Bijlage 5: Forest plots

Diet

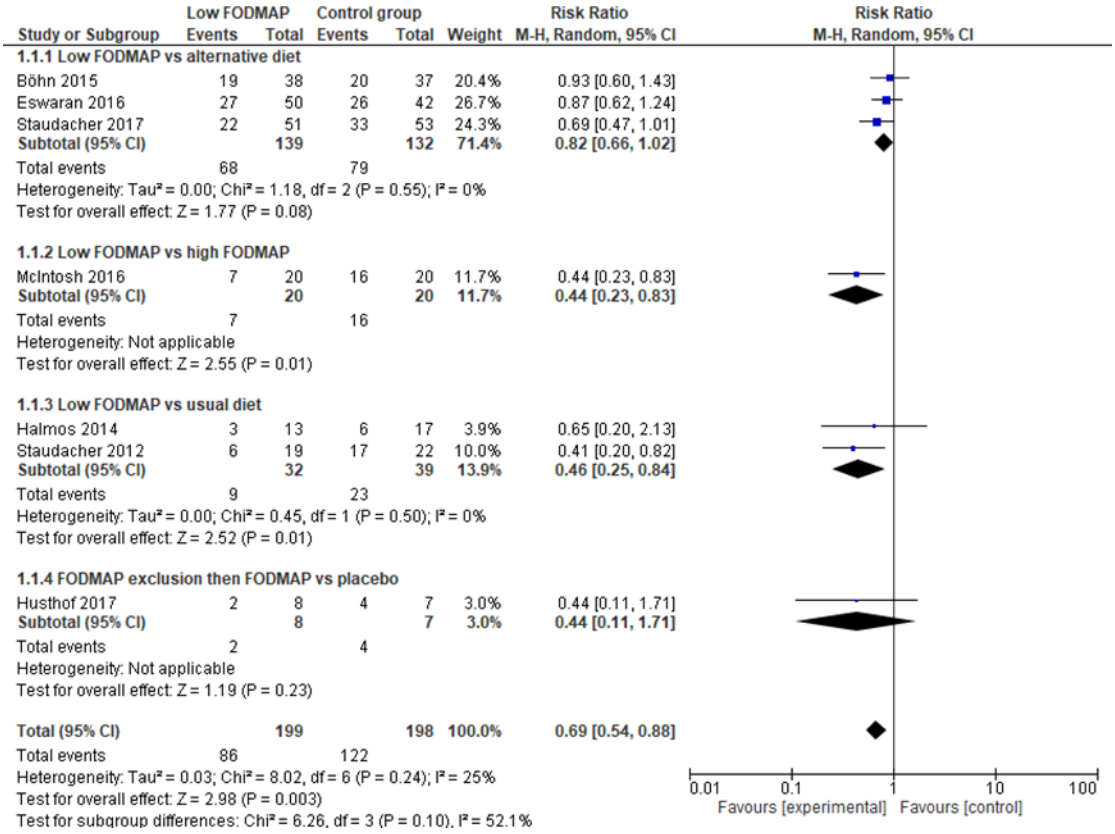


Figure 1: Low FODMAP diet and global improvement in IBS symptoms (data from Dionne 2018)

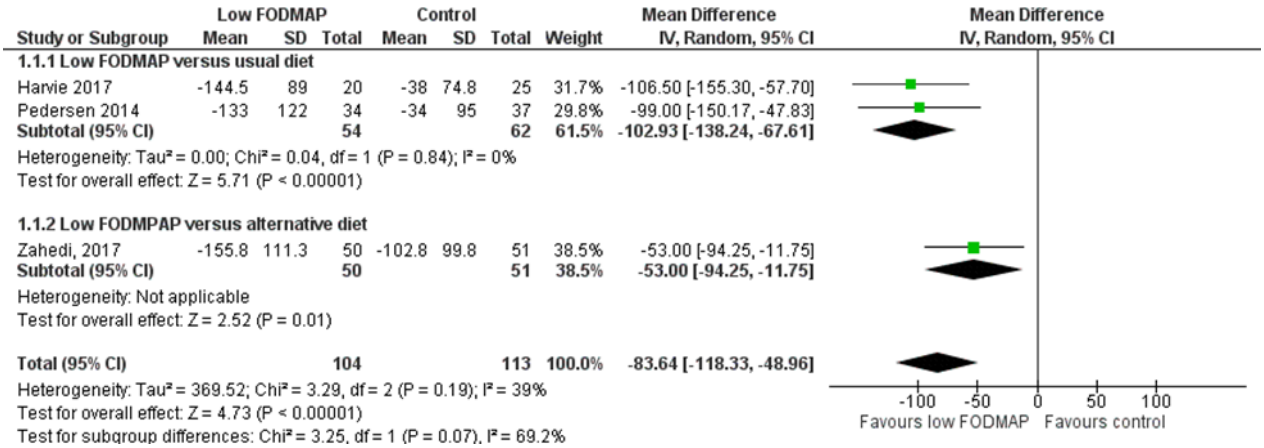
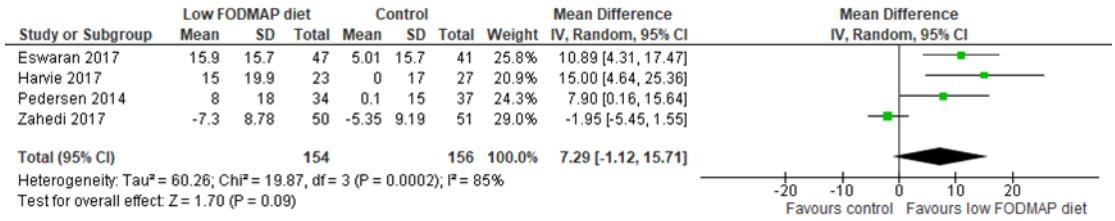


Figure 2: Low FODMAP diet of mean difference in IBS-SSS score



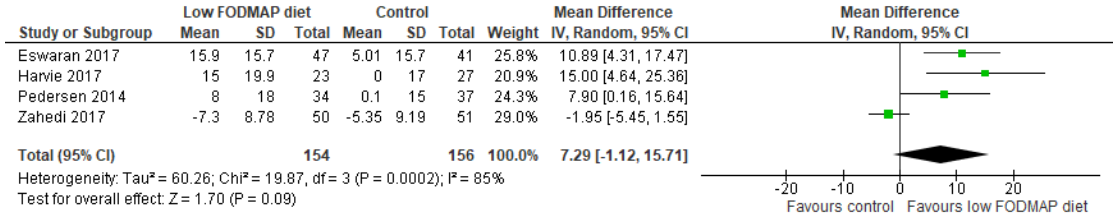


Figure 3: Low FODMAP diet, pooled mean difference IBS-QoL

Probiotics

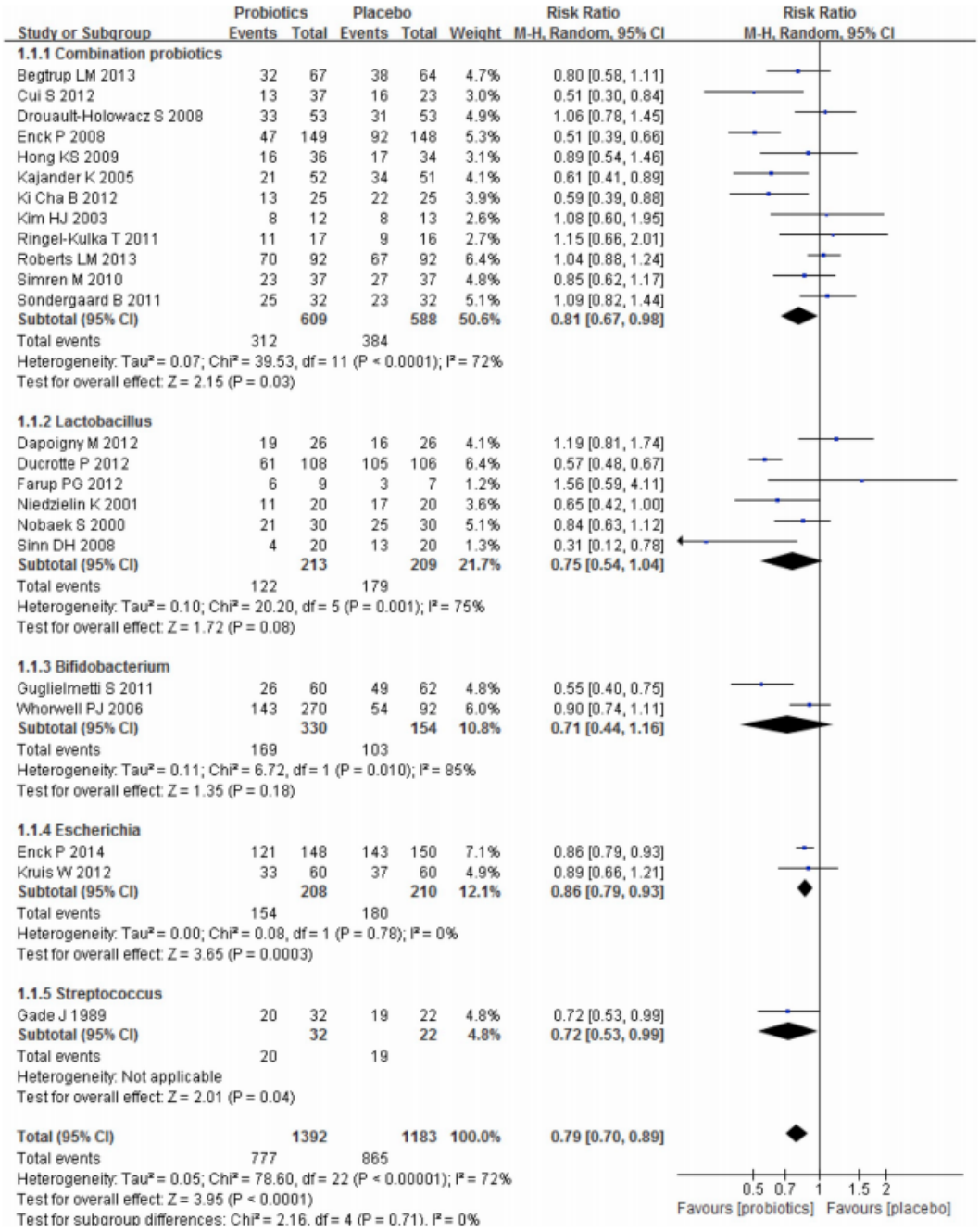


Fig. 2. Forest plot of comparison between probiotics and placebo in term of persistence of symptoms for IBS.

Figure 1. Meta-analysis from systematic review Niu (2020) probiotics and outcome 'persistence of symptoms'.

Figure from systematic review Niu (2020) probiotics and outcome 'general symptom score (GSS) or abdominal pain score (APS)'.

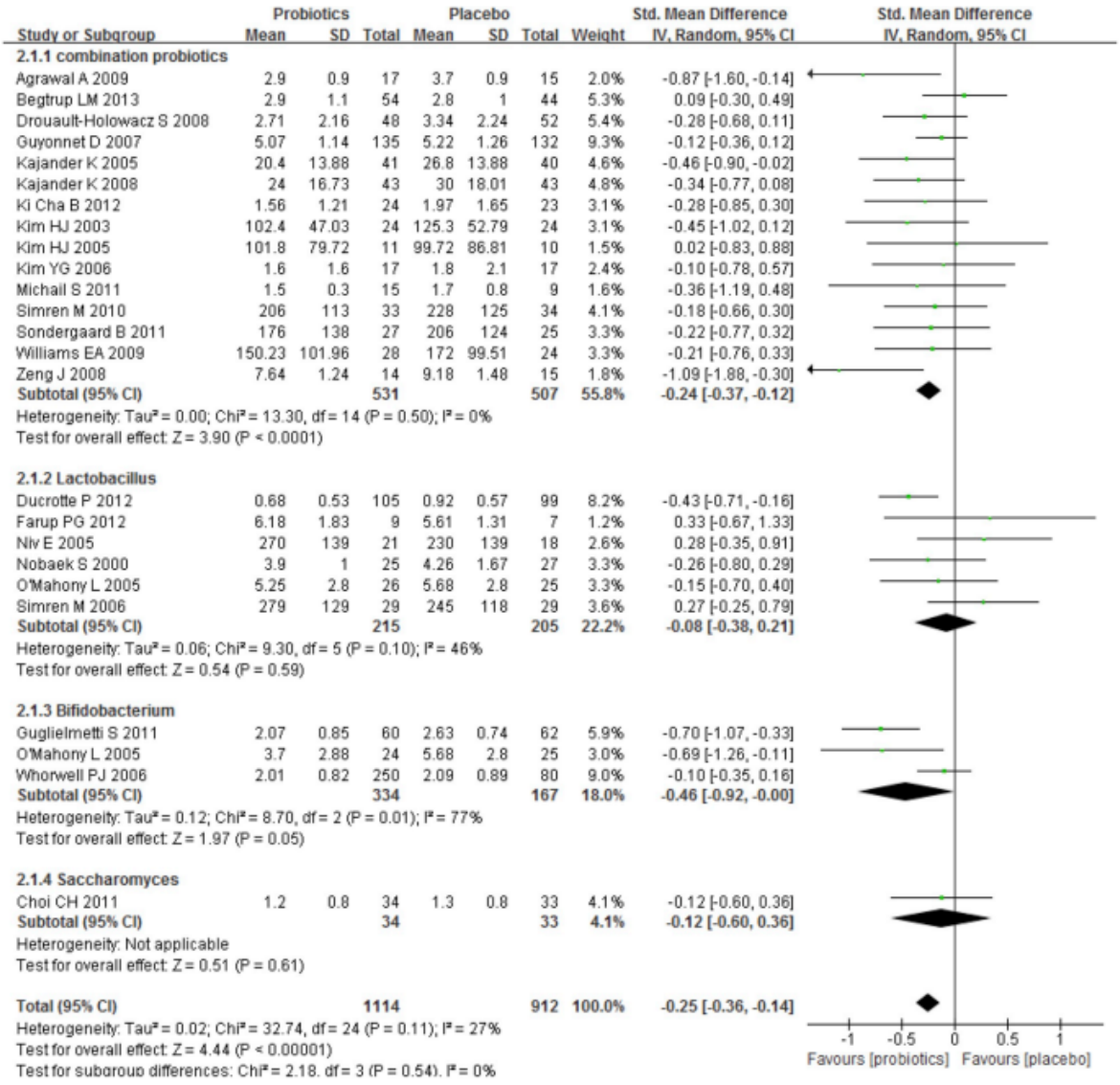
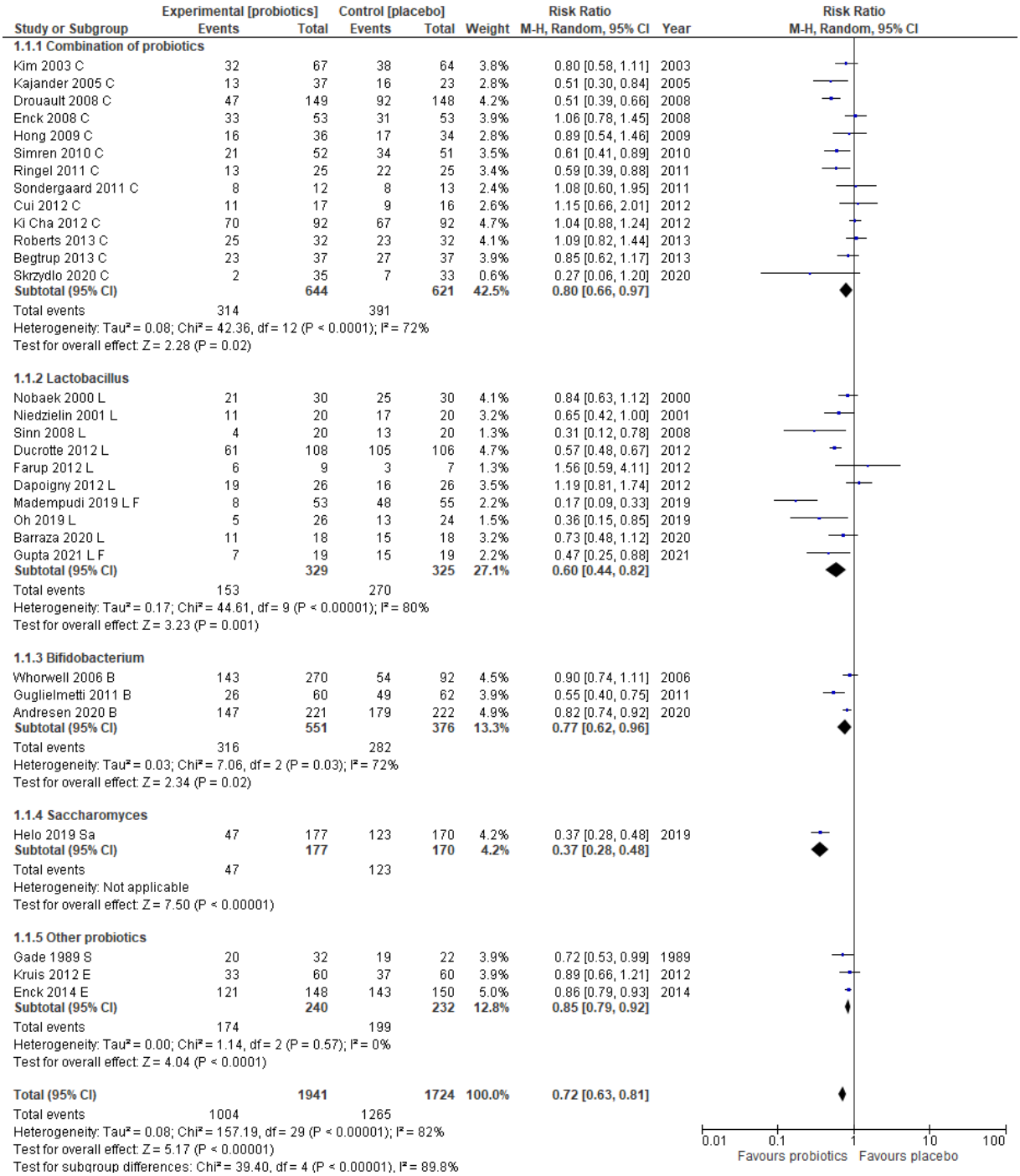
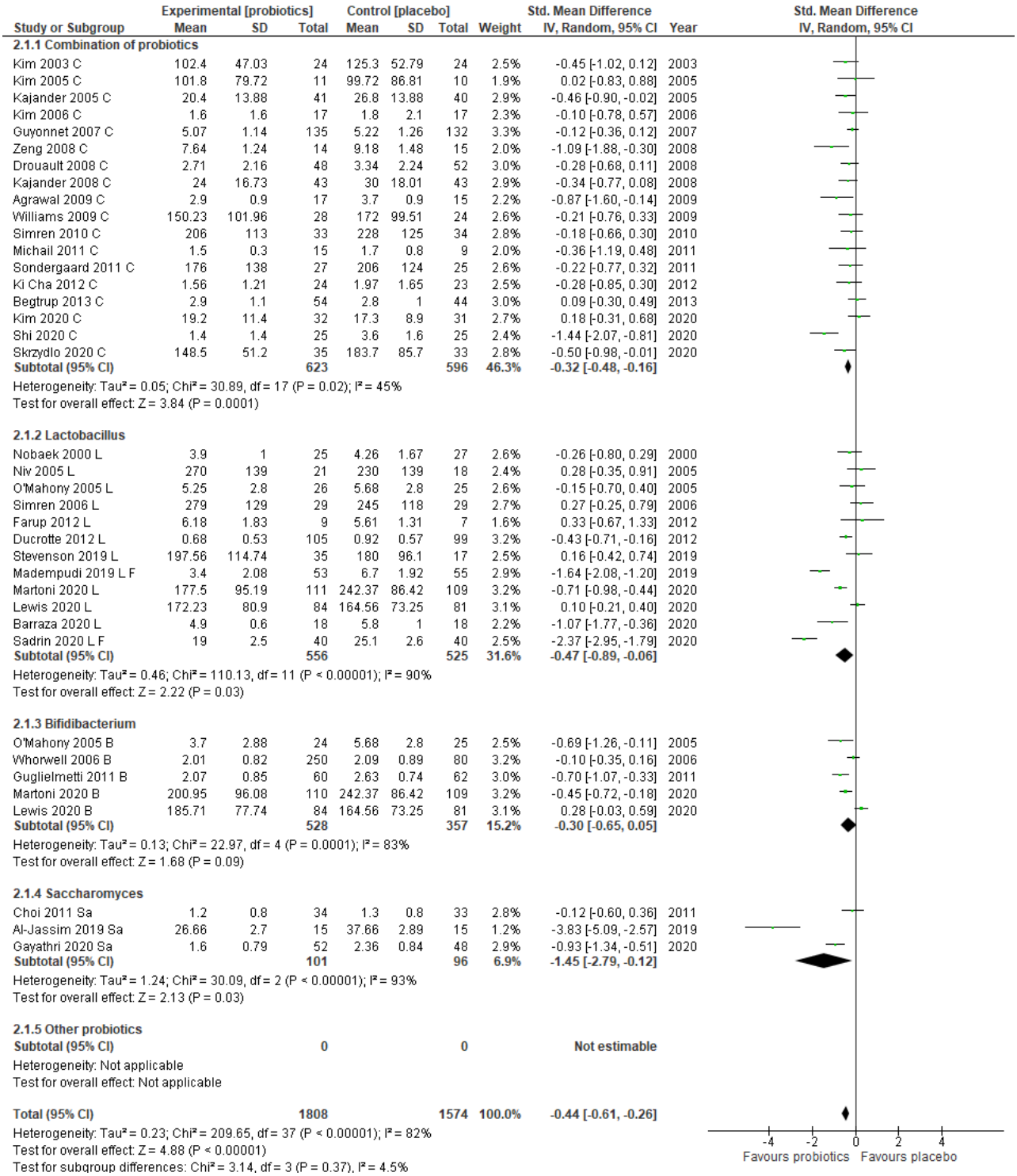


Fig. 3. Forest plot of comparison between probiotics and placebo in term of GSS or APS for IBS.

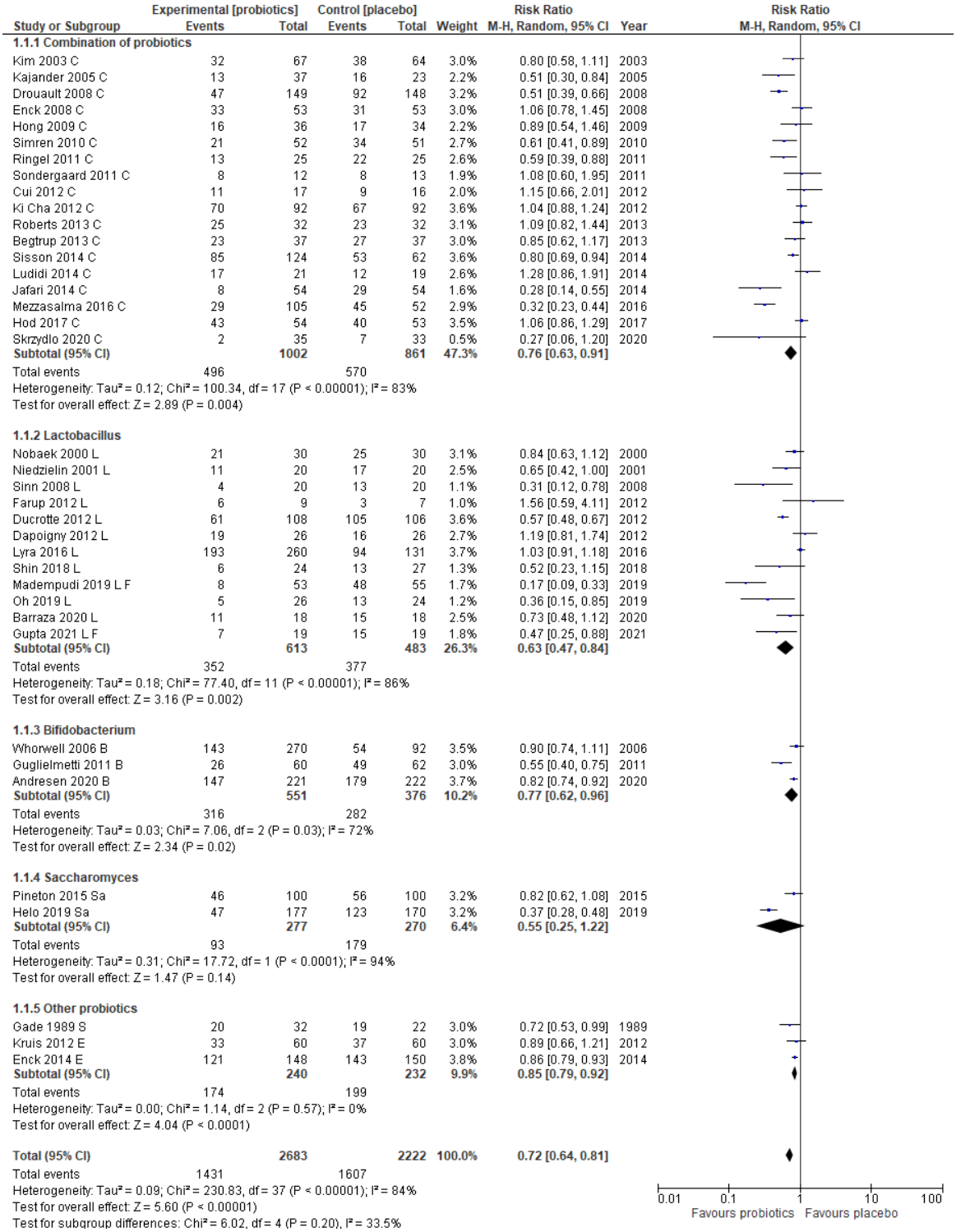
Forest plot with analysis of review Niu (2020) PLUS RCT's published after the search data of Niu (April 2019): probiotics and outcome 'persistence of symptoms'.



Forest plot with analysis of review Niu (2020) PLUS RCT's published after the search data of Niu (April 2019): probiotics and outcome 'general symptom score (GSS) or abdominal pain score (APS)'.

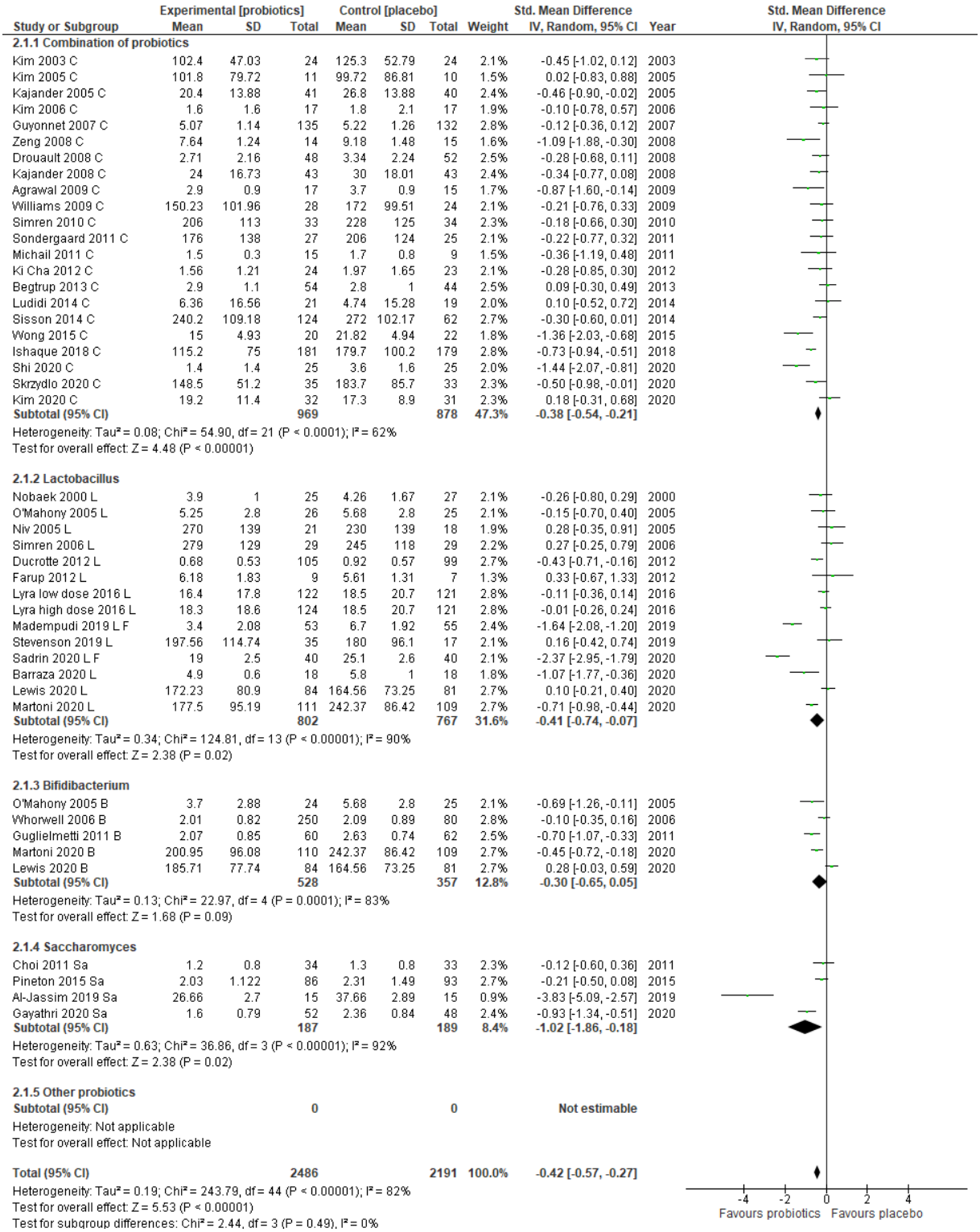


Forest plot with analysis of review Niu (2020) PLUS RCT's published after the search data of Niu (April 2019) PLUS Sun (2020): probiotics and outcome 'persistence of symptoms'.
[*RR was 0,79 (0,70-0,89), toen 0,72 (0,63-0,81), nu 0,72 (0,64-0,81)***]**



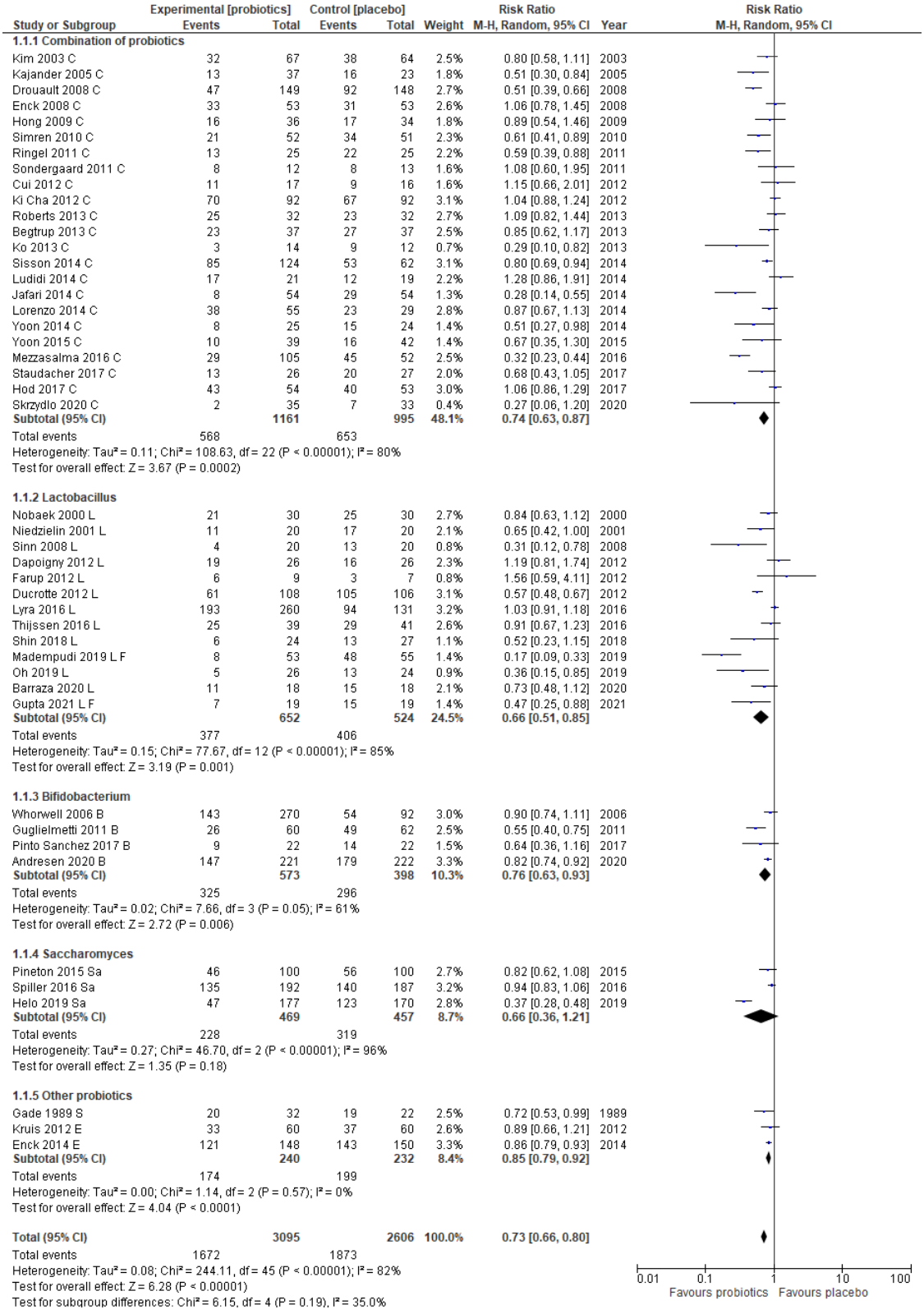
Forest plot with analysis of review Niu (2020) PLUS RCT's published after the search data of Niu (April 2019) PLUS Sun (2020): probiotics and outcome 'general symptom score (GSS) or abdominal pain score (APS)'.

[*SMD was -0,25, toen -0,44 (-0,61 – -0,26) is nu -0,42 (-0,57 – -0,27)***]**



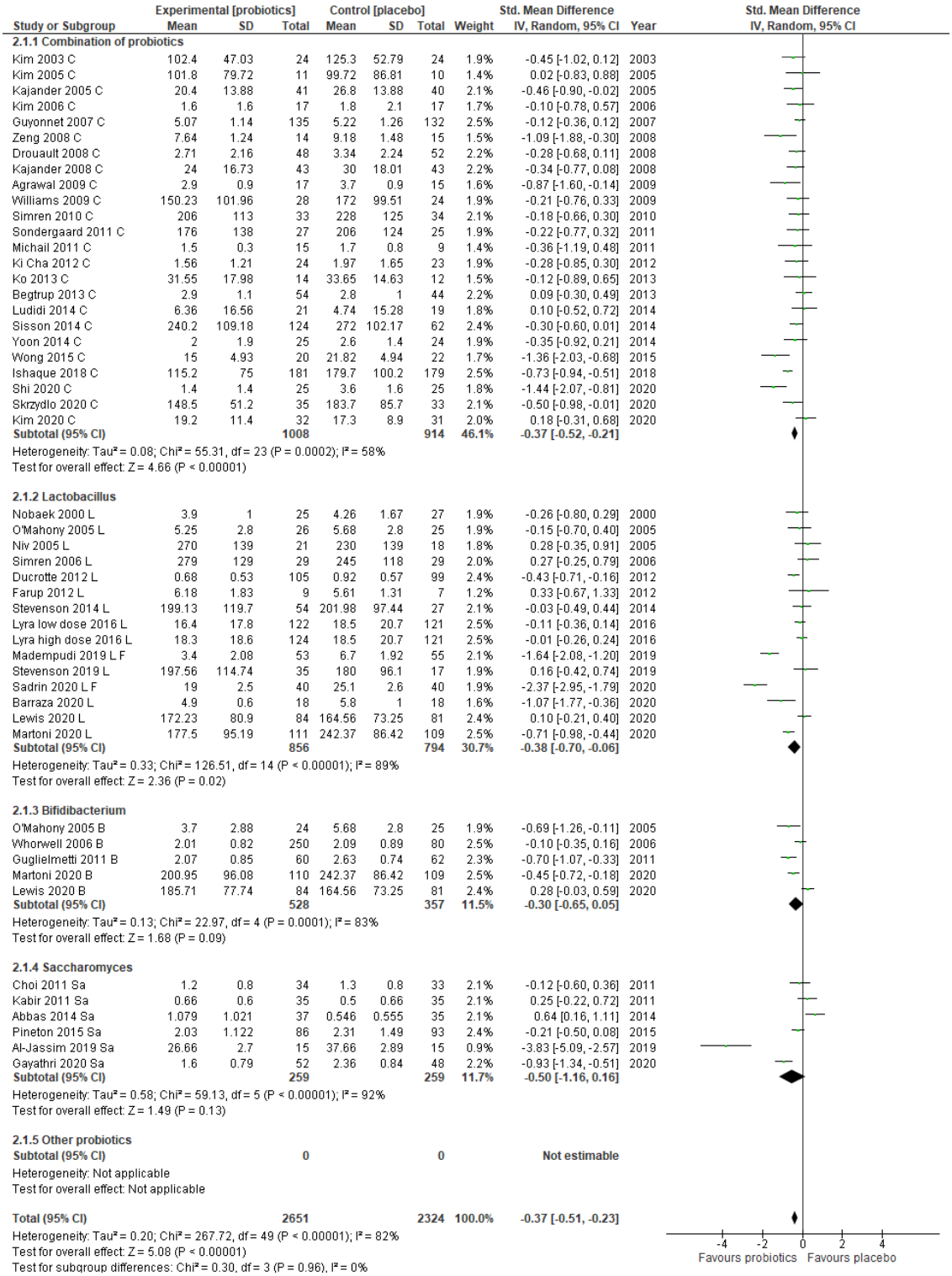
Forest plot with analysis of review Niu (2020) PLUS RCT's published after the search data of Niu (April 2019) PLUS Sun (2020) PLUS Ford (2018): probiotics and outcome 'persistence of symptoms'.

[*RR was 0,79 (0,70-0,89), toen 0,72 (0,63-0,81), daarna 0,72 (0,64-0,81) en nu 0,73 (0,66-0,89)***]** (*8 RCT's uit Ford toegevoegd*)



Forest plot with analysis of review Niu (2020) PLUS RCT's published after the search data of Niu (April 2019) PLUS Sun (2020) PLUS Ford (2018): probiotics and outcome 'general symptom score (GSS) or abdominal pain score (APS)'.

[*SMD was -0,25, toen -0,44 (-0,61 – -0,26) daarna -0,42 (-0,57 – -0,27) en nu -0,37 (-0,52 – -0,23)***]** (*5 RCT's uit Ford*)

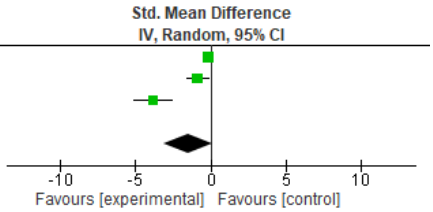


Analysis subtype IBS (C and D)

Forest plot IBS-C Outcome General symptom score or abdominal pain score

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Guyonnet 2007 C	5.07	1.14	135	5.22	1.26	132	36.2%	-0.12 [-0.36, 0.12]	2007
Agrawal 2009 C	2.9	0.9	17	3.7	0.9	15	34.0%	-0.87 [-1.60, -0.14]	2009
Al-Jassim 2019 Sa	26.66	2.7	15	37.66	2.89	15	29.9%	-3.83 [-5.09, -2.57]	2019
Total (95% CI)			**167**			**162**	**100.0%**	**-1.48 [-3.10, 0.14]**	

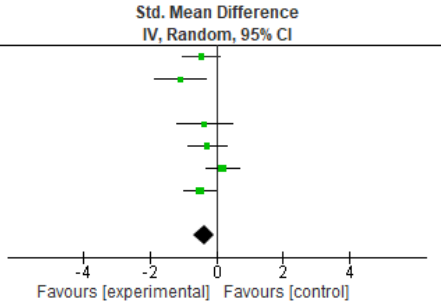
Heterogeneity: Tau² = 1.88; Chi² = 34.37, df = 2 (P < 0.00001); I² = 94%
Test for overall effect: Z = 1.79 (P = 0.07)



Forest plot IBS-D Outcome General symptom score or abdominal pain score

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Kim 2003 C	102.4	47.03	24	125.3	52.79	24	17.7%	-0.45 [-1.02, 0.12]	2003
Zeng 2008 C	7.64	1.24	14	9.18	1.48	15	11.7%	-1.09 [-1.88, -0.30]	2008
Ringel 2011 C	0	0	0	0	0	0		Not estimable	2011
Michail 2011 C	1.5	0.3	15	1.7	0.8	9	10.8%	-0.36 [-1.19, 0.48]	2011
Ki Cha 2012 C	1.56	1.21	24	1.97	1.65	23	17.7%	-0.28 [-0.85, 0.30]	2012
Kim 2020 C	19.2	11.4	32	17.3	8.9	31	20.8%	0.18 [-0.31, 0.68]	2020
Skrzydlo 2020 C	148.5	51.2	35	183.7	85.7	33	21.3%	-0.50 [-0.98, -0.01]	2020
Total (95% CI)			**144**			**135**	**100.0%**	**-0.36 [-0.68, -0.05]**	

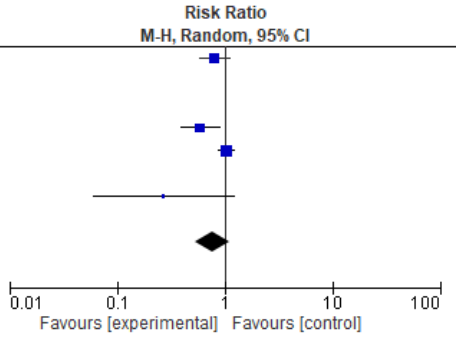
Heterogeneity: Tau² = 0.06; Chi² = 8.38, df = 5 (P = 0.14); I² = 40%
Test for overall effect: Z = 2.25 (P = 0.02)



Forest plot IBS-D Outcome Persistence of symptoms

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Kim 2003 C	32	67	38	64	30.7%	0.80 [0.58, 1.11]	2003
Zeng 2008 C	0	0	0	0		Not estimable	2008
Michail 2011 C	0	0	0	0		Not estimable	2011
Ringel 2011 C	13	25	22	25	26.9%	0.59 [0.39, 0.88]	2011
Ki Cha 2012 C	70	92	67	92	37.3%	1.04 [0.88, 1.24]	2012
Kim 2020 C	0	0	0	0		Not estimable	2020
Skrzydlo 2020 C	2	35	7	33	5.0%	0.27 [0.06, 1.20]	2020
Total (95% CI)		**219**		**214**	**100.0%**	**0.77 [0.54, 1.11]**	
Total events	117		134				

Heterogeneity: Tau² = 0.08; Chi² = 10.86, df = 3 (P = 0.01); I² = 72%
Test for overall effect: Z = 1.41 (P = 0.16)



Peppermint oil

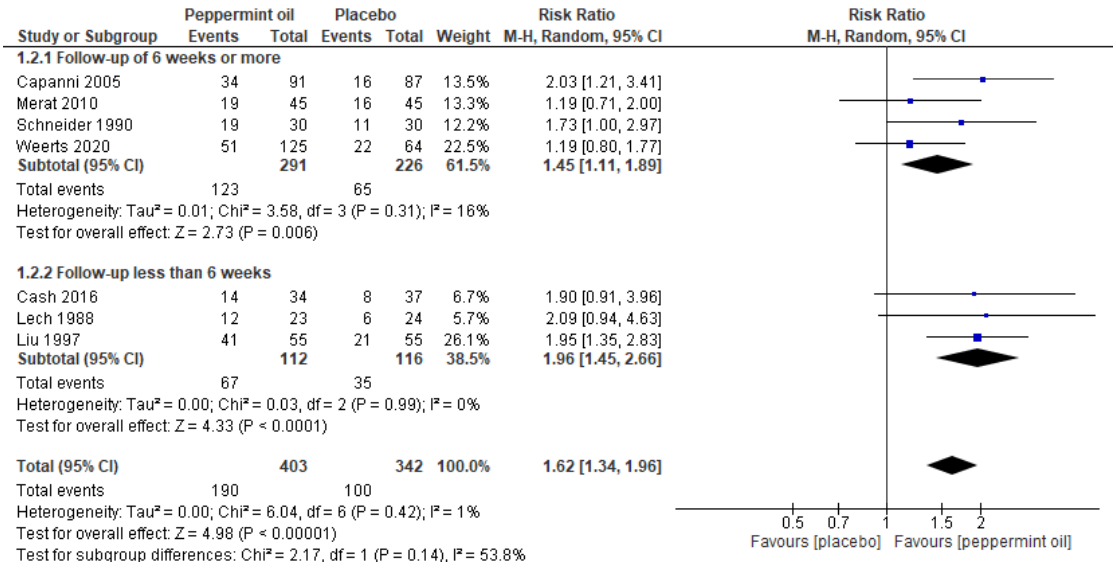


Figure 1. Forest plot of peppermint oil compared with placebo on abdominal pain.

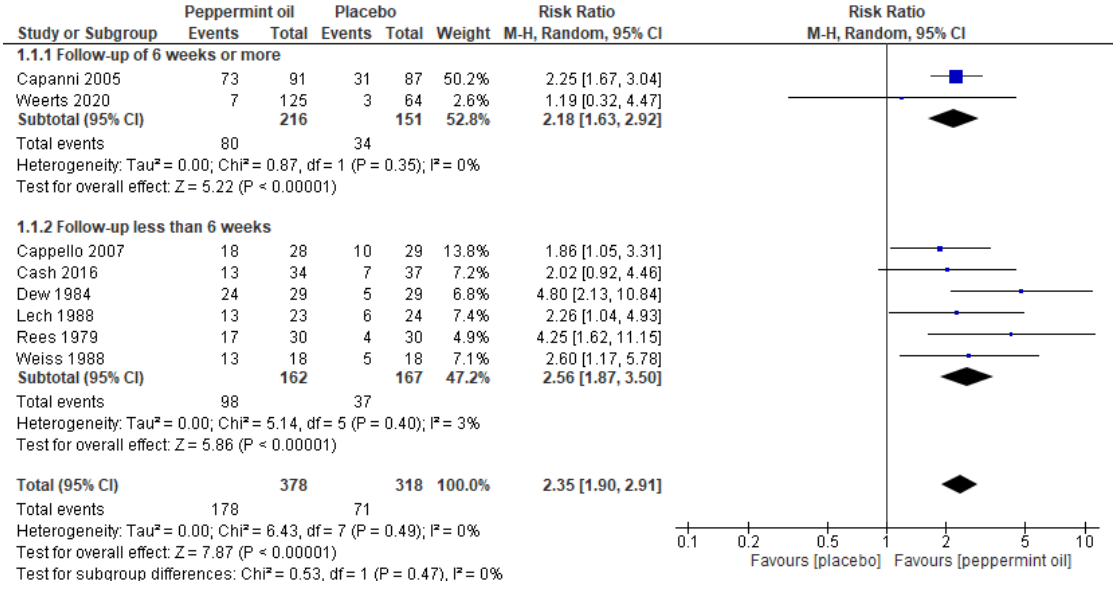


Figure 2. Forest plot of peppermint oil compared with placebo on global improvement.

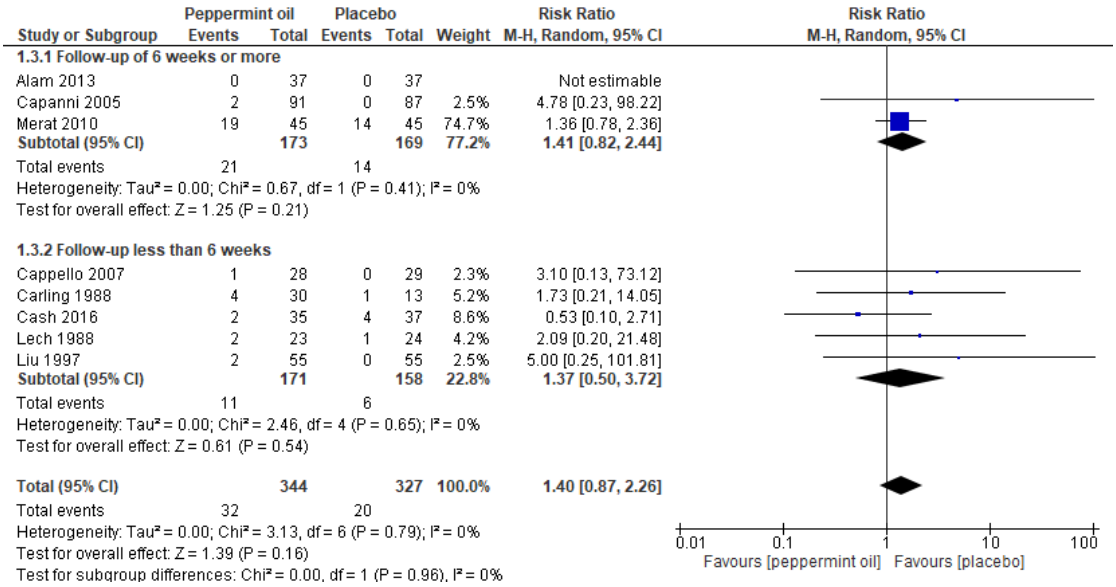


Figure 3. Forest plot of peppermint oil compared with placebo on adverse events.

Linaclotide

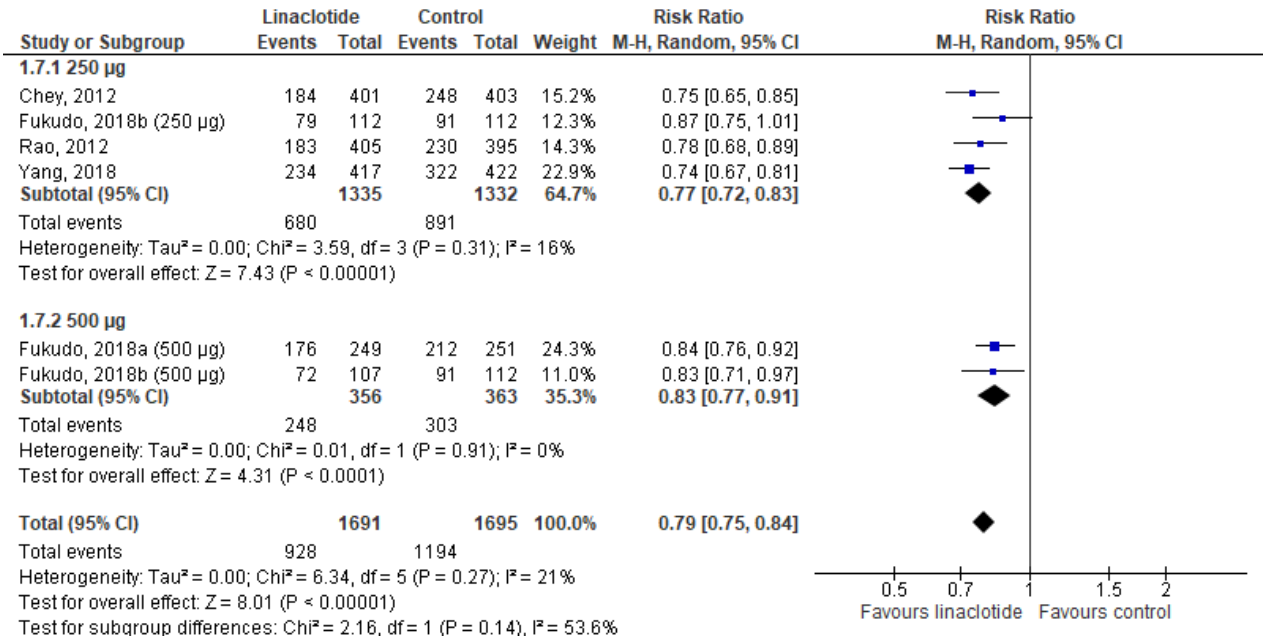


Figure 1. Forest plot of linaclotide compared with placebo showing clinically meaningful improvement in abdominal pain.

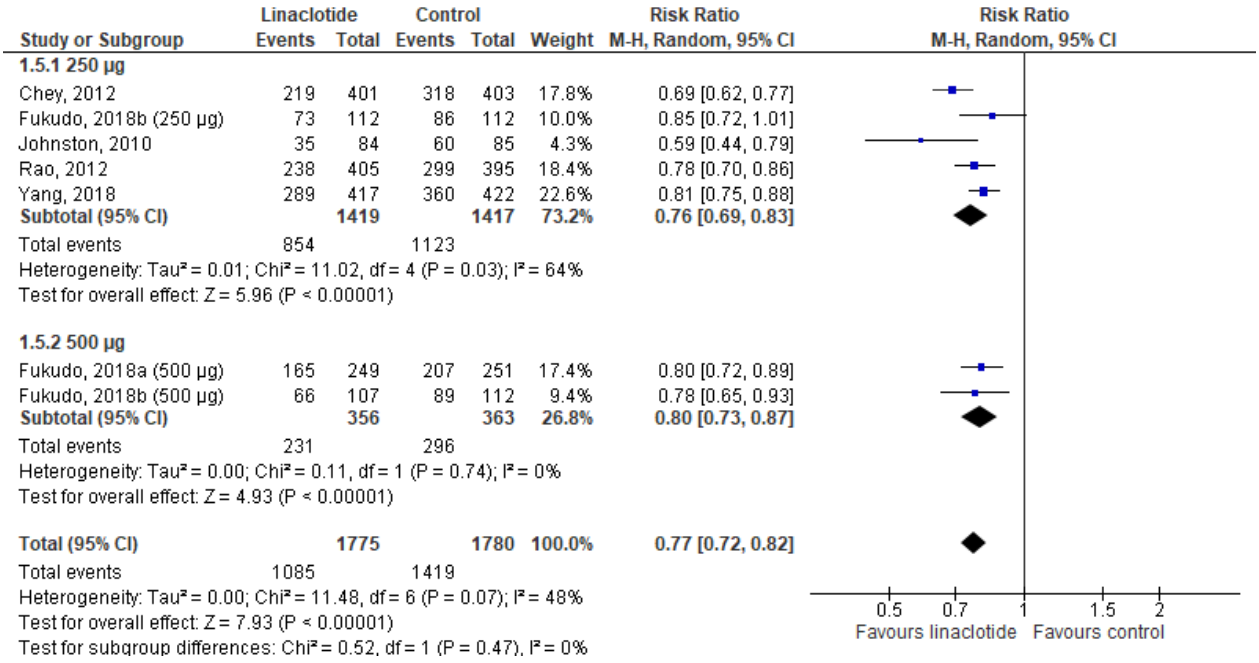


Figure 2: Forest plot of linaclotide compared with placebo showing failure to achieve global relief response (RevMan)

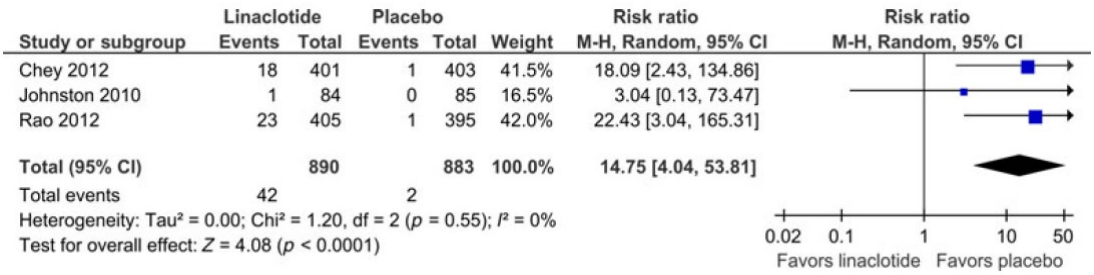


Figure 3. Forest plot of linaclotide compared with placebo showing incidence of diarrhea necessitating discontinuation of treatment. (Atluri, 2014)

Antidepressants
Forest-plots, based on Ford

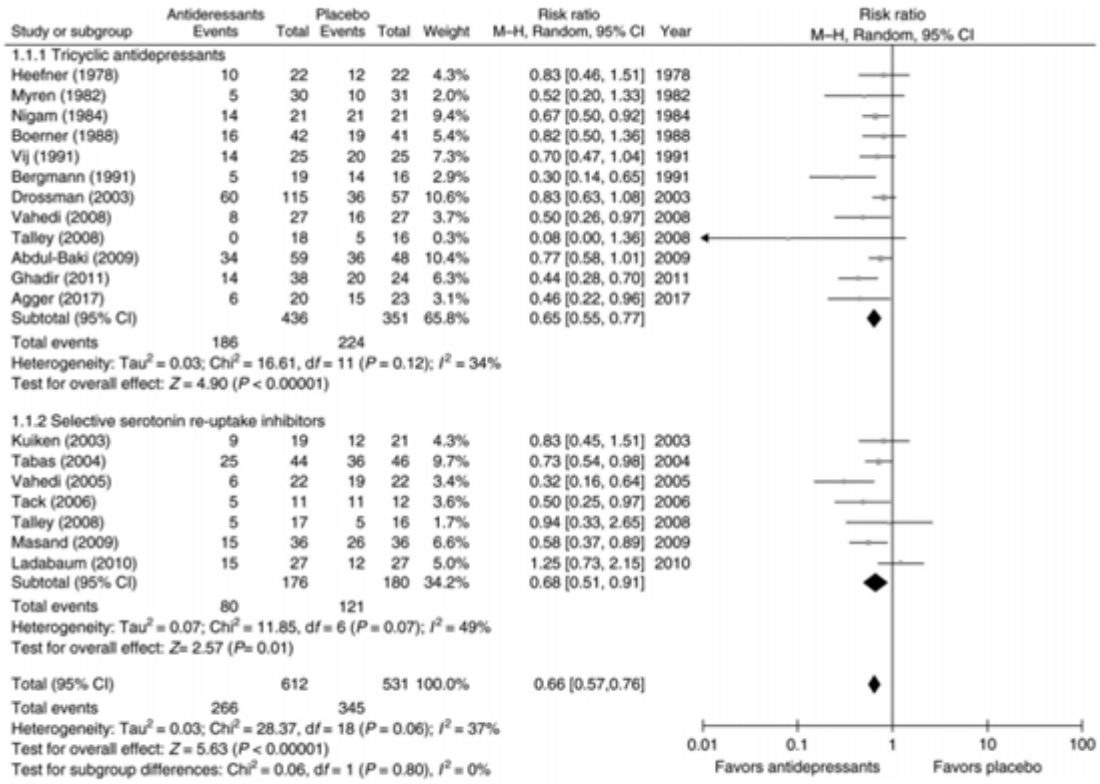


Fig. 2 Forest plot of randomized controlled trials of antidepressants versus placebo in irritable bowel syndrome

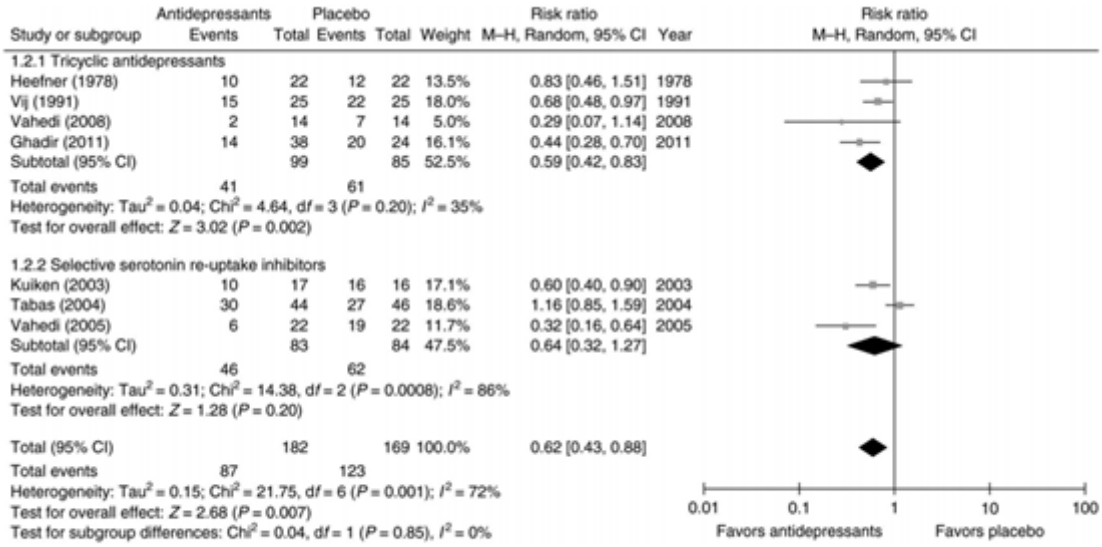


Fig. 3 Forest plot of randomized controlled trials of antidepressants versus placebo in terms of effect on abdominal pain in irritable bowel syndrome

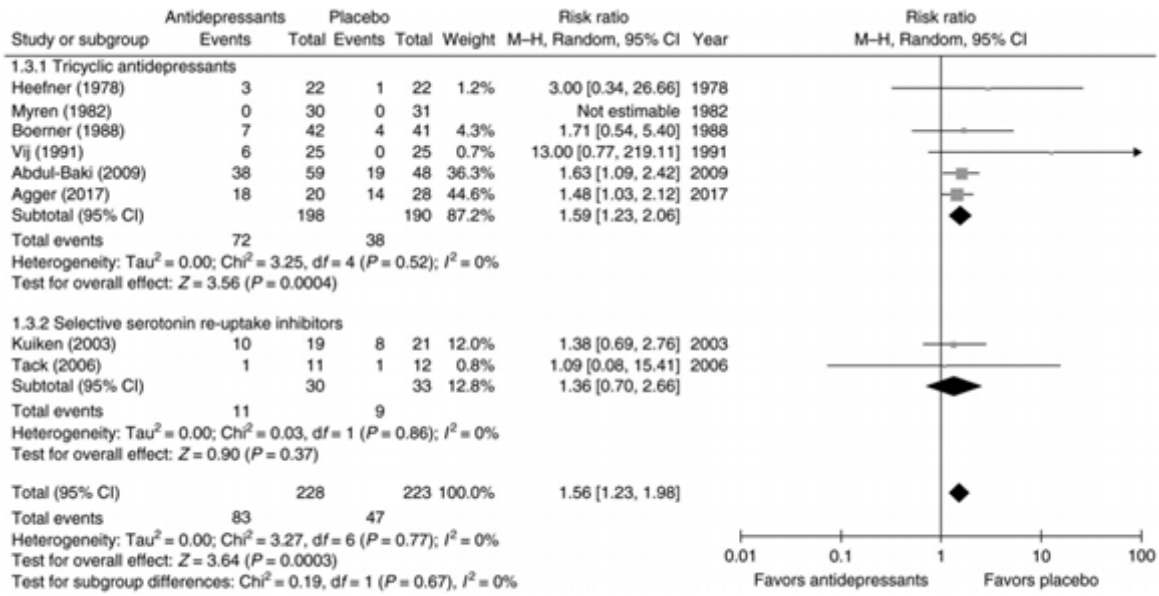
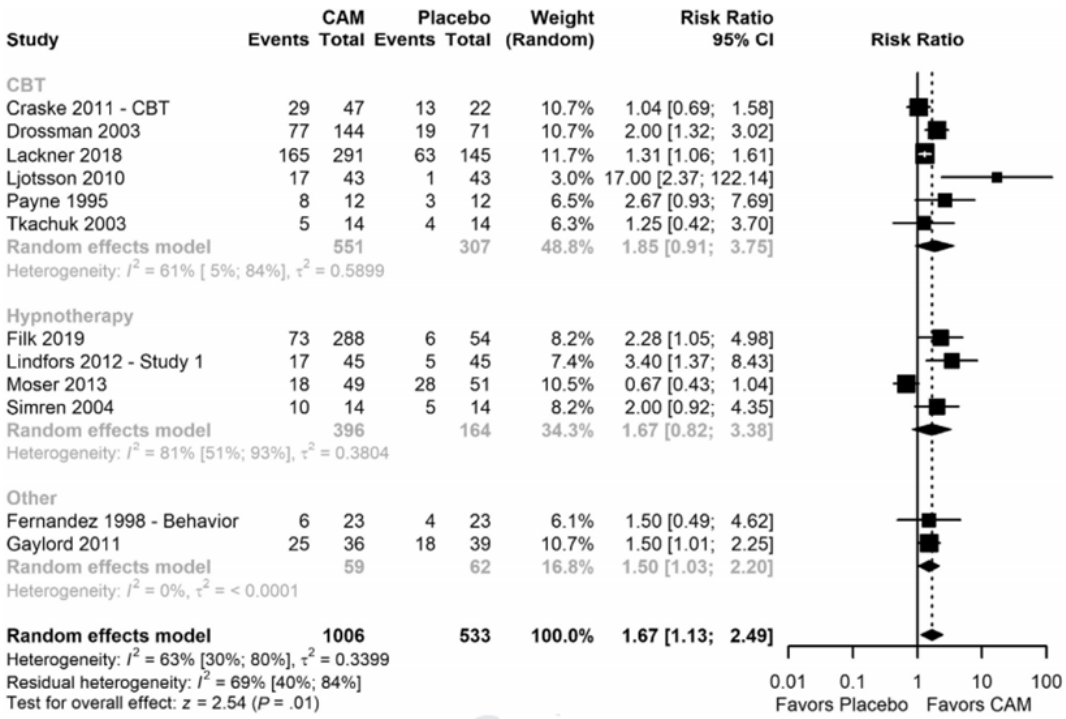


Fig. 4 Forest plot of adverse events in randomized controlled trials of antidepressants versus placebo in irritable bowel syndrome

Psychological therapies



Supplementary Figure 10. Forest plot of studies of mind-body based therapy vs placebo or sham with effect on overall response by intervention (between-group *P* value = .87). CAM, complementary and alternative medicine; CBT, cognitive behavioral therapy; CI, confidence interval.

Figure from systematic review Billings (2020) mind-body therapy (cognitive behavioural therapy and hypnotherapy) and outcome 'overall response'.

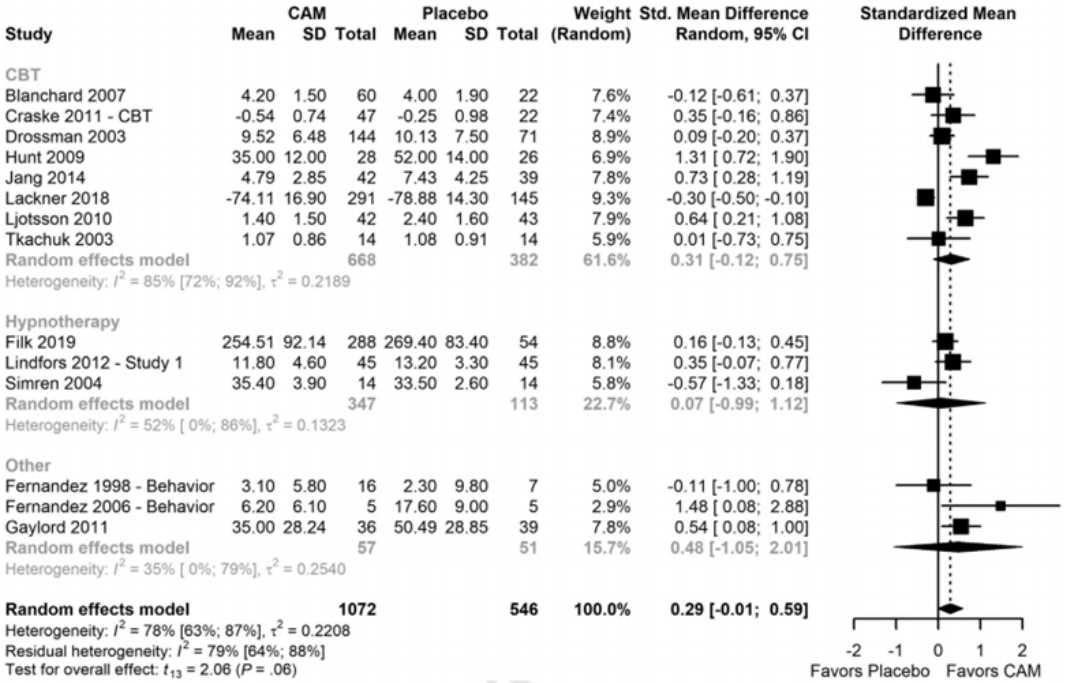


Figure 3. Forest plot of studies of mind-body based therapy vs placebo or sham with effect on abdominal pain by intervention. CAM, complementary and alternative medicine; CBT, cognitive behavioral therapy.

Figure from systematic review Billings (2020) mind-body therapy (cognitive behavioural therapy and hypnotherapy) and outcome 'effect on abdominal pain'.

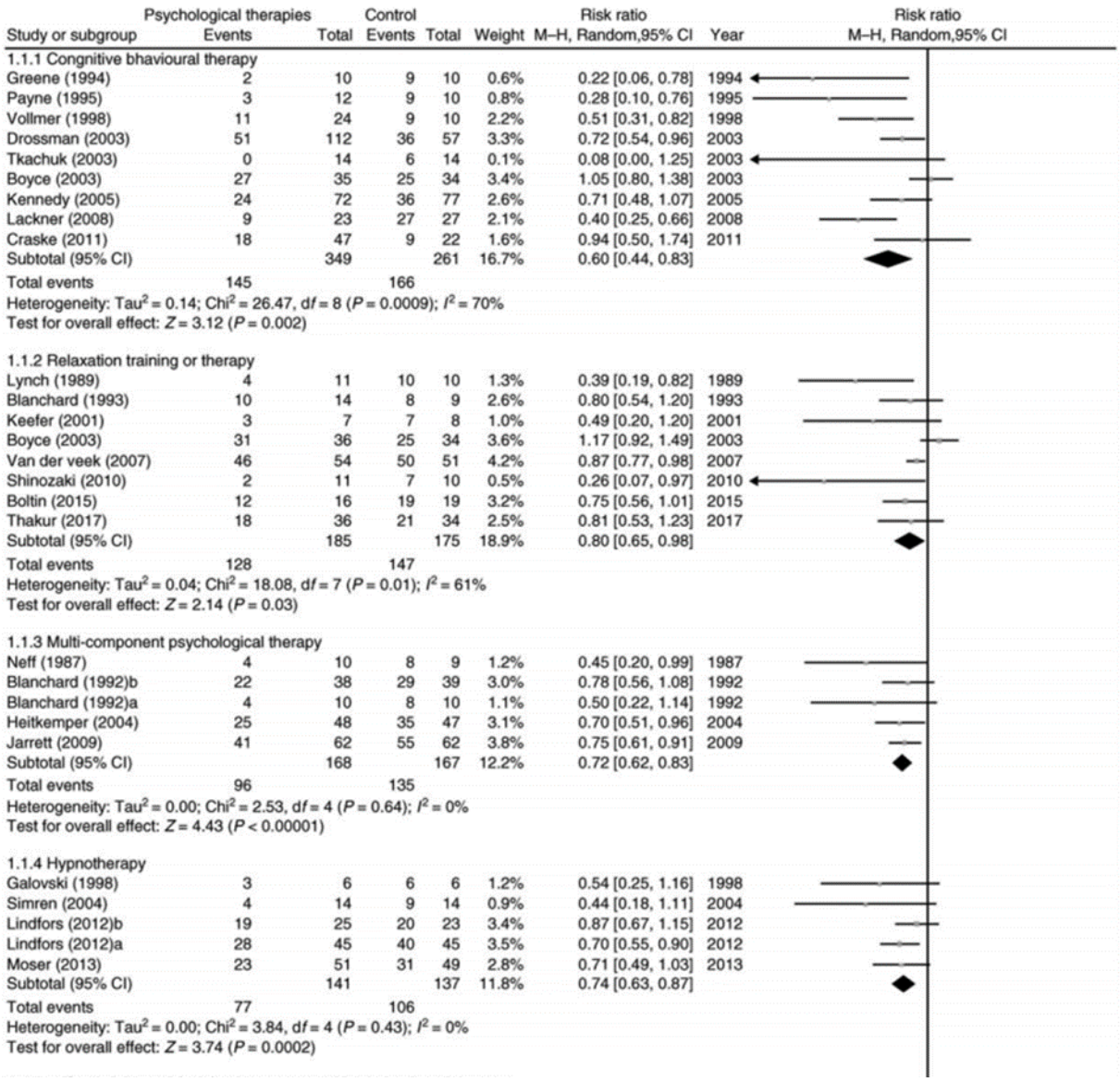
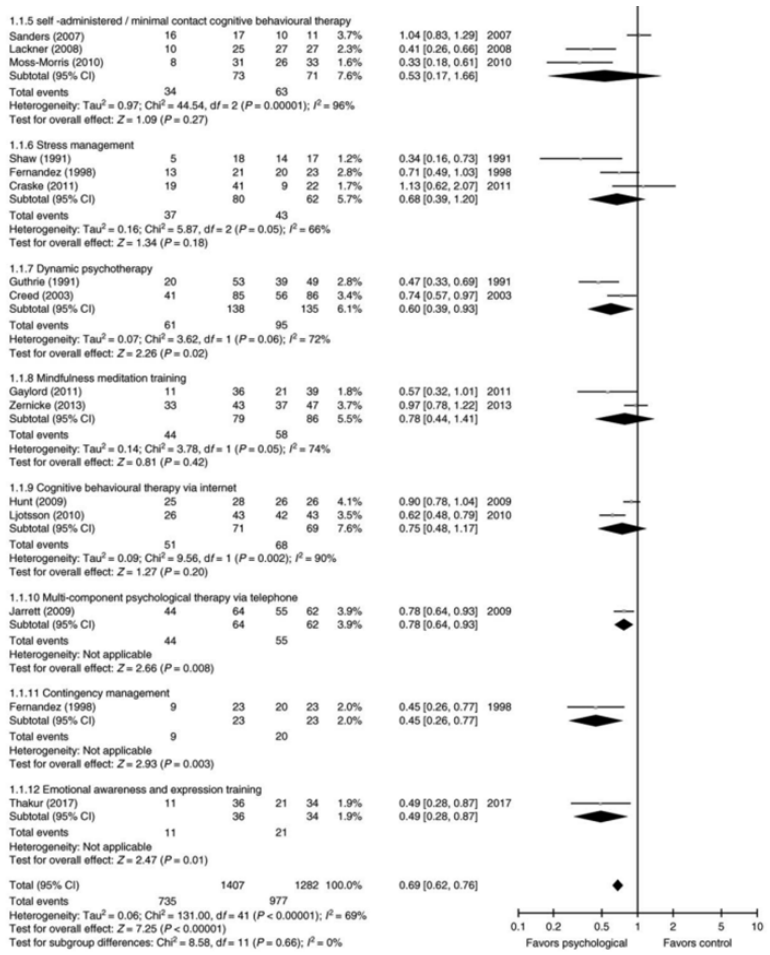


Figure from systematic review Ford (2019) Cognitive behavioural therapy, relaxation therapy, hypnotherapy and outcome 'no improvement in IBS symptoms'.



omized controlled trials of psychological therapies versus control in irritable bowel syndrome

Figure from systematic review Ford (2019) Cognitive behavioural therapy, relaxation therapy, hypnotherapy and outcome 'no improvement in IBS symptoms'.

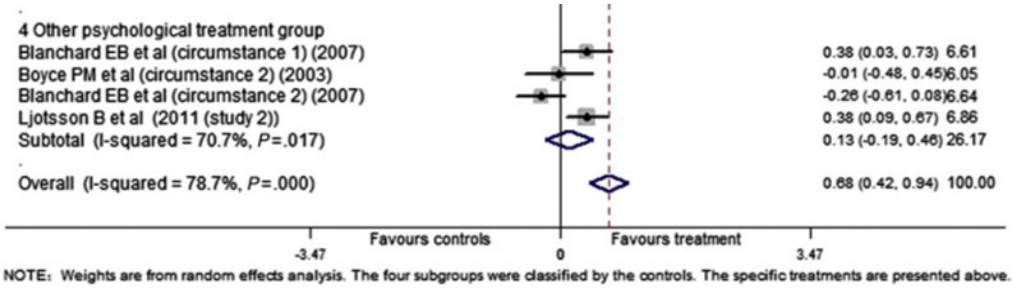


Fig. 2. Effect size estimates for the efficacy of CBT compared to controls in IBS symptom improvement at post-treatment.

Figure from systematic review Li (2014) other psychological treatments and outcome 'IBS symptom improvement' (post treatment).

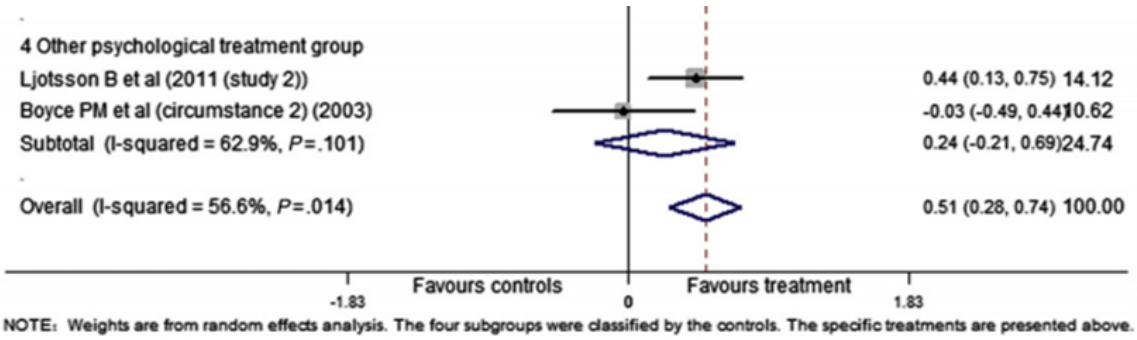


Fig. 3. Effect size estimates for the efficacy of CBT compared to controls in IBS symptom improvement at short-term follow-up.

Figure from systematic review Li (2014) other psychological treatments and outcome 'IBS symptom improvement' (at short-term follow-up).

Fig. 4. Effect size estimates for the efficacy of CBT compared to controls in improvement of IBS QOL.

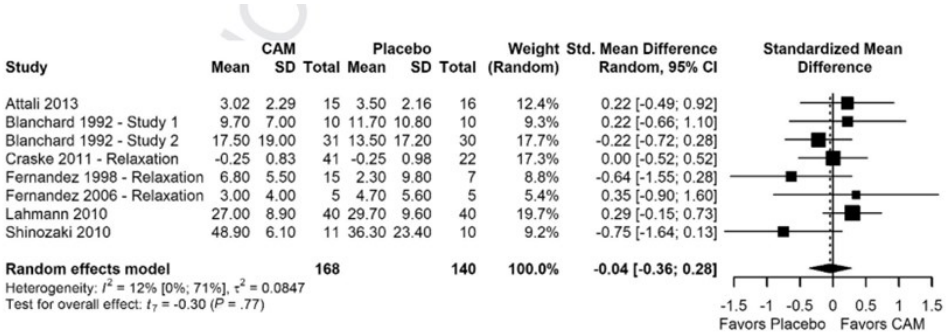
Figure from systematic review Li (2014) other psychological treatments and outcome 'improvement of IBS QOL'.

Table 2. Change in Overall Gastrointestinal Symptom Score

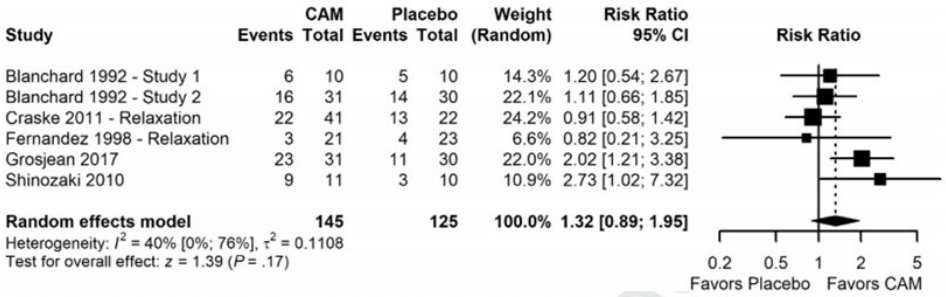
Author (yr)	Outcome measurement	3 months		*P*-value	12 months		*P*-value
		Intervention (SD)	Control (SD)		Intervention (SD)	Control (SD)	
Galovski et al[21] (1998)	CPSR[a]	-0.55 (0.53)	0.32 (0.49)	0.00047	NA	NA	NA
Roberts et al[23] (2006)	Full symptom score	-13.00 (10.50)	-4.5 (13.90)	0.008	-9.10 (14.00)	-6.40 (14.70)	0.440
Lindfors et al[20] (2012) study 1	GI-symptom questionnaire	-4.50 (8.60)	-0.80 (7.30)	< 0.05	NA	NA	NA
Lindfors et al[20] (2012) study 2	GSRS-IBS	-0.43 (0.90)	-0.10 (1.00)	0.220	NA	NA	NA

[a]CPSR was measured at right after end of treatment.
SD, standard deviation; CPSR, composite primary symptom reduction; NA, not allowed; GSRS, gastrointestinal symptom rating scale; IBS, irritable bowel syndrome.

Figure from systematic review Lee (2014) other psychological treatments and outcome 'Quality Of Life'.



Supplementary Figure 2. Forest plot of studies of body-based therapy vs placebo or sham with effect on abdominal pain. CAM, complementary and alternative medicine; CI, confidence interval; SD, standard deviation.



Supplementary Figure 3. Forest plot of studies of body-based therapy vs placebo or sham with effect on overall response. CAM, complementary and alternative medicine; CI, confidence interval.

Figure from systematic review Billings (2020) body-based therapy (relaxation therapy) and outcome 'effect on abdominal pain' and 'overall response'.

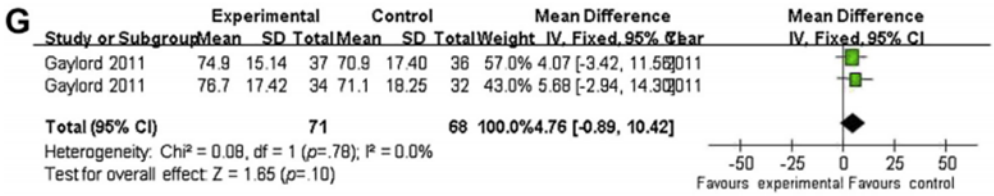


Figure 3. (*continued*).

Figure 3. Comparing outcomes of relaxation therapy versus control: (A) Improved irritable bowel syndrome (IBS) symptom. (B) Total IBS symptom severity score. (C) Abdominal pain frequency in IBS symptom severity score. (D) Dissatisfaction with bowel habit in IBS symptom severity score. (E) Bloating in IBS symptom severity score. (F) Anxiety. (G) Quality of life. *Note.* CI = confidence interval; IV = inverse variance.

Figure from systematic review Park (2014) relaxation therapy and outcome 'quality of life'.