Nonpharmacologic Treatment of Functional Abdominal Pain Disorders: A Systematic Review

Juliette M.T.M. Rutten, MD[a]*, Judith J. Korterink, MD[a]*, Leonie M.A.J. Venmans, PhD[b], Marc A. Benninga, MD, PhD[a], Merit M. Tabbers, MD, PhD[a]

abstract

BACKGROUND AND OBJECTIVE: Various nonpharmacologic treatments are available for pediatric abdominal pain–related functional gastrointestinal disorders (AP-FGIDs). Data on efficacy and safety are scarce. The goal of this study was to summarize the evidence regarding nonpharmacologic interventions for pediatric AP-FGIDs: lifestyle interventions, dietary interventions, behavioral interventions, prebiotics and probiotics, and alternative medicine.

METHODS: Searches were conducted of the Medline and Cochrane Library databases. Systematic reviews and randomized controlled trials (RCTs) concerning nonpharmacologic therapies in children (aged 3–18 years) with AP-FGIDs were included, and data were extracted on participants, interventions, and outcomes. The quality of evidence was assessed by using the GRADE approach.

RESULTS: Twenty-four RCTs were found that included 1390 children. Significant improvement of abdominal pain was reported after hypnotherapy compared with standard care/wait-list approaches and after cognitive behavioral therapy compared with a variety of control treatments/wait-list approaches. Written self-disclosure improved pain frequency at the 6-month follow-up only. Compared with placebo, *Lactobacillus rhamnosus* GG (LGG) and VSL#3 were associated with significantly more treatment responders (LGG relative risk: 1.31 [95% confidence interval: 1.08 to 1.59]; VSL#3: $P < .05$). Guar gum significantly improved irritable bowel syndrome symptom frequency; however, no effect was found for other fiber supplements (relative risk: 1.17 [95% confidence interval: 0.75 to 1.81]) or a lactose-free diet. Functional disability was not significantly decreased after yoga compared with a wait-list approach. No studies were found concerning lifestyle interventions; gluten-, histamine-, or carbonic acid–free diets; fluid intake; or prebiotics. No serious adverse effects were reported. The quality of evidence was found to be very low to moderate.

CONCLUSIONS: Although high-quality studies are lacking, some evidence shows efficacy of hypnotherapy, cognitive behavioral therapy, and probiotics (LGG and VSL#3) in pediatric AP-FGIDs. Data on fiber supplements are inconclusive.

[a]*Department of Pediatric Gastroenterology and Nutrition, Emma's Children's Hospital, Academic Medical Center, Amsterdam, Netherlands; and* [b]*Pediatric Association of the Netherlands, Utrecht, Netherlands*

Drs Rutten and Korterink participated in the design of the study, judged the eligibility and validity of the studies, and drafted the initial manuscript; Dr Venmans participated in the design of the study, performed the literature search, and judged the eligibility and validity of the studies; Dr Benninga participated in the design of the study and critically reviewed and revised the manuscript; Dr Tabbers participated in the design of the study, performed the literature search, judged the eligibility and validity of the studies, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

*Drs Rutten and Korterink contributed equally.

www.pediatrics.org/cgi/doi/10.1542/peds.2014-2123

DOI: 10.1542/peds.2014-2123

Accepted for publication Nov 25, 2014

Abdominal pain–related functional gastrointestinal disorders (AP-FGIDs), diagnosed according to the Rome III criteria, are defined as chronic or recurrent abdominal pain, not explained by underlying organic disorders.[1] AP-FGIDs affect ~20% of children worldwide and include functional dyspepsia, irritable bowel syndrome (IBS), abdominal migraine, functional abdominal pain (FAP), and functional abdominal pain syndrome.[1,2] AP-FGIDs have a significant impact on children and adolescents' quality of life, daily activities, and school absenteeism and can have long-term psychological implications.[3] Moreover, patients with AP-FGIDs are at risk for continued symptoms in adulthood, and the costs are substantial.[4–6]

Standard medical care consists of reassurance, education, and dietary advice.[7] Despite ongoing efforts to identify causal and contributing factors in AP-FGIDs, successful management is complicated by an incomplete pathophysiologic understanding of the disorders. The biopsychosocial model, based on a complex interplay of genetic, physiologic, and psychological factors, is conceptualizing the etiology of FGIDs.

It is hypothesized that pediatric AP-FGIDs are strongly associated with stress and psychological disorders such as anxiety and depression,[8] wherein the coping potentials of children with AP-FGIDs are low compared with those of healthy children.[9] Therefore, interventions such as cognitive behavioral therapy (CBT), hypnotherapy (HT), and yoga aim to teach alternative responses to stress.[10] Systematic reviews have concluded that CBT and HT offer beneficial effects for children with AP-FGIDs.[11,12]

The role of food in FGIDs has been revisited recently in the adult literature.[13,14] Food may trigger symptoms in FGID patients who already have physiologic alterations, subsequently making them susceptible for hypersensitivity.[13] However, recognizing which specific food components trigger symptoms is difficult and can lead to a profusion of investigations and dietary therapies, largely based on expert opinion.[14] Two previous systematic reviews reported that fiber supplements are ineffective in treating AP-FGIDs, whereas conclusions were contradictory regarding probiotics.[15,16] Treatment of children who have AP-FGIDs can be challenging, especially because high-quality evidence for pharmacologic interventions is lacking.[17] Although several systematic reviews summarizing different nonpharmacologic interventions exist,[11,15,18] the present systematic review provides an up-to-date overview regarding the efficacy and safety of all nonpharmacologic treatments for pediatric AP-FGIDs. Such a comprehensive and recent overview is warranted.

METHODS

Literature Search

The Cochrane Library and Medline databases were searched for systematic reviews and randomized controlled trials (RCTs) from inception to October 2013. Search terms used items related to pediatric AP-FGIDs and various nonpharmacologic treatments. To identify additional studies, reference lists of reviews and included studies were searched by hand. The full search strategy and key words are available from the authors.

Study Inclusion

Two authors (L.M.A.J.V. and M.M.T.) independently assessed the eligibility of all abstracts. In cases of disagreement, consensus was reached through discussion. Inclusion criteria were: (1) study was a systematic review or RCT; (2) study population comprised children aged 3 to 18 years; (3) diagnosis of recurrent abdominal pain (RAP), FAPS, IBS, functional dyspepsia, or abdominal migraine as defined by the authors; (4) interventions were lifestyle advice such as physical exercise, dietary interventions (fiber supplements; lactose-, gluten-, histamine-, and carbonic acid–free diets; and fluid intake), behavioral interventions such as HT and CBT, prebiotics and probiotics, and alternative medicine (acupuncture, homeopathy, mind–body therapy, musculoskeletal manipulations such as osteopathic and chiropractic manipulations, and spiritual therapies such as yoga); (5) the intervention was compared with placebo, no treatment, any other nonpharmacologic treatment, or a pharmacologic agent; and (6) outcomes were abdominal pain intensity and/or frequency, quality of life, functional disability (eg, school absence), and adverse effects. Exclusion criteria were: (1) treatment arm with <10 patients; and (2) language other than English. Potentially relevant studies and studies in which the title and abstract provided insufficient information were retrieved as full-text articles.

Quality Assessment and Data Extraction

Two authors (L.M.A.J.V. and M.M.T.) independently rated the methodologic quality of the included studies by using the Cochrane risk of bias tool. For each outcome, quality of evidence was assessed by using the GRADE approach and was categorized as very low, low, moderate, or high.[19–21]

The same authors extracted data from included studies by using structured data extraction forms containing items on participants, study setting, interventions, and outcomes. Disagreements were resolved through consensus or by a third reviewer (M.A.B.).

Data Analysis

Dichotomous outcomes were analyzed as odds ratios (ORs) or

relative risk (RRs) along with 95% confidence intervals (CIs). For continuous outcomes, the mean differences (MDs) with 95% CIs were reported. Heterogeneity was quantified by using χ^2 tests and the I^2 statistic, which can be interpreted as the percentage of the total variation between studies that is attributable to heterogeneity rather than chance. A value of 0% indicates no observed heterogeneity, whereas larger values show increasing heterogeneity. If heterogeneity was not revealed, results of the fixed effect model are presented. If there was substantial heterogeneity (>50%), the random effect model was used.

RESULTS

A total of 568 potentially relevant articles and abstracts were identified (Fig 1). After removal of duplicates (n = 316) and screening of abstracts (n = 210), 42 full-text articles were assessed for eligibility. Twenty-nine articles were excluded because of the following: adult study population (n = 6), irrelevant outcome measures, such as improvement in rectal sensitivity or gastrointestinal symptoms without abdominal pain (n = 2), no systematic review or RCT (n = 15), or inclusion only of trials that were already included by another systematic review (n = 6). Thirteen articles remained for analysis: 7 systematic reviews[11,12,15,16,18,22,23] (including 18 RCTs) and 6 RCTs.[24–29] Two included trials concerned follow-up studies,[26,30] which will be discussed by using their original studies.[31,32]

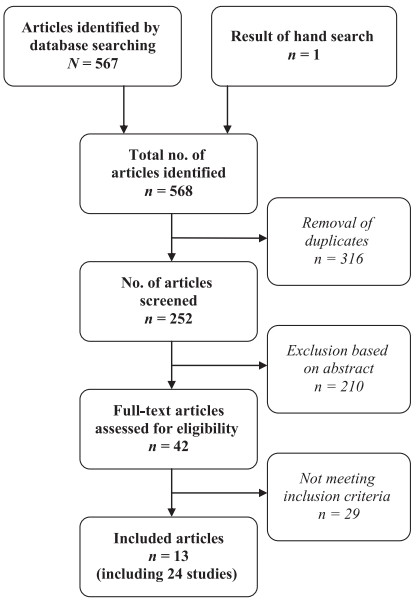

FIGURE 1
Flow chart showing results of the literature search and study inclusion.

Two systematic reviews[11,12] included studies with <10 patients per treatment arm, and these studies were therefore excluded.[33–35]

Data of 1390 children aged 3 to 18 years were included for analysis. Sample sizes ranged from 21 to 200, and follow-up varied from 2 weeks to 5 years. Four trials investigated fiber supplements compared with placebo,[24,36–38] and 2 trials studied a lactose-free diet.[39,40] Four trials investigated probiotics,[27,41–43] and 3 trials compared HT versus standard care or a wait-list.[25,32,44] Seven studies compared CBT with standard care, physiotherapy, fiber supplements, biofeedback, and/or parental support.[28,31,45–49] One trial compared yoga with a wait-list,[50] and 1 trial evaluated written self-disclosure (WSD) in addition to standard care.[29] No studies were included on lifestyle advice or prebiotics. A range of different outcomes were measured, and even if the same outcome was measured, different measurement instruments were used. All trials measured abdominal pain as the primary or secondary outcome.

Nine studies reported disability or school absenteeism.[25,31,32,38,42,44,47,49,50] Four studies assessed quality of life,[25,28,29,44] and 8 studies assessed adverse effects.[24,25,37,38,41–44] Data of 3 studies were pooled to perform a meta-analysis of the efficacy of fiber supplements,[36–38] and 3 studies were used to perform a meta-analysis on probiotics.[41–43] Table 1 presents the characteristics of the included studies.

Methodologic Quality

The overall quality of evidence was very low to moderate. The Supplemental Appendix displays the GRADE evidence profiles.

Concealment of allocation was unclear in 6 studies.[36,44–46,48,49] Due to the nature of HT, CBT, WSD, and yoga, blinding was not possible for the caregiver or patient.[25,28,29,31,32,44–50] Dropout was considerable in 4 studies[36,40,41,47] or vaguely described in 3 others.[31,46,50] Two studies excluded patients due to poor compliance.[40,41] The method of randomization was unclear in 3 studies.[27,31,50] Alfvén and Lindstrom[48] provided no information on outcome blinding or treatment duration. Six trials did not present results with absolute numbers and were therefore not included in the meta-analysis.[27,39,40,44,47,48] Analyses for follow-up were uncontrolled for baseline differences by Levy et al.[31] Because participants were recruited through physician referral and flyers, these patients were therefore seriously motivated, which can cause bias.

Dietary Interventions

No studies were included evaluating gluten-, histamine-, and carbonic acid–free diets or fluid intake.

Fiber Supplements

Two systematic reviews[15,16] including 3 RCTs[36–38] and 1 RCT[24] evaluated the efficacy of fiber supplements compared with placebo for RAP. A systematic review by Huertas-Ceballos et al[15] included 2 RCTs, involving 92 children aged 3 to 15 years.[36,37] Children received fiber supplements for 6 weeks. No information was available regarding daily fiber intake before and/or during intervention weeks. Information about abdominal pain was collected through the use of diaries, but the authors did not clarify how these diaries were analyzed. The systematic review by Horvath et al[16] included a third trial with 90 children

TABLE 1 Study Characteristics of Included Studies

Study	Participants	Intervention	Outcome Measures and Instruments	Quality
Fiber supplements and guar gum				
Christensen[36] (1986); Denmark	Children aged 3–14 y (N = 40) RAP (at least 10 episodes of abdominal pain during the last 6 wk, organic causes of pain were excluded)	Fibers (ispaghula husk) vs placebo Dosage: Visiblin 5 mL twice daily; crushed crisp bread with 66% fiber Treatment period: 6 wk	Abdominal pain frequency score Improvement: <10 episodes of pain during the study period Instrument: pain diary	Low
Feldman et al[37] (1985); Canada	Children aged 5–15 y (N = 52) RAP (organic causes of pain were excluded on the basis of history, examination, and simple laboratory test results)	Fiber cookies vs placebo Dosage: 5 g of corn fiber per cookie; 1 cookie twice daily Treatment period: 6 wk	Abdominal pain frequency score Improvement: 50% decrease in frequency of attack Instrument: pain diary	Low
Horvath et al[38] (2013); Poland	Children aged 7–17 y (N = 90) IBS, FAP, and functional dyspepsia (Rome III criteria)	GNN vs placebo Dosage: 2.52 g/d Treatment period: 4 wk Follow-up: no follow-up	Severity of pain Improvement: no pain or a decrease ≥2/6 points on the FPS-R Instrument: FPS-R School absenteeism Changes in daily activity Instrument: self-reported at baseline and final visit	Low
Romano et al[24] (2013); Italy	Children aged 8–16 y (N = 60) IBS-C and IBS-D (Rome III criteria)	PHGG vs placebo Dosage: 5 g/d Treatment period: 4 wk Follow-up: 4 wk	IBS symptoms Treatment success: improvement IBS symptoms Instrument: Birmingham IBS Symptom Questionnaire score Intensity of abdominal pain Instrument: Wong-Baker FACES Pain Rating Scale	Moderate
Fructose and lactose				
Dearlove et al[39] (1983); United Kingdom	Children aged >3 y (N = 21) RAP (> 1/4 d in the last 3 mo)	Lactose vs placebo Dosage: 2 g/kg Treatment period: 2 wk Follow-up: 3 mo	Abdominal pain Instrument: reported at final visit (better, worse, same)	NA
Lebenthal et al[40] (1981); United States	Children aged 6–14 y (N = 38) RAP (intermittent episodes of unexplained abdominal pain, in a 4-mo period)	Lactose versus lactose-free formula Dosage: 2dd 200 mL Treatment period: 6 wk Follow-up: 12 mo	Abdominal pain (severity and frequency) Instrument: pain diary	NA
HT				
Gulewitsch et al[25] (2013); Germany	Children aged 6–12 y (N = 38) FAP and IBS (Rome II criteria)	HT program consists of 4 sessions: 2 children's sessions and 2 parent's sessions in a weekly sequence Control: wait-list Treatment duration: 4 wk Follow-up: 3 mo	Abdominal pain index Clinical remission: >80% decrease in days of pain, duration, and intensity of abdominal pain Instrument: abdominal pain dairy Quality of life Instrument: German KINDL questionnaire Disability Instrument: Pediatric Pain Disability Index School absenteeism Instrument: abdominal pain dairy	Low

TABLE 1 Continued

Study	Participants	Intervention	Outcome Measures and Instruments	Quality
van Tilburg et al[44] (2009); United States	Children aged 6–15 y (N = 34) FAP (abdominal pain at least once a week in the past 3 mo)	Standard care + guided imagery; 3 biweekly sessions, including 1 booster session + 3 daily sessions. Listen to CD with self exercises ≥5 d/wk Control: standard care Treatment period: 2 mo Follow-up: 6 mo	Improvement of abdominal pain Treatment response: >50% reduction of abdominal pain score Instrument: abdominal pain index Quality of life Instrument: PedsQL Disability Instrument: Functional Disability Inventory School absenteeism Instrument: abdominal pain dairy	Low
Vlieger et al[30,32] (2007/2012); the Netherlands	Children aged 8–18 y (N = 53) FAP and IBS (Rome II criteria)	6 HT sessions Control: Standard medical care + supportive therapy Treatment period: 3 mo Follow-up: 1 y and 5 y	Abdominal pain score Clinical remission: >80% decrease of intensity and frequency of abdominal pain Instrument: abdominal pain dairy School absenteeism Instrument: abdominal pain dairy	Low
CBT				
Duarte et al[45] (2006); Brazil	Children aged 5–14 y (N = 32) RAP (Apley's criteria)	4 monthly sessions of CBT-family Control: standard care Treatment period: 4 mo Follow-up: no follow-up	Abdominal pain intensity Instrument: red and white VAS Abdominal pain frequency Instrument: daily numbers of pain in pain dairy	Low
Sanders et al[46] (1994); Australia	Children aged 7–14 y (N = 44) RAP (Apley's criteria)	6-session CBT-family Control: standard care Treatment period: 8 wk Follow-up: 6 and 12 mo	Abdominal pain intensity Instrument: VAS	Very low
Robins et al[47] (2005); United States	Children aged 6–16 y (N = 69) RAP (Apley's criteria)	5-session CBT-family + standard care Control: standard care Treatment period: 10 mo Follow-up: 3 and 6 mo	Abdominal pain Instrument: Abdominal pain index Disability Instrument: Functional Disability Inventory School absenteeism Instrument: Record of school attendance	Low
Levy et al[26,31] (2010/2013); United States	Children aged 7–17 y (N = 200) RAP (≥3 episodes of abdominal pain during a 3-mo period)	3-session social learning + CBT-family Control: education + support intervention Treatment period: 3 wk Follow-up: 12 mo	Abdominal pain intensity Instrument: FPS-R Disability Instrument: Functional Disability Inventory	Very low
Alfvén and Lindstrom[48] (2007); Sweden	Children aged 6–18 y (N = 48) RAP (Apley's criteria)	Psychological + psychotherapy Control: physiotherapy Treatment period: at least 2 sessions, according to the expressed needs Follow-up: 12 mo	Abdominal pain intensity Instrument: VAS Pain score at 1-year follow-up Instrument: VAS + duration (min) + frequency (per week)	Very low
Humphreys and Gevirtz[49] (2000); United States	Children aged 4–18 y (N = 64) RAP	4 groups: 1. Fiber + biofeedback + CBT + parental support 2. Fiber + biofeedback + CBT 3. Fiber + biofeedback 4. Fiber Treatment period: 8-session CBT Dosage: 10+ g/d fiber cookies or bars Follow-up: no follow-up	Abdominal pain intensity Instrument: VAS School absenteeism Instrument: Record of school attendance	Moderate

TABLE 1 Continued

Study	Participants	Intervention	Outcome Measures and Instruments	Quality
Groß and Warschburger[28] (2013); Germany	Children aged 6–12 y (N = 29) CAP (Rome III criteria)	6-session CBT (group sessions) + listen to CD with self exercises Control: wait-list Treatment period: 2 mo Follow-up: 3 mo	Abdominal pain intensity Instrument: VAS Abdominal pain frequency (times per day)/duration (hours per day) Instrument: pain diary Quality of life Instrument: PedsQL	Low
WSD				
Wallander et al[29] (2011); United States	Children aged 11–17 y (N = 63) RAP (Apley's criteria)	WSD + standard care: 3 writing sessions of 20 min Control: standard care Treatment period: 5 d Follow-up: 6 mo	Abdominal pain frequency Instrument: abdominal pain frequency rating Quality of life Instrument: PedsQL	Low
Probiotics				
Bausserman and Michail[41] (2005); United States	Children aged 6–17 y (N = 64) IBS (Rome II criteria)	LGG versus placebo Dosage:10^{10} CFU, twice daily Treatment period: 6 wk Follow-up: no follow-up	Abdominal pain severity Responders: decreased pain score of ≥1 point Instrument: severity of symptom scale	Moderate
Francavilla et al[43] (2010); Italy	Children aged 5–14 y (N = 141) IBS and FAP (Rome II criteria)	LGG vs placebo Dosage: 3×10^9 CFU, twice daily Treatment period: 8 wk Follow-up: 8 wk	Abdominal pain (frequency/severity) Treatment success: a decrease of at least 50% in the number of episodes and intensity of pain Instrument: VAS	Moderate
Gawrońska et al[42] (2007); Poland	Children aged 6–16 y (N = 104) FAP, functional dyspepsia, and IBS (Rome II criteria)	LGG versus placebo Dosage: 3×10^9 CFU, twice daily Treatment period: 4 wk Follow-up: no follow-up	Abdominal pain intensity Improvement: no pain or a change in the FPS-R by at least 2 faces Instrument: FPS-R School absenteeism Instrument: Record of school attendance	Moderate
Guandalini et al[27] (2010); Italy and India	Children aged 4–18 y (N = 59) IBS (Rome II criteria)	VSL#3 vs placebo Dosage: 4–11 y, 1 sachet; 12–18 y, 2 sachets Treatment period: 6 wk Follow-up: no follow-up	Abdominal pain score (frequency and intensity) Responders: decreased pain score of ≥1 point Instrument: self-administered questionnaire	Very low
Alternative medicine				
Kuttner et al[50] (2006); Canada	Children aged 11–18 y (N = 25) IBS (Rome I criteria)	Yoga intervention for 1 h followed by daily home practice guided by a video Control: wait-list Treatment period: 4 wk Follow-up: no follow-up	Abdominal pain intensity Instrument: numeric rating scale Disability Instrument: Functional Disability Inventory	Very low

CAP, chronic abdominal pain; FD, functional dyspepsia; FPS-R, Faces Pain Scale–Revised; GNN, glucomannan; IBS-C, irritable bowel syndrome, constipation predominant; IBS-D, irritable bowel syndrome, diarrhea predominant; NA, not applicable; PedsQL, Pediatric Quality of Life Inventory.

(aged 7–17 years) receiving 4 weeks of glucomannan or identical placebo.[38] Pain severity was assessed by using the Faces Pain Scale–Revised (6 faces ranging from relaxed to intense pain).[51] School absenteeism and changes in daily activities were self-reported. The primary outcome in all studies was degree of improvement based on abdominal pain frequency or intensity. After pooling, there was no significant difference between the fiber group in experiencing "no pain" and/or "satisfactory improvement" (52.4%) and the placebo group (43.5%) (RR: 1.17 [95% CI: 0.75 to 1.81]). Concerning secondary outcomes, no significant differences for school absenteeism (10% vs 14%; P = .56) or daily activities (27% vs 19%; P = .37) after glucomannan treatment compared with placebo were found.[38]

Romano et al[24] enrolled 60 patients (aged 8–16 years) and compared 4 weeks of partially hydrolyzed guar gum (PHGG), a water-soluble, dietary fiber, with placebo. Symptoms were assessed by using the Birmingham IBS Symptom Questionnaire, which contains questions on frequency of IBS symptoms (0 = none, 5 = all the time),[52] and the Wong-Baker FACES Pain Rating Scale, which was used to evaluate abdominal pain severity (0 = no hurt, 5 = hurts worst).[53] The primary outcome was reduction in the frequency and intensity of IBS symptoms. Improvement in the frequency of IBS symptoms was significantly more likely in the PHGG group compared with the control group (43% vs 5%; $P = .025$) after 8 weeks. Effects on pain intensity were not significant.

Three studies assessed adverse effects.[24,37,38] Unknown small numbers of children in both groups reported gas or diarrhea in the trial by Feldman et al.[37] Horvath et al[38] and Romano et al[24] reported no adverse effects.

Lactose-Free Diet

Huertas-Ceballos et al[15] included 2 trials evaluating a lactose-free diet in RAP.[39,40] Lebenthal et al[40] enrolled 95 participants. After an intestinal biopsy was conducted, those patients with abnormal lactase activity (12–20 U) were excluded: 69 children received 6 weeks of lactose-containing or lactose-free infant formula. Abdominal pain was documented in diaries by parents. Remarkably, 31 children were excluded due to a lack of compliance; 38 children remained. A lactose tolerance test was performed, the results of which were used to divide children into 2 groups: lactose malabsorbers ($n = 21$) and lactose absorbers ($n = 17$). Increased symptoms were described in 48% of the lactose malabsorbers and 24% of the lactose absorbers after lactose intake; however, P values were not reported. Forty of the 69 children continued with a 12-month lactose-free diet. Improvement of abdominal pain after 12 months was similar in both groups (40% vs 38%). Detailed data were not reported, however, and meta-analysis and GRADE evidence profiling were therefore not possible.

Dearlove et al[39] included 21 children with RAP in a double-blind, single crossover study. After 2 weeks of collecting baseline data, all children underwent a 2-week lactose-free diet, followed by another 2 weeks of lactose tonic (2 g/kg) or similarly flavored placebo. Primary and secondary outcomes were not specified. After 3 months, parents were asked whether their child's symptoms (including abdominal pain) were better, worse, or the same. There was no difference in the number of children claiming relief from the lactose-free or lactose-containing formula.

Hypnotherapy

One systematic review[11] (including 2 RCTs[32,44]) and 1 RCT[25] evaluated the effects of HT for FAP and IBS. Two studies examined HT by therapists[25,32] and 1 examined HT with self exercises on a CD.[44] All studies used diaries to assess pain intensity and frequency. Gulewitsch et al[25] recalculated pain scores into an abdominal pain index. The abdominal pain index, disability, and school absenteeism were the primary outcomes. Clinical remission was defined as a >80% decrease on the abdominal pain index: 55% (11 of 20) of children showed clinical remission after HT, compared with 5.6% (1 of 18) of wait-list control subjects (RR: 9.90 [95% CI: 1.14 to 69.28]).

Vlieger et al[30,32] included 53 children in their research. Clinical remission, defined as a >80% reduction in abdominal pain scores, was the primary outcome. After 3 months of HT, 59% showed clinical remission compared with 12% receiving standard care ($P < .001$). Differences persisted after 1 year (85% vs 25%; $P < .001$) and after 5 years (68% vs 20%; $P = .005$).

Van Tilburg et al[44] compared 19 children receiving 2 months of standard care plus HT through self exercises on a CD with 15 children receiving standard care. Primary or secondary outcomes were not specified. Efficacy was based on an abdominal pain index,[54] with higher scores indicating more abdominal pain (range: 0–40). After treatment, children receiving HT reached an improvement of 9.7 points compared with 3.1 points in the control subjects ($P = .02$). Significantly more children responded to HT compared with control subjects (63% vs 27%; $P = .03$). At 6 months' follow-up, beneficial effects persisted in 62.5% of the HT group.

Two trials assessed quality of life, but the results were conflicting.[25,44] To evaluate this secondary outcome, Gulewitsch et al[25] used the validated German KINDL questionnaire. No significant effects were reported by children ($P = .120$) or parents ($P = .678$) compared with control subjects. Van Tilburg et al[44] demonstrated a significant quality of life improvement compared with standard care ($P = .049$), measured by using the validated Pediatric Quality of Life Inventory. Two studies reported significant improvement in disability.[25,44] Gulewitsch et al used the Pediatric Pain Disability Index to assess impairment in 12 daily activities. HT had a significant beneficial effect on the self-reported disability compared with control subjects (MD: –9.14 [95% CI: –14.41 to –3.87]).[25] Van Tilburg et al used the Functional Disability Inventory. Children receiving HT exhibited a significant reduction in disability compared with control subjects ($P = .01$).

Two studies did not describe differences in school absenteeism between either treatment group.[32,44] In 1 trial, school absenteeism was seldom reported, and therefore no

calculation was performed.[25] One child dropped out because of transient headaches after listening to the CD.[44] Gulewitsch et al[25] reported no adverse effects.

Cognitive Behavioral Therapy

Two systematic reviews[12,22] (including 6 RCTs[31,45–49]) and 1 RCT[28] were included in the assessment of the various CBT methods. Four trials evaluated the efficacy of family-focused CBT (ie, CBT-family).[31,45–47] A visual analog scale (VAS)[45,46] and the Faces Pain Scale–Revised[31] were used to assess pain intensity. Robins et al[47] used the abdominal pain index for assessments. Only Levy et al[31] specified primary outcomes, which were abdominal pain intensity and disability scores. A significantly higher proportion of children in the trial by Sanders et al[46] were pain free after CBT-family compared with standard care (MD: −3.61 [95% CI: −5.76 to −1.46]); these changes persisted at 6 months ($P = .02$) but had disappeared at the 12-month follow-up. Duarte et al[45] reported significantly decreased abdominal pain frequency at 3 months' follow-up ($P = .001$), but no effect was seen for pain intensity. In the study by Robins et al,[47] CBT-family added to standard care resulted in a significantly lower abdominal pain index compared with standard care alone ($P < .05$), with continuing effects at 6 and 12 months of follow-up. Levy et al[31] compared CBT-family with education and support intervention in 200 children. A significant reduction in pain intensity as indicated by parents was reported after 3 sessions of CBT-family ($P < .01$). This reduction persisted for 12 months but was not significant when reported by children.[26] There was no beneficial effect of CBT-family for disability,[31,47] but a significant improvement in school absenteeism was reported after CBT-family plus standard care ($P = .047$).[47]

Two studies evaluated the effects of individual CBT. Alfvén and Lindstrom[48] randomized children to undergo CBT plus physiotherapy ($n = 25$) or physiotherapy alone ($n = 23$). Pain intensity score (1–3), frequency score (1–3), and duration score (1–3) were summed into individual pain scores ranging from 3 to 9. Pain score reduction at the 1-year follow-up was not significantly different between groups (46% vs 44%; P value not reported). Humphreys and Gevirtz[49] divided 64 patients (aged 4–18 years) into 4 groups to compare CBT, fiber supplements, biofeedback, and parental support in different combinations. Children kept diaries and reported pain intensity by using a VAS; the primary outcome was the number of self-reported pain-free days. Results of the first 3 groups (CBT, biofeedback, and parental support) were combined and compared with a group receiving fiber supplements. After treatment, 33 (72%) of 46 children in the intervention groups were pain free compared with 1 (7.1%) of 14 children taking fiber supplements only (OR: 33.0 [95% CI: 3.9 to 278.5]).[22] Humphreys and Gevirtz investigated school absenteeism and reported significant effects favoring CBT.

Groß and Warschburger[28] compared children in the CBT group sessions ($n = 15$) versus wait-list control subjects ($n = 14$). Pain intensity was assessed by using a VAS. Although primary outcomes on pain intensity ($P = .001$), frequency ($P = .003$), and duration ($P = .002$) significantly improved after CBT, only pain duration was still significant at 3 months' follow-up ($P = .014$). Quality of life was measured as a secondary outcome by using the Pediatric Quality of Life Inventory. A significant improvement favoring CBT was reported on physical functioning ($P < .001$), psychological functioning ($P = .003$), social functioning ($P = .044$), and school functioning ($P = .012$). However, results disappeared after 3 months of follow-up.

Written Self-Disclosure

Wallander et al[29] evaluated WSD in addition to standard care in 63 children (aged 11–18 years) with RAP. In three 20-minute sessions, patients were asked to write about their "deepest thoughts and feelings about the most distressing experience in their life." Primary and secondary outcomes were not specified. Seven patients were lost to follow-up and were excluded from analyses. Abdominal pain frequency was rated by using a 6-point scale. Although there were no differences at 3 months, pain frequency was significantly less after WSD and standard care at the 6-month follow-up compared with standard care alone (F [1,51] = 6.50, $P = .014$, Cohen's $d = 0.61$). Physical and psychosocial quality of life was measured by using the Pediatric Quality of Life Inventory, and no significant differences were reported.

Prebiotics or Probiotics

One systematic review[18] (including 3 RCTs[41–43]) evaluated the effects of *Lactobacillus rhamnosus* GG (LGG) compared with placebo. Data were pooled by Horvath et al for treatment responders and treatment success, which were secondary outcomes. Bausserman and Michail[41] classified children as responders if abdominal pain severity decreased ≥1 point on a 4-point Likert scale. Francavilla et al[43] used a VAS and defined treatment success as a decrease of >50% of pain episodes and intensity. Gawrońska et al[42] defined treatment success as no pain or change in the Faces Pain Scale–Revised by ≥2 faces. LGG supplementation was associated with significantly more treatment responders (67%) compared with placebo (51%) ($n = 290$; RR: 1.31 [95% CI: 1.08 to 1.59]; number needed to treat: 7 [95% CI: 4 to 22]).[18] Subgroup analysis showed results being mainly applicable for IBS ($n = 167$; RR: 1.70 [95% CI: 1.27 to 2.27]; number needed to treat: 4 [95% CI: 3 to 8]). Guandalini et al[27]

conducted a crossover trial, comparing 6 weeks of VSL#3 versus placebo in 59 children with IBS. VSL#3 is a probiotic mixture comprising 8 different strains of *Bifidobacterium, Lactobacillus,* and *Streptococcus.* After a 2-week washout period, each patient switched to the other group for another 6 weeks of treatment. Abdominal pain was measured as a secondary outcome: frequency and intensity were rated on a 5-point Likert scale. After treatment, a significant reduction in the abdominal pain score of 1.0 ± 0.2 was reported in the VSL#3 group versus 0.5 ± 0.2 in control subjects ($P < .05$). One study evaluated school absenteeism, but no significant difference was found.[42] No adverse effects of LGG were reported, although it was unclear in 2 studies how adverse effects were assessed.[41,42]

No studies were included on prebiotics.

Alternative Medicine

One study of the systematic review by Birdee et al[23] was included regarding alternative therapy. Kuttner et al[50] compared 14 children receiving yoga versus 11 wait-list control subjects. After 4 weeks, questionnaires were completed, and control subjects received 4 weeks of yoga and completed additional questionnaires. Pain intensity was measured on a numeric scale of 0 to 10. Results before the crossover phase were not reported because of baseline differences. Functional disability decreased after yoga but increased in control subjects (MD: −9.60 [95% CI: −19.66 to 0.46]). Primary or secondary outcomes were not specified.

No studies were included evaluating acupuncture, homeopathy, mind–body therapy, or musculoskeletal manipulations such as osteopathic and chiropractic manipulations.

DISCUSSION

This systematic review includes 24 studies that were of very low to moderate methodologic quality. Some evidence was found indicating beneficial effects of PHGG, HT, CBT, and probiotics (LGG and VSL#3). No beneficial effects were reported for fiber supplementation other than PHGG and a lactose-restricted diet. No studies were included on lifestyle advice, other dietary advice, or prebiotics. No serious adverse effects were reported.

Dietary interventions are frequently used in AP-FGIDs because many patients and some physicians consider symptoms to be meal related.[55] Fiber supplementation is believed to be helpful because it softens stools and enhances colonic transit.[56] However, studies in children and adolescents evaluating ispaghula husk and glucomannan found no favorable effects.[36,38] Improvement in abdominal pain frequency was reported after administration of corn fiber,[37] but questions were raised whether the statistical analyses were adequate. Re-analyses by Huertas-Ceballos et al[15] failed to replicate the findings. Adult studies produced conflicting results and a meta-analysis reported only beneficial effects for ispaghula husk.[56] The main component of PHGG is galactomannan, which softens stool, improves fecal output, and increases bulk capacities.[57] PHGG treatment in IBS children found a reduced frequency in IBS symptoms, but pain intensity was not decreased.[24] Results of an open-label PHGG trial in adult patients with IBS produced significant improvements in gastrointestinal symptoms, quality of life, and psychological distress, but the effects tended to diminish after the 12-week treatment period.[57]

Malabsorption and intolerance to carbohydrates such as fructose and lactose are believed to cause symptoms such as bloating, diarrhea, and abdominal pain.[55] However, neither lactose nor fructose intolerance was established as a cause of pain in 220 children with RAP in a recent study,[58] and lactose restriction did not improve symptoms in pediatric trials.[39,40] Recently, diets of low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) have been extensively studied in adults. FODMAPs are poorly absorbed short-chain carbohydrates, which may cause gas production, bloating, and abdominal pain.[59] A low FODMAP diet seemed beneficial in adult IBS trials, but due to heterogeneity in study design and outcomes and because of unknown long-term safety and efficacy, definitive conclusions cannot be drawn.[60] Recently, a randomized, double-blind, crossover trial in 33 children with IBS reported improvement in abdominal pain after receiving a 48-hour low FODMAP diet.[61] Although these results seem promising, more long-term studies are needed to further assess the efficacy and safety of a low FODMAP diet in children and adolescents.

In HT, suggestions toward control and normalization of gut functioning, ego strengthening, and stress reduction are conveyed to patients after inducing a hypnotic state.[62] Results of studies in children and adolescents found significantly lower abdominal pain levels and symptom scores after HT, either through individual or group sessions with therapists or with self exercises on a CD.[25,32,44] Effects persist up to 5 years after treatment.[30] Results are in accordance with adult IBS trials showing that HT is superior to a variety of control treatments, with long-lasting effects.[63–66] Working mechanisms of HT are still poorly understood, but outcomes of adult studies hypothesize that HT affects both physiologic processes, such as colonic motility and pain-processing brain regions, and psychological factors, such as stress and dysfunctional cognitions.[67–69]

CBT aims to change attitudes, cognitions, and behavior that may play a role in generating or maintaining symptoms and is effective in improving pain and other IBS symptoms in adults.[70] Trials in children and adolescents also indicate beneficial effects of CBT, especially CBT-family, in improving pain and disability, and the effects seem to be long-lasting.[26,28,31,45–47] Results of the trial by Levy et al are of particular interest because it included 200 children and adolescents.[31] An RCT on individual CBT published shortly after the literature search for the present systematic review showed improvement in 60% of children with FAP after CBT, but the results did not differ compared with standard care (including 6 supportive sessions with the pediatric gastroenterologist).[71] However, children receiving CBT reported significantly fewer symptoms of anxiety or depression compared with children receiving standard care.

WSD targets psychosocial stress and may work through changing expression and increasing insight about emotions. It is reportedly effective in a wide variety of adult organic and functional disorders.[72] WSD in addition to standard care significantly reduced pain frequency after 6 months in pediatric RAP but not after 3 months. Although further research is needed, WSD may be a useful adjunct to other treatment regimens because it can be easily integrated, requires little training, and has low costs.[29]

Probiotics are beneficial species of bacteria that may improve AP-FGID symptoms by preventing overgrowth of potentially pathogenic bacteria, maintaining integrity of gut mucosa, and/or altering intestinal inflammatory responses.[73] RCTs in children and adolescents evaluating LGG and VSL#3 in FAP, IBS, and functional dyspepsia indicate beneficial effects over placebo, but probiotics seem mostly effective in IBS.[27,41–43] Probiotics also seem effective in adults with AP-FGIDs, but future research must clarify which probiotic strains are most effective.[74]

Although >40% of children with IBS and FAP use complementary and alternative medicine,[75] data are lacking on the efficacy and safety of almost all forms of this treatment in children and adolescents. Yoga may address psychosocial factors and decrease stress.[76] Kuttner et al[50] reported significantly lower levels of functional disability and gastrointestinal symptoms after yoga, but it is noteworthy that *P* values <.1 were considered reflective of statistical trends worthy of interpretation. However, a pilot study in children and adolescents aged 8 to 18 years with IBS and FAP also found significant short-term improvement in abdominal pain frequency and intensity.[76] It thus seems worthwhile to further explore the efficacy of yoga. Because treatment protocols in CBT, HT, and yoga all incorporate relaxation exercises, one might hypothesize that relaxation training alone can also be beneficial in AP-FGIDs. This therapeutic approach may be interesting to address in future research because it has been shown to be effective in children and adolescents with recurrent headaches as well.[77]

The methodologic quality of the included studies varied from very low to moderate, and the results should therefore be interpreted cautiously. The low quality was mainly due to small sample sizes, lack of adequate follow-up, substantial dropout rates, or considerable risk of bias. However, it should be taken into account that blinding of patients and caregivers is not possible in psychological therapies such as HT or CBT. By using validated diagnostic criteria for AP-FGIDs, applicability of results is increased, which strengthens the results. Due to considerable heterogeneity of studies, meta-analysis could only be conducted for fiber supplementation and probiotics. Other possible limitations of this systematic review include the possibility of publication bias and language restriction to English. However, by conducting a comprehensive and contemporaneous literature search, we attempted to minimize the risk of missing relevant studies. Use of a wide variety of definitions for clinical improvement also hampers the interpretation of results. Clinical relevance of a 1-point reduction on a 4-point Likert scale may be questioned,[41] whereas an 80% reduction in abdominal pain frequency and intensity scores seems overly conservative.[30,32] Unfortunately, a standard definition of improvement for therapeutic studies on AP-FGIDs is lacking. Consensus on a standard definition is necessary because it increases the homogeneity of future trials and allows better comparison of results. In addition, performing analyses on number needed to treat and RR is often restricted because most RCTs fail to report on numbers or percentages of patients experiencing significant improvement.

A limited number of RCTs (*n* = 8) reported on adverse effects, thereby hindering interpretation of results on safety. However, in those studies, no serious adverse effects were shown, apart from a small number of children reporting gas or diarrhea.[37] In interpreting FGID trials, the placebo effect may play an important role. Placebo responses in trials of adults with IBS vary from 16.0% to 71.4%,[78] and high placebo rates up to 53% were reported in RCTs on children and adolescents.[41,43,79] High placebo responses may also display natural course of FGIDs with fluctuating symptoms.[80] Improving the patient-practitioner relationship and active listening approaches are essential in mediating placebo responses. This may be especially important in nonpharmacologic therapies in which

contact with therapists is mostly frequent.[81,82]

CONCLUSIONS

To date, high-quality studies on nonpharmacologic treatments in pediatric AP-FGIDs are lacking, and the need for these studies is evident. However, available evidence indicates beneficial effects of HT, CBT and probiotics (LGG and VSL#3) in some children. Data on fiber supplementation for children and adolescents with AP-FGIDs are inconclusive, but PHGG may be an option. No serious adverse effects were reported.

Because symptoms may resolve without active treatment in a significant proportion of children, the first step in management may consist of physician reassurance and education. However, approximately one-third of children continue to experience symptoms.[83] Clinicians may consider HT, CBT, or probiotics (LGG and VSL#3), especially in children with persistent symptoms. Additional high-quality studies are required in children with mild as well as severe symptoms to further assess the effectiveness of nonpharmacologic therapies and to identify factors predicting response, with the goal of optimizing and tailoring individual treatments. Because abdominal pain is the key symptom in AP-FGIDs and to decrease heterogeneity, we emphasized the importance of including abdominal pain severity, frequency, and/or intensity as a primary outcome measure in trials evaluating nonpharmacologic treatments for AP-FGIDs. In addition, adverse effects need to be reported systematically to better assess safety.

Address correspondence to Juliette M.T.M. Rutten, MD, Emma Children's Hospital, Academic Medical Center, Room C2-312, PO Box 22700, 1100 DD Amsterdam. E-mail: j.m.rutten@amc.nl

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

REFERENCES

1. Rasquin A, Di Lorenzo C, Forbes D, et al. Childhood functional gastrointestinal disorders: child/adolescent. *Gastroenterology*. 2006;130(5):1527–1537
2. Chitkara DK, Rawat DJ, Talley NJ. The epidemiology of childhood recurrent abdominal pain in Western countries: a systematic review. *Am J Gastroenterol*. 2005;100(8):1868–1875
3. Chiou E, Nurko S. Management of functional abdominal pain and irritable bowel syndrome in children and adolescents. *Expert Rev Gastroenterol Hepatol*. 2010;4(3):293–304
4. Di Lorenzo C, Colletti RB, Lehmann HP, et al; AAP Subcommittee; NASPGHAN Committee on Chronic Abdominal Pain. Chronic abdominal pain in children: a technical report of the American Academy of Pediatrics and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr*. 2005;40(3):249–261
5. Howell S, Poulton R, Talley NJ. The natural history of childhood abdominal pain and its association with adult irritable bowel syndrome: birth-cohort study. *Am J Gastroenterol*. 2005;100(9):2071–2078
6. Dhroove G, Chogle A, Saps M. A million-dollar work-up for abdominal pain: is it worth it? *J Pediatr Gastroenterol Nutr*. 2010;51(5):579–583
7. Drossman DA. The functional gastrointestinal disorders and the Rome III process. *Gastroenterology*. 2006;130(5):1377–1390
8. Campo JV, Bridge J, Ehmann M, et al. Recurrent abdominal pain, anxiety, and depression in primary care. *Pediatrics*. 2004;113(4):817–824
9. Walker LS, Smith CA, Garber J, Claar RL. Appraisal and coping with daily stressors by pediatric patients with chronic abdominal pain. *J Pediatr Psychol*. 2007;32(2):206–216
10. Levy RL, Olden KW, Naliboff BD, et al. Psychosocial aspects of the functional gastrointestinal disorders. *Gastroenterology*. 2006;130(5):1447–1458
11. Rutten JM, Reitsma JB, Vlieger AM, Benninga MA. Gut-directed hypnotherapy for functional abdominal pain or irritable bowel syndrome in children: a systematic review. *Arch Dis Child*. 2013;98(4):252–257
12. Eccleston C, Palermo TM, de C Williams AC, et al. Psychological therapies for the management of chronic and recurrent pain in children and adolescents. *Cochrane Database Syst Rev*. 2012;12:CD003968
13. Chey WD. The role of food in the functional gastrointestinal disorders: introduction to a manuscript series. *Am J Gastroenterol*. 2013;108(5):694–697
14. Gibson PR, Shepherd SJ. Food choice as a key management strategy for functional gastrointestinal symptoms. *Am J Gastroenterol*. 2012;107(5):657–666, quiz 667
15. Huertas-Ceballos A, Logan S, Bennett C, Macarthur C. Dietary interventions for recurrent abdominal pain (RAP) and irritable bowel syndrome (IBS) in childhood. *Cochrane Database Syst Rev*. 2008;23(1):CD003019

16. Horvath A, Dziechciarz P, Szajewska H. Systematic review of randomized controlled trials: fiber supplements for abdominal pain-related functional gastrointestinal disorders in childhood. *Ann Nutr Metab*. 2012;61(2):95–101

17. Huertas-Ceballos A, Logan S, Bennett C, Macarthur C. Pharmacological interventions for recurrent abdominal pain (RAP) and irritable bowel syndrome (IBS) in childhood. *Cochrane Database Syst Rev*. 2008;23(1):CD003017

18. Horvath A, Dziechciarz P, Szajewska H. Meta-analysis: Lactobacillus rhamnosus GG for abdominal pain-related functional gastrointestinal disorders in childhood. *Aliment Pharmacol Ther*. 2011;33(12):1302–1310

19. Guyatt GH, Oxman AD, Vist GE, et al; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336(7650):924–926

20. Higgins JPT, Altman DG, Gøtzsche PC, et al; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928

21. Schünemann H, Oxman A, Vist G, et al. Interpreting results and drawing conclusions. In: Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 510 (updated March 2011)*; The Cochrane Collaboration 2012. Available at: www.cochrane-handbook.org. Accessed December 19, 2014

22. Huertas-Ceballos A, Logan S, Bennett C, Macarthur C. Psychosocial interventions for recurrent abdominal pain (RAP) and irritable bowel syndrome (IBS) in childhood. *Cochrane Database Syst Rev*. 2008;(1):CD003014

23. Birdee GS, Yeh GY, Wayne PM, Phillips RS, Davis RB, Gardiner P. Clinical applications of yoga for the pediatric population: a systematic review. *Acad Pediatr*. 2009;9(4):212–, e1–e9

24. Romano C, Comito D, Famiani A, Calamarà S, Loddo I. Partially hydrolyzed guar gum in pediatric functional abdominal pain. *World J Gastroenterol*. 2013;19(2):235–240

25. Gulewitsch MD, Müller J, Hautzinger M, Schlarb AA. Brief hypnotherapeutic-behavioral intervention for functional abdominal pain and irritable bowel syndrome in childhood: a randomized controlled trial. *Eur J Pediatr*. 2013;172(8):1043–1051

26. Levy RL, Langer SL, Walker LS, et al. Twelve-month follow-up of cognitive behavioral therapy for children with functional abdominal pain. *JAMA Pediatr*. 2013;167(2):178–184

27. Guandalini S, Magazzù G, Chiaro A, et al. VSL#3 improves symptoms in children with irritable bowel syndrome: a multicenter, randomized, placebo-controlled, double-blind, crossover study. *J Pediatr Gastroenterol Nutr*. 2010;51(1):24–30

28. Groß M, Warschburger P. Evaluation of a cognitive-behavioral pain management program for children with chronic abdominal pain: a randomized controlled study. *Int J Behav Med*. 2013;20(3):434–443

29. Wallander JL, Madan-Swain A, Klapow J, Saeed S. A randomised controlled trial of written self-disclosure for functional recurrent abdominal pain in youth. *Psychol Health*. 2011;26(4):433–447

30. Vlieger AM, Rutten JM, Govers AM, Frankenhuis C, Benninga MA. Long-term follow-up of gut-directed hypnotherapy vs. standard care in children with functional abdominal pain or irritable bowel syndrome. *Am J Gastroenterol*. 2012;107(4):627–631

31. Levy RL, Langer SL, Walker LS, et al. Cognitive-behavioral therapy for children with functional abdominal pain and their parents decreases pain and other symptoms. *Am J Gastroenterol*. 2010;105(4):946–956

32. Vlieger AM, Menko-Frankenhuis C, Wolfkamp SC, Tromp E, Benninga MA. Hypnotherapy for children with functional abdominal pain or irritable bowel syndrome: a randomized controlled trial. *Gastroenterology*. 2007;133(5):1430–1436

33. Sanders MR, Rebgetz M, Morrison M, et al. Cognitive-behavioral treatment of recurrent nonspecific abdominal pain in children: an analysis of generalization, maintenance, and side effects. *J Consult Clin Psychol*. 1989;57(2):294–300

34. Hicks CL, von Baeyer CL, McGrath PJ. Online psychological treatment for pediatric recurrent pain: a randomized evaluation. *J Pediatr Psychol*. 2006;31(7):724–736

35. Weydert JA, Shapiro DE, Acra SA, Monheim CJ, Chambers AS, Ball TM. Evaluation of guided imagery as treatment for recurrent abdominal pain in children: a randomized controlled trial. *BMC Pediatr*. 2006;6:29

36. Christensen MF. Recurrent abdominal pain and dietary fiber. *Am J Dis Child*. 1986;140(8):738–739

37. Feldman W, McGrath P, Hodgson C, Ritter H, Shipman RT. The use of dietary fiber in the management of simple, childhood, idiopathic, recurrent, abdominal pain. Results in a prospective, double-blind, randomized, controlled trial. *Am J Dis Child*. 1985;139(12):1216–1218

38. Horvath A, Dziechciarz P, Szajewska H. Glucomannan for abdominal pain-related functional gastrointestinal disorders in children: a randomized trial. *World J Gastroenterol*. 2013;19(20):3062–3068

39. Dearlove J, Dearlove B, Pearl K, Primavesi R. Dietary lactose and the child with abdominal pain. *Br Med J (Clin Res Ed)*. 1983;286(6382):1936

40. Lebenthal E, Rossi TM, Nord KS, Branski D. Recurrent abdominal pain and lactose absorption in children. *Pediatrics*. 1981;67(6):828–832

41. Bausserman M, Michail S. The use of Lactobacillus GG in irritable bowel syndrome in children: a double-blind randomized control trial. *J Pediatr*. 2005;147(2):197–201

42. Gawrońska A, Dziechciarz P, Horvath A, Szajewska H. A randomized double-blind placebo-controlled trial of Lactobacillus GG for abdominal pain disorders in children. *Aliment Pharmacol Ther*. 2007;25(2):177–184

43. Francavilla R, Miniello V, Magistà AM, et al. A randomized controlled trial of Lactobacillus GG in children with functional abdominal pain. *Pediatrics*. 2010;126(6). Available at: www.pediatrics.org/cgi/content/full/126/6/e1445

44. van Tilburg MA, Chitkara DK, Palsson OS, et al. Audio-recorded guided imagery treatment reduces functional abdominal pain in children: a pilot study. *Pediatrics*. 2009;124(5). Available at: www.pediatrics.org/cgi/content/full/124/5/e890

45. Duarte MA, Penna FJ, Andrade EM, Cancela CS, Neto JC, Barbosa TF.

Treatment of nonorganic recurrent abdominal pain: cognitive-behavioral family intervention. *J Pediatr Gastroenterol Nutr*. 2006;43(1):59–64

46. Sanders MR, Shepherd RW, Cleghorn G, Woolford H. The treatment of recurrent abdominal pain in children: a controlled comparison of cognitive-behavioral family intervention and standard pediatric care. *J Consult Clin Psychol*. 1994;62(2):306–314
47. Robins PM, Smith SM, Glutting JJ, Bishop CT. A randomized controlled trial of a cognitive-behavioral family intervention for pediatric recurrent abdominal pain. *J Pediatr Psychol*. 2005; 30(5):397–408
48. Alfvén G, Lindstrom A. A new method for the treatment of recurrent abdominal pain of prolonged negative stress origin. *Acta Paediatr*. 2007;96(1):76–81
49. Humphreys PA, Gevirtz RN. Treatment of recurrent abdominal pain: components analysis of four treatment protocols. *J Pediatr Gastroenterol Nutr*. 2000;31(1):47–51
50. Kuttner L, Chambers CT, Hardial J, Israel DM, Jacobson K, Evans K. A randomized trial of yoga for adolescents with irritable bowel syndrome. *Pain Res Manag*. 2006;11(4):217–223
51. Hicks CL, von Baeyer CL, Spafford PA, van Korlaar I, Goodenough B. The Faces Pain Scale-Revised: toward a common metric in pediatric pain measurement. *Pain*. 2001;93(2):173–183
52. Roalfe AK, Roberts LM, Wilson S. Evaluation of the Birmingham IBS symptom questionnaire. *BMC Gastroenterol*. 2008;8:30
53. Chambers CT, Craig KD. An intrusive impact of anchors in children's faces pain scales. *Pain*. 1998;78(1):27–37
54. Walker LS, Smith CA, Garber J, Van Slyke DA. Development and validation of the pain response inventory for children. *Psychol Assessment*. 1997;9(4):392–405
55. Simrén M, Månsson A, Langkilde AM, et al. Food-related gastrointestinal symptoms in the irritable bowel syndrome. *Digestion*. 2001;63(2):108–115
56. Ford AC, Talley NJ, Spiegel BM, et al. Effect of fibre, antispasmodics, and peppermint oil in the treatment of irritable bowel syndrome: systematic review and meta-analysis. *BMJ*. 2008;337: a2313
57. Parisi G, Bottona E, Carrara M, et al. Treatment effects of partially hydrolyzed guar gum on symptoms and quality of life of patients with irritable bowel syndrome. A multicenter randomized open trial. *Dig Dis Sci*. 2005;50(6): 1107–1112
58. Gijsbers CF, Kneepkens CM, Büller HA. Lactose and fructose malabsorption in children with recurrent abdominal pain: results of double-blinded testing. *Acta Paediatr*. 2012;101(9):e411–e415
59. Shepherd SJ, Lomer MCE, Gibson PR. Short-chain carbohydrates and functional gastrointestinal disorders. *Am J Gastroenterol*. 2013;108(5):707–717
60. Fedewa A, Rao SS. Dietary fructose intolerance, fructan intolerance and FODMAPs. *Curr Gastroenterol Rep*. 2014; 16(1):370
61. Chumpitazi B, Tsai C, McMeans A, Shulman R. A low FODMAPs diet ameliorates symptoms in children with irritable bowel syndrome: a double blind, randomized crossover trial. *Gastroenterology*. 2014;146(5):S-144
62. Green JP, Barabasz AF, Barrett D, Montgomery GH. Forging ahead: the 2003 APA Division 30 definition of hypnosis. *Int J Clin Exp Hypn*. 2005;53(3):259–264
63. Webb AN, Kukuruzovic RH, Catto-Smith AG, Sawyer SM. Hypnotherapy for treatment of irritable bowel syndrome. *Cochrane Database Syst Rev*. 2007;17(4): CD005110
64. Gonsalkorale WM, Miller V, Afzal A, Whorwell PJ. Long term benefits of hypnotherapy for irritable bowel syndrome. *Gut*. 2003;52(11):1623–1629
65. Lindfors P, Unge P, Nyhlin H, et al. Long-term effects of hypnotherapy in patients with refractory irritable bowel syndrome. *Scand J Gastroenterol*. 2012; 47(4):414–420
66. Moser G, Trägner S, Gajowniczek EE, et al. Long-term success of GUT-directed group hypnosis for patients with refractory irritable bowel syndrome: a randomized controlled trial. *Am J Gastroenterol*. 2013;108(4):602–609
67. Palsson OS, Turner MJ, Johnson DA, Burnett CK, Whitehead WE. Hypnosis treatment for severe irritable bowel syndrome: investigation of mechanism and effects on symptoms. *Dig Dis Sci*. 2002;47(11):2605–2614
68. Gonsalkorale WM, Toner BB, Whorwell PJ. Cognitive change in patients undergoing hypnotherapy for irritable bowel syndrome. *J Psychosom Res*. 2004;56(3): 271–278
69. Faymonville ME, Roediger L, Del Fiore G, et al. Increased cerebral functional connectivity underlying the antinociceptive effects of hypnosis. *Brain Res Cogn Brain Res*. 2003;17(2):255–262
70. Ford AC, Talley NJ, Schoenfeld PS, Quigley EM, Moayyedi P. Efficacy of antidepressants and psychological therapies in irritable bowel syndrome: systematic review and meta-analysis. *Gut*. 2009;58(3):367–378
71. van der Veek SM, Derkx BH, Benninga MA, Boer F, de Haan E. Cognitive behavior therapy for pediatric functional abdominal pain: a randomized controlled trial. *Pediatrics*. 2013;132(5). Available at: www.pediatrics.org/cgi/content/full/132/5/e1163
72. Frattaroli J. Experimental disclosure and its moderators: a meta-analysis. *Psychol Bull*. 2006;132(6):823–865
73. Quigley EM. Probiotics in functional gastrointestinal disorders: what are the facts? *Curr Opin Pharmacol*. 2008;8(6): 704–708
74. Simrén M, Barbara G, Flint HJ, et al; Rome Foundation Committee. Intestinal microbiota in functional bowel disorders: a Rome foundation report. *Gut*. 2013;62(1):159–176
75. Vlieger AM, Blink M, Tromp E, Benninga MA. Use of complementary and alternative medicine by pediatric patients with functional and organic gastrointestinal diseases: results from a multicenter survey. *Pediatrics*. 2008; 122(2). Available at: www.pediatrics.org/cgi/content/full/122/2/e446
76. Brands MM, Purperhart H, Deckers-Kocken JM. A pilot study of yoga treatment in children with functional abdominal pain and irritable bowel syndrome. *Complement Ther Med*. 2011; 19(3):109–114
77. Trautmann E, Lackschewitz H, Kröner-Herwig B. Psychological treatment of recurrent headache in children and adolescents—a meta-analysis. *Cephalalgia*. 2006;26(12):1411–1426
78. Patel SM, Stason WB, Legedza A, et al. The placebo effect in irritable bowel

syndrome trials: a meta-analysis. *Neurogastroenterol Motil*. 2005;17(3):332–340

79. Saps M, Youssef N, Miranda A, et al. Multicenter, randomized, placebo-controlled trial of amitriptyline in children with functional gastrointestinal disorders. *Gastroenterology*. 2009;137(4):1261–1269
80. Drossman DA, Camilleri M, Mayer EA, Whitehead WE. AGA technical review on irritable bowel syndrome. *Gastroenterology*. 2002;123(6):2108–2131
81. Kelley JM, Lembo AJ, Ablon JS, et al. Patient and practitioner influences on the placebo effect in irritable bowel syndrome. *Psychosom Med*. 2009;71(7):789–797
82. Kaptchuk TJ, Kelley JM, Conboy LA, et al. Components of placebo effect: randomised controlled trial in patients with irritable bowel syndrome. *BMJ*. 2008;336(7651):999–1003
83. Gieteling MJ, Bierma-Zeinstra SM, Passchier J, Berger MY. Prognosis of chronic or recurrent abdominal pain in children. *J Pediatr Gastroenterol Nutr*. 2008;47(3):316–326

WARM WATER BLUES: *When I was a teen, I would occasionally go cod fishing off the coast of Maine or Massachusetts with my father. While we did not catch particularly large numbers of fish, we always caught enough cod for several dinners. In those days, cod was a staple of New England fish restaurants. That has changed. The cod population off of the coast of New England has collapsed – so much so that, as reported in* The New York Times *(U.S.: December 15, 2014), cod fishing has been banned since November for six months as regulators decide how to address the problem.*

While overfishing has certainly contributed, a problem that cannot easily be addressed by state and federal regulators is the warming of the Gulf of Maine waters. Historically, the water temperature in the Gulf of Maine had warmed on average about one degree every two decades or so. In the past decade, the water has warmed by about one degree every two years. This has led to changes in the ecosystem. Maine shrimp have fled for colder climates, leading regulators to cancel the Maine shrimp harvest for the second year in a row. Black sea bass, native to warmer southern waters and previously rarely seen off the coast of Maine, have become abundant. Blue crab, so closely linked to the Chesapeake, has made an appearance. Lobsters have become much more plentiful with record harvests for several years in a row, but the center of the lobster industry has moved at least 50 miles to the north. The toll on the economy and human life may be quite severe. Precluded from fishing for at least six months, Maine's fishermen have few options to support themselves. This is just another example of how intertwined humans and animals are with the ecosystems and the complex interplay between each and all its parts.

Noted by WVR, MD

Nonpharmacologic Treatment of Functional Abdominal Pain Disorders: A Systematic Review

Juliette M.T.M. Rutten, Judith J. Korterink, Leonie M.A.J. Venmans, Marc A. Benninga and Merit M. Tabbers

Pediatrics 2015;135;522
DOI: 10.1542/peds.2014-2123 originally published online February 9, 2015;

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Nonpharmacologic Treatment of Functional Abdominal Pain Disorders: A Systematic Review

Juliette M.T.M. Rutten, Judith J. Korterink, Leonie M.A.J. Venmans, Marc A. Benninga and Merit M. Tabbers

Pediatrics 2015;135;522
DOI: 10.1542/peds.2014-2123 originally published online February 9, 2015;