren 1984	Randomised placebo-controlled	428	Trimipramine up to 60mg, 6 weeks	Improved pain with higher doses, but tiredness in early stage
	Greenbaum 1987	Crossover placebo-controlled	28 (9 c-IBS, 19 d-IBS)	Desipramine 150mg vs atropine, 6 weeks	Global improvement 54% vs 21% atropine vs 18% placebo; d-IBS did best
	Vij 1991	Randomised placebo-controlled	50 (predominantly male)	Doxepin up to 75mg, 6 weeks	Improved pain and bowel function – patient assessed
	Tanum 1996	Randomised placebo-controlled	49	Mianserin 120mg, 7 weeks	Improved pain and overall function (p<0.001)
	Rajgopalan 1998	Randomised placebo-controlled	40 (Rome I)	Amitriptyline up to 75mg, 12 weeks	Improved pain and global symptoms (p<0.01), abdominal pain (p<0.05) and functioning (p<0.001)

SSRIs	Creed 2003	Randomised placebo-controlled, multiple interventions	257 (Rome I)	Paroxetine 20mg vs psychotherapy vs standard care, 12 weeks	Global improvement ($p<0.001$) and physical aspects QoL ($p<0.001$) vs standard care
	Kuiken 2003	Randomised placebo-controlled	40 (Rome I)	Fluoxetine 20mg, 6 weeks	Non-significant improvements in pain and global score
	Tabas 2004	Randomised placebo-controlled, multiple agents	110 (Rome I)	Paroxetine 10-20mg + high fibre diet vs high fibre diet, 12 weeks	Global improvement ($p<0.01$) and less food avoidance ($p<0.03$)
	Tack 2006	Crossover placebo-controlled	23 (Rome II, 4 c-IBS, 5 d-IBS, 14 a-IBS)	Citalopram up to 40mg, 6 weeks	Improved pain, bloating QoL (all $p<0.05$). (Effect independent of mood.)
Bulking agents	Soltoft 1976	Randomised placebo-controlled	52	Wheat bran 30gm/day, 6 weeks	No advantage over placebo
	Manning 1977	Randomised, NOT placebo-controlled	24	Wheat fibre 20gm/day, 6 weeks	Improved pain and bowel function
	Ritchie 1979	Randomised placebo-controlled	24	Ispaghula 30mg bid, 12 weeks	Improved ease of bowel opening
	Logstreth 1981	Randomised placebo-controlled	60	Psyllium 6.4gm tid, 8 weeks	No advantage over placebo
	Golecha 1982	Crossover placebo-controlled	26	Ispaghula – uncertain dose, 3 weeks	Improved ease of bowel opening

Bulking agents	Arthurs 1983	Randomised placebo-controlled	78	Ispaghula-polaxamer, 2 sachets/day, 4 weeks	No advantage over placebo
	Arfmann 1985	Crossover placebo-controlled	18	Wheat bran 30gm/day, 6 weeks	No advantage over placebo
	Lucey 1987	Crossover placebo-controlled	28	Wheat bran 12.8gm/day, 12 weeks	No advantage over placebo
	Prior 1987	Randomised placebo-controlled	80	Ispaghula 30mg tid, 12 weeks	Global improvement 82% vs 53%, bowel function improved ($p<0.03$ both)
	Cook 1990	Crossover placebo-controlled	9	Corn fibre 10gm bid, 12 weeks	No advantage over placebo
	Jalihal 1990	Crossover placebo-controlled	20	Ispaghula 30mg qid, 4 weeks	Improved global score and bowel satisfaction (both $p<0.001$)
	Fowlie 1992	Randomised placebo-controlled	49 (c-IBS, a-IBS)	Fibre (soluble and insoluble) 4.1gm qid, 3 months	No advantage over placebo
	Toskes 1993	Crossover placebo-controlled	23 (all IBS subtypes)	Calcium polycarbonate 1.5gm qid, 12 weeks	c-IBS and a-IBS patients “preferred” active treatment, no symptom differences found
	Snook 1994	Crossover placebo-controlled	71	Wheat bran 40gm/day, 7 weeks	No advantage over placebo
	Aller 2004	Randomised	56 (Rome II)	Fibre 10.4gm qid	Improved pain, bowel

		placebo-controlled		vs 30gm/day, 3 months	function and global scores (all p<0.05)
	Rees 2005	Randomised placebo-controlled	28 (Rome I, c-IBS)	Coarse wheat bran 10-20gm qid, 8-12 weeks	No improvement in symptoms, increased stool weight (p<0.05)
Anti-diarrhoeals	Cann 1984	Crossover placebo-controlled	28	Loperamide 2-12mg/day, 5 weeks	Improved stool frequency and consistency and urgency (all p<0.05)
	Hovdenak 1987	Randomised placebo-controlled	58	Loperamide 4mg/day, 3 weeks	Improvement in patients with painless diarrhoea (stool frequency and consistency, p<0.01) and a-IBS (stool frequency and consistency, p<0.02)
	Lavo 1987	Randomised placebo-controlled	25 (d-IBS)	Loperamide 2-8mg/day	Improved global score (p<0.03), pain (p<0.02), stool consistency (p<0.001) and urgency (p<0.03)
	Efskind 1996	Randomised placebo-controlled	69	Loperamide 2-6mg/day, 5 weeks	Improved stool frequency and consistency (p<0.05)
$5HT_4$ agonists	Lefkowitz 1999	Randomised placebo-controlled	799 (Rome I c-IBS)	Tegaserod 4mg and 12mg qid, 12 weeks	Improved pain and bowel frequency (both p<0.01)
	Whorwell 2000	Randomised	799 (Rome I)	Tegaserod 2 or	Retrospectively defined

		placebo-controlled		6mg bid, 12 weeks	end-point of global improvement
$5HT_4$ agonists	Muller-Lissner 2001	Randomised placebo-controlled	881 (Rome I)	Tegaserod 2 or 6mg bid, 12 weeks	Global improvement over placebo 12.7% and 11.8% for 2 and 6mg respectively. Also improved pain and bowel function (both $p<0.05$)
	Kellow 2003	Randomised placebo-controlled	520 (Rome I)	Tegaserod 6mg bid, 12 weeks	Global improvement 62% vs 44% (tegaserod vs placebo, $p<0.0001$). Improved pain and bowel function
	Novick 2003	Randomised placebo-controlled	1519 (Rome I)	Tegaserod 6mg bid, 12 weeks	Improved global score ($p<0.05$) and rapid relapse on withdrawal
	Nyhlin 2004	Randomised placebo-controlled	647 (Rome II, no d-IBS)	Tegaserod 6mg bid, 12 weeks	Improved global state ($p<0.0001$)
	Tack 2004	Crossover placebo-controlled	2660 (Rome II, c-IBS)	Tegaserod 6mg bid, 4 weeks	Improved global score and pain (both $p<0.0001$) and improved aspects of QoL ($p<0.05$)
$5HT_3$ antagonists	Steadman 1994	Crossover placebo-controlled	14 (d-IBS)	Ondansetron 16mg tid, 4 weeks	Improved stool consistency ($p<0.05$)
	Goldberg 1996	Crossover placebo-controlled	9 (no criteria used)	Ondansetron 16mg tid, 4 weeks	Improved pain ($p=0.03$) and stool consistency ($p<0.01$)

	Maxton 1996	Crossover placebo-controlled	50 (Rome I,	Ondansetron 4mg tid, 4 weeks	Improved stool consistency (p=0.002) and frequency (p=0.035)
	Camilleri 1999	Randomised placebo-controlled	370 (Rome I, 53% female)	Alosetron 1, 2, 4 or 8mg bid, 12 weeks	Alosetron 1 and 2mg improved global score in women only (p<0.05). Improved bowel function and urgency in women only, all doses (p<0.05)
	Jones 1999	Randomised vs mebeverine	623 (Rome I)	Alosetron 1mg bid vs mebeverine 135mg tid, 12 weeks	58% vs 48% responders at trial end (alosetron vs mebeverine, respectively, p=0.009). Improved bowel function (p<0.01)
	Bardhan 1999	Randomised placebo-controlled	462 (Rome I, all d-IBS)	Alosetron 0.1, 0.5 and 2mg bid, 12 weeks	Improved pain and diarrhoea VAS (p<0.05) for 2mg dose only.
	Camilleri 2000	Randomised placebo-controlled	647 (Rome I)	Alosetron 1mg bid, 12 weeks	Adequate response in 41% vs 29% (p<0.05). Improved bowel function and urgency (all p<0.05)
	Lembo 2001	Randomised placebo-controlled	801 (Rome I)	Alosetron 1mg bid, 12 weeks	Global improvement 76% vs 33% (p<0.01)
	Camilleri 2001	Randomised placebo-controlled	626 (Rome I, all d-IBS)	Alosetron 1mg bid, 12 weeks	Improved pain, bowel function and urgency (all p<0.001)
	Chey 2004	Randomised placebo-controlled	714 (Rome I, all d-IBS)	Alosetron 1mg bid, 48 weeks	End trial greater overall relief (p=0.01) and urgency (p<0.001)

	Lembo 2004	Randomised placebo-controlled	492 (Rome II, all d-IBS)	Alosetron 1mg bid, 12 weeks	Improved global score and urgency (both p<0.001)
	Bradette 2004	Randomised placebo-controlled	792 (Rome I, all d-IBS)	Cilansetron 2mg tid, 6 months	Improved pain and bowel function at 3 and 6 months (all p<0.001)
	Coremans 2004	Subset analysis	3 month 205 d-IBS (men) 6 month 358 d-IBS (men)	Cilansetron 2mg tid, 6 months	Improved pain and bowel function at 3 and 6 months (p<0.002 at least). Global relief only at 3 months (p<0.001)
Other 5HT agents in development	Camilleri 2004	Randomised placebo-controlled	48 (Rome II, all c-IBS)	Renzapride 1, 2 or 4mg/day	No change in symptoms, but accelerated colon transit in highest dose (p<0.05)
	Henderson 2004	Randomised placebo-controlled	168 (Rome II, all a-IBS)	Renzapride 1, 2 or 4mg/day	No significant advantage over placebo
	Meyers 2004	Randomised placebo-controlled	510 (Rome II, all c-IBS)	Renzapride 2 or 4mg/day	Increased bowel frequency (p<0.005) and consistency (p<0.05)