Supplemental Information

APPENDIX. GRADE PROFILES

The GRADE approach was categorized as follows:

- Very low ⊕OOO: Any estimate of effect is uncertain.
- Low ⊕⊕OO: Further research is very likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- Moderate ⊕⊕⊕O: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- High ⊕⊕⊕⊕: Further research is unlikely to change our confidence in the estimate of effect.

GRADE EVIDENCE PROFILES

Dietary advice ($n = 4$)

Question: Should fiber supplements versus placebo be used for recurrent abdominal pain?

Settings: Private practices (Feldman), hospital (Christensen)

Bibliography: Christensen et al,[36] 1986; Feldman et al,[37] 1985; Horvath et al,[38] 2013

Quality Assessment							No. of Patients		Effect		Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Fiber Supplements	Placebo	Relative (95% CI)	Absolute		
No pain and/or satisfactory improvement												
3	Randomized trials	Serious[a]	No serious inconsistency[b]	No serious indirectness	Serious[c]	None	43/82 (52.4%)	37/85 (43.5%) 0%	RR: 1.17 (0.75 to 1.81)	76 more per 1000 (from 111 fewer to 361 more) —	⊕⊕OOLow	Critical

[a] Christensen: >20% were lost to follow-up.
[b] Moderate: I = 40%.
[c] Total number of events is <300 and 95% CI around the pooled estimate of effect includes both: (1) no effect; and (2) appreciable benefit or appreciable harm.

Question: Should guar gum versus placebo be used for chronic abdominal pain and IBS?

Settings: Gastroenterology unit, university

Bibliography: Romano et al,[24] 2013

Quality Assessment							No. of Patients		Effect		Quality	Importance
No. of Studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Guar Gum	Placebo	Relative (95% CI)	Absolute		
Intensity abdominal pain (follow-up, 8 wk; measured with Wong-Baker FACES Pain Rating Scale; better indicated by lower values)												
1	Randomized trials	No serious risk of bias	No serious inconsistency[a]	No serious indirectness	Serious[b]	None	30	30	—	MD: 0.42 lower (0.51 to 0.33 lower)	⊕⊕⊕O Moderate	Critical

[a] One study only.
[b] Low sample size (<400).

Hypnotherapy ($n = 3$)

Question: Should HT versus standard care/wait-list be used for functional abdominal pain or IBS?

Settings: Diverse

Bibliography: Vlieger et al,[32] 2007; van Tilburg et al,[44] 2009; Gulewitsch et al,[25] 2013

Quality Assessment							No. of Patients		Effect		Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Hypnotherapy	Standard care/Wait-List	Relative (95% CI)	Absolute		
Abdominal pain index[a] (follow-up, 2 wk; assessed with diary [days with pain, duration, and intensity])												
1	Randomized trials	Serious[b]	No serious inconsistency[c]	No serious indirectness	Serious[d]	None	11/20 (55%)	1/18 (5.6%)	RR: 9.90 (1.41 to 69.28)	494 more per 1000 (from 23 more to 1000 more)	⊕⊕OO Low	Critical
								0%		—		
Abdominal pain score[e] (follow-up, 2 mo; measured with Likert scale [0–40]; better indicated by lower values)												
1	Randomized trials	Serious[f]	No serious inconsistency[c]	No serious indirectness	Serious[d]	None	19	15	—	MD: 6.6 higher[g]	⊕⊕OO Low	Critical
Abdominal pain score[h] (follow-up, 12 mo; assessed with diary card [>80% of patients with complete remission of pain])												
1	Randomized trials	Serious[i]	No serious inconsistency	No serious indirectness	Serious[d]	None	22/26 (84.6%)	6/24 (25%)	RR: 3.38 (1.66 to 6.9)	595 more per 1000 (from 165 more to 1000 more)	⊕⊕OO Low	Critical
								0%		—		
Quality of life [g,i] (measured with question; better indicated by lower values)												
1	Randomized trials	Serious[f]	No serious inconsistency[c]	No serious indirectness	Serious[d]	None	19	15	—	MD: 18.9 higher	⊕⊕OO Low	Critical
School absence[h] (follow-up, 5 y; assessed with question)												
1	Randomized trials	Serious[i]	No serious inconsistency[c]	No serious indirectness	Serious[d]	None	7/22 (31.8%)	3/27 (11.1%)	RR: 0.35 (0.10 to 1.19)	72 fewer per 1000 (from 100 fewer to 21 more)	⊕⊕OO Low	Critical
Disability score[a] (follow-up, 2 wk; measured with questionnaire; better indicated by higher values)												
1	Randomized trials	Serious[b]	No serious inconsistency[d]	No serious indirectness	Serious[d]	None	20	18	—	MD: 9.14 lower (14.41 to 3.87 lower)	⊕⊕OO Low	Critical

[a] Gulewitsch (2013).
[b] A wait-list design does not control for attention or expectation of a future symptom improvement.
[c] One study only.
[d] Low sample size.
[e] Van Tilburg (2009).
[f] Concealment of allocation unclear. Intervention unblinded.
[g] In the article, insufficient data are given to present (complete) results.
[h] Vlieger (2007).
[i] Intervention unblinded.

Cognitive behavioral therapy ($n = 7$)

Question: Should CBT-family versus standard pediatric care be used for recurrent abdominal pain?

Settings: Diverse

Bibliography: Sanders et al,[46] 1994; Robins et al,[47] 2005; Duarte et al,[45] 2006

Quality Assessment							No. of Patients		Effect		Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	CBT-Family	Standard Pediatric Care	Relative (95% CI)	Absolute		
Pain intensity (follow-up, 6 mo; better indicated by lower values)												
1	Randomized trials	Very serious[a]	No serious inconsistency[b]	No serious indirectness	Serious[c]	None	22	22	—	MD: 3.61 lower (5.76 to 1.46 lower)	⊕OOO Very low	Critical
Median frequency of episodes of pain (better indicated by lower values)												
1	Randomized trials	Serious[d]	No serious inconsistency[b]	No serious indirectness	Serious[c]	None	15	17	—	Median 6 higher (0 to 0 higher)[e]	⊕⊕OO Low	Critical
Abdominal pain index (better indicated by lower values)												
1	Randomized trials	Serious[f]	No serious inconsistency[b]	No serious indirectness	Serious[c]	None	40	29	—	MD: 3.3 higher (0 to 0 higher)[e]	⊕⊕OO Low	Critical

[a] Concealment of allocation was unclear. Outcome was assessed by parents and children who could not be blinded. In total, 38 of 44 participants completed the study, but we were unable to ascertain the numbers by group to which they were allocated.
[b] One study only.
[c] Low sample size.
[d] Concealment of allocation was unclear.
[e] In the article, insufficient data are given to present (complete) results.
[f] There is significant differential loss to follow-up in this study with outcome data available for 40 of 46 patients in the intervention group and 29 of 40 in the control group.

Question: Should CBT interventions and dietary fiber versus dietary fiber alone be used for recurrent abdominal pain?

Settings: Community in southern California, United States

Bibliography: Humphreys et al,[49] 1998

Quality Assessment							No. of Patients		Effect		Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	CBT Interventions and Dietary Fiber	Dietary Fiber Alone	Relative (95% CI)	Absolute		
Pain free (follow-up, 8 wk; assessed with child's pain diary)												
1	Randomized trials	Serious[a]	No serious inconsistency[b]	No serious indirectness	No serious imprecision	None	33/46 (71.7%)	1/14 (7.1%)	OR: 33.0 (3.9 to 278.5)	646 more per 1000 (from 159 more to 884 more)	⊕⊕⊕O Moderate	Critical
								0%		—		
School absences (follow-up, 8 wk; assessed with record of school attendance)												
1	Randomized trials	Serious[a]	No serious inconsistency[b]	No serious indirectness	No serious imprecision	None	—	—	—	—	⊕⊕⊕O Moderate	Critical
								0%		—		

[a] Concealment of allocation was unclear.
[b] One study only.

Question: Should psychological treatment and physiotherapy versus physiotherapy only be used for recurrent abdominal pain?

Settings: Primarily, secondarily, and tertiary referred children from suburban areas of Stockholm

Bibliography: Alfvén and Lindstrom,[48] 2007

Quality Assessment							No. of Patients		Effect		Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Psychological Treatment and Physiotherapy	Physiotherapy Only	Relative (95% CI)	Absolute		
Pain intensity (follow-up, 1 y; measured with VAS scale; better indicated by lower values)												
1	Randomized trials	Very serious[a]	No serious inconsistency[b]	No serious indirectness	Serious[c]	None	25	23	—	MD: 0.2 higher (0 to 0 higher)[d]	⊕OOO Very low	Critical

[a] Concealment of allocation and blinding of outcomes was unclear. Duration of treatment has not been described.
[b] One study only.
[c] Low sample size ($n = 48$).
[d] In the article, insufficient data are given to present (complete) results.

Question: Should CBT versus education be used for functional abdominal pain?

Settings: Seattle, Washington, and Morristown

Bibliography: Levy et al,[31] 2010

Quality Assessment							No. of Patients		Effect		Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	CBT	Education	Relative (95% CI)	Absolute		
Pain reported by parents (follow-up, 12 mo; measured with the Faces Pain Scale–Revised; better indicated by lower values)												
1	Randomized trials	Very serious[a]	No serious inconsistency[b]	Serious[c]	No serious imprecision	None	75	63	—	MD: 0.77 lower (1.66 lower to 0.13 higher)	⊕OOO Very low	Critical
Functional disability reported by parents (follow-up, 12 mo; measured with Functional Disability Inventory; better indicated by lower values)												
1	Randomized trials	Very serious[a]	No serious inconsistency[b]	Serious[c]	No serious imprecision	None	75	63	—	MD: 0.16 lower (0.48 lower to 0.15 higher)	⊕OOO Very low	Critical
Pain reported by child (follow-up, 12 mo; measured with the Faces Pain Scale–Revised; better indicated by lower values)												
1	Randomized trials	Very serious[a]	No serious inconsistency[b]	Serious[c]	No serious imprecision	None	75	63	—	MD: 0.55 lower (1.31 lower to 0.2 higher)	⊕OOO Very low	Critical

[a] Attrition is described; significant differences between completers and noncompleters are not reported. Randomization unclear. Baseline differences.
[b] One study only.
[c] Participants were a volunteer group who had been referred by providers or responded to notices regarding the study. Consequently, they may not be representative of the larger population of families and children with FAP.

Question: Should CBT group versus wait-list be used for functional abdominal pain?

Settings: Not reported

Bibliography: Groß and Warschburger,[28] 2013

Quality Assessment							No. of Patients		Effect		Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	CBT Group Therapy	Wait-List	Relative (95% CI)	Absolute		
Pain intensity (follow-up, 3 mo; measured with VAS scale; better indicated by lower values)												
1	Randomized trials	Serious[a]	No serious inconsistency[b]	No serious indirectness	Serious[c]	None	15	14	—	MD: 1.47 lower (1.45 lower to 0.01 higher)	⊕⊕OO Low	Critical
Pain frequency (follow-up, 3 mo; times per day measured with pain diary; better indicated by lower values)												
1	Randomized trials	Serious[a]	No serious inconsistency[b]	No serious indirectness	Serious[c]	None	15	14	—	MD: 0.38 lower (0.38 lower to 0.03 lower)	⊕⊕OO Low	Critical
Pain duration (follow-up, 3 mo; hours per day measured with pain diary; better indicated by lower values)												
1	Randomized trials	Serious[a]	No serious inconsistency[b]	No serious indirectness	Serious[c]	None	15	14	—	MD: 0.59 lower (0.71 lower to 0.19 lower)	⊕⊕OO Low	Critical
Quality of life (follow-up, 3 mo; measured with PedsQL; better indicated by higher values)												
1	Randomized trials	Serious[a]	No serious inconsistency[b]	No serious indirectness	Serious[c]	None	15	14	—	Physical functioning: MD, 35.96 higher (31.66 higher to 11.16 lower) Psychological functioning: MD, 18.36 higher (25.33 higher to 2.85 higher) Social functioning: MD, 11.4 higher (11.33 higher to 1.07 lower) School functioning: MD, 17.62 higher (18 higher to 1.79 lower)	⊕⊕OO Low	Critical

PedsQL, Pediatric Quality of Life Inventory.

[a] No blinding

[b] One study only.

[c] Low sample size.

Written self-disclosure ($n = 1$)

Question: Should WSD + standard care versus standard care be used for functional abdominal pain?

Settings: GI clinic, United States

Bibliography: Wallander et al,[29] 2011

Quality Assessment							No. of Patients		Effect		Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	WSD + Standard Care	Standard Care	Relative (95% CI)	Absolute		
Pain frequency (follow-up, 6 mo; measured with abdominal pain frequency rating; better indicated by lower values)												
1	Randomized trials	Serious[a]	No serious inconsistency[b]	No serious indirectness	Serious[c]	None	32	24	—	MD: 0.97 lower (0.58 lower to 0.29 higher)	⊕⊕OO Low	Critical
Quality of life (follow-up, 6 mo; measured with PedsQL; better indicated by higher values)												
1	Randomized trials	Serious[a]	No serious inconsistency[b]	No serious indirectness	Serious[c]	None	32	24	—	Physical functioning: MD, 2.51 higher (1.96 higher to 0.51 lower) Psychological functioning: MD, 1.91 higher (2.35 higher to 1.56 higher)	⊕⊕OO Low	Critical

PedsQL, Pediatric Quality of Life Inventory.

[a] No blinding.

[b] One study only.

[c] Low sample size.

Probiotics ($n = 4$)

Question: Should LGG versus placebo be used for abdominal pain–related functional gastrointestinal disorders?

Settings: Countries: Poland, Italy, and the United States

Bibliography: Horvath et al,[18] 2011

Quality Assessment							No. of Patients		Effect		Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	LGG	Placebo	Relative (95% CI)	Absolute		
Pain intensity												
3	Randomized trials	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	97/144 (67.4%)	75/146 (51.4%)	RR: 1.31 (1.08 to 1.59)	159 more per 1000 (from 41 more to 303 more)	⊕⊕⊕O Moderate	Critical
								0%		—		

[a] In Bausserman, the loss to follow up was >20%.

Question: Should VSL#3 vs placebo be used for IBS (Rome II)?

Settings: Five pediatric tertiary care centers in Italy and India

Bibliography: Guandalini et al,[27] 2010

Quality Assessment							No. of Patients		Effect		Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	VSL#3	Placebo	Relative (95% CI)	Absolute		
Abdominal pain (follow-up, 6 wk)												
1	Randomized trials	Serious[a]	No serious inconsistency[b]	Serious[c]	Serious[d]	None	—	—	—	—	⊕OOO Very low	Critical[e]

[a] No details about randomization mentioned.
[b] One study only.
[c] Only children with IBS have been included.
[d] Low sample size.
[e] In the article, insufficient data are given to present (complete) results.

Alternative medicine ($n = 1$)

Question: Should yoga versus wait-list be used for IBS?

Settings: Gastroenterology clinic at the local children's hospital and community (posters)

Bibliography: Birdee et al,[23] 2009

Quality Assessment							No. of Patients		Effect		Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Yoga	Wait-List	Relative (95% CI)	Absolute		
Functional disability (follow-up 5 wk; better indicated by lower values)												
1	Randomized trials	Serious[a]	No serious inconsistency[b]	Serious[c]	Serious[d]	None	14	11	—	MD: 9.60 lower (19.66 lower to 0.46 higher)	⊕OOO Very low	Critical

[a] No details about randomization. No description of the reasons for lost to follow-up.
[b] One study only.
[c] Children aged 11 to 18 years with IBS.
[d] Low sample size (n=25).