Appendix F: Grading the evidence

Antidepressant review

Antimotility review

Antispasmodics review

CBT review

Hypnotherapy review

Laxatives review

Psychotherapy review

Evidence Summary: antidepressants review

Comparison: tricyclics versus placebo

Outcome	*Meta-analysis Evidence details*	*Summary Statistics*	*p(hetero) and 12*	*Comments:*	*Study Quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*Rating*
Global improvement of IBS symptoms (no. patients)	3 trials; 180 patients; from meta-analysis	RR=1.31 (95%CI 1.04, 1.64)	p=0.27; I2 =23%	Statistically significant in favour of tricyclics. NNT 6, for control group rate 22-68%	Good	Indirect setting-minor, secondary care OPD	Precise	Consistent	---	1/3 was CCT. 2/3 had some patients with depression. 1/3 primary care.	Moderate
Global IBS symptom score	1 trial; 28 patients; from RCT	MD=-8.86 (95%CI -24.02, 6.3)		Not statistically significant; scale not given	Good	Indirect setting-minor, secondary care OPD	Sparse data	Consistent	---	Small study (28 patients). Setting not stated. Drug from industry. Severe and refractory IBS. >5% with depression.	Moderate
No of patients with less pain	2 trials; 84 patients; from meta-analysis	RR=3.91 (95%CI 1.93, 7.93)	p=0.81; I2 =0%	Statistically significant, favours tricyclic NNT 2, for control group rate 16-18%.	Good	Indirect patients - minor, closely related conditn	Fairly wide CI	Consistent	---	60% IBS in 1/2 studies (Tanum & Malt); 24% dropouts in other (Vij). Secondary care. 1/2 had patients with depression; 1/2 had refractory IBS.	Moderate
Pain score	1 trial; 47 patients; from RCT	MD=-25.9 (95%CI -38.82, -12.98)		Statistically significant, favours tricyclic; scale 100	Good	Indirect patients - minor, comorbidity	Precise	Consistent	---	Tanum & Malt 60% patients IBS. Secondary care; refractory IBS	Moderate

Comparison: tricyclics versus placebo

Outcome	*Meta-analysis Evidence Details*	*Summary Statistics*	*p(hetero) and 12*	*Comments:*	*Study Quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*Rating*
Improvement in pain score	1 trial; 79 patients; from RCT	median diff=0.3 (95%CI 0, 0)		Statistically significant in favour of antidepressant; p<0.05; scale 0-4	Good	Indirect setting-minor, secondary care OPD	Precise	Consistent	---	Primary and secondary care; some patients had depression. Detail limited - German translation	Moderate
Improvement in feeling of fullness	1 trial; 79 patients; from RCT	Median diff=0.23 (95%CI 0, 0)		Not statistically significant; scale 0-4	Good	Indirect setting-minor, secondary care OPD	Precise	Consistent	---	Primary and secondary care; some patients had depression. Detail limited - German translation	Moderate
No of patients with improved bowel habit	1 trial; 44 patients; from RCT	RR=2.41 (95%CI 1, 5.79)		borderline significance; favours tricyclic; wide CI	Good	Indirect setting-minor, secondary care OPD	Wide CI	Consistent	---	Wide CI. 57% psychiatric comorbidities; secondary care.	Low

Comparison: SSRIs versus placebo/usual care

Outcome	Evidence details	Summary Statistics	p(hetero) and I2	Comments:	Study Quality	Directness	Imprecision	Inconsistency	Reporting Bias	GRADE Comments	Rating
Global improvement of IBS symptoms (no. patients)	3 trials; 254 patients; from meta-analysis	RR=1.8 (95%CI 1.38, 2.34)	p=0.48; I2 =0%	Statistically significant, favours SSRI. NNT 4, for control group rate 28-41%	Good	Indirect setting-minor, secondary care OPD	Precise	Consistent	---	1/3 had 34% discontinuing treatment in SSRI arm. 2/3 studies had patients with refractory IBS and 1/3 selected non-responders to placebo. 2/3 had patients with depression. Mainly	Moderate
Pain number of patients	1 trial; 34 patients; from RCT	RR=0.69 (95%CI 0.41, 1.16)		Not statistically significant	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	Consistent	Poor - studies, industry	Kuiken 2003. Non-depressed patients; refractory IBS. Tertiary referral. Sponsored by drug co.	Low
No of patients with less pain	1 trial; 66 patients; from RCT	RR=0.88 (95%CI 0.54, 1.45)		Not statistically significant	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	Consistent	---	Primary and secondary care. Tabas excluded pts with major psychiatric illness; but 33% had depression. Non-responders to placebo; refractory IBS.	Moderate
Pain score	1 trial; 153 patients; from RCT	MD=-9.2 (95%CI -18.35, -0.05)		Statistically significant, favours SSRI, scale 100	Good	Indirect setting-minor, secondary care OPD	Precise	Consistent	---	Pain severity at 3 months. Creed study. 34% discontinued treatment in SSRI arm, but ITT. Refractory IBS. Approx half pts had depression. Secondary care.	Moderate
No of patients with bloating	1 trial; 34 patients; from RCT	RR=1.25 (95%CI 0.66, 2.38)		Not statistically significant	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	Consistent	Poor - studies, industry	Kuiken 2003. Non-depressed patients; refractory IBS. Tertiary referral. Sponsored by drug co.	Low

Comparison: SSRIs versus placebo/usual care

Outcome	Evidence Details	Summary Statistics	p(hetero) and I2	Comments:	Study Quality	Directness	Imprecision	Inconsistency	Reporting Bias	GRADE Comments	Rating
No of patients with less bloating	1 trial; 66 patients; from RCT	RR=0.94 (95%CI 0.51, 1.76)		Not statistically significant	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	Consistent	---	Primary and secondary care. Tabas excluded pts with major psychiatric illness; but 33% had depression. Non-responders to placebo; refractory IBS.	Moderate
No of patients with improved bowel habit	1 trial; 66 patients; from RCT	RR=1.7 (95%CI 0.97, 2.97)		Not statistically significant, favours SSRI	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	Consistent	---	Primary and secondary care. Tabas excluded pts with major psychiatric illness; but 33% had depression. Non-responders to placebo; refractory IBS.	Moderate
SF36 mental health component	1 trial; 122 patients; from RCT	MD=4.2 (95%CI -0.45, 8.85)		Not statistically significant	Poor - incomplete follow-up	Indirect setting-minor, secondary care OPD	Precise	Consistent	---	32% loss to follow up in paroxetine arm; 34% discontinued treatment in SSRI arm, but ITT. Refractory IBS. Approx half pts had depression. Secondary care.	Low
SF36 physical health component	1 trial; 122 patients; from RCT	MD=2.9 (95%CI -0.23, 6.03)		Not statistically significant, favours antidepressant. Scale 0-100.	Poor - incomplete follow-up	Indirect setting-minor, secondary care OPD	Precise	Consistent	---	32% loss to follow up in paroxetine arm; 34% discontinued treatment in SSRI arm, but ITT. Refractory IBS. Approx half pts had depression. Secondary care.	Low
Number of patients discontinuing treatment	1 trial; 172 patients; from RCT	Peto OR=10.93 (95%CI 4.93, 24.23)		Statistically significant, favours placebo	Good	Indirect setting-minor, secondary care OPD	Wide CI	Consistent	---	Refractory IBS. Approx half pts had depression. Secondary care.	Moderate

Comparison: dose 1 versus Dose 2

Outcome	*Evidence Details*	*Summary Statistics*	*p(hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*Rating*
Global assessment	1 trial; 171 patients; from RCT	Median=0.2 (95%CI -1.74, 2.14)		Not statistically significant	Good	Indirect setting-minor, secondary care OPD	Precise	Consistent	---	50 vs 35mg. Physician assessment of effect of treatment. Primary & secondary care	Moderate
Global assessment	1 trial; 154 patients; from RCT	Median=1 (95%CI -0.55, 2.55)		Not statistically significant	Good	Indirect setting-minor, secondary care OPD	Precise	Consistent	---	50mg vs 3 x 10mg; Physician assessment of effect of treatment. Primary & Secondary care	Moderate
Global assessment	1 trial; 175 patients; from RCT	Median=0.2 (95%CI -1.66, 2.06)		Not statistically significant	Good	Indirect setting-minor, secondary care OPD	Precise	Consistent	---	50mg divided doses vs 35mg nocte. Physician assessment of effect of treatment. Primary & Secondary care. About 50% not taking drugs at start of study.	Moderate
Global assessment	1 trial; 158 patients; from RCT	Median=1 (95%CI -0.45, 2.45)		Not statistically significant	Good	Indirect setting-minor, secondary care OPD	Precise	Consistent	---	50mg divided doses vs 30mg in divided doses. Physician assessment of effect of treatment.Primary & Secondary care. About 50% not taking drugs at start of study.	Moderate

Evidence Summary: antimotiltiy agents review

Acute studies

Comparison: co-phenotrope versus placebo

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Stool freq	1 trial; 4 patients; from RCT; (crossover + washout design)	MD= -2.35 /day (95%CI -5.34, 0.64)		Not statistically significant; wide confidence interval	Poor - subgroup only	Direct	Sparse data	Consistent	---	Subgroup of 4 IBS patients; crossover study; 3 day duration	Low
Stool freq	1 trial; 15 patients; from RCT; (crossover + washout design)	MD= -2.29 /day (95%CI -4.47, -0.11)		Statistically significant, favours cophenotrope	Good	Indirect patients - minor, closely related conditn	Fairly wide CI	Consistent	---	Only 4/15 patients had IBS crossover study	Low
Stool weight	1 trial; 4 patients; from RCT; (crossover + washout design)	MD= -98 g/day (95%CI -213, 17)		Not statistically significant; favours co-phenotrope	Poor - subgroup only	Direct	Sparse data	Consistent	---	Subgroup of 4 patients; crossover study; 3 day duration	Low
Stool weight	1 trial; 15 patients; from RCT; (crossover + washout design)	MD= -203 g/day (95%CI -542, 135)		Not statistically significant	Good	Indirect patients - minor, closely related conditn	Wide CI	Consistent	---	Only 4/15 patients had IBS; crossover study	Low

Acute studies

Comparison: co-phenotrope versus placebo

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
No of patients with no unformed stools at 1h	1 trial; 107 patients; from RCT; (parallel design)	RR= 0.83 (95%CI 0.59, 1.16)		Not statistically significant	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	Amery 1975. Industry funded; not IBS population; some children	Low
No of patients with no unformed stools at 2h	1 trial; 107 patients; from RCT; (parallel design)	RR= 0.9 (95%CI 0.61, 1.34)		Not statistically significant	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	Amery 1975. Industry funded; not IBS population; some children	Low
No of patients with no unformed stools at 4h	1 trial; 107 patients; from RCT; (parallel design)	RR= 1.17 (95%CI 0.72, 1.89)		Not statistically significant	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	Amery 1975. Industry funded; not IBS population; some children	Low
No of patients with no unformed stools at 24h	1 trial; 107 patients; from RCT; (parallel design)	RR= 1.33 (95%CI 0.98, 1.82)		Not statistically significant, but favours co-phenotrope	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	Amery 1975. Industry funded; not IBS population; some children	Low

Acute studies

Comparison: loperamide versus placebo

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
No of patients with no unformed stools at 1h	1 trial; 115 patients; from RCT; (acute parallel design)	RR= 1.25 (95%CI 0.99, 1.59)		Not statistically significant, but favours loperamide	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	Amery 1975. Industry funded; not IBS population; some children	Low
No of patients with no unformed stools at 2h	1 trial; 115 patients; from RCT; (parallel design)	RR= 1.33 (95%CI 0.98, 1.82)		Not statistically significant, but favours loperamide	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	Amery 1975. Industry funded; not IBS population; some children	Low
No of patients with no unformed stools at 4h	1 trial; 115 patients; from RCT; (parallel design)	RR= 1.66 (95%CI 1.1, 2.49)		Statistically significant in favour of loperamide. NNT 5 (95%CI 3, 17), for control group rate of 36%	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	Amery 1975. Industry funded; not IBS population; some children	Low
No of patients with no unformed stools at 24h	1 trial; 115 patients; from RCT; (parallel design)	RR= 1.73 (95%CI 0.99, 3.01)		Borderline significant, favours loperamide	Good	Indirect patients - minor, closely related conditn	Fairly wide CI	Consistent	Poor - studies, industry	Amery 1975. Industry funded; not IBS population; some children	Low

Acute studies

Comparison: loperamide versus placebo

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
No of patients with no unformed stools at 72h	1 trial; 213 patients; from RCT; (parallel design)	RR= 1.2 (95%CI 1.03, 1.4)		Statistically significant, favours loperamide	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	Dettmar 1998. Industry funded. Not IBS population	Low
No of patients with first relief	1 trial; 242 patients; from RCT; (parallel design)	OR= 4.23 (95%CI 1.13, 15.82)		Statistically significant, favours loperamide	Good	Indirect patients - minor, closely related conditn	Wide CI	Consistent	Poor - studies, industry	Dreverman 0.5mg vs placebo. Unclear what precision, but assumed reasonable because large study. Industry sponsored. Not IBS	Low
No of patients with first relief	1 trial; 242 patients; from RCT; (parallel design)	OR= 6.25 (95%CI 1.74, 22.42)		Statistically significant, favours loperamide	Good	Indirect patients - minor, closely related conditn	Wide CI	Consistent	Poor - studies, industry	Dreverman 1.0mg vs placebo. Unclear what precision, but assumed reasonable because large study. Industry sponsored. Not IBS	Low
Time to first relief	1 trial; 242 patients; from RCT; (parallel design)	Median difference= 4.5 hours		Details not given, but statistically significant in favour of loperamide (p=0.012)	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	Dreverman 0.5mg vs placebo. Unclear what precision, but assumed reasonable because large study. Industry sponsored. Not IBS	Low

Acute studies

Comparison: loperamide versus placebo

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Time to first relief	1 trial; 242 patients; from RCT; (parallel design)	Median difference= 9.3 hours		Details not given, but statistically significant in favour of loperamide (p=0.003)	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	Dreverman 1.0mg vs placebo. Unclear what precision, but assumed reasonable because large study. Industry sponsored. Not IBS	Low

Acute studies

Comparison: co-phenotrope versus loperamide

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Stool score	1 trial; 614 patients; from RCT; (parallel design)	MD= -0.99		Statistically significant, in favour of loperamide (p=0.011)	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	---	Dom 1974. Change in mean number of stools. Not IBS. Precision probably OK because large study.	Moderate
No of patients with no unformed stools at 1h	1 trial; 104 patients; from RCT; (parallel design)	RR= 0.66 (95%CI 0.49, 0.9)		Statistically significant, favours loperamide; NNT 4 (95%CI 3, 12)	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	Amery 1975. Industry funded; not IBS population; some children	Low
No of patients with no unformed stools at 2h	1trial; 104 patients; from RCT; (parallel design)	RR= 0.68 (95%CI 0.47, 0.96)		Statistically significant, favours loperamide; NNT 5 (9%CI 3, 34)	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	Amery 1975. Industry funded; not IBS population; some children	Low

Acute studies

Comparison: co-phenotrope versus loperamide

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
No of patients with no unformed stools at 4h	1 trial; 104 patients; from RCT; (parallel design)	RR= 0.71 (95%CI 0.47, 1.05)		Not statistically significant, favours loperamide	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	Amery 1975. Industry funded; not IBS population; some children	Low
No of patients with no unformed stools at 24h	3 trials; 1066 patients; from meta-analysis; (parallel design)	RR= 0.78 (95%CI 0.62, 0.98)	p=0.15; I2 =47%	Statistically significant, favours loperamide. Some heterogeneity. NNT 20, control rate 21-41%	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	2/3 studies had industry funding. Not IBS population	Low
No of patients with no unformed stools at 48h	2 trials; 954 patients; from meta-analysis; (parallel design)	RR= 0.81 (95%CI 0.73, 0.89)	p=0.94; I2 =0%	Statistically significant, favours loperamide.	Good	Indirect patients - minor, closely related conditn	Precise	Consistent	Poor - studies, industry	1/2 studies was industry sponsored	Moderate
Time to first unformed stools	1 trial; 104 patients; from RCT; (parallel design)	Median difference= 22 hours		Statistically significant favouring loperamide (p=0.024)	Good	Indirect patients - minor, closely related conditn	----	Consistent	Poor - studies, industry	Amery 1975. Industry funded; not IBS population; some children	Low

Acute studies

Comparison: co-phenotrope versus loperamide

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Adverse effects	1 trial; 104 patients; from RCT; (parallel design)	OR= 3.67 (95%CI 0.37, 36.47)		Not statistically significant; very wide CI	Good	Indirect patients - minor, closely related conditn	Wide CI	Consistent	Poor - studies, industry	Amery 1975. Industry funded; not IBS population; some children	Very low

Acute studies

Comparison: co-phenotrope versus morphine

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
No. of patients with normal stools	1 trial; 164 patients; from RCT; (parallel design)	RR= 3.19 (95%CI 1.75, 5.83)		Significantly in favour of co-phenotrope. NNT 4 for control group risk of 14%	Poor - not blinded	Indirect patients - minor, closely related conditn	Precise	Consistent	---	Frequency. At 12 hours. Lee 1968. Not IBS and not blinded	Low
No. of patients with normal stools	1 trial; 164 patients; from RCT; (parallel design)	RR= 3.49 (95%CI 1.6, 7.6)		Significantly in favour of co-phenotrope. NNT 5 for control group risk of 9%	Poor - not blinded	Indirect patients - minor, closely related conditn	Precise	Consistent	---	Consistency. At 12 hours. Lee 1968. Not IBS and not blinded	Low

Maintenance studies

Comparison: loperamide versus placebo

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (no. patients)	1 trial; 32 patients; from RCT; (parallel design)	RR= 1.84 (95%CI 0.94, 3.58)		Not statistically significant; favours loperamide; fairly wide CI.	Poor - subgroup only	Direct	Fairly wide CI	Consistent	---	32/55 patients (subgroup IBS-A); 3 weeks duration.	Low
Global improvement of IBS symptoms (no. patients)	1 trial; 16 patients; from RCT; (parallel design)	RR= 4 (95%CI 1.2, 13.28)		Statistically significant, in favour of loperamide; NNT 2 (95%CI 1, 3); for 25% control group rate.	Poor - subgroup only	Direct	Wide CI	Consistent	---	16/55 patients (IBS-D subgroup); 3 weeks duration.	Low
Global improvement of IBS symptoms (no. patients)	1 trial; 46 patients; from RCT; (parallel design)	RR= 2 (95%CI 1.15, 3.48)		Statistically significant, in favour of loperamide; NNT 3 for control group rate 39%	Good	Direct	Fairly wide CI	Consistent	---	46/55 patients (IBS-C not included); 3 weeks duration. Setting not stated.	Moderate
Global improvement of IBS symptoms (mean score)	1 trial; 25 patients; from RCT; (parallel design)	MD=		results not stated, but statistically significant, in favour of loperamide; p<0.03	Good	Indirect setting- minor, secondary care OPD	Sparse data	Consistent	---	Insufficient detail to give higher rating. May be moderate. Small study (n=25) Secondary care.	Low

Maintenance studies

Comparison: loperamide versus placebo

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
No of patients with less pain	2 trials; 70 patients; from meta-analysis; (parallel design)	RR= 2.6 (95%CI 1.02, 6.61)	p=0.17; I2 =48%	Statistically significant; favours loperamide; some inconsistency. NNT 5 (95%CI 3, 25).	Poor - subgroup only	Indirect setting-minor, secondary care OPD	Wide CI	Consistent	---	IBS subgroups + Lavo. Study quality: 1/2 IBS subgroups combined. 1/2 (smaller study) secondary care	Low
No of patients with more pain	2 trials; 40 patients; from meta-analysis; (parallel design)	RR= 0.36 (95%CI 0.14, 0.96)	p=0.33; I2 =0%	Statistically significant, favouring loperamide; NNT 3 (95%CI 2, 13).	Poor - subgroup only	Indirect setting-minor, secondary care OPD	Wide CI	Consistent	---	IBS-D subgroup + Lavo. 1/2 studies was a subgroup; 1/2 studies was secondary care. May be moderate if CIs not too wide.	Low
No of patients with more pain	2 trials; 70 patients; from meta-analysis; (parallel design)	RR= 0.38 (95%CI 0.15, 0.96)	p=0.36; I2 =0%	Statistically significant; favours loperamide; NNT 5 (95%CI 3, 25).	Poor - subgroup only	Indirect setting-minor, secondary care OPD	Fairly wide CI	Consistent	---	IBS subgroups + Lavo. Study quality: 1/2 IBS subgroups combined. 1/2 (smaller study) secondary care	Low
No of patients with improved bowel habit	1 trial; 32 patients; from RCT; (parallel design)	RR= 2.4 (95%CI 1.32, 4.35)		Statistically significant; favours loperamide; NNT 2 (95%CI 2, 4)	Poor - subgroup only	Direct	Fairly wide CI	Consistent	---	IBS-A subgroup. Stool frequency. 32/55 patients (subgroup)	Low

Maintenance studies

Comparison: loperamide versus placebo

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
No of patients with improved bowel habit	2 trials; 40 patients; from meta-analysis; (parallel design)	RR= 2.83 (95%CI 1.43, 5.63)	p=0.86; I2 =0%	Statistically significant, favouring loperamide; fairly wide CI. NNT 2 (95%CI 2, 4)	Poor - subgroup only	Indirect setting-minor, secondary care OPD	Fairly wide CI	Consistent	---	IBS-D subgroup + Lavo. Stool frequency. 1/2 studies was a subgroup; 1/2 studies was secondary care.	Low
No of patients with improved bowel habit	1 trial; 32 patients; from RCT; (parallel design)	RR= 2.1 (95%CI 1.23, 3.58)		Statistically significant; favours loperamide; fairly wide CI. NNT 3 (95%CI 2, 5)	Poor - subgroup only	Direct	Fairly wide CI	Consistent	---	IBS-A subgroup. Stool consistency. 32/55 patients (subgroup); 3 weeks duration.	Low
No of patients with improved bowel habit	2 trials; 70 patients; from meta-analysis; (parallel design)	RR= 2.38 (95%CI 1.53, 3.7)	p=0.58; I2 =0%	Statistically significant; favours loperamide; NNT 2 (95%CI 2, 4)	Poor - subgroup only	Indirect setting-minor, secondary care OPD	Precise	Consistent	---	IBS subgroups + Lavo. Stool frequency. Study quality: 1/2 IBS subgroups combined. 1/2 (smaller study) secondary care	Moderate
Stool score	1 trial; 69 patients; from RCT; (parallel design)	=		Results not given, but said to be statistically significantly better consistency for loperamide group (p<0.002)	Good	Direct	----	Consistent	Poor - studies, industry	Stool consistency. >20% dropouts from trial, but occurred before interventions. Precision unclear. Industry supported trial. May be moderate.	Low

Maintenance studies

Comparison: loperamide versus placebo

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Stool score	1 trial; 69 patients; from RCT; (parallel design)	=		Results not given, but said to be statistically significantly better consistency for loperamide group (p<0.05)	Good	Direct	----	Consistent	Poor - studies, industry	Stool frequency. >20% dropouts from trial, but occurred before interventions. Precision unclear. Industry supported trial. May be moderate.	Low
Stool score	1 trial; 25 patients; from RCT; (parallel design)	MD=		results not stated, but statistically significant in favour of loperamide; p<0.001	Good	Indirect setting-minor, secondary care OPD	Sparse data	Consistent	---	Stool consistency. Insufficient detail to give higher rating. Small study (n=25)	Low
Stool score	1 trial; 25 patients; from RCT; (parallel design)	MD=		results not stated, but not statistically significant	Good	Indirect setting-minor, secondary care OPD	Sparse data	Consistent	---	Stool frequency. Insufficient detail to give higher rating. May be moderate. Small study (n=25)	Low
Urgency	1 trial; 25 patients; from RCT; (parallel design)	RR= 3 (95%CI 1.07, 8.43)		statistically significant in favour of loperamide; wide CI; NNT 2 (95%CI 2, 7).	Good	Indirect setting-minor, secondary care OPD	Wide CI	Consistent	---	Number of patients with less urgency. Small study (n=25)	Low

Maintenance studies

Comparison: loperamide versus yoga

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Bowel symptom score	1 trial; 22 patients; from RCT; (parallel design)	MD= 1.2 (95%CI -0.25, 2.65)		Not statistically significant	Poor - not blinded	Indirect patients - minor, closely related conditn	Fairly wide CI	Consistent	---	2 months Not blinded	Low
Bowel symptom score	1 trial; 22 patients; from RCT; (parallel design)	MD= 0.66 (95%CI -0.32, 1.64)		Not statistically significant	Poor - not blinded	Indirect patients - minor, closely related conditn	Fairly wide CI	Consistent	---	1 month Not blinded	Low

Evidence Summary: anti-spasmodics review

Comparison: all antispasmodics vs placebo

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (no. patients)	8 trials; 731 patients; from meta analysis; (parallel design);	RR=1.32 (95%CI 1.18, 1.48)	p=0.09; I2 =43%	statistically significant, favours antispasmodic; NNT 6	Good	Indirect Setting - minor, secondary care OPD	Precise	minor inconsistency		Some heterogeneity. 1/8 studies had >20% missing data; secondary care	Moderate
pain number of patients with less pain	4 trials; 301 patients; from meta analysis; (parallel design);	RR=1.61 (95%CI 1.36, 1.91)	p=0.13; I2 =0.473%	statistically significant, favours antispasmodics; significant heterogeneity in smooth muscle relaxant group (I2: 63.4%)	Good	Indirect Setting - minor, secondary care OPD	Precise	consistent	---	1/4 studies had missing data >20%; 1 was not comparable at baseline for stool frequency.	Moderate
pain number of patients with less pain	3 trials; 114 patients; from meta analysis; (parallel design);	RR=1.83 (95%CI 1.46, 2.29)	p=0.62; I2 =0%	Statistically significant in favour of antispasmodics	Poor - incomplete follow up	Indirect Setting - minor, secondary care OPD	Precise	consistent	---	Sensitivity analysis without Mitchell study. No heterogeneity. 1/3 studies not comparable at baseline for stool frequency; 1/3 studies had missing data >20%.	Moderate
No of patients with improved bowel habit	1 trials; 71 patients; from RCT; (parallel design);	RR=1.58 (95%CI 1.14, 2.19)		statistically significant, in favour of antispasmodic	Poor - incomplete follow up	Indirect Setting - minor, secondary care OPD	Precise	consistent	---	Attrition bias in 1 study (Page).	Low
Stool score	1 trials; 69 patients; from RCT; (parallel design);	WMD=-0.46 (95%CI -0.86, -0.06)		statistically significant, in favour of antispasmodic; scale 1 to 4	Good	Indirect Setting - minor, secondary care OPD	Precise	consistent	---		Moderate

Comparison: smooth muscle relaxant vs placebo

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (no. patients)	4 trials; 243 patients; from meta analysis; (parallel design);	RR=1.33 (95%CI 1.06, 1.68)	p=0.23; I2 =30.3%	Statistically significant, favours smooth muscle relaxants	Good	Indirect Setting - minor, secondary care OPD	Precise	consistent	---	Smooth muscle relaxants. 1/4 had uncertain randomisation	Moderate

Comparison: antimuscarinic vs placebo

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (no. patients)	4 trials; 483 patients; from meta analysis; (parallel design);	RR=1.38 (95%CI 1.22, 1.57)	p=0.08; I2 =57%	statistically significant, favours antimuscarinic agent	Good	Indirect Setting - minor, secondary care OPD	Precise	minor inconsistency	---	Antimuscarinic agents subgroup. 1/4 had missing data. Sensitive to random effects/fixed effects model	Low

Comparison: mebeverine MR vs mebeverine conventional

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (no. patients)	2 trials; 208 patients; from meta analysis; (parallel design);	RR=1.03 (95%CI 0.88, 1.2)	p=0.28; I2 =0.153%	no significant difference between types	Good	Direct	Precise	consistent	---	I of the 2 studies took place in primary care. 1/2 studies was not blinded and duration < 4w. Overall downgraded to moderate.	Moderate

Evidence Summary: CBT review

Comparison: CBT versus placebo/no treatment/symptom monitoring

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (no. patients)	4 trials; 102 patients; from meta-analysis	RR=6.11 (95%CI 2.33, 16.07)	p=0.91; I2 =0%	statistically significantly in favour of CBT; large effect; NNT 3 for a for a control group risk of 7 to 10%	Good	Indirect patients - minor, comorbidity	Precise	consistent	Adequate	Sensitivity analysis without Gong, Blanchard, Lynch. Indirect population: 2/4 secondary care and all had concurrent psychiatric illness	Moderate
Global improvement of IBS symptoms (mean score)	4 trials; 74 patients; from meta-analysis	WMD=-0.57 (95%CI -0.73, -0.42)	p=0.89; I2 =0%	Large statistically significant effect in favour of CBT (scale -1 to +1)	Good	Indirect patients - minor, comorbidity	Precise	consistent	Not applicable	Global symptom improvement score (CPSR). All studies had psychiatric comorbidities.	Moderate
Global IBS symptom score	3 trials; 173 patients; from meta-analysis	SMD=-0.64 (95%CI -0.94, -0.33)	p=0.90; I2 =0%	Statistically significant, favours CBT	Good	Indirect patients - minor, comorbidity	Precise	consistent	Not applicable	Largest study in primary care; 2/3 studies had psychiatric comorbidities.	Moderate
pain score	6 trials; 347 patients; from meta-analysis	SMD=-0.12 (95%CI -0.33, 0.1)	p=0.99; I2 =0%	No significant difference; highly homogeneous; scales all high = severe	Good	Indirect patients - minor, comorbidity	Precise	consistent	Adequate	4/6 had psychiatric comorbidities; most secondary care; 2/6 comparisons had only 78% patients with IBS; funnel plot seems OK.	Moderate
Bloating score	4 trials; 80 patients; from meta-analysis	SMD=-0.23 (95%CI -0.69, 0.22)	p=0.36; I2 =7%	No significant difference	Good	Indirect patients - minor, comorbidity	Precise	consistent	Not applicable	All had patients with psychiatric comorbidities; secondary care.	Moderate

Comparison: CBT versus placebo/no treatment/symptom monitoring

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Diarrhoea	1 trials; 20 patients; from RCT	WMD=-5.7 (95%CI -11.19, -0.21)		Statistically significant, favours CBT. Scale 0-4 daily added over 4 weeks (i.e. max 112)	Good	Indirect patients - minor, comorbidity	sparse data	consistent	---	Greene; psychiatric comorbidity,	Low
Constipation	1 trials; 20 patients; from RCT	WMD=-2.9 (95%CI -9.22, 3.42)		No significant difference. Scale 0-4 daily added over 4 weeks	Good	Indirect patients - minor, comorbidity	sparse data	----	---	Psychiatric comorbidity	Low
Quality of life	1 trials; 215 patients; from RCT	WMD=2.95 (95%CI -0.98, 6.88)		IBS-QOL Scale 0-84; not statistically significant	Good	Indirect patients - minor, comorbidity	Precise	----	---	CBT vs attention control; only 78% patients had IBS; no concurrent psychiatric illness; secondary care. IBS-QOL. May be moderate.	Low
Beck depression inventory	4 trials; 96 patients; from meta-analysis	WMD=-4.68 (95%CI -6.79, -2.57)	p=0.82; I2 =0%	Scale max 63; homogeneous; stat sig; favours CBT	Good	Indirect patients - minor, comorbidity	Precise	consistent	---	3/4 had psychiatric comorbidities	Moderate
State-Trait Anxiety Inventory	4 trials; 94 patients; from meta-analysis	WMD=-1.08 (95%CI -4.09, 1.93)	p=0.54; I2 =0%	Scale 20-80; no significant difference	Good	Indirect patients - minor, comorbidity	Precise	consistent	---	3/4 studies had psychiatric comorbidities	Moderate

Comparison: CBT + medical treatment versus medical treatment

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global symptoms - change in overall wellbeing	1 trials; 24 patients; from meta-analysis	MD=-1.88 (95%CI -2.33, -1.43)		Statistically significant, favours CBT + medical treatment; scale 1 to 7 (high=worse)	Good	Indirect setting- - minor, secondary	sparse data	----	Not applicable	Small study (n=24) but precise data; no pyschiatric comorbidities; secondary care.	Low
Quality of life	1 trials; 24 patients; from meta-analysis	MD=21.73 (95%CI 9.04, 34.42)		Scale max 144; stat sig; favours CBT+medical treatment	Good	Indirect setting- - minor, secondary	sparse data	consistent	---	GI QoL instrument; no psychiatric comorbidities; secondary care. Small RCT	Low

Comparison: CBT + mebeverine versus mebeverine

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global IBS symptom score	1 trials; 149 patients; from RCT	MD=-71 (95%CI -107, -35)		Scale 0 to 500; statistically significant, favours CBT+mebeverine	Good	Indirect patients - minor, comorbidity	Precise	consistent	Not applicable	About half patients had psychiatric comorbidities. Primary care settting.	Moderate
Global IBS symptom score	1 trials; 101 patients; from RCT	MD=-82.27 (95%CI -122.59, -41.95)		Statistically significant, in favour of CBT+mebeverine, scale 0-500	Poor - incomplete follow up	Indirect patients - minor, closely	Precise	consistent	---	Follow up 13 weeks. 28% and 36% drop outs, some had psychiatric comorbidities.	Moderate
Global IBS symptom score	1 trials; 111 patients; from RCT	WMD=-40 (95%CI -80, 0.4)		Scale 0 to 500; borderline significance, favours CBT+mebeverine	Poor - incomplete follow up	Indirect patients - minor, comorbidity	Precise	consistent	Not applicable	Follow up 26 weeks. 38/149 (26%) drop outs, some had psychiatric comorbidities.	Moderate
Global IBS symptom score	1 trials; 110 patients; from RCT	MD=-26 (95%CI -66, 16.38)		Scale 0 to 500; not statistically significant	Poor - incomplete follow up	Indirect patients - minor, comorbidity	Precise	consistent	Not applicable	Follow up 52 weeks. 39/149 (26%) drop outs, some had psychiatric comorbidities.	Moderate
Quality of life(social functioning)	1 trials; 149 patients; from RCT	WMD=-4.7 (95%CI -7.43, -1.97)		statistically significant, favours CBT+mebeverine; scale maximum 40;	Good	Indirect patients - minor, comorbidity	Precise	----	---	work and social adjustment score; some had psychiatric comorbidities; primary care.	Moderate
Quality of life(social functioning)	1 trials; 112 patients; from RCT	MD=-3.2 (95%CI -6.39, -0.01)		statistically significant; , favours CBT+mebeverine; scale maximum 40	Poor - incomplete follow up	Indirect patients - minor, comorbidity	Precise	consistent	---	Follow up at 26 weeks. Work and social adjustment score. Drop out 39/149 (26%), some had psychiatric comorbidities; primary care.	Moderate
Quality of life(social functioning)	1 trials; 109 patients; from RCT	MD=-3.8 (95%CI -7.18, -0.42)		statistically significant; favours CBT+mebeverine; scale maximum 40	Poor - incomplete follow up	Indirect patients - minor, comorbidity	Precise	consistent	---	Follow up at 52 weeks. Work and social adjustment score. Drop out 40/149 (27%); some had psychiatric comorbidities; primary care.	Moderate

Evidence Summary: hypnotherapy review

Comparison: Hypnotherapy vs waiting list control

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (no of patients)	2 trials; 41 patients; from MA; (parallel design);	OR=3.85 (95%CI 2.03, 7.29)	p=0.18; I2=45%	Statistically significant, favours hypnotherapy; OR calculated for 1 study	Good	Indirect setting-minor, secondary care OPD	Sparse data	consistent	---	Overall improvement of symptoms and general well being. 1/2 severe refractory IBS. Secondary care.	Moderate
Global improvement of IBS symptoms (mean score)	1 trial; 30 patients; from RCT; (parallel design);	MD=2.43 (95%CI 0, 0)		Statistically significant, favours hypnotherapy; SDs not given, but p<0.0001. Scale 0-3.	Good	Indirect setting-minor, secondary care OPD	Sparse data	consistent	---	Overall improvement of symptoms and general well being. Severe refractory IBS. Secondary care. Two therapies delivered by same therapist - possible therapist effect.	Moderate/Low
Global IBS symptom score	1 trial; 81 patients; from RCT; (parallel design);	MD=-8.5 (95%CI -14.54, -2.46)		Statistically significant, favours hypnotherapy. Baseline scores ~40; scale probably 22 to 154	Good	Direct	Precise	consistent	---	Change from baseline at 12 weeks (follow up 7 weeks after end of treatment); primary care; refractory IBS	High
Global IBS symptom score	1 trial; 81 patients; from RCT; (parallel design);	MD=-2.7 (95%CI -10.48, 5.08)		Not significant. Baseline scores ~40; scale probably 22 to 154	Poor drop outs	Direct	Precise	consistent	---	Change from baseline at 52 weeks; primary care; refractory IBS; 35% missing data (said to be missing-at-random)	Moderate

Comparison: Hypnotherapy vs waiting list control

Outcome	*Meta-analysis and I2*	*Summary Statistics Rating*	*p (hetero)*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence details*
pain score	1 trial; 81 patients; from RCT; (parallel design);	MD=-14.4 (95%CI -24.69, -4.11)		Statistically significant, favours hypnotherapy. Baseline scores ~54	Good	Direct	Precise	consistent	--	Change from baseline at 12 weeks (follow up 7 weeks after end of treatment); primary care; refractory IBS	High
pain score	1 trial; 81 patients; from RCT; (parallel design);	MD=-0.6 (95%CI -13.27, 12.07)		Not significant. Baseline scores ~54	Poor drop outs	Direct	Precise	consistent	---	Change from baseline at 52 weeks; primary care; refractory IBS; 35% missing data (said to be missing-at-random)	Moderate
pain score	1 trial; 30 patients; from RCT; (parallel design);	MD=-9.4 (95%CI 0, 0)		Statistically significant, favours hypnotherapy; SDs not given, but p<0.0001. Scale 0-21.	Good	Indirect setting-minor, secondary care OPD	Sparse data	consistent	---	Severe refractory IBS. Secondary care. Two therapies delivered by same therapist - possible therapist effect.	Moderate/Low
Bloating score	1 trial; 30 patients; from RCT; (parallel design);	MD=-10 (95%CI 0, 0)		Statistically significant, favours hypnotherapy; SDs not given, but p<0.0001. Scale 0-21.	Good	Indirect setting-minor, secondary care OPD	Sparse data	consistent	---	Severe refractory IBS. Secondary care. Two therapies delivered by same therapist - possible therapist effect.	Moderate/Low

Comparison: Hypnotherapy vs waiting list control

Outcome	*Meta-analysis and I2*	*Summary Statistics Rating*	*p (hetero)*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence details*
Diarrhoea	1 trial; 81 patients; from RCT; (parallel design);	MD=-7.9 (95%CI -16.29, 0.49)		Not statistically significant, favours hypnotherapy. Baseline scores ~33	Good	Direct	Precise	consistent	---	Change from baseline at 12 weeks (follow up 7 weeks after end of treatment); primary care; refractory IBS	High
Constipation	1 trial; 81 patients; from RCT; (parallel design);	MD=-2.4 (95%CI -11.61, 6.81)		Not statistically significant, favours hypnotherapy. Baseline scores ~38	Good	Direct	Precise	consistent	---	Change from baseline at 12 weeks (follow up 7 weeks after end of treatment); primary care; refractory IBS	High
Quality of life	1 trial; 81 patients; from RCT; (parallel design);	MD=8.7 (95%CI -2.82, 20.22)		Not significant, favours hypnotherapy. Baseline score ~50	Good	Direct	Fairly wide CI	consistent	---	Overall QoL scores at 12 weeks (follow up 7 weeks after end of treatment); primary care; refractory IBS	Moderate
Quality of life	1 trial; 81 patients; from RCT; (parallel design);	MD=9.5 (95%CI -3.67, 22.67)		Not significant, favours hypnotherapy. Baseline score ~50	Good	Direct	Fairly wide CI	consistent	---	Overall QoL scores at 6 months; primary care; refractory IBS	Moderate
Quality of life	1 trial; 81 patients; from RCT; (parallel design);	MD=9.6 (95%CI -3.75, 22.95)		Not significant, favours hypnotherapy. Baseline score ~50	Poor drop outs	Direct	Fairly wide CI	consistent	---	Overall QoL scores at 12 months; primary care; refractory IBS; 35% missing data (said to be missing-at-random)	Moderate/Low

Comparison: Hypnotherapy vs waiting list control

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
other medication use	1 trial; 81 patients; from RCT; (parallel design);	RR=0.61 (95%CI 0.4, 0.94)		Statistically significant, favours hypnotherapy. Control group rate 79%	Poor drop outs	Direct	Fairly wide CI	consistent	---	Prescription medication over 12 months; primary care; refractory IBS; 35% missing data (said to be missing-at-random)	Moderate/Low

Comparison: group vs individual hypnotherapy

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (no. patients)	1 trial; 36 patients; from RCT; (parallel design);	RR=1.41 (95%CI 0.79, 2.52)		Not significant	Good	Indirect setting-minor, secondary care OPD	Sparse data	consistent	---	Refractory IBS. 36% patients had pyschological problems.	Low

Comparison: hypnotherapy vs relaxation

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global IBS symptom score	1 trial; 52 patients; from RCT; (parallel design);	RR=1.28 (95%CI 0.87, 1.88)		Not significant	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	consistent	---	12 weeks end of therapy. IBS medication continued. Secondary care. 37% psychiatric cases. Refractory IBS. Delivered by same therapist so possible therapist effect.	Moderate

Evidence Summary: *laxatives review*

short term relief

Comparison: stimulant laxative versus placebo (Bisacodyl versus placebo)

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Impre-cision*	*Inconsist ency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
No of patients with improved bowel habit	2 trials; 112 patients; from meta-analysis; (short term relief design)	RR=1.34 (95%CI 1.02, 1.76)	p=0.89; I2 =0%	Statistically significant, favours laxative. NNT 6, for a control group risk of 52 to 61%	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Unclear if IBS population. Industry trials	Moderate
Stool score (consistency)	1trial; 54 patients; from RCT; (short term relief design)	MD=-1.4 (95%CI -2.04, -0.76)		statistically significant, favours Bisacodyl. Scale 1-5 normal stool = 3; placebo group 4.2	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Unclear if IBS population	Moderate
Stool score (consistency)	1trial; 57 patients; from RCT; (short term relief design)	RR=1.51 (95%CI 1.06, 2.15)		Statistically significant, favours laxative	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	May be IBS; industry study	Moderate
Stool freq	1trial; 54 patients; from RCT; (short term relief design)	MD=0.85 (95%CI 0.24, 1.46)		Statistically significant: higher stool frequency for Bisacodyl (stools per day) Scale 1-5; placebo group 0.95/day	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Unclear if IBS population	Moderate

long term maintenance

Comparison: osmotic laxative versus placebo (PEG versus placebo)

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Impre-cision*	*Inconsist ency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (no. patients)				No evidence for this outcome	----	---	----	----	---		----
No of patients not using rescue medication	1trial; 48 patients; from RCT; (long term maintenance design)	RR=1.61 (95%CI 1.05, 2.47)		Statistically significant, favours PEG; NNT 4 for control group risk of 52%	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	Laxatives as rescue medication. Probably some IBS patients, but secondary care. Corazziari 1996	Moderate
rescue medication use	1trial; 48 patients; from RCT; (long term maintenance design)	RR=0.33 (95%CI 0.12, 0.9)		statistically significant at 8 weeks, favours PEG. NNT 4	Good	Indirect setting-minor, secondary care OPD	Wide CI	consistent	---	Laxatives as rescue medication. Probably some IBS patients, but secondary care. Corazziari 1996	Low
rescue medication use	1trial; 65 patients; from RCT; (long term maintenance design)	MD=-1.5 (95%CI -2.96, -0.04)		statistically significant; in favour of PEG at 8 weeks. Placebo group 2.2 per 4 weeks.	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	consistent	---	Number of laxatives used/4 weeks (rescue). Probably some IBS patients, but secondary care. Corazziari 2000. Withdrawal of laxative after 4 weeks in responders	Low
pain number of patients	1trial; 48 patients; from RCT; (long term maintenance design)	RR=0.69 (95%CI 0.28, 1.69)		not statistically significant at 8 weeks; placebo group rate 35%	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	consistent	---	Probably includes some IBS patients, but secondary care.	Low

Comparison: osmotic laxative versus placebo (PEG versus placebo)

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Impre-cision*	*Inconsist ency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
No of patients with bloating	1trial; 48 patients; from RCT; (long term maintenance design)	RR=0.69 (95%CI 0.42, 1.13)		no statistically significant difference at 8 weeks; control group rate 70%	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	Probably includes some IBS patients, but secondary care.	Moderate
Bloating score	1trial; 65 patients; from RCT; (long term maintenance design)			Statistically significant difference at 8 weeks in severity of bloating (p<0.001)	Good	Indirect setting-minor, secondary care OPD	----	----	---	Reported by authors. Probably some IBS patients, but secondary care. Corazziari 2000. Withdrawal of laxative after 4 weeks in responders	----
No of patients with improved bowel habit	1trial; 65 patients; from RCT; (long term maintenance design)	RR=3.95 (95%CI 1.86, 8.42)		Large statistically significant effect at 8 weeks, favours PEG. NNT 2. Placebo group rate 18%	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	consistent	---	Probably some IBS patients, but secondary care. Corazziari 2000. Withdrawal of laxative after 4 weeks in responders	Moderate
Stool freq	1trial; 48 patients; from RCT; (long term maintenance design)	MD=2 (95%CI 0.89, 3.11)		Statistically significant increase in stool frequency per week for patients given PEG at 8 weeks. Placebo group 2.8/week	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	Probably some IBS patients, but secondary care. Corazziari 1996.	Moderate
Stool freq	1trial; 65 patients; from RCT; (long term maintenance design)	MD=3.13 (95%CI 1.35, 4.91)		Large statistically significant increase in stool frequency in PEG group at 8 weeks. Control group 4.39 / week	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	Probably some IBS patients, but secondary care. Corazziari 2000. Withdrawal of laxative after 4 weeks in responders	Moderate
Use of laxatives	1trial; 65 patients; from RCT; (long term maintenance design)	MD=-10 (95%CI -16.09, -3.91)		Statistically significant at 8 weeks. Favours PEG. Placebo group 43 sachets/4 weeks.	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	Number of intervention laxatives used/4 weeks. Probably some IBS patients, but secondary care. Corazziari 2000. Withdrawal of laxative after 4 weeks in responders	Moderate

Comparison: osmotic laxative versus placebo (PEG versus placebo)

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Impre-cision*	*Inconsist ency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Number of withdrawals	1trial; 65 patients; from RCT; (long term maintenance design)	RR=0.13 (95%CI 0.03, 0.53)		Statistically significant at 20 weeks; favours PEG. NNT 3 for placebo group rate of 46%	Good	Indirect setting-minor, secondary care OPD	Wide CI	consistent	---	Probably some IBS patients, but secondary care. Corazziari 2000. Withdrawal of laxative after 4 weeks in responders	Low

Comparison: osmotic laxative versus stimulant laxative (PEG versus Lactulose)

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Impre-cision*	*Inconsist ency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (mean score)	1trial; 99 patients; from RCT; (long term maintenance design)	MD=2.2 (95%CI 1.05, 3.35)		statistically significant, in favour of PEG. Scale 1-10, high score= good response. Lactulose: 5.20.	Poor - patients could take other laxatives ad lib	Indirect setting-minor, secondary care OPD	Precise	consistent	---	Patients with chronic constipation, some may have had IBS; in secondary care. Attar 1999. Patients could take other laxatives during trial ad-lib.	Low
No of patients using rescue microenemas	1trial; 115 patients; from RCT; (long term maintenance design)	RR=0.48 (95%CI 0.25, 0.95)		Statistically significant. More patients used microenemas in the lactulose group. NNT 6 for lactulose group rate of 35%	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	consistent	---	Rescue medication. Patients with chronic constipation, some may have had IBS; in secondary care. Patients could take other laxatives during trial ad-lib.	Low
No of patients not using rescue medication	1trial; 115 patients; from RCT; (long term maintenance design)	RR=1.27 (95%CI 1.02, 1.59)		Statistically significant. Favours PEG. NNT 6 for lactulose group rate of 65%	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	Rescue medication. Patients with chronic constipation, some may have had IBS; in secondary care. Patients could take other laxatives during trial ad-lib.	Moderate
pain number of patients	2 trials; 180 patients; from meta-analysis; (long term maintenance design)	OR=0.55 (95%CI 0.25, 1.22)	p=0.80; I2 =0%	Not statistically significant. No heterogeneity.	Poor - patients could take other laxatives ad lib	Indirect setting-minor, secondary care OPD	Fairly wide CI	consistent	Poor - studies, industry	Patients with chronic constipation, some may have had IBS; 1/2 in secondary care. In 1/2 patients could take other laxatives during trial ad-lib. 1/2 industry sponsored	Low
No of patients with bloating	2 trials; 180 patients; from meta-analysis; (long term maintenance design)	RR=0.63 (95%CI 0.39, 1.04)	p=0.16; I2 =49.6%	Not statistically significant, favours PEG. Some heterogeneity. May be dose dependent.	Poor - patients could take other laxatives ad lib	Indirect setting-minor, secondary care OPD	Precise	minor inconsistency	Poor - studies, industry	Patients with chronic constipation, some may have had IBS; 1/2 in secondary care. In 1/2 patients could take other laxatives during trial ad-lib. 1/2 industry sponsored	Low
Stool freq	2 trials; 180 patients; from meta-analysis; (long term maintenance design)	WMD=0.27 (95%CI 0.09, 0.45)	p=0.16; I2 =50%	Statistically significant difference in stools per day in favour of PEG, some heterogeneity	Poor - patients could take other laxatives ad lib	Indirect setting-minor, secondary care OPD	Precise	minor inconsistency	Poor - studies, industry	Patients with chronic constipation, some may have had IBS; 1/2 in secondary care. In 1/2 patients could take other laxatives during trial ad-lib. 1/2 industry sponsored	Low

Comparison: Stimulant laxative 1 versus Stimulant laxative 2 (Bisacodyl versus sodium picosulphate)

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Impre-cision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Stool freq	1trial; 142 patients; from RCT; (long term maintenance design)	MD=-0.05 (95%CI -0.18, 0.08)		not statistically significant. Frequency per day.	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	May be IBS, and secondary care	Moderate

Comparison: Laxative sub type 1versus Laxative subtype 2 (PEG 3350 electrolyte versus PEG 4000 no electrolyte)

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Impre-cision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
pain score	2 trials; 211 patients; from RCT; (long term maintenance design)	WMD=0.1 (95%CI -0.11, 0.31)	p=0.35; I2 =0%	Not statistically significant. No heterogeneity. Pain Scale 1-4. (4= severe). PEG 4000 score 1.6 or 1.8.	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Moderate
Bloating score	2 trials; 211 patients; from RCT; (long term maintenance design)	WMD=0.15 (95%CI -0.06, 0.35)	p=0.64; I2 =0%	Not statistically significant, favours PEG 4000. Scale 1-4 (4=severe). No heterogeneity.	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Moderate
Stool score (consistency)	2 trials; 211 patients; from RCT; (long term maintenance design)	WMD=0.14 (95%CI -0.09, 0.37)	p=0.09; I2 =65%	Not statistically significant; heterogeneity. Favours PEG 4000 at standard dose. Scale 1(liquid) to 6 (very hard). PEG 4000 at 3.2 and 3.4	Good	Indirect patients - minor, comorbidity	Precise	minor inconsistency	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Low
Stool freq	2 trials; 211 patients; from meta-analysis; (long term maintenance design)	WMD=0.75 (95%CI -0.5, 2)	p=0.76; I2 =0%	no significant difference at 4 weeks between types of PEG. No heterogeneity. PEG 4000: 6.2 or 7.2 / week	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Moderate
No. of patients with normal stool	2 trials; 270 patients; from meta-analysis; (long term maintenance design)	RR=1 (95%CI 0.69, 1.44)	p=0.21; I2 =37.6%	Not statistically significant. PEG 4000 rate 10 or 33%	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Moderate
Diarrhoea	2 trials; 211 patients; from RCT; (long term maintenance design)	RR=0.9 (95%CI 0.57, 1.42)	p=0.68; I2 =0%	No significant difference. No heterogeneity. PEG 4000 rate 14 and 30%	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Moderate

Comparison: Laxative sub type 1versus Laxative subtype 2 (PEG 3350 electrolyte versus PEG 4000 no electrolyte)

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Impre-cision*	*Inconsist ency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Quality of life	2 trials; 211 patients; from RCT; (long term maintenance design)	WMD=-2.65 (95%CI -8.57, 3.29)	p=0.93; I2 =0%	No significant difference. Highly homogeneous. VAS to 100.	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Moderate
Adverse effects	2 trials; 211 patients; from RCT; (long term maintenance design)	RR=1.07 (95%CI 0.86, 1.33)	p=0.58; I2 =0%	No significant difference. No heterogeneity for PEG 4000 group rate of 51 and 54%	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Moderate

Comparison: laxative dose 1 versus laxative dose 2 (standard dose versus maximum dose)

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Impre-cision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
pain score	2 trials; 211 patients; from meta-analysis; (long term maintenance design)	WMD=-0.09 (95%CI -0.3, 0.11)	p=0.64; I2 =0%	No significant difference between doses. No heterogeneity.	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Moderate
Bloating score	2 trials; 211 patients; from meta-analysis; (long term maintenance design)	WMD=-0.05 (95%CI -0.26, 0.16)	p=0.64; I2 =0%	Not statistically significant. Bloating Scale 1-4 (4= severe). No heterogeneity.	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Moderate
Stool score (consistency)	2 trials; 211 patients; from meta-analysis; (long term maintenance design)	WMD=0.42 (95%CI 0.19, 0.65)	p=0.09; I2 =65.4%	Statistically significant; favours maximum dose. Heterogeneity by type of PEG.	Good	Indirect patients - minor, closely related conditn	Precise	minor inconsistency	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Low
Stool freq	2 trials; 211 patients; from meta-analysis; (long term maintenance design)	WMD=-0.89 (95%CI -2.04, 0.26)	p=0.76; I2 =0%	Not statistically significant, favours maximum dose. Stool frequency per week. No heterogeneity.	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Moderate
No. of patients with normal stool	2 trials; 211 patients; from meta-analysis; (long term maintenance design)	RR=1.68 (95%CI 1.14, 2.48)	p=0.21; I2 =37%	Statistically significantly more normal stools for standard dose. NNT 7 for max rate of 19 or 25%	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Moderate
Diarrhoea	2 trials; 211 patients; from meta-analysis; (long term maintenance design)	RR=0.41 (95%CI 0.24, 0.7)	p=0.68; I2 =0%	Statistically significant, favours standard dose. Rate for maximum dose 29-30%. NNT 6	Good	Indirect patients - minor, closely related conditn	Fairly wide CI	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Low

Comparison: laxative dose 1 versus laxative dose 2 (standard dose versus maximum dose)

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Impre-cision*	*Inconsist ency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Quality of life	2 trials; 211 patients; from meta-analysis; (long term maintenance design)	WMD=-3.04 (95%CI -8.96, 2.88)	p=0.93; I2 =0%	Not statistically significant. Highly homogeneous. VAS to 100.	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Moderate
Adverse effects	2 trials; 211 patients; from meta-analysis; (long term maintenance design)	RR=0.89 (95%CI 0.71, 1.11)	p=0.58; I2 =0%	No significant difference. No heterogeneity. Maximum dose rate 54 and 61%.	Good	Indirect patients - minor, closely related conditn	Precise	consistent	Poor - studies, industry	Meta-analysis of 2 comparisons in 1 study (Chaussade). Probably some had IBS; primary care. Industry sponsored (by PEG 3350).	Moderate

Comparison: laxative versus fibre (lactulose versus ispaghula)

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Impre-cision*	*Inconsist ency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (no. patients)	2 trials; 427 patients; from meta-analysis; (long term maintenance design)	RR=0.92 (95%CI 0.85, 1)	p=0.05; I2 =74%	Borderline significance favouring fibre at 4 weeks (p=0.06).	Good	Indirect patients - minor, closely related conditn	Precise	minor inconsistency	Poor - studies, industry	Patients with chronic constipation and unlikely to be IBS, in primary care. Lactulose subgroup of Dettmar study combined with Rouse. Dettmar industry funded.	Low
pain number of patients	1trial; 112 patients; from RCT; (long term maintenance design)	RR=0.94 (95%CI 0.5, 1.74)		No significant difference. Placebo group rate 31%	Good	Indirect patients - minor, closely related conditn	Fairly wide CI	consistent	---	Patients with chronic constipation, not IBS; in primary care.	Low
No of patients with bloating	1trial; 78 patients; from RCT; (long term maintenance design)	RR=1 (95%CI 0.49, 2.03)		No significant difference between interventions at 4 weeks. Fibre rate 28%.	Poor - short crossover	Indirect patients - minor, closely related conditn	Fairly wide CI	consistent	---	Patients with chronic constipation, not IBS; in secondary care. Crossover study, 1 week washout.	Low
No of patients with bloating	1trial; 315 patients; from RCT; (long term maintenance design)	RR=0.84 (95%CI 0.46, 1.55)		No significant difference; fibre group rate 16%	Poor - post-hoc subgroup	Indirect patients - minor, closely related conditn	Fairly wide CI	consistent	Poor - studies, industry	Patients with chronic constipation, not IBS; in primary care. Study authors from manufacturers of fibogel. Post-hoc subgroup for lactulose.	very low
Stool score (consistency)	1trial; 78 patients; from RCT; (long term maintenance design)	MD=0.5 (95%CI 0, 1)		Borderline significant at 4 weeks; lower score for lactulose on scale of 0 to 5 (loose), 3 normal. Fibre group 2.9 (ie arguably closer to normal)	Poor - short crossover	Indirect patients - minor, closely related conditn	Precise	consistent	Not applicable	Patients with chronic constipation, not IBS; in secondary care. Crossover study, 1 week washout.	Low
Stool freq	1trial; 78 patients; from RCT; (long term maintenance design)	MD=1.8 (95%CI -0.12, 3.72)		No significant difference between interventions; favoured lactulose. Fibre group 5.5/week	Poor - short crossover	Indirect patients - minor, closely related conditn	Precise	consistent	Not applicable	Patients with chronic constipation, not IBS; in secondary care. Crossover study, 1 week washout.	Low

Comparison: laxative vs fibre (lactulose versus ispaghula)

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Impre-cision*	*Inconsist ency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
improvement in bowel score	1trial; 78 patients; from RCT; (long term maintenance design)	MD=1.4 (95%CI 0.19, 2.61)		Statistically significant, favours lactulose after 4 weeks; scale 0-10 (excellent). Fibre group 4.8	Poor - short crossover	Indirect patients - minor, closely related conditn	Precise	consistent	Not applicable	Patients with chronic constipation, not IBS; in secondary care. Crossover study, 1 week washout.	Moderate
patient preference	1trial; 78 patients; from RCT; (long term maintenance design)	RR=1.71 (95%CI 1.05, 2.79)		statistically significantly more patients preferred lactulose. Fibre proportion 44%.	Poor - short crossover	Indirect patients - minor, closely related conditn	Fairly wide CI	consistent	Not applicable	Patients with chronic constipation, not IBS; in secondary care. Crossover study, 1 week washout.	Low
Adverse effects	1trial; 315 patients; from RCT; (long term maintenance design)	OR=0.98 (95%CI 0.3, 3.225)		No significant difference	Poor - post-hoc subgroup	Indirect patients - minor, closely related conditn	Wide CI	consistent	Poor - studies, industry	Patients with chronic constipation, not IBS; in primary care. Study authors from manufacturers of fibogel. Post-hoc subgroup for lactulose.	very low

Evidence Summary: psychotherapy review

Comparison: psychotherapy+medical vs medical

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (no. patients)	1 trial; 102 patients; from RCT; (parallel design);	RR=3.08 (95%CI 1.74, 5.47)		Statistically significant, favours psychotherapy + medical care. NNT 3, control group rate 23%	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	consistent	---	Rated by assessor (not patients) at 12 weeks. Refractory IBS, secondary care (tertiary referral). 48% psychological problems.	Moderate /low
Global improvement of IBS symptoms (no. patients)	1 trial; 101 patients; from RCT; (parallel design);	RR=1.68 (95%CI 1.14, 2.49)		Statistically significant, favours psychotherapy + medical care. NNT 4, control group rate 40%.	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	Patients' assessment at 15 months. Long term IBS, but unclear if refractory. Patients had to commit to longterm trial. Secondary care. 70% had previous psychological comorbidities.	Moderate
Global IBS symptom score	1 trial; 101 patients; from RCT; (parallel design);	MD=-4.56 (95%CI -8.77, -0.35)		Statistically significant, favours psychotherapy + medical care. Scale may be 114 max. Control group score 37.5.	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	Patients' assessment at 12 weeks. Long term IBS, but unclear if refractory. Patients had to commit to longterm trial. Secondary care. 70% had previous psychological comorbidities.	Moderate
Global IBS symptom score	1 trial; 101 patients; from RCT; (parallel design);	MD=-8.1 (95%CI -12.31, -3.89)		Statistically significant, favours psychotherapy + medical care. Scale may be 114 max. Control group score 38.0.	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	Patients' assessment at 15 months. Long term IBS, but unclear if refractory. Patients had to commit to longterm trial. Secondary care. 70% had previous psychological comorbidities.	Moderate

Comparison: psychotherapy+medical vs medical

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
pain score	1 trial; 101 patients; from RCT; (parallel design);	MD=-1.01 (95%CI -1.95, -0.07)		Statistically significant, favours psychotherapy + medical care. Scale unclear. Control group score 7.8.	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	Patients' assessment at 12 weeks. Long term IBS, but unclear if refractory. Patients had to commit to longterm trial. Secondary care. 70% had previous psychological comorbidities.	Moderate
pain score	1 trial; 101 patients; from RCT; (parallel design);	MD=-2.3 (95%CI -3.43, -1.17)		Statistically significant, favours psychotherapy + medical care. Scale unclear. Control group score 7.8.	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	Patients' assessment at 15 months. Long term IBS, but unclear if refractory. Patients had to commit to longterm trial. Secondary care. 70% had previous psychological comorbidities.	Moderate
mental health	1 trial; 101 patients; from RCT; (parallel design);	RR=7.33 (95%CI 2.34, 22.95)		Statistically significant, favours psychotherapy + medical care	Good	Indirect setting-minor, secondary care OPD	Wide CI	consistent	---	Raters' assessment at 12 weeks. Mental improvement. Long term IBS, but unclear if refractory. Patients had to commit to longterm trial. Secondary care. 70% had previous psychological comorbidities.	Moderate/ low
mental health	1 trial; 101 patients; from RCT; (parallel design);	RR=4.9 (95%CI 2.03, 11.8)		Statistically significant, favours psychotherapy + medical care	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	consistent	---	Raters' assessment at 15 months. Mental improvement. Long term IBS, but unclear if refractory. Patients had to commit to longterm trial. Secondary care. 70% had previous psychological comorbidities.	Moderate /low

Comparison: psychotherapy+medical vs medical

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
mental health	1 trial; 101 patients; from RCT; (parallel design);	RR=0.94 (95%CI 0.48, 1.86)		Not statistically significant	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	consistent	---	Patients' assessment at 15 months. Mental improvement. Long term IBS, but unclear if refractory. Patients had to commit to longterm trial. Secondary care. 70% had previous psychological comorbidities.	Moderate /low
mental health	1 trial; 101 patients; from RCT; (parallel design);	RR=1.44 (95%CI 0.86, 2.4)		Not statistically significant	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	consistent	---	Patients' assessment at 15 months. Psychological subgroup. Mental improvement. Long term IBS, but unclear if refractory. Patients had to commit to longterm trial. Secondary care. 70% had previous psychological	Moderate /low

Comparison: psychotherapy only vs medical treatment

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (no. patients)	1 trial; 171 patients; from RCT; (parallel design);	RR=1.59 (95%CI 1.13, 2.23)		Statistically significant, favours psychotherapy. NNT 5, control group rate 38%	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	12 weeks. 16% discontinued treatment in the psychotherapy arm, but ITT. Refractory IBS. Approx half pts had depression. Secondary care.	Moderate
Global improvement of IBS symptoms (no. patients)	1 trial; 171 patients; from RCT; (parallel design);	RR=1.21 (95%CI 0.92, 1.6)		Not significant	poor possibly confounded	Indirect setting-minor, secondary care OPD	Precise	consistent	---	12 months follow up. 16% discontinued treatment in the psychotherapy arm, but ITT. May be confounded by 10% psych in usual care arm during follow up. Refractory IBS. Approx half pts had depression. Secondary care.	Low
pain score	1 trial; 171 patients; from RCT; (parallel design);	MD=-4.7 (95%CI -13.55, 4.15)		Not significant	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	12 weeks. 16% discontinued treatment in the psychotherapy arm, but ITT. Refractory IBS. Approx half pts had depression. Secondary care.	Moderate
pain score	1 trial; 171 patients; from RCT; (parallel design);	MD=0.6 (95%CI -8.75, 9.95)		Not significant	Poor possibly confounded	Indirect setting-minor, secondary care OPD	Precise	consistent	---	12 months follow up. 16% discontinued treatment in the psychotherapy arm, but ITT. May be confounded by 10% psych in usual care arm during follow up. Refractory IBS. Approx half pts had depression. Secondary care.	Low

Comparison: psychotherapy only vs medical treatment

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Quality of life	1 trial; 171 patients; from RCT; (parallel design);	MD=2.7 (95%CI 0.22, 5.18)		Statistically significant, favours psychotherapy. Small effect. Scale 0-100	Poor loss to follow up	Indirect setting-minor, secondary care OPD	Precise	consistent	---	SF36 physical health. 12 weeks. 16% discontinued psychotherapy, but ITT. Refractory IBS. ~50% depression. Secondary care. 32% missing data psychotherapy.	Low
Quality of life	1 trial; 171 patients; from RCT; (parallel design);	MD=5.5 (95%CI 2.13, 8.87)		Statistically significant, favours psychotherapy. Small effect. Scale 0-100	Poor possibly confounded	Indirect setting-minor, secondary care OPD	Precise	consistent	---	SF36 physical health. 12 months follow up. 16% discontinued treatment in the psychotherapy arm, but ITT. Refractory IBS. Approx half pts had depression. May be confounded 10% psych in usual care follow up period.	Low
Quality of life	1 trial; 171 patients; from RCT; (parallel design);	MD=5.9 (95%CI 1.35, 10.45)		Statistically significant, favours psychotherapy. Small effect. Scale 0-100	poor loss to follow up	Indirect setting-minor, secondary care OPD	Precise	consistent	---	SF36 mental health. 12 weeks. 16% discontinued psychotherapy, but ITT. Refractory IBS. ~50% depression. Secondary care. 32% missing data psychotherapy.	Low
Quality of life	1 trial; 171 patients; from RCT; (parallel design);	MD=-1.9 (95%CI -6.45, 2.65)		Not statistically significant	poor loss to follow up	Indirect setting-minor, secondary care OPD	Precise	consistent	---	SF36 mental health. 12 months follow up. 16% discontinued psychotherapy, but ITT. Refractory IBS. 32% missing data psychotherapy. 50% depression. May be confounded 10% psych in	Low

Comparison: psychotherapy only vs medical treatment

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Number requiring other medication	1 trial; 171 patients; from RCT; (parallel design);	RR=0.85 (95%CI 0.47, 1.54)		Not significant	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	consistent	---	Number requiring prescriptions for antidepressants over 12m. Refractory IBS. 50% depression.	Low
Number discontinuing treatment	1 trial; 171 patients; from RCT; (parallel design);	Peto OR=8.83 (95%CI 2.97, 26.27)		Statistically significant, favours usual care.	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	consistent	---	Refractory IBS. 50% depression.	Low

Comparison: psychotherapy vs antidepressant

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Global improvement of IBS symptoms (no. patients)	1 trial; 172 patients; from RCT; (parallel design);	RR=0.9 (95%CI 0.7, 1.15)		Not significant	Good	Indirect setting-minor, secondary care OPD	Precise	consistent	---	12 weeks. 16% discontinued psychotherapy and 34% SSRI, but ITT. Refractory IBS. 50% depression. Secondary care.	Moderate
Global improvement of IBS symptoms (no. patients)	1 trial; 172 patients; from RCT; (parallel design);	RR=1.09 (95%CI 0.84, 1.41)		Not significant; may be confounded.	Poor probably confounded	Indirect setting-minor, secondary care OPD	Precise	consistent	---	12 months. May be confounded by different use of SSRI in follow up. 16% discontinued psychotherapy and 34% SSRI, but ITT. Refractory IBS. 50% depression. Secondary care.	very low
pain score	1 trial; 172 patients; from RCT; (parallel design);	MD=4.5 (95%CI -4.95, 13.95)		Not significant	poor loss to follow up	Indirect setting-minor, secondary care OPD	Precise	consistent	---	12 weeks. 16% discontinued psychotherapy and 34% SSRI, but ITT. Refractory IBS. 50% depression. Secondary care. 26% missing data.	Low
Quality of life	1 trial; 172 patients; from RCT; (parallel design);	MD=-0.2 (95%CI -3.35, 2.95))		Not significant	poor loss to follow up	Indirect setting-minor, secondary care OPD	Precise	consistent	---	SF36 physical component. 12 weeks. 16% discontinued psychotherapy and 34% SSRI, but ITT. Refractory IBS. 50% depression. Secondary care. 32% missing data.	low

Comparison: psychotherapy vs antidepressant

Outcome	*Meta-analysis details*	*Summary Statistics*	*p (hetero) and I2*	*Comments:*	*Study quality*	*Directness*	*Imprecision*	*Inconsistency*	*Reporting Bias*	*GRADE Comments*	*GRADE Evidence Rating*
Quality of life	1 trial; 172 patients; from RCT; (parallel design);	MD=1.7 (95%CI -3.05, 6.45))		Not significant	poor loss to follow up	Indirect setting-minor, secondary care OPD	Precise	consistent	---	SF36 mental component. 12 weeks. 16% discontinued psychotherapy and 34% SSRI, but ITT. Refractory IBS. 50% depression. Secondary care. 32% missing data.	low
Number requiring other medication	1 trial; 172 patients; from RCT; (parallel design);	RR=0.45 (95%CI 0.27, 0.75)		Statistically significant, favours psychotherapy. NNH 5, antidepressant group rate 42%	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	----	---	Number requiring prescriptions for antidepressants over 12m. Refractory IBS. 50% depression.	Low
Number discontinuing treatment	1 trial; 172 patients; from RCT; (parallel design);	RR=0.49 (95%CI 0.28, 0.86)		Statistically significant, favours psychotherapy. NNH 6, antidepressant group rate 34%	Good	Indirect setting-minor, secondary care OPD	Fairly wide CI	consistent	---	Refractory IBS, secondary care, 50% depression	Low