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Dietary interventions for recurrent abdominal pain in childhood (Review)

Newlove-Delgado TV, Martin AE, Abbott RA, Bethel A, Thompson-Coon J, Whear R, Logan S

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[Intervention Review]

Dietary interventions for recurrent abdominal pain in childhood

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ABSTRACT

Background

This is an update of the original Cochrane review, last published in 2009 (Huertas-Ceballos 2009). Recurrent abdominal pain (RAP), including children with irritable bowel syndrome, is a common problem affecting between 4% and 25% of school-aged children. For the majority of such children, no organic cause for their pain can be found on physical examination or investigation. Many dietary inventions have been suggested to improve the symptoms of RAP. These may involve either excluding ingredients from the diet or adding supplements such as fibre or probiotics.

Objectives

To examine the effectiveness of dietary interventions in improving pain in children of school age with RAP.

Search methods

We searched CENTRAL, Ovid MEDLINE, Embase, eight other databases, and two trials registers, together with reference checking, citation searching and contact with study authors, in June 2016.

Selection criteria

Randomised controlled trials (RCTs) comparing dietary interventions with placebo or no treatment in children aged five to 18 years with RAP or an abdominal pain-related, functional gastrointestinal disorder, as defined by the Rome III criteria (Rasquin 2006).

Data collection and analysis

We used standard methodological procedures expected by Cochrane. We grouped dietary interventions together by category for analysis. We contacted study authors to ask for missing information and clarification, when needed. We assessed the quality of the evidence for each outcome using the GRADE approach.

Main results

We included 19 RCTs, reported in 27 papers with a total of 1453 participants. Fifteen of these studies were not included in the previous review. All 19 RCTs had follow-up ranging from one to five months. Participants were aged between four and 18 years from eight different countries and were recruited largely from paediatric gastroenterology clinics. The mean age at recruitment ranged from 6.3 years to 13.1 years. Girls outnumbered boys in most trials. Fourteen trials recruited children with a diagnosis under the broad umbrella of RAP or functional gastrointestinal disorders; five trials specifically recruited only children with irritable bowel syndrome. The studies fell into four categories: trials of probiotic-based interventions (13 studies), trials of fibre-based interventions (four studies), trials of low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diets (one study), and trials of fructose-restricted diets (one study).

We found that children treated with probiotics reported a greater reduction in pain frequency at zero to three months postintervention than those given placebo (standardised mean difference (SMD) -0.55, 95% confidence interval (CI) -0.98 to -0.12; 6 trials; 523 children). There was also a decrease in pain intensity in the intervention group at the same time point (SMD -0.50, 95% CI -0.85 to -0.15; 7 studies; 575 children). However, we judged the evidence for these outcomes to be of low quality using GRADE due to an unclear risk of bias from incomplete outcome data and significant heterogeneity.

We found that children treated with probiotics were more likely to experience improvement in pain at zero to three months postintervention than those given placebo (odds ratio (OR) 1.63, 95% CI 1.07 to 2.47; 7 studies; 722 children). The estimated number needed to treat for an additional beneficial outcome (NNTB) was eight, meaning that eight children would need to receive probiotics for one to experience improvement in pain in this timescale. We judged the evidence for this outcome to be of moderate quality due to significant heterogeneity.

Children with a symptom profile defined as irritable bowel syndrome treated with probiotics were more likely to experience improvement in pain at zero to three months postintervention than those given placebo (OR 3.01, 95% CI 1.77 to 5.13; 4 studies; 344 children). Children treated with probiotics were more likely to experience improvement in pain at three to six months postintervention compared to those receiving placebo (OR 1.94, 95% CI 1.10 to 3.43; 2 studies; 224 children). We judged the evidence for these two outcomes to be of moderate quality due to small numbers of participants included in the studies.

We found that children treated with fibre-based interventions were not more likely to experience an improvement in pain at zero to three months postintervention than children given placebo (OR 1.83, 95% CI 0.92 to 3.65; 2 studies; 136 children). There was also no reduction in pain intensity compared to placebo at the same time point (SMD -1.24, 95% CI -3.41 to 0.94; 2 studies; 135 children). We judged the evidence for these outcomes to be of low quality due to an unclear risk of bias, imprecision, and significant heterogeneity.

We found only one study of low FODMAP diets and only one trial of fructose-restricted diets, meaning no pooled analyses were possible.

We were unable to perform any meta-analyses for the secondary outcomes of school performance, social or psychological functioning, or quality of daily life, as not enough studies included these outcomes or used comparable measures to assess them.

With the exception of one study, all studies reported monitoring children for adverse events; no major adverse events were reported.

Authors' conclusions

Overall, we found moderate- to low-quality evidence suggesting that probiotics may be effective in improving pain in children with RAP. Clinicians may therefore consider probiotic interventions as part of a holistic management strategy. However, further trials are needed to examine longer-term outcomes and to improve confidence in estimating the size of the effect, as well as to determine the optimal strain and dosage. Future research should also explore the effectiveness of probiotics in children with different symptom profiles, such as those with irritable bowel syndrome.

We found only a small number of trials of fibre-based interventions, with overall low-quality evidence for the outcomes. There was therefore no convincing evidence that fibre-based interventions improve pain in children with RAP. Further high-quality RCTs of fibre supplements involving larger numbers of participants are required. Future trials of low FODMAP diets and other dietary interventions are also required to facilitate evidence-based recommendations.

PLAIN LANGUAGE SUMMARY

Dietary interventions for recurrent abdominal pain in children

Review question

We reviewed the evidence on the effects of dietary interventions on pain in children aged between five and 18 years with recurrent abdominal pain (RAP).

Background

Recurrent abdominal pain, or RAP, is a term used for unexplained episodes of stomachache or abdominal pain in children. Recurrent abdominal pain is a common condition, and most children are likely to be helped by simple measures. However, a range of treatments have been recommended to relieve abdominal pain, including making changes to the child's eating habits by adding supplements or excluding certain foods.

Study characteristics

This evidence is current to June 2016.

Nineteen studies met our inclusion criteria, including 13 studies of probiotics and four studies of fibre interventions. We also found one study of a diet low in substances known as FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) and one study of a fructose-restricted diet.

All of the studies compared dietary interventions to a placebo or control. The trials were carried out in eight countries and included a total of 1453 participants, aged between five and 18 years. Most children were recruited from outpatient clinics. Most interventions lasted four to six weeks.

Key results

Probiotics

We found evidence from 13 studies suggesting that probiotics might be effective in improving pain in the shorter term. Most studies did not report on other areas such as quality of daily life. No harmful effects were reported, other than dry mouth in one study. We judged this evidence to be of moderate or low quality because some studies were small, showed varying results, or were at risk of bias.

Fibre supplements

We found no clear evidence of improvement of pain from four studies of fibre supplements. Most studies did not report on other areas such as quality of daily life. No harmful effects were reported. There were few studies of fibre supplements, and some of these studies were at risk of bias. We judged this evidence to be of low quality.

Low FODMAP diets

We found only one study evaluating the effectiveness of low FODMAP diets in children with RAP.

Fructose-restricted diets

We found only one study evaluating the effectiveness of fructose-restricted diets in children with RAP.

Conclusion

We found some evidence suggesting that probiotics may be helpful in relieving pain in children with RAP in the short term. Clinicians may therefore consider probiotic interventions as part of the management strategy for RAP. Further trials are needed to find out how effective probiotics are over longer periods of time and which probiotics might work best.

We did not find convincing evidence that fibre supplements are effective in improving pain in children with RAP. Future larger, high-quality studies are needed to test the effectiveness of fibre and low FODMAP diet treatments.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Probiotics compared to placebo for recurrent abdominal pain in childhood

Patient or population: Children with recurrent abdominal pain
Settings: Mixed settings, including paediatric gastroenterology clinics
Intervention: Probiotics
Comparison: Placebo

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo	Probiotics				
Change in pain frequency: 0 to 3 months' postintervention Different measures were used to assess pain frequency, such as a visual analogue scale and the Wong-Baker FACES Pain Rating Scale (McGrath 1996; Wong 1988).	-	The mean change in pain frequency: 0 to 3 months' postintervention scores in the intervention groups was **0.55 SDs lower** (0.98 to 0.12 lower).	-	523 (6 studies)	⊕⊕◯◯ **Low**[1,2]	As a rule of thumb, 0.2 SD represents a small difference, 0.5 SD a moderate difference, and 0.8 SD a large difference
Change in pain intensity: 0 to 3 months' postintervention Different measures were used to assess pain intensity, as above	-	The mean change in pain intensity: 0 to 3 months' postintervention scores in the intervention groups was **0.50 SDs lower** (0.85 to 0.15 lower).	-	575 (7 studies)	⊕⊕◯◯ **Low**[1,2]	As a rule of thumb, 0.2 SD represents a small difference, 0.5 SD a moderate difference, and 0.8 SD a large difference

Improvement in pain: 0 to 3 months' postintervention Different measures and definitions were used for improvement in pain, such as Likert scale, visual analogue scale, and Subject's Global Assessment of Relief Scale (McGrath 1996; Muller-Lissner 2003).	**421 per 1000**[3]	**542 per 1000** (438 to 642)	**OR 1.63** (1.07 to 2.47) NNTB = 8	722 (7 studies)	⊕⊕⊕○ **Moderate**[4]	-
Improvement in pain: 0 to 3 months' postintervention Subgroup (irritable bowel syndrome) Different measures were used to assess improvement in pain, as above	**359 per 1000**	**627 per 1000** (498 to 742)	**OR 3.01** (1.77 to 5.13) NNTB = 4	344 (4 studies)	⊕⊕⊕○ **Moderate**[5]	-
Improvement in pain: 3 to 6 months' postintervention Different measures were used to assess improvement in pain, as above	**589 per 1000**	**736 per 1000** (612 to 831)	**OR 1.94** (1.10 to 3.43) NNTB = 7	224 (2 studies)	⊕⊕⊕○ **Moderate**[5]	-

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **NNTB**: number needed to treat for an additional beneficial outcome, based on the absolute risk reduction between the intervention and comparison group probable outcomes; **OR:** odds ratio; **SD:** standard deviation.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Downgraded one level due to incomplete outcome data in a number of included studies leading to an unclear or high risk of bias.
[2]Downgraded one level for evidence of significant heterogeneity (I^2 > 70%; Chi^2 P < 0.001).
[3]Assumed risk is based on the mean outcome of the control groups in all included studies.
[4]Downgraded one level due to evidence of heterogeneity (I^2 = 45%; Chi^2 P = 0.09).
[5]Downgraded one level for imprecision.

BACKGROUND

Description of the condition

This review is an update of a previously published review in the Cochrane Library on 'Psychosocial interventions for recurrent abdominal pain and irritable bowel syndrome in childhood' (Huertas-Ceballos 2009). Recurrent abdominal pain (RAP) is a common problem in paediatric practice. It has been suggested that 4% to 25% of school-aged children will at some point suffer from recurrent or chronic abdominal pain that interferes with their activities of daily living (Konijnenberg 2005; Williams 1996; Youssef 2006), with a recent meta-analysis estimating that 13.5% of children worldwide may be affected (Korterink 2015). Recurrent abdominal pain is often regarded as a relatively benign condition, but it is important to note the associated morbidity and the anxiety it causes for children and caregivers (Paul 2013). The condition is associated with school absences, hospital admissions, emotional disorders and, on occasion, unnecessary surgical intervention (Scharff 1997; Stickler 1979; Størdal 2005; Walker 1998; Youssef 2008). The abdominal pain is also commonly associated with other symptoms, including headaches, recurrent limb pains, pallor, and vomiting (Abu-Arafeh 1995; Devanarayana 2011; Hyams 1995). Symptoms sometimes continue into adulthood; childhood RAP is associated with a higher risk of anxiety disorders in adults (Horst 2014; Shelby 2013).

Apley first sought to define the condition in the 1950s and suggested that the diagnostic label should be based on the presence of at least three episodes of severe abdominal pain (often, but not necessarily, with associated systemic symptoms) over three months (Apley 1958), with no established organic cause. Historically diverse terms have since been used to describe these conditions, some implying causation. These include: "abdominal migraine" (Bain 1974; Farquar 1956; Hockaday 1992; Symon 1986), "abdominal epilepsy" (Stowens 1970), "the irritable bowel syndrome in childhood" (Stone 1970), "allergic-tension-fatigue syndrome" (Sandberg 1973; Speer 1954), "neurovegetative dystonia" (Peltonen 1970; Rubin 1967), "functional gastrointestinal disorder" (Drossman 1995), and "the irritated colon syndrome" (Harvey 1973; Painter 1964).

It is now generally accepted that RAP in children represents a group of functional gastrointestinal disorders that have an unclear aetiology. The latest Rome Foundation criteria state that such disorders are defined by symptoms related to motility disturbance; visceral hypersensitivity; altered mucosal and immune function; altered gut microbiota; and altered central nervous system processing, and are "the product of ... interactions of psychosocial factors and altered gut physiology via the brain-gut axis" (Drossman 2016). The Rome Foundation has produced criteria for this group of conditions since 1994 by international consensus. Most studies included in this review use the Rome III criteria from 2006, which included a symptom-based classification system with specific categories for paediatric presentations (Rasquin 2006). Throughout this review we have therefore used RAP as an umbrella term to refer to the five subcategories included within the Rome III category of childhood abdominal pain-related functional gastrointestinal disorders, which are: functional dyspepsia, irritable bowel syndrome, abdominal migraine, functional abdominal pain, and functional abdominal pain syndrome. It should be noted that the pain classification for each of the Rome III diagnoses is defined by at least one episode per week for at least two months; this varies from Apley's original definition of RAP (Apley 1958). The Rome IV criteria were produced in spring 2016; in this new iteration the category of childhood functional abdominal pain disorders includes functional dyspepsia, irritable bowel syndrome, abdominal migraine, and functional abdominal pain not otherwise specified (Drossman 2016). However, the Rome classification is not based on known pathophysiological differences between the conditions, but rather on the constellation of clinical features. It is unclear the extent to which separating children into these categories defines groups that are distinct clinical entities that are likely to respond differently to treatment.

There is no consensus about which of the numerous proposed causal pathways result in the heterogeneous presentations of chronic abdominal pain, although it is suggested that physical, emotional, and environmental factors may contribute to the manifestation of unexplained abdominal pain. When considering the diverse proposed mechanisms, it is unsurprising that a variety of treatments have been suggested. The treatment approaches can be grouped as pharmacological, dietary, or psychosocial (psychological or behavioural, or both). This review focused on any intervention with dietary changes intended to improve the symptoms of RAP, and hence dietary approaches only are discussed below. Updated companion reviews of pharmacological interventions, Martin 2014a, and psychosocial interventions, Abbott 2017, for RAP have been published.

Description of the intervention

Dietary interventions may involve excluding or reducing a food group or specific ingredient from the diet or supplementing it and therefore increasing its intake. Such dietary interventions include eliminating or restricting food groups or food components, such as dairy products or fructose (Bain 1974; Bayless 1971; Wirth 2014), and taking fibre supplements (Horvath 2013). Probiotics, which are living micro-organisms such as *Lactobacillus*, have also been used in managing children with RAP (Wilhelm 2008). More recently there has been interest in the use of low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diets in the management of irritable bowel syndrome, although the majority of studies have included adult populations (Rao 2015), with one recent randomised controlled trial in children (Chumpitazi 2015).

How the intervention might work

Probiotic-based interventions containing living micro-organisms are thought to improve symptoms through restoring the gut's microbial balance. It has also been suggested that they might alter the intestinal inflammatory response in the lining of the gut (Quigley 2008). Fibre-based interventions might be effective in children with irritable bowel syndrome in particular, by modifying bowel habits and the transit time through the gut, as well as by decreasing intracolonic pressure (Romano 2013). It has been suggested that alterations in diet, such as low FODMAP interventions, may work in irritable bowel syndrome by reducing osmotic effects, fermentation, and gas production, hence decreasing distension and pain (Nanayakkara 2016).

Why it is important to do this review

Recurrent abdominal pain in children is very common, and in daily clinical practice there is no consensus on which treatments to offer patients. The approach to treating RAP is therefore inconsistent. This review, an update of one last carried out in 2009 (Huertas-Ceballos 2009), is important to establish if there is new evidence for the effectiveness of dietary interventions in children with RAP. Together with updated reviews of pharmacological interventions, Martin 2014a, and psychosocial interventions, Abbott 2017, for RAP, this review can guide clinicians, patients, and their families in treatment decisions.

OBJECTIVES

To examine the effectiveness of dietary interventions in improving pain in children of school age with RAP.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs).

Types of participants

Children aged five to 18 years old with RAP or an abdominal pain-related functional gastrointestinal disorder, as defined by the Rome III criteria (Rasquin 2006).

Recurrent abdominal pain is defined as at least three episodes of pain interfering with normal activities within a three-month period. The Rome III criteria recognise five abdominal pain-related categories: "abdominal migraine", "irritable bowel syndrome", "functional dyspepsia", "functional abdominal pain", and "functional abdominal pain syndrome" (Rasquin 2006).

Types of interventions

Any dietary intervention compared to placebo, waiting list, no treatment, or standard care.

Types of outcome measures

Primary outcomes

1. Pain intensity, duration, or frequency.

There is no standard method for measuring pain in this condition. Studies may use any validated measurement of pain, and may report the proportion of participants with significant improvement in pain as defined by the trial author. We expected studies to vary in their duration of postintervention follow-up. We therefore grouped studies according to duration of follow-up: postintervention (immediately or the earliest data available following the end of treatment), medium-term follow-up (three to six months' postintervention), and long-term follow-up (six months or longer). See Differences between protocol and review.

Secondary outcomes

As measured by a validated tool:

1. school performance (to include measures such as school functioning, behaviour, or school attendance);
2. social or psychological functioning (to include measures such as anxiety or depression); and
3. quality of daily life (to include measures such as quality of life or impairment to daily activities, functional disability, or activity limitations).

We also reported on adverse events, where these were monitored. See Differences between protocol and review.

We presented all outcomes in Summary of findings for the main comparison and Summary of findings 2.

Search methods for identification of studies

Electronic searches

We ran the first literature searches in April 2013 and updated them in April 2014, March 2015, and again in June 2016. We searched the electronic databases and trial registers listed below.

1. Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 5) in the Cochrane Library, and which includes the Cochrane Developmental, Psychosocial and Learning Problems Specialised Register (searched 10 June 2016).

2. Ovid MEDLINE In-Process & Other Non-Indexed Citations and Ovid MEDLINE (1946 to current; searched 9 June 2016).
3. Embase Ovid (1974 to current; searched 9 June 2016).
4. CINAHL Healthcare Databases Advanced Search (Cumulative Index to Nursing and Allied Health Literature; 1981 to current; searched 9 June 2016).
5. PsycINFO Ovid (1806 to current; searched 9 June 2016).
6. ERIC ProQuest (Educational Resources Information Center; 1966 to current; searched 9 June 2016).
7. BEI ProQuest (British Education Index; 1975 to current; searched 9 June 2016).
8. ASSIA ProQuest (Applied Social Sciences Index and Abstracts; 1987 to current; searched 9 June 2016).
9. AMED Healthcare Databases Advanced Search (Allied and Complementary Medicine; 1985 to current; searched 9 June 2016).
10. LILACS (Latin American and Caribbean Literature in Health Sciences; lilacs.bvsalud.org/en; searched 9 June 2016).
11. OpenGrey (opengrey.eu; searched 9 June 2016).
12. ClinicalTrials.gov (clinicaltrials.gov; searched 9 June 2016).
13. World Health Organization International Clinical Trials Registry Platform (WHO ICTRP; apps.who.int/trialsearch; searched 9 June 2016).

The search terms were revised from the original Cochrane RAP reviews (Huertas-Ceballos 2008a; Huertas-Ceballos 2008b; Huertas-Ceballos 2009); consequently, searches were run for all available years. We used RCT filters where appropriate and imposed no language limits. We translated any non-English language studies identified so that they could be screened and considered for inclusion. The search strategies for each database are reported in Appendix 1.

Searching other resources

We used the Science Citation Index to locate relevant studies using the bibliographic details, and authors' names of relevant papers for forward and backward citations. We contacted researchers who have published studies in this field to ask for details of any relevant trials. We also checked the bibliographies of papers retrieved to establish if all pertinent references were found by our search.

Data collection and analysis

Selection of studies

Two review authors (TVN, AEM, RAA, AB, or RW) independently screened the titles and abstracts of studies for relevance. We obtained the full-text reports of all potentially relevant papers and screened them for inclusion against the eligibility criteria (see Criteria for considering studies for this review). Any disagreements were resolved through discussion with a third review author (JTC). We recorded our decisions in a PRISMA diagram (Moher 2009).

Data extraction and management

Two review authors (TVN, AEM, RAA, AB, JTC, or RW) extracted the data and entered the data into Cochrane's statistical software, Review Manager 5 (Review Manager 2014). All review authors used the same data extraction form. We collected the following data.

1. Study characteristics: number of participating children, inclusion and exclusion criteria, type of intervention and comparison, intervention characteristics (duration, frequency, setting), number of withdrawals.
2. Participant characteristics: sex, age, diagnosis (e.g. RAP or other syndrome, as defined by the Rome III criteria) (Rasquin 2006).
3. Outcome measures: measurement of pain and any secondary outcomes measured. See Types of outcome measures.

Assessment of risk of bias in included studies

We assessed the risk of bias of each included study using the Cochrane 'Risk of bias' tool (Higgins 2011a). We assessed the following categories of bias: selection bias (random sequence generation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting), and other potential sources of bias that could have altered the estimate of treatment effect; for example, any evidence of differential loss to follow-up, whether the data collection tools were valid, whether there was sufficient power in terms of appropriate sample size, whether baseline parameters were similar, and whether data analyses were appropriate. Two review authors (TVN, AEM, RAA, AB, JTC, or RW) independently assessed and classified each study as being at 'low', 'high', or 'unclear' risk of bias across each of these domains, based on the methods detailed in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a); see Table 1 for more information. We considered a trial as having an overall low risk of bias if most of the above categories of bias were assessed as low risk of bias.

Measures of treatment effect

We reported our study results as follows.

Continuous data

For continuous data (e.g. pain intensity or frequency), we analysed means and standard deviations (SDs), where available or could be calculated, and providing there was no clear evidence of skew in the distribution. When different scales were used to measure

the same clinical outcome, we combined standardised mean differences (SMDs) across the studies. We presented the pooled estimates with 95% confidence intervals (CIs).

Dichotomous data

For dichotomous data (e.g. pain improved, yes or no), we analysed the data using odds ratios (ORs) and 95% CIs.
The definition of pain improvement varied across the studies. We used the author definition of improvement.

Unit of analysis issues

Cross-over trials

We considered the results of this type of trial using the guidance in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b), in particular assessing whether an appropriate washout period was used. Given that RAP can be a stable and chronic condition, we considered a washout period of two to three weeks to be sufficient.
Please see Appendix 2 and our protocol, Martin 2014b, for additional methods for handling unit-of-analysis issues archived for use in future updates of this review.

Dealing with missing data

In the few cases where there were missing data, such as standard deviations, we contacted the original investigators to request if the missing data were available. When it was not possible to obtain the data from the original investigators, we did not impute values; this was a decision made a priori in our protocol (Martin 2014b). Studies for which authors provided additional data not originally published are detailed in the Characteristics of included studies.

Assessment of heterogeneity

We anticipated finding considerable heterogeneity among included studies. We assessed clinical heterogeneity by examining the distribution of relevant participant characteristics (e.g. age, definition of RAP) and study differences (e.g. concealment of randomisation, blinding of outcome assessors, interventions, or outcome measures). We described the statistical heterogeneity (observed variability in study results that is greater than that expected to occur by chance) by reporting the I^2 statistic (Higgins 2003). The I^2 statistic describes approximately the proportion of variation in point estimates due to heterogeneity rather than sampling error. A value of more than 50% may indicate significant heterogeneity. We used the Chi^2 test to further assess the strength of evidence of the heterogeneity. We regarded any result with a P value lower than 0.10 as indicating significant statistical heterogeneity. We interpreted this cautiously and used it to help quantify the impact of heterogeneity on the results of the meta-analysis and ultimately on the GRADE quality rating (see Data synthesis). We also reported Tau^2 when using the random-effects model (see Differences between protocol and review), which provides an estimate of the between-study variance (Deeks 2011).

Assessment of reporting biases

We did not have more than 10 trials for each outcome, and so did not perform these analyses (see Appendix 2; Martin 2014b).

Data synthesis

We used Review Manager 5 for statistical analysis (Review Manager 2014). Two review authors (TVN, AEM, RAA, AB, JTC) independently entered data into Review Manager 5 (Review Manager 2014).
We anticipated significant statistical and clinical heterogeneity. We reported summary statistics for continuous data as mean differences (MDs) or SMDs using a random-effects model, weighted using the inverse-variance method. For dichotomous data, we also used a random-effects model and calculated the ORs using Mantel-Haenszel methods, as this has been shown to have better statistical properties where event rates are low or study size small (Deeks 2011).
We only conducted meta-analyses if it was appropriate to do so, that is if the studies were sufficiently homogeneous. We thus only carried out a meta-analysis using data from studies with equivalent dietary interventions. Where meta-analysis was not appropriate, we provided a narrative description of the results.
For all outcomes where we conducted a meta-analysis, we produced a 'Summary of findings' table detailing the number of trials and participants, the results of the analysis, and the GRADE rating of quality of evidence for the outcome; the procedure for this is described below.

Assessing the quality of evidence for each outcome

We used the GRADE approach to assess the overall quality of the body of evidence for a specific outcome (The Grade Working Group 2013). We used GRADEpro software to assess and present the findings in the 'Summary of findings' tables (GRADEpro GDT 2015). We completed a 'Summary of findings' table for each main treatment comparison (Summary of findings for the main comparison; Summary of findings 2).
For the dichotomous outcome of pain improvement, we calculated the probable outcome of events per 1000 for both the control group and those receiving the intervention, following the guidance in the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2011a), similar to other reviews that include people with pain conditions (e.g. Eccleston 2014). We judged the studies included for each outcome using five criteria: risk of bias, indirectness, inconsistency, imprecision, and publication bias. We used limitations in the design and implementation to assess the

overall risk of bias of included studies for each outcome, downgrading an outcome if the majority of studies had unclear or high risk of bias. We assessed indirectness if a population, intervention, or outcome was not of direct interest to the review. Inconsistency was determined by the heterogeneity of results. If there was evidence of significant statistical heterogeneity (see Assessment of heterogeneity), we downgraded the quality of the outcome. We assessed imprecision by the number of participants included in an outcome and by CIs; we downgraded outcomes when only a small number of participants could be included in the analysis or the analysis had wide CIs. Finally, we downgraded for publication bias if studies failed to report outcomes in the published manuscript or if there was a suspicion that null findings had not been published or reported (Schünemann 2011b).

We gave each outcome a quality rating ranging from 'very low' to 'high'. High-quality ratings are given when "further research is unlikely to change our estimate of effect". Moderate-quality ratings are given when "further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate". Low-quality ratings are given when "further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate". Finally, very low-quality ratings are given when "we are very uncertain about the estimate" (Balshem 2011).

Subgroup analysis and investigation of heterogeneity

Where data were available, we carried out subgroup analyses by subtype of RAP and by duration of follow-up, as specified in our protocol (Martin 2014b).

Sensitivity analysis

In our protocol we planned to carry out sensitivity analyses to assess the robustness of our conclusions in relation to two aspects of study design (Martin 2014b). We intended to assess: 1) the effect of inadequate allocation concealment, and 2) the effect of inadequate blinding to treatment, by removal of studies judged to be at high or unclear risk of bias in these domains. We performed sensitivity analyses where pooled analyses included such studies.

RESULTS

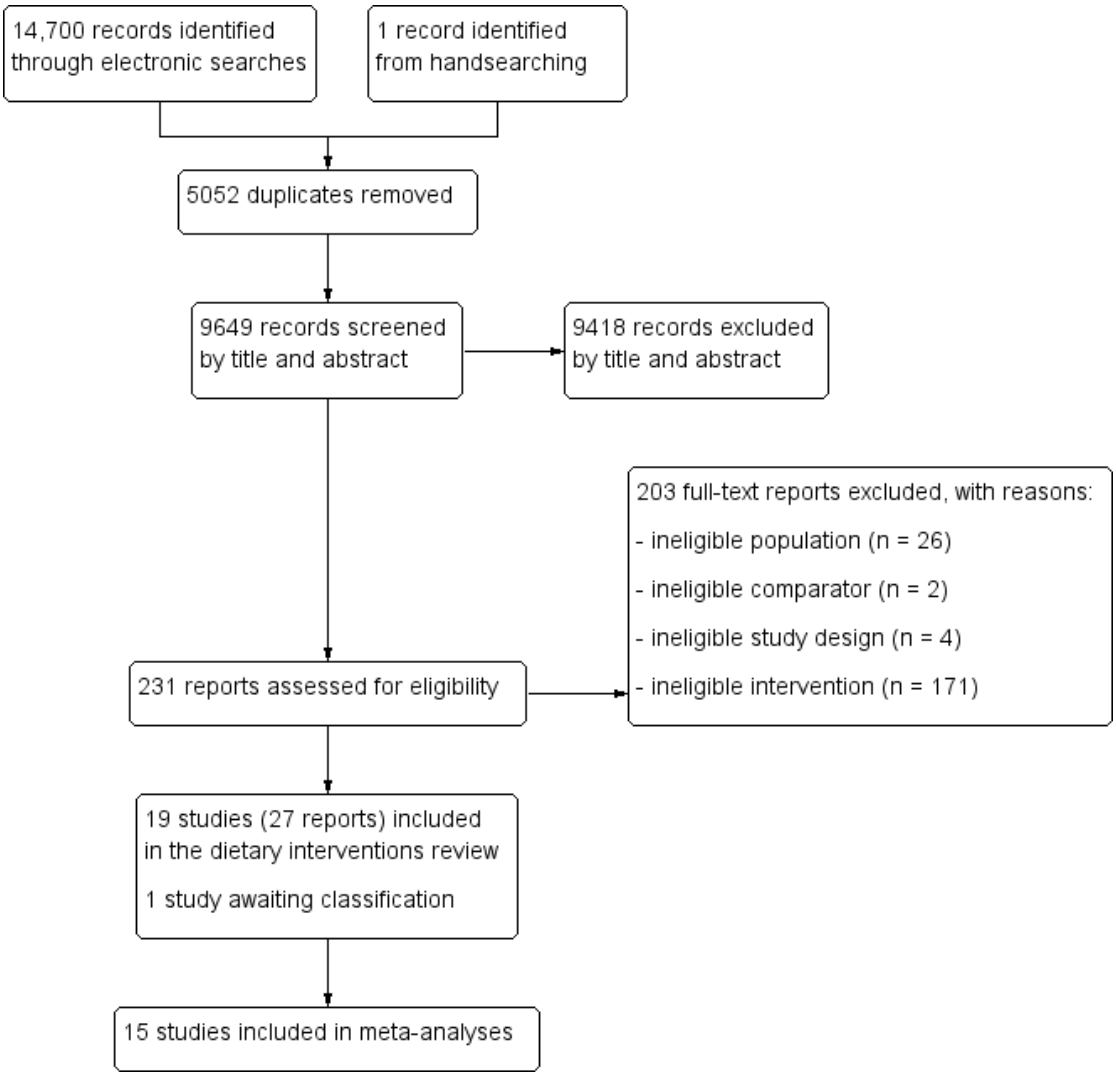
Description of studies

For a full description of the main characteristics of the studies, including details on participants and setting, intervention aspects, and outcome measures, see: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification.

Results of the search

For this updated review, we chose to redesign the search strategy in order to include the recognised terms for different types of RAP, as defined by the Rome criteria (Rasquin 2006). Consequently, we ran our searches across the databases with no date restriction. The results of the searching and screening are shown in the PRISMA flow chart (Figure 1). We screened a total of 9649 titles and abstracts, of which 231 were carried forward for further screening at full text. We excluded 203 reports at full text and included 27 reports (19 studies) in the review. One study is awaiting classification (Jarocka-Cyrta 2002).

Figure 1. PRISMA study flow diagram



Included studies

We included 19 studies in this review, which were reported in 27 papers, four of which were included in the previous version of our review (Bausserman 2005; Feldman 1985; Gawronska 2007; Young 1997). Two of the included studies were only reported as abstracts, and we were unable to obtain further details of the methods or results; either we could not contact the authors of the studies or the authors were unable to provide the details requested (Sabbi 2011; Young 1997). However, based on the data in the abstracts, the studies met the inclusion criteria (Sabbi 2011; Young 1997).

Thirteen studies were trials of probiotic-based interventions (Asgarshirazi 2015; Bausserman 2005; Eftekhari 2015; Francavilla 2010; Gawronska 2007; Giannetti 2017; Guandalini 2010; Kianifar 2015; Romano 2010; Sabbi 2011; Saneian 2015; Weizman 2016; Young 1997), and four studies were trials of fibre-based interventions (Feldman 1985; Horvath 2013; Romano 2013; Shulman 2016). One study was a trial of a low FODMAP diet (Chumpitazi 2015), and one was a trial of a fructose-restricted diet (Wirth 2014). All included studies were written in English. We contacted the authors of Romano 2010 and Shulman 2016, and they provided raw data for pain frequency and intensity outcomes, as these were not included in the published paper. The au-

thors of Asgarshirazi 2015 also provided additional data. For more information, please see below and the Characteristics of included studies tables.

Participants

The 19 included studies involved a total of 1453 children. Thirteen studies, with a total of 1017 children, investigated the effects of probiotics versus placebo (Asgarshirazi 2015; Bausserman 2005; Eftekhari 2015; Francavilla 2010; Gawronska 2007; Giannetti 2017; Guandalini 2010; Kianifar 2015; Romano 2010; Sabbi 2011; Saneian 2015; Weizman 2016; Young 1997). Four studies, with a total of 299 children, investigated the effects of fibre-based interventions versus placebo (Feldman 1985; Horvath 2013; Romano 2013; Shulman 2016). The single study of the FODMAP diet versus typical diet included 34 children (Chumpitazi 2015), and the trial of a fructose-restricted diet included 103 children (Wirth 2014). Eleven included trials randomised between 50 and 90 children; the smallest study included only 11 children (Young 1997), and the six largest more than 100 each (Asgarshirazi 2015; Francavilla 2010; Gawronska 2007; Shulman 2016; Weizman 2016; Wirth 2014). Participants were aged between four and 18 years, with the mean age at recruitment ranging from 6.3 years to 13.1 years. Girls outnumbered boys in most included trials. Fourteen trials recruited children with a diagnosis under the broad umbrella of RAP or functional gastrointestinal disorders; five trials specifically recruited only children with irritable bowel syndrome (Bausserman 2005; Chumpitazi 2015; Guandalini 2010; Kianifar 2015; Shulman 2016). In Shulman 2016, children were only randomised if they first failed to respond to an eight-day exclusion diet eliminating carbohydrates (defined as 75% or less improvement in abdominal pain frequency and severity).

Settings

The majority of studies took place in paediatric gastroenterology clinics. In Francavilla 2010, children were recruited from primary care paediatric practices, and in Feldman 1985 children came from private general practice practices and community paediatric clinics. Children in Shulman 2016 and Weizman 2016 came from care networks, including both primary and tertiary care. Chumpitazi 2015 advertised for participants from community settings as well as recruiting from paediatric gastroenterology clinics.

Location

Trials took place across eight countries. Six studies were conducted in Italy (Francavilla 2010; Giannetti 2017; Guandalini 2010; Romano 2010; Romano 2013; Sabbi 2011), four in Iran (Asgarshirazi 2015; Eftekhari 2015; Kianifar 2015; Saneian 2015), four in the USA (Bausserman 2005; Chumpitazi 2015; Shulman 2016; Young 1997), two in Poland (Gawronska 2007; Horvath 2013), and one each in Canada (Feldman 1985), Israel (Weizman 2016), Germany (Wirth 2014), and India (Guandalini 2010).

Interventions

We classified interventions into four groups: probiotic-based interventions, fibre-based interventions, low FODMAP-based diet interventions, and fructose-restricted diets. We did not include peppermint oil as a dietary intervention but categorised it as pharmacological; trials of this intervention are therefore considered in the companion pharmacological review (Martin 2014a).

Probiotic interventions

Thirteen trials used probiotic-based interventions. Not all trials assessed the same probiotic-based intervention. Five trials used *Lactobacillus rhamnosus* GG in slightly different preparations (Bausserman 2005; Francavilla 2010; Gawronska 2007; Kianifar 2015; Sabbi 2011). Three other trials used *Lactobacillus reuteri* (Eftekhari 2015; Romano 2010; Weizman 2016). The probiotic in Young 1997 was *Lactobacillus plantarum* (LP299V). Guandalini 2010 was a cross-over trial where the intervention was VSL#3, a probiotic preparation of different strains. Giannetti 2017 was a cross-over trial using a mixture of three *Bifidobacterium* species. Saneian 2015 and Asgarshirazi 2015 used *Bacillus coagulans* plus fructo-oligosaccharides. The treatment period ranged from four weeks, in Asgarshirazi 2015, Bausserman 2005, Eftekhari 2015, Gawronska 2007, Kianifar 2015, Romano 2010, Saneian 2015, and Weizman 2016, to eight weeks, in Francavilla 2010. In most studies, outcomes were measured immediately postintervention; the longest period of follow-up was 16 weeks, in Francavilla 2010. Only two studies measured outcomes at three to 12 months' postintervention (Francavilla 2010; Saneian 2015).

Fibre interventions

Four trials used fibre-based interventions. These included a fibre biscuit containing 5 g of corn fibre (Feldman 1985), a preparation of partially hydrolysed guar gum (PHGG) (Romano 2013), a preparation of glucomannan (GNN) (Horvath 2013), and psyllium fibre (Shulman 2016). The treatment period ranged from four weeks, in Romano 2013 and Horvath 2013, to six weeks, in Feldman 1985 and Shulman 2016. Three of the studies measured outcomes immediately postintervention (Feldman 1985; Horvath 2013; Shulman 2016), and the fourth measured outcomes immediately postintervention and four weeks afterwards (Romano 2013).

Low FODMAP interventions

Only one included trial examined a low FODMAP diet intervention. Chumpitazi 2015 was a cross-over trial comparing a two-day low FODMAP diet intervention with a control of a typical

American childhood diet (TACD). Outcomes were measured immediately after intervention at two days. We found no other RCTs of low FODMAP diets.

Fructose-restricted diets

We found one trial of a fructose-restricted diet (Wirth 2014), where participants with RAP for more than three months were randomised to a specified low-fructose diet or a standard diet for two weeks, with outcomes measured immediately postintervention. We found no other eligible RCTs of this type of intervention.

Comparators

All included trials assessed the dietary intervention against a placebo comparison, with the exception of Chumpitazi 2015 and Wirth 2014, where the comparator was a standard diet. Asgarshirazi 2015 was a three-arm trial where probiotics were compared against peppermint oil and placebo; however, only the probiotics versus placebo comparison was reported in this review.

Outcomes

The primary outcomes of this review related to abdominal pain, and pain outcomes were reported in every trial. Studies reported on pain in terms of pain improvement (usually defined as a percentage or number of points improved from baseline, or being pain-free), pain severity/intensity, or pain frequency; or a combination of all three. Pain was most commonly assessed using versions of the Faces Pain Scale (Bieri 1990; McGrath 1996; Wong 1988), or by using a standard visual analogue scale, typically with a range of 0 to 10. Other studies used more general measures to assess improvement in symptoms, including pain, such as the Subject's Global Assessment of Relief Child version (SGARC) (Muller-Lissner 2003). A number of studies specified that the outcome was child reported (Francavilla 2010; Gawronska 2007; Guandalini 2010; Shulman 2016). In other studies it was not specified whether the parent or child was completing the measure, or it was stated that pain was reported by "child or family/parent". As the age range in most studies was wide, this is likely to have influenced who was reporting on the measures. Authors usually reported that pain was assessed on a daily basis (Asgarshirazi 2015; Bausserman 2005; Chumpitazi 2015; Feldman 1985; Francavilla 2010; Giannetti 2017; Guandalini 2010; Romano 2010; Shulman 2016; Weizman 2016). Wirth 2014 reported that symptoms were recorded at the end of the intervention. In the remaining studies the frequency of measure completion was not clearly described.

Secondary outcomes included in this review were school performance, social or psychological functioning, and quality of daily life. Not all studies measured these outcomes. Gawronska 2007, Horvath 2013, and Weizman 2016 reported on school absenteeism, and Guandalini 2010 and Horvath 2013 reported on disruption of daily activities. Participants in Kianifar 2015 reported on both absence from school and disruption of social activities as part of functional changes on a three-point Likert scale. In Giannetti 2017, participants completed the Functional Disability Inventory (Claar 2006), which assesses physical and psychosocial functions and quality of life. In Shulman 2016, participants completed Paediatric Quality of Life Generic Core Scales (Varni 2015).

Adverse events

All studies except Feldman 1985 and Wirth 2014 reported that they monitored children for adverse events. This information was not available in the two included abstracts, and the authors either did not respond to requests for further information (Sabbi 2011), or they were unable to provide details (Young 1997).

Funding

Ten studies did not report their source of funding (Asgarshirazi 2015; Feldman 1985; Francavilla 2010; Giannetti 2017; Horvath 2013; Romano 2010; Romano 2013; Weizman 2016; Wirth 2014; Young 1997). Four studies reported being funded by their university (Eftekhari 2015; Gawronska 2007; Kianifar 2015; Saneian 2015); one was funded by "locally available grants", although the intervention and placebo were provided by industry (Guandalini 2010), and one study was funded by a university seed grant (Bausserman 2005). Shulman 2016 was funded by various organisations, including the US National Institutes of Health and the US Department of Agriculture. Chumpitazi 2015 was funded by an academic society in conjunction with Nestlé and the National Institutes of Health.

Excluded studies

The PRISMA diagram (Figure 1) outlines the number of studies excluded at the full-text screening stage (n = 231). The majority of these clearly involved an ineligible population (e.g. adults) or ineligible interventions (psychosocial or pharmacological), and therefore we have not listed or described these further. However, we excluded six studies for less obvious reasons, and have described these here and listed them in the Characteristics of excluded studies section.

We excluded three studies that were included in the 2009 review, Huertas-Ceballos 2009, on the grounds of study design (Christensen 1982; Dearlove 1983; Lebenthal 1981). Christensen 1982 and Dearlove 1983 did not appear to be RCTs. It was also unclear whether participants in Lebenthal 1981 were randomised, and as we were unable to clarify this with the authors, we also excluded this study.

From our updated search in 2016, we excluded one study that was not a RCT (Agah 2015). We excluded two further studies because they used ineligible comparators (Chumpitazi 2014; Edwards 1991).

Risk of bias in included studies

We rated all included studies for risk of bias across the following categories: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other potential sources of bias (other bias). Figure 2 displays the review authors' assessments of risk of bias for each study individually, and Figure 3 represents the authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

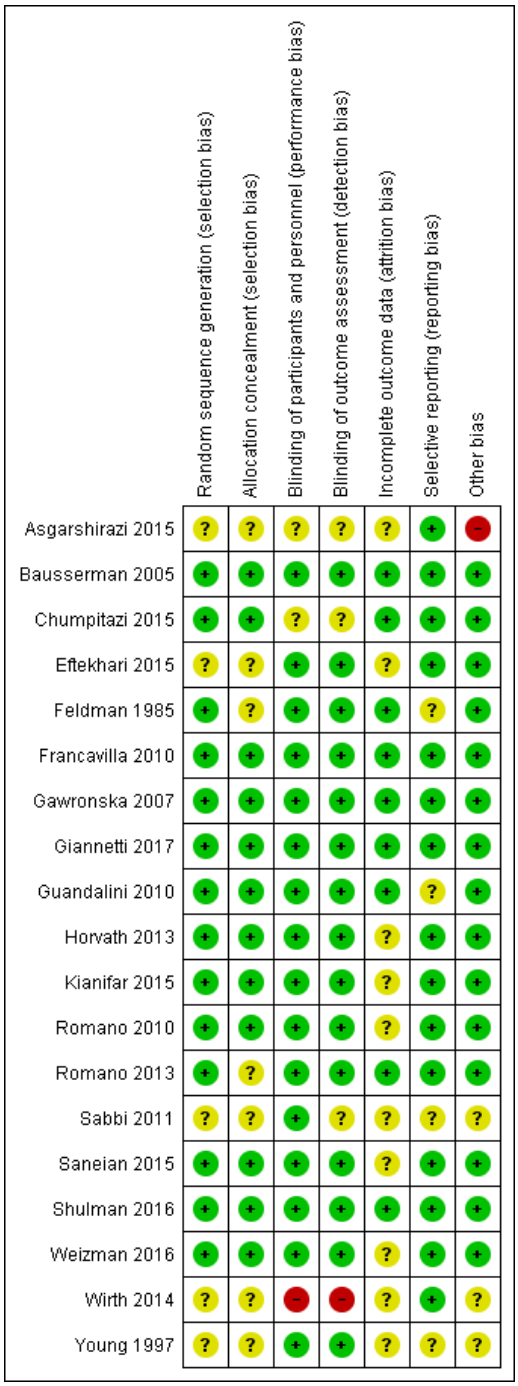
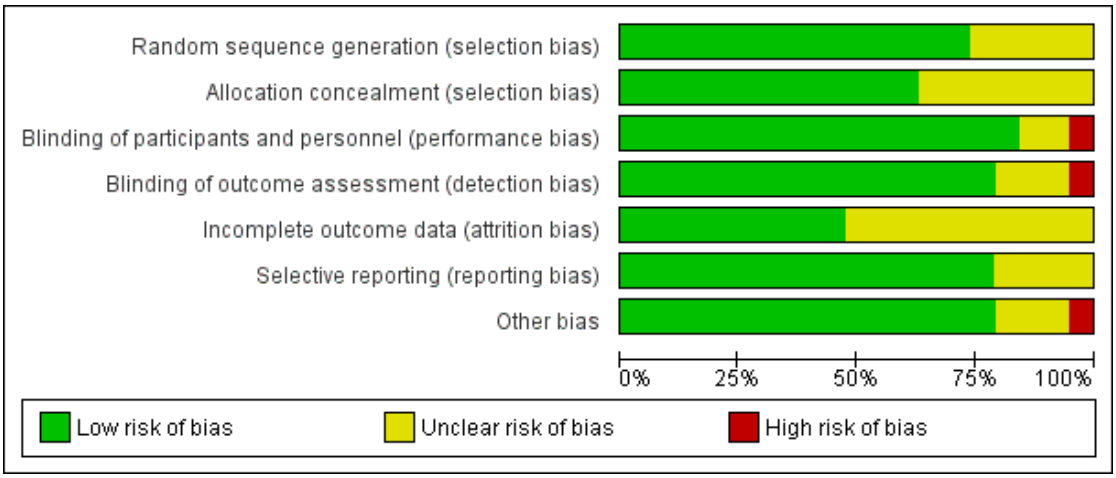


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

We rated no studies as being at high risk of bias in this domain.

Random sequence generation

We judged that the majority of studies had adequately randomised their participants as they used appropriate methods of randomisation as detailed in Table 1, such as computer-generated random numbers. The exceptions were Asgarshirazi 2015, Eftekhari 2015, and Wirth 2014, all of which we rated as being at unclear risk in this domain due to insufficient detail provided about how randomisation was performed. We also rated the two studies for which only abstracts were available as at unclear risk of bias in this domain due to insufficient detail provided about randomisation (Sabbi 2011; Young 1997).

Allocation concealment

The most frequently encountered issue in assessing the risk of selection bias was poorly described allocation sequence concealment. The authors of seven studies provided insufficient detail on how this was done, leading to an assessment of unclear risk of bias (Asgarshirazi 2015; Eftekhari 2015; Feldman 1985; Romano 2013; Sabbi 2011; Wirth 2014; Young 1997).

Blinding

Blinding of participants and personnel

Most studies described the use of identical placebos and double-blinding of participants and personnel, and so we judged them to be at low risk of performance bias. However, we rated Asgarshirazi 2015 as being at unclear risk of bias for this outcome, as although the study was blinded, the placebo regimen of folic acid tablets was different in timing and frequency to the intervention regimen, and the authors did not discuss the possible impact of this. In Chumpitazi 2015, the study was described as double-blinded, but it was unclear whether the intervention and control diets were delivered in identical containers or what clues there might have been to the allocation, hence we also rated this study as being at unclear risk of bias. We rated one study as being at high risk of bias for this domain, as the children who rated their own symptoms were not blinded (Wirth 2014).

Blinding of outcome assessment

Outcomes were assessed by parents, children, and clinicians; the issues described above regarding blinding of participants and personnel also applied to the blinding of outcome assessment, consequently we rated all studies as being at low risk of bias for this do-

main with the exception of Asgarshirazi 2015, Chumpitazi 2015, Sabbi 2011, and Wirth 2014.

Incomplete outcome data

We rated 10 studies as being at unclear risk of attrition bias; many studies did not fully report outcome data, making it difficult to assess the risk of attrition bias (Asgarshirazi 2015; Eftekhari 2015; Horvath 2013; Kianifar 2015; Romano 2010; Sabbi 2011; Saneian 2015; Weizman 2016; Wirth 2014; Young 1997). For example, in Asgarshirazi 2015, 32 children were excluded during the trial after randomisation and not analysed because they did not complete the one-month intervention; according to the authors this was "due to journey or lack of 2 weeks visit", but information was insufficient to determine if this could have resulted in attrition bias. Also, in Weizman 2016, the authors state that an intention-to-treat analysis was carried out, but the paper also states that eight participants were excluded due to "poor compliance and violation of the protocol" and not analysed, hence the exact methodology was unclear. Again, for the two studies for which only abstracts were available, insufficient detail was provided, so they too were rated as being unclear risk of bias for this domain (Sabbi 2011; Young 1997).

Selective reporting

We did not rate any studies as being at high risk of bias for this domain. Feldman 1985 presented insufficient information to assess reporting bias and so was judged to be at unclear risk of bias. We also judged Guandalini 2010 to be at unclear risk of reporting bias as comparisons were made pre/post and not between intervention and control at six weeks. Again, for the two studies for which only abstracts were available, insufficient detail was provided, so they too were rated as being unclear risk of bias for this domain (Sabbi 2011; Young 1997).

Other potential sources of bias

We rated the risk of other potential biases (such as validity of data collection tools, appropriate sample size, similarity of baseline details) as low for included studies for which we had the full text, as we did not find any other major sources of bias that would likely affect the results. The exceptions were Asgarshirazi 2015, which we rated at high risk of bias as there were imbalances in measures of pain at baseline; Wirth 2014, which we rated as being at unclear risk of bias as no details were given regarding the use of validated tools or of adherence; and Sabbi 2011 and Young 1997, which we also rated at unclear risk of bias due to insufficient information in the abstracts.

Effects of interventions

See: **Summary of findings for the main comparison** Probiotics compared to placebo for recurrent abdominal pain in childhood; **Summary of findings 2** Fibre versus placebo for recurrent abdominal pain in childhood

We were able to perform a total of 10 analyses across the studies. We performed analyses within intervention type, as the mechanisms of action of each dietary intervention are different. We only performed analyses on those studies that provided equivalent outcome data in comparable formats, therefore not all studies within each intervention type were entered into the analyses.

For probiotic-based interventions, we were able to perform three analyses for our primary outcomes (effects on pain frequency, pain intensity, and pain improvement), at zero to three months' postintervention. As four studies included only children with irritable bowel syndrome, or reported outcomes for this group separately, as per our protocol (Martin 2014b), we were also able to perform a subgroup analysis for this group for the outcome of improvement in pain at zero to three months' postintervention. We were able to perform one analysis for the outcome of improvement in pain at three to six months' postintervention. We also were able to perform sensitivity analyses for three outcomes, by removing studies judged to be at unclear or high risk of bias in the domains of allocation concealment, blinding of participants and personnel, and/or blinding of outcome assessment.

For fibre-based interventions, we were able to perform two analyses: effect on pain improvement and change in pain intensity postintervention (zero to three months).

We were unable to perform any analyses for low FODMAP diet interventions or for fructose-restricted diets, as we found only one study in each category eligible for inclusion.

We were unable to perform any pooled analyses of secondary outcomes for any dietary intervention, as these were either not reported or reported in formats that were not comparable. The results of individual studies are briefly presented below, followed by the results of the pooled analyses.

We assessed the quality of evidence using the GRADE criteria (The Grade Working Group 2013), and presented our ratings in 'Summary of findings' tables, which we constructed using GRADEpro software (GRADEpro GDT 2015). Within probiotic-based interventions, we scored the evidence for the three improvement in pain outcomes as moderate quality, meaning that further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. For the change in pain intensity and frequency outcomes, we rated the evidence as low quality, meaning that future research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. See Summary of findings for the main comparison. For fibre-based interventions, we rated the evidence for the change in pain intensity and improvement in pain outcomes as low quality. See Summary of findings 2.

Comparison 1: Probiotic interventions versus placebo

Thirteen included studies assessed the effects of probiotics (Asgarshirazi 2015; Bausserman 2005; Eftekhari 2015; Francavilla 2010; Gawronska 2007; Giannetti 2017; Guandalini 2010; Kianifar 2015; Romano 2010; Sabbi 2011; Saneian 2015; Weizman 2016; Young 1997).

Primary outcomes

Results of individual studies

Here, we briefly present the results of the individual studies (please note, we could only provide exact P values when these were available in the original report).

Change in pain frequency, change in pain intensity, and improvement in pain

Asgarshirazi 2015 reported on pain severity, duration, and frequency immediately following a four-week intervention with *Bacillus coagulans* plus fructo-oligosaccharides. Mean decrease in pain duration and pain frequency was greater in the probiotic group compared to the placebo group (P = 0.012 and P < 0.001, respectively).

Bausserman 2005 reported no difference between the probiotic arm and placebo arm in response to treatment, defined as improvement in abdominal pain of one or more levels, at six weeks (OR 1.18, 95% CI 0.38 to 3.63). There was also no difference between the two groups in terms of mean change in pain (P = 0.175) as measured by the Gastrointestinal Symptoms Rating Scale (Svedlund 1988).

Eftekhari 2015 reported no significant difference in pain intensity, pain frequency, or improvement in pain between probiotic and placebo arms at four and eight weeks' postintervention. At both time points, pain intensity and severity in both groups were significantly reduced from baseline (P < 0.001).

Francavilla 2010 reported results at eight and 16 weeks' postintervention. At eight weeks, treatment success was experienced by 72% of children in the probiotic group and 53% of children in the placebo group (OR 2.18, 95% CI 1.07 to 4.45), and the difference was maintained at 16 weeks (79% intervention, 62% control; P < 0.03). Pain intensity was lower in the intervention group at eight weeks (P < 0.01), and pain frequency was reduced at eight weeks (P < 0.01) and 12 weeks (P < 0.02).

Gawronska 2007 reported that at four weeks, 25% of the intervention group experienced treatment success in terms of no pain compared to 9.6% of the placebo group (OR 3.1, 95% CI 1.03 to 9.56). Overall, 25 children receiving probiotics experienced improvement in pain compared to 23 receiving placebo (OR 1.17, 95% CI 0.62 to 2.21). No other significant differences in outcome measure were reported, including change in pain frequency and intensity.

Guandalini 2010 reported only pre/post comparisons on change in pain frequency and intensity at week six, and we could obtain no additional information for these outcomes to enter in the meta-analysis. At six weeks, 44 of 59 children experienced an improvement in pain in the intervention arm of the cross-over, compared to 29 children in the placebo group (OR 3.03, 95% CI 1.4 to 6.6).

Giannetti 2017 was a cross-over RCT with a six-week treatment period and a two-week washout period. The primary outcome was being pain-free at six weeks. In children with irritable bowel syndrome, 42% experienced full resolution on probiotic versus 14% on placebo (P = 0.003); in those with functional dyspepsia there was no improvement (21% versus 32%; P = 0.5).

Kianifar 2015 measured pain severity at four weeks; the mean score in the probiotic group was significantly lower than the mean score in the placebo group at this time point (P < 0.001).

In Romano 2010, the intervention group experienced a significant decrease in pain intensity at eight weeks (P < 0.001), and both groups had a decrease in pain frequency at the same time point (P < 0.05).

Sabbi 2011 reported outcomes at six and 10 weeks. In the probiotic group, there was a significant reduction of both frequency (P < 0.01) and severity (P < 0.01) of abdominal pain at six weeks. These differences were still present at 10-week follow-up (P < 0.02 and P < 0.001, respectively).

In Saneian 2015, a higher proportion of children in the intervention group (60%) compared to the control group (39.5%) were defined as treatment responders at four weeks (P = 0.044), but this difference was not sustained at 12 weeks (64.4% intervention, 53.4% control; P = 0.204). The authors reported no statistically significant difference between intervention and control in terms of physician-rated global pain severity or global improvement.

In Weizman 2016, pain intensity was significantly reduced in the intervention group compared to the placebo group at four weeks (P < 0.01) and eight weeks (P < 0.02); the difference in pain frequency was significant at four weeks (P < 0.02) but was not sustained at eight weeks (P = 0.09).

Young 1997 was a cross-over RCT. In the abstract the authors report that children treated with probiotic had a significant reduction in symptoms at four weeks when compared to baseline, whereas placebo treatment did not produce significant improvement.

Results of pooled analyses

See Summary of findings for the main comparison.

Change in pain frequency

We pooled data from six studies at zero to three months' postintervention in a meta-analysis to examine change in pain frequency (Asgarshirazi 2015; Eftekhari 2015; Francavilla 2010; Gawronska 2007; Romano 2010; Weizman 2016). The SMD of effect across the studies was -0.55 (95% CI -0.98 to -0.12; Z = 2.52; P = 0.01; 523 children; Analysis 1.1). However, there was significant statistical heterogeneity (Tau^2 = 0.23; Chi^2 = 28.10; I^2 = 82%; P for heterogeneity < 0.001). Using GRADE, we rated the quality of evidence for this outcome as low, downgrading it two levels due to risk of bias in the included studies and the statistical heterogeneity. For our planned sensitivity analysis, we identified two included studies where there was an unclear risk of bias in relation to allocation concealment or blinding of participants and personnel and/or blinding of outcome assessment (Asgarshirazi 2015; Eftekhari 2015), and repeated the pooled analysis after excluding these two studies. The estimate of effect was a SMD of -0.54 (95% CI -0.94 to -0.14; Z = 2.62; P = 0.009; 4 studies; 389 children; Tau^2 = 0.12; Chi^2 = 11.24; I^2 = 73%; P for heterogeneity = 0.01; Analysis 1.2). Removing these studies therefore did not appreciably change the estimate of effect from the main analysis in Analysis 1.1.

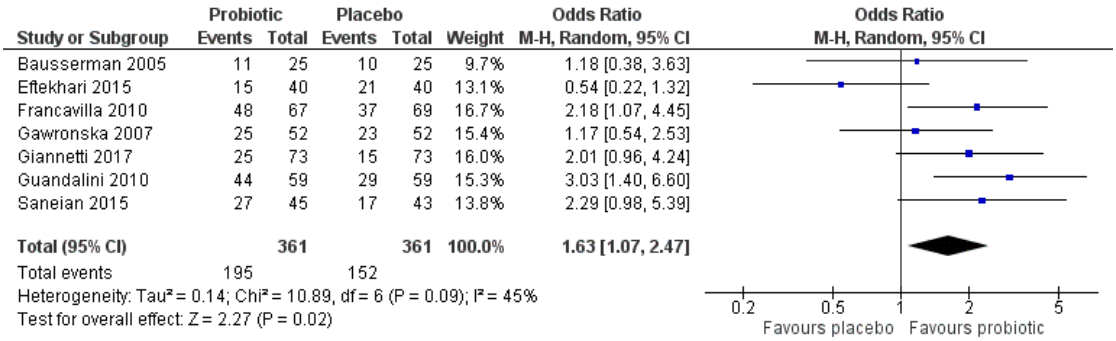
Change in pain intensity

We entered data from seven studies into the meta-analysis of change in pain intensity (Asgarshirazi 2015; Eftekhari 2015; Francavilla 2010; Gawronska 2007; Kianifar 2015; Romano 2010; Weizman 2016). The SMD of effect across the studies was -0.50, (95% CI -0.85 to -0.15; Z = 2.80; P = 0.005; 575 children; Analysis 1.3), and again there was considerable statistical heterogeneity (Tau^2 = 0.17; Chi^2 = 24.95; I^2 = 76%; P for heterogeneity < 0.001). Using GRADE, we rated the quality of evidence for this outcome as low, downgrading it two levels due to risk of bias in the included studies and the statistical heterogeneity. We were able to perform a sensitivity analysis (again excluding Asgarshirazi 2015 and Eftekhari 2015). The estimate of effect in the sensitivity analysis was a SMD of -0.68 (95% CI -1.05 to -0.30; P = 0.001; 5 studies; 441 children; Tau^2 = 0.13; Chi^2 = 14.00; I^2 = 71%; P for heterogeneity = 0.007; Analysis 1.4). Again, this did not result in appreciable change to the estimate of effect from the main analysis in Analysis 1.3.

Improvement in pain

Seven studies (722 children) were eligible for meta-analysis for the outcome of improvement in pain (Bausserman 2005; Eftekhari 2015; Francavilla 2010; Gawronska 2007; Giannetti 2017; Guandalini 2010; Saneian 2015). The OR for pain improvement at zero to three months' postintervention was 1.63 (95% CI 1.07 to 2.47; Z = 2.27; P = 0.02; Tau^2 = 0.14; Chi^2 = 10.98; I^2 = 45%; P for heterogeneity = 0.09; Analysis 1.5), with eight as the number needed to treat for an additional beneficial outcome (NNTB) (see Figure 4). Using GRADE, we rated the quality of the evidence for this outcome as moderate, downgrading it one level due to evidence of statistical heterogeneity. In this analysis, the heterogeneity appeared to have been introduced by one of the new studies in the update search (Eftekhari 2015); prior to its inclusion in the pooled analysis there was no significant evidence of statistical heterogeneity (Tau^2 = 0.00; I^2 = 0%; P for heterogeneity = 0.41). On examination of the forest plot (see Figure 4), Eftekhari 2015 was also the only study where the point estimate of effect favours placebo rather than probiotic (OR 0.54, 95% CI 0.22 to 1.32). We carried out a planned sensitivity analysis by removing Eftekhari 2015 from the pooled analysis due to our judgement on the risk of bias present in this study. The resulting estimate of effect was an OR of 1.95 (95% CI 1.40 to 2.70; Z = 3.97; P < 0.001; 6 studies; 642 children; Tau^2 = 0.00; Chi^2 = 3.96; I^2 = 0%; P for heterogeneity = 0.56; Analysis 1.6).

Figure 4. Forest plot of comparison: 1 Probiotics versus placebo, outcome: Improvement in pain 0 to 3 months' postintervention.



We were able to perform one subgroup analysis of improvement in pain at zero to three months' postintervention for 344 children with irritable bowel syndrome only (Analysis 1.7). This included four studies (Bausserman 2005; Francavilla 2010; Giannetti 2017; Guandalini 2010). The OR for pain improvement at zero to three months' postintervention was 3.01 (95% CI 1.77 to 5.13; Z = 4.06; P < 0.001; Tau² = 0.06; Chi² = 3.77; I² = 21%; P for heterogeneity = 0.29), with a NNTB of four. Using GRADE, we rated the quality of the evidence for this outcome as moderate, downgrading it one level for imprecision, due to small numbers of participants in included studies.

Only two studies (224 children) were eligible for inclusion in an analysis of improvement in pain at three to six months' postintervention (Francavilla 2010; Saneian 2015), as most studies had short follow-up periods. The OR for pain improvement at three to six months' postintervention was 1.94 (95% CI 1.10 to 3.43; Z = 2.28; P = 0.02; Tau² = 0.00; Chi² = 0.41; I² = 0%; P for heterogeneity = 0.52; Analysis 1.8), with a NNTB of seven. Using GRADE, we rated the quality of the evidence for this outcome as moderate, downgrading it one level due to imprecision.

Secondary outcomes

Results of individual studies

School performance

Gawronska 2007 assessed school absenteeism (included as a secondary outcome) as a dichotomous measure in 104 children (reported in diaries) and found no difference between control and intervention groups (P = 0.44). In Weizman 2016, the 101 included children kept a school absence diary; postintervention there was no significant difference in the number of days of absence between the two groups (2.7 versus 1.9 days per four weeks, in the placebo and the probiotic groups, respectively; P = 0.08). Kianifar 2015 assessed "functional changes", which included disruption of social activities, need to see a doctor, use of medications, and days of absence from school, on a three-point Likert scale. The authors reported that this measure improved significantly in the probiotic group at four weeks' postintervention (2.4 (SD 0.5) in the probiotic group, 1.9 (SD 0.4) in the placebo group; P < 0.001).

Social or psychological functioning

Kianifar 2015 included "disruption of social activities" as part of their "functional changes" outcome, the results of which are reported above.

Quality of daily life

In Guandalini 2010, caregivers of 59 children were asked to assess family life disruption; the trial reported improvement in family life disruption after six weeks in the intervention group (P < 0.001), which was not present in the placebo group. Giannetti 2017 used the Functional Disability Assessment to measure quality of life (Claar 2006). An improved quality of life was reported by 46% of children with irritable bowel syndrome after probiotics, versus 16% after placebo (P = 0.002). There was no difference in the functional dyspepsia group.

Adverse events

Ten of the 13 studies included in this comparison reported that the probiotic was well tolerated and that there were no adverse events. In Saneian 2015, participants were specifically asked about a checklist of adverse effects; the only symptom where there was a significant difference was that of dry mouth, reported by 44% of the intervention group and 23% of the control group. The studies by Sabbi 2011 and Young 1997 were reported in abstracts and did not report on adverse events.

Results of pooled analyses

No pooled analyses were possible.

Comparison 2: Fibre*interventions* versus placebo

Four studies assessed the effects of fibre in various forms (Feldman 1985; Horvath 2013; Romano 2013; Shulman 2016).

Primary outcomes

Results of individual studies

Change in pain frequency

Feldman 1985 only reported figures for improvement in frequency of pain at six weeks: 13 out of 26 children in the fibre cookie group and 7 out of 26 children in the placebo group experienced the outcome of improvement in pain following intervention (OR 2.71, 95% CI 0.85 to 8.64). No numerical data were given for the other outcome of improved intensity of pain, which was simply described as "not significant".

In Shulman 2016, the authors reported a significant reduction in pain frequency in the fibre group compared with the placebo group using the Numerical Rating Scale (NRS-11) (McGrath 1996) after the six-week intervention (P = 0.03).

Change in pain intensity

In Romano 2013, pain intensity was rated at baseline and at eight weeks' follow-up using the Wong-Baker FACES Pain Rating Scale (Wong 1988); whilst there was a greater decrease in intensity in the intervention group, this was not statistically significant at the P < 0.05 level.

Improvement in pain

Horvath 2013 measured improvement in pain using the Faces Pain Scale at four weeks (Bieri 1990): 23 out of 41 children in the intervention arm and 20 out of 43 in the placebo arm experienced the outcome of improvement in pain following intervention (OR 1.47, 95% CI 0.62 to 3.47).

Results of pooled analyses

See Summary of findings 2.

Change in pain frequency

We were not able to pool data for this outcome as it was either not reported in these studies or there was no equivalent outcome data.

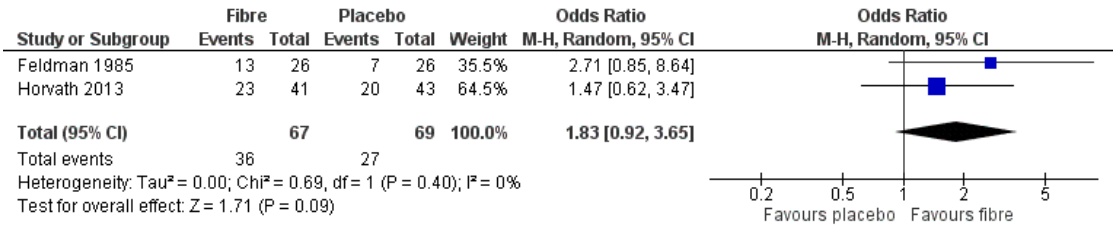
Change in pain intensity

We were able to pool data from Romano 2013 and Shulman 2016 in a meta-analysis for the outcome of change in pain intensity at zero to three months' postintervention. Both studies included only children with irritable bowel syndrome. The SMD of effect across the studies was -1.24 (95% CI -3.41 to 0.94; Z = 1.11; P = 0.27; 2 studies; 135 children; Tau^2 = 2.38; Chi^2 = 28.91; I^2 = 97%; P for heterogeneity < 0.001; Analysis 2.1). The 95% CIs for the point estimates of SMD in both studies did not overlap, and very high statistical heterogeneity was detected according to Chi^2 and I^2 tests. Romano 2013 used a tertiary clinic sample, and Shulman 2016 used a mixed population recruited from primary and specialist care. Using GRADE, we downgraded the quality of evidence for this outcome by two levels to low, based on the high levels of heterogeneity and the imprecision of the estimate.

Improvement in pain

We pooled data from Feldman 1985 and Horvath 2013 (136 children) in a meta-analysis for the dichotomous outcome of improvement in pain at zero to three months' postintervention. The total number of events in the meta-analysis was fewer than 70, with a consequently imprecise estimate. The pooled OR was 1.83 (95% CI 0.92 to 3.65; Z = 1.71; P = 0.09; 2 studies; 136 children; Tau^2 = 0.00; Chi^2 = 0.69; I^2 = 0%; P for heterogeneity = 0.40; Analysis 2.2; Figure 5). Using GRADE, we rated the quality of evidence for this outcome as low due to an unclear risk of bias in a number of domains in the included studies and the small numbers of events (fewer than 100).

Figure 5. Forest plot of comparison: 2 Fibre versus placebo, outcome: Improvement in pain 0 to 3 months' postintervention.



Secondary outcomes

Results of individual studies

School performance

Horvath 2013 reported on the frequency of school absenteeism in 84 children as described by parents (no specific measure reported), and found no significant difference between intervention and control groups (P = 0.56).

Social or psychological functioning

No studies reported data on this outcome.

Quality of daily life

Horvath 2013 reported no difference between intervention and control groups in changes in daily activities in 84 children (no measure reported) (P = 0.37). Shulman 2016 reported on health-related quality of life using the Pediatric Quality of Life Generic Core Scales (Varni 2015); no difference was found between the

intervention and control groups on child report (P = 0.73) or parent report (P = 0.99).

Adverse events

Horvath 2013 reported that no adverse events had occurred, although four children in the intervention group complained of symptom exacerbation compared to two in the placebo group; Romano 2013 and Shulman 2016 also reported that no adverse events had occurred. Feldman 1985 did not report adverse events.

Results of pooled analyses

No pooled analyses were possible.

Comparison 3: Low FODMAP diet versus normal diet

We found only one eligible study that examined the effect of a low FODMAP diet. Chumpitazi 2015 compared two days of a low FODMAP diet to two days of a typical American childhood diet (TACD) in 33 children using a cross-over study design.

Primary outcomes

Results of individual studies

Change in pain frequency

Fewer episodes of abdominal pain per day occurred during the low FODMAP diet versus the control diet (P < 0.05), and compared to baseline, children had fewer daily abdominal pain episodes during the low FODMAP diet (P < 0.01), but more episodes during the control diet (P < 0.01). Exact P values were not reported in the paper.

Change in pain intensity

Median pain severity decreased on both diets in comparison to baseline (low FODMAP diet P < 0.001, TACD P < 0.01; exact P values not reported in the paper).

Improvement in pain

Eight children were categorised as responders (children who had significant improvement in pain on the low FODMAP diet only), 15 as non-responders (children who did not have significant improvement on the low FODMAP diet or TACD), and 10 as placebo responders (children who improved on both diets or only on the TACD).

Results of pooled analyses

No pooled analyses were possible.

Secondary outcomes

Results of individual studies

No studies reported data on school performance, social or psychological functioning, or quality of daily life. No adverse effects were reported.

Results of pooled analyses

No pooled analyses were possible.

Comparison 4: Fructose-restricted diet versus normal diet

We found only one eligible study that examined the effect of a fructose-restricted diet. In Wirth 2014, children with RAP for more than three months were randomised to two weeks of a fructose-restricted diet or two weeks of a normal diet. Pain intensity and frequency were measured at baseline and postintervention.

Primary outcomes

Results of individual studies

Change in pain frequency

In Wirth 2014, 37 out of 50 (74%) of children in the intervention group and 29 out of 51 (57%) in the control group reported a reduction in the number of pain episodes per week; both reductions were described as 'statistically significant'.

Change in pain intensity

Wirth 2014 reported a significant decrease in pain intensity in the intervention group after treatment (P < 0.001), and no difference in pain intensity in the control group.

Improvement in pain

No studies reported this outcome.

Results of pooled analyses

No pooled analyses were possible.

Secondary outcomes

No studies reported data on school performance, social or psychological functioning, or quality of daily life. Wirth 2014 did not report on adverse effects.

Results of pooled analyses

No pooled analyses were possible.

ADDITIONAL SUMMARY OF FINDINGS [*Explanation*]

Fibre versus placebo for recurrent abdominal pain in childhood

Patient or population: Children with recurrent abdominal pain
Settings: Mixed settings, predominantly outpatient gastroenterology clinics
Intervention: Fibre
Comparison: Placebo

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo	Fibre				
Change in pain intensity: 0 to 3 months' postintervention Pain intensity was measured using different scales in the 2 included studies: the Wong Baker FACES Pain Rating Scale, Wong 1988, and the Numerical Rating Scale (von Baeyer 2009).	-	The mean change in pain intensity 0 to 3 months' postintervention score in the intervention groups was **1.24 SDs lower** (3.41 lower to 0.94 higher)	-	135 (2 studies)	⊕⊕◯◯ **Low**[2,3]	-
Improvement in pain: 0 to 3 months' postintervention Improvement in pain was defined and measured differently in the 2 included studies: using a "stomach ache diary" and the Faces Pain	**391 per 1000**[1]	**541 per 1000** (372 to 701)	**OR 1.83** (0.92 to 3.65) NNTB = 6.7	136 (2 studies)	⊕⊕◯◯ **Low**[2,4]	-

Scale (Bieri 1990).	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **NNTB:** number needed to treat for an additional beneficial outcome, based on the absolute risk reduction between the intervention and comparison group probable outcomes; **OR:** odds ratio; **SD:** standard deviation.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Assumed risk in control group is based on the mean outcome of the control group in the two included studies.
[2]Downgraded one level due to imprecision.
[3]Downgraded one level due to evidence of significant heterogeneity.
[4]Downgraded one level, as one study contained insufficient information regarding allocation concealment, outcome assessment, and selective reporting.

DISCUSSION

Summary of main results

We included 19 studies with a total of 1453 participants in this review. With the exception of two studies, all studies assessed a treatment arm of probiotic or fibre-based interventions against placebo, with an average treatment duration of six weeks. The remaining two studies assessed a dietary intervention (low FODMAP diet or fructose-restricted diet) against a normal control diet. This update extends the evidence base in this area through the inclusion of 15 new studies, along with four from the original review (Huertas-Ceballos 2009); 10 pooled analyses were possible.

Evidence for probiotic interventions

Overall, the data in this review provided some evidence suggesting that probiotics may be effective in the management of children with RAP, based on the results of 13 studies. Trials used a range of probiotic preparations: five used *Lactobacillus rhamnosus* GG in slightly different preparations; three used *Lactobacillus reuteri;* two used *Bacillus coagulans* with fructo-oligosaccharides; one used a patented mixture; one used *Lactobacillus plantarum*; and one used a mixture of *Bifidobacterium* species.

The majority of studies measured short-term outcomes at zero to three months' postintervention only. We found that probiotics improved pain in the meta-analysis of seven probiotic trials at this time point (OR 1.63, 95% CI 1.07 to 2.47; P = 0.02), with an estimated NNTB of eight, meaning that eight children would need to receive probiotics for one to experience improvement in pain in this timescale. The planned sensitivity analysis removing studies where the risk of bias for allocation concealment or blinding of participants and personnel and/or blinding of outcome assessment was high or unclear also found that children treated with probiotics were more likely to experience an improvement in pain (OR 1.95, 95% CI 1.40 to 2.70; P < 0.001). The planned subgroup analysis of children identified as having irritable bowel syndrome only at the same time point resulted in a pooled OR of 3.01 (95% CI 1.77 to 5.13; P < 0.001), and an estimated NNTB of four.

For all children, we also found a reduction in pain frequency (SMD -0.55, 95% CI -0.98 to -0.12; P = 0.012) and pain intensity (SMD -0.50, 95% CI -0.85 to -0.15; P = 0.005), in those treated with probiotics compared to placebo at zero to three months' postintervention.

We were able to perform only one pooled analysis of two studies for outcomes at three to six months' postintervention, for the outcome of improvement in pain. The pooled OR was 1.94 (95% CI 1.10 to 3.43; P = 0.023), with a NNTB of seven.

Using the GRADE approach, we rated the quality of the evidence for all the improvement in pain outcomes as moderate, and the quality of evidence for change in pain frequency and intensity as low.

Evidence for fibre interventions

As in the previous version of this review (Huertas-Ceballos 2009), the data in this analysis did not provide convincing evidence suggesting that fibre supplements are effective in RAP, on the grounds of a paucity of studies and a lack of moderate- or high-quality evidence. We performed two meta-analyses, neither of which found that fibre interventions were effective in improving pain.

Only two studies were eligible for inclusion in the meta-analysis for the outcome of improvement of pain, with a pooled OR of 1.83 (95% CI 0.92 to 3.65; P = 0.09). Two different studies were eligible for pooled analysis for the outcome of change in pain intensity: the SMD of effect across the studies was -1.24 (95% CI -3.41 to 0.94; P = 0.27); both studies included only children with irritable bowel syndrome. Using GRADE, we assessed the quality of the evidence for both outcomes as low.

Evidence for low FODMAP diet and fructose-restricted diet

We found only one study each that examined the effects of a low FODMAP diet and a fructose-restricted diet on pain in children with RAP. We were therefore unable to perform any pooled analyses for these two interventions.

Overall completeness and applicability of evidence

There are some important considerations relating to the overall completeness and applicability of the evidence from this study. First, 11 out of 13 included probiotic studies measured outcomes at zero to three months' postintervention only, and most interventions lasted only between four and six weeks. Only two included studies measured outcomes at 12 weeks or more, although the pooled analysis did find that improvement in pain was sustained at this time point. Consequently, the evidence base for the longer-term effectiveness of probiotics in the included studies needs to be strengthened. Second, we were only able to perform one subgroup analysis by category of RAP, which was for probiotics for children with irritable bowel syndrome. However, the pooled analysis suggested that a significant improvement in pain was experienced by this group at short-term follow-up. Third, we were only able to identify one study of low FODMAP diets and one of fructose-restricted diets eligible for inclusion. A number of RCTs of low FODMAP diets have been conducted in adults with irritable bowel syndrome (Nanayakkara 2016), but it appears that the area of exclusion diets in children requires further research before evidence-based recommendations regarding the use of these interventions can be made.

We would also like to highlight that few studies reported on our secondary outcomes relating to school absence, social or psychological functioning, and quality of life, which represents a gap in the completeness of the evidence base. These 'secondary' outcomes

are important, as they are likely to indicate disability and to be highly significant for the child and family.
Finally, we also note that the majority of studies took place in paediatric gastroenterology clinics, with three taking place in mixed settings and one in "primary care paediatrics". We were therefore unable to comment on any potential difference in outcome by setting.

Quality of the evidence

The overall quality of evidence within this review as assessed by the GRADE approach ranged from 'low' to 'moderate'. We rated the quality of the evidence for the three improvement in pain outcomes in the probiotic and placebo comparison as moderate, downgrading for imprecision or heterogeneity. This means we judged that further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. We rated the quality of the evidence for the change in pain frequency and intensity outcomes for the same comparison as being low due to significant levels of heterogeneity and risk of bias introduced by incomplete outcome data. This means that future research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
In the case of the two pooled analyses comparing fibre interventions to placebo, we rated the quality of the evidence as low due to significant heterogeneity, imprecision, and an unclear risk of bias in a number of domains in the included studies. Future research in this area is therefore very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Potential biases in the review process

We conducted a comprehensive search of electronic databases, but did not find sufficient studies to perform a formal assessment of the likelihood of publication bias; consequently it is possible that smaller studies may have been missed. Two review authors independently carried out screening and 'Risk of bias' assessments, discussing any areas of disagreement with another review author. Two review authors also checked data extraction. The methods used were therefore unlikely to introduce bias.

Agreements and disagreements with other studies or reviews

The findings of this review are in keeping with other systematic reviews of dietary interventions in RAP. Horvath 2011, and more recently Rutten 2015, reported that *Lactobacillus rhamnosus* GG was associated with significantly more treatment responders than placebo in their meta-analyses; the same authors found only inconclusive data regarding the effects of fibre supplements (Horvath 2012; Rutten 2015).

Issues for consideration

We rated the quality of the evidence provided by the included studies as moderate or low (for probiotics) or low (for fibre). There were additionally further issues for consideration. As discussed above, the majority of studies were short term. We also noted variety in the definition and scales used to assess improvement in pain, meaning that this outcome does not reflect a universally agreed clinically significant benchmark. It is therefore harder to draw conclusions as to whether the reported improvements in pain were clinically meaningful, although this is to some extent a matter of judgement. The outcome of improvement in pain in most included studies represented either a change to no pain or a decrease by 50%, which could be argued to be clinically important. This observation also applied to the assessment of other outcomes, such as pain intensity and frequency.
As previously mentioned, many studies did not collect data on the prespecified secondary outcomes of interest, such as school performance or quality of daily life, meaning that the effect of dietary interventions on these important outcomes was not measured and that it was therefore not possible to conduct pooled analyses. Data on these outcomes would also assist in determining the clinical relevance of improvements in pain.
We performed no subgroup analyses by type or concentration of probiotic, as we did not specify this in our protocol (Martin 2014b); each pooled analysis included studies using different strains of probiotic, the most common being *L rhamnosus* GG and *L reuteri.*
Finally, the majority of studies included children under the broad umbrella of RAP and did not present results by RAP subtype. Consequently, we were only able to perform one pooled analysis for the subtype of irritable bowel syndrome for probiotic interventions, although the eligible studies for the pooled analysis for pain intensity in fibre interventions also included only children with irritable bowel syndrome.

AUTHORS' CONCLUSIONS

Implications for practice

Overall, there is some evidence to suggest that probiotics may be effective in the treatment of RAP, in terms of improving pain in the shorter term. Clinicians may therefore consider probiotic interventions as part of the management strategy for children with RAP. However, we were unable to recommend the optimum strain and dosage of probiotic based on this review.

We did not find convincing evidence that fibre interventions were effective in improving pain in children with RAP. The evidence for other dietary interventions (e.g. low FODMAP or lactose- or fructose-free diets) is also currently lacking, therefore we were unable to make evidence-based recommendations regarding their use in practice. For a holistic approach, the evidence from this review regarding the effectiveness of dietary interventions should also be considered in conjunction with evidence from the companion Cochrane reviews covering pharmacological interventions, Martin 2014a, and psychosocial interventions, Abbott 2017, for RAP in childhood.

Implications for research

The evidence for the effectiveness of probiotics was based largely on shorter-term outcomes. Further trials are required to assess whether improvements in pain are maintained over the longer term; these trials should also consider the importance of using validated and consistent scales to measure pain and other outcomes. Such studies could attempt to examine the effects of probiotics on a wider range of outcomes important to children and their parents, such as quality of life, school attendance, and disability. Future research should also address the question of the optimal strain and dosage schedule for probiotic interventions, as well as consider the effectiveness of probiotics in different settings (the majority of these studies were conducted in gastroenterology clinics in Europe). It has been suggested that there are distinct subtypes of RAP and that these could guide treatment choice (Drossman 2016). We therefore thought it important in this review to estimate whether subtype predicted response to different treatment modalities, however this needs further investigation to allow a tailored approach to management.

In the case of fibre-based interventions and low FODMAP and other exclusion diets, further high-quality RCTs involving larger numbers of participants are needed to examine the effectiveness of these interventions.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Asgarshirazi 2015

Methods	3-arm RCT with placebo control **Follow-up:** 4 weeks
Participants	**Location**: Iran **Setting:** Paediatric gastroenterology outpatient clinic **Sample size:** 120 children (40 probiotic, 40 peppermint oil, 40 control) **Sex:** Not given for whole sample; for those analysed: 48 girls, 40 boys **Dropouts/withdrawals:** 32 withdrawals, number analysed = 88 **Diagnosis:** Functional gastrointestinal disorders diagnosed using Rome III (Rasquin 2006) **Mean age:** 7.44 (SD 2.44) years probiotic intervention, 7.42 (SD 2.49) years control
Interventions	**Intervention:** Synbiotic Lactol tablet (150 million spores of *Bacillus coagulans* + fructo-oligosaccharide) (Bioplus Life Sciences), 1 tablet, 3 x day **Control:** Folic acid tablet (1 mg), 1 tablet, 2 x day **Third arm:** Peppermint oil. Please see Pharmacological review, Martin 2014a, for this comparison.
Outcomes	1. Pain severity (using Numerical Rating Scale 0-to-10) 2. Pain duration: minutes per day 3. Pain frequency: episodes per week
Notes	**Study dates:** September 2012 to August 2014 **Funding:** Not stated **Declarations of interest:** Not reported

Risk of bias ***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** Authors describe using block randomisation (Asgarshirazi 2016 [pers comm]), but no further detail given.
Allocation concealment (selection bias)	Unclear risk	**Comment:** Allocation concealment not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** The nurse that carried out the questionnaire was blinded. However, the placebo regimen of folic acid tablets differed in timing and frequency to the intervention regimen, which could have introduced bias

Asgarshirazi 2015 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** As above.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** All children accounted for, however, 15 in control group and 11 in probiotic group were excluded during trial after randomisation and not analysed as "they did not complete one-month drug consumption (due to journey or lack of 2 weeks visit)". No further explanation given
Selective reporting (reporting bias)	Low risk	**Comment:** All outcomes reported.
Other bias	High risk	The intervention and placebo groups differed at baseline, as duration of pain in the intervention group was 67.05 mean minutes/day (SD ± 36.97) and the placebo group was 53.4 mean minutes/day (SD ± 16.81)

Bausserman 2005

Methods	RCT with placebo control **Follow-up:** Post-treatment (6 weeks) follow-up
Participants	**Location:** USA **Setting:** Paediatric gastroenterology outpatient clinic **Sample size:** 50 children (25 intervention, 25 control) **Sex:** 10 boys, 40 girls **Dropouts/withdrawals:** 6 withdrawals, 6 dropouts lost to follow-up, and 2 excluded due to poor compliance; number analysed = 50 **Diagnosis:** Irritable bowel syndrome diagnosed using Rome II (Thompson 2000) **Mean age:** 11.6 (SD 3.2) years intervention, 12.4 (SD 2.9) years control
Interventions	**Intervention:** *Lactobacillus* GG in capsule form in concentration of 10^{10} CFU of bacteria with inulin, 1 capsule, 2 x day **Control:** Inulin-only capsule identical in size, taste, and colour, 1 capsule, 2 x day
Outcomes	1. Improvement in pain, defined as number of responders with a decrease of 1 or more points on a severity-of-symptom Likert scale, versus non-responders 2. Pain severity (Gastrointestinal Symptoms Rating Scale (Svedlund 1988))
Notes	**Study dates:** July 2003 to June 2004 **Funding:** Wright State University School of Medicine seed grant **Declarations of interest:** Not reported

Bausserman 2005 (*Continued*)

Risk of bias		*Risk of bias*
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Comment:** Computer-generated randomisation.
Allocation concealment (selection bias)	Low risk	**Comment:** Pharmacist dispensed drugs.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Double-blind with placebo control.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** Double-blind with placebo control.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** 2 children in the intervention group were removed postrandomisation due to poor compliance and were not analysed. 3 lost to follow-up in each arm and not analysed. 6 withdrew from the study before data were collected but postrandomisation and were therefore not analysed
Selective reporting (reporting bias)	Low risk	**Comment:** All outcomes mentioned are reported.
Other bias	Low risk	**Comment:** Aside from outcome data, overall well reported.

Chumpitazi 2015

Methods	Cross-over RCT with 'typical diet' control **Follow-up:** Postintervention at 2 days
Participants	**Location:** USA **Setting:** Paediatric gastroenterology outpatient clinic and self referral via community advertisements **Sample size:** 34 children **Sex:** 22 girls, 12 boys **Dropouts/withdrawals:** 1 excluded postrandomisation; 33 analysed **Diagnosis:** Irritable bowel syndrome diagnosed using Rome III (Rasquin 2006) **Mean age:** 11.5 (SD 3) years

Chumpitazi 2015 (*Continued*)

Interventions	**Intervention:** Low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diet containing 0.15 g/kg/day (maximum 9 g/day) of FODMAPs. 2-day diet, preprepared and delivered to participants **Control:** Typical American childhood diet (TACD) containing 0.7 g/kg/day (maximum 50 g/day) of FODMAPs. 2-day diet, preprepared and delivered to participants **Washout:** 5-day washout period in between.
Outcomes	1. Improvement in pain, defined as participants who had a ≥ 50% decrease in the number of daily abdominal pain episodes 2. Pain severity (pain diary using a 1-to-10 Likert scale) 3. Pain frequency (episodes per day recorded in diary)
Notes	**Study dates:** September 2011 to December 2013 **Funding:** North American Society for Pediatric Gastroenterology, Hepatology and Nutrition Foundation/Nestlé Nutrition Career Development Award and US National Institutes of Health (NIH) K23 DK101688 (BPC) **Declarations of interest:** Bruno Chumpitazi received funding from the NIH, QOL Medical Inc., and is a consultant for Mead Johnson Nutrition. Robert Shulman received funding from the NIH and Mead Johnson Nutrition and is a consultant for Nutrinia Ltd. and Gerson Lehrman Group. James Versalovic received funding from the NIH and BioGaia AB. The remaining authors do not have personal interests to disclose

Risk of bias ***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Comment:** Computer-generated block randomisation.
Allocation concealment (selection bias)	Low risk	**Comment:** Randomisation handled by external research dietician.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** Double-blind but unclear whether both diets were delivered in identical containers or whether there were other ways for participants to guess the allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** Double-blind but unclear whether both diets were delivered in identical containers or whether there were other ways for participants to guess the allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** All participants accounted for.
Selective reporting (reporting bias)	Low risk	**Comment:** All stated outcomes reported.
Other bias	Low risk	**Comment:** Well-conducted study.

Eftekhari 2015

Methods	RCT with placebo control **Follow-up:** 4 weeks postintervention (at 8 weeks)
Participants	**Location:** Iran **Setting:** Paediatric gastroenterology outpatient clinic **Sample size:** 80 children **Sex:** 40 girls, 40 boys **Dropouts/withdrawals:** Not discussed/no information given **Diagnosis:** RAP diagnosed using Rome III (Rasquin 2006) **Mean age:** 6.26 (SD 2.10) years intervention, 6.26 (SD 2.10) years control
Interventions	**Intervention:** *Lactobacillus reuteri* 5 drops per day orally equivalent to 10^8CFU for 4 weeks **Control:** Placebo (no further details given)
Outcomes	1. Improvement in pain, defined as percentage with no pain 2. Pain severity using Wong-Baker FACES Pain Rating Scale (Wong 1988) 3. Pain frequency using Wong-Baker FACES Pain Rating Scale (Wong 1988)
Notes	**Study dates:** 2012 to 2013 (14 months) **Funding:** Zanjan University of Medical Sciences **Declarations of interest:** Not mentioned

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	**Comment:** Only detail given is: randomised allocation (computer registration)
Allocation concealment (selection bias)	Unclear risk	**Comment:** Only detail given is: randomised allocation (computer registration)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Double-blind study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** Double-blind study.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** Does not mention loss to follow-up or withdrawals.
Selective reporting (reporting bias)	Low risk	**Comment:** Reports all outcomes mentioned.
Other bias	Low risk	**Comment:** No other major sources of bias.

Feldman 1985

Methods	RCT with placebo control **Follow-up:** 6 weeks
Participants	**Location:** Canada **Setting:** Private GP practices and community paediatric clinics **Sample size:** 52 children (26 intervention, 26 control) **Sex:** 17 boys, 35 girls **Dropouts/withdrawals:** None reported **Diagnosis:** At least 1 attack per week of unexplained abdominal pain over 2 months **Mean age:** 9.31 (SD 3.2) years intervention, 9.44 (SD 2.9) years control
Interventions	**Intervention:** Fibre cookie (5 g corn per cookie), twice a day **Control:** Placebo cookie, twice a day, identically wrapped to the intervention cookie (cookies tasted different but believed to be no cross-over)
Outcomes	1. Frequency of pain (stomachache diary) 2. Pain intensity (stomachache diary)
Notes	**Study dates:** Not given **Funder:** Not reported **Declarations of interest:** Not reported

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Comment:** Computer-generated random number system.
Allocation concealment (selection bias)	Unclear risk	**Comment:** Insufficient information reported.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Cookies wrapped identically.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** Parents, children, and clinicians blinded to allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** Have complete outcome data on all included children.
Selective reporting (reporting bias)	Unclear risk	**Comment:** Insufficient information. Does not report all numerical data
Other bias	Low risk	**Comment:** No other major sources of bias.

Francavilla 2010

Methods	RCT with placebo control **Follow-up:** 8 weeks and 16 weeks
Participants	**Location**: Italy **Setting:** Primary care paediatric practices **Sample size:** 141 children (71 intervention, 70 control) **Sex:** Not given for whole sample **Dropouts/withdrawals:** 4 dropped out (2 from intervention, 2 from control) and 1 withdrew (from control) **Diagnosis:** Irritable bowel syndrome or functional abdominal pain diagnosed using Rome II (Thompson 2000) **Mean age:** 6.5 (SD 2.1) years intervention, 6.3 (SD 2.0) years control
Interventions	**Intervention:** Oral *Lactobacillus* GG (3 x 10^{10} CFU), twice per day for 8 weeks **Control:** Identical-looking/tasting placebo twice per day for 8 weeks
Outcomes	1. Pain episodes and severity (visual analogue scale and Faces Pain Scale combined (McGrath 1996)) 2. Treatment success (as above; success defined as 50% reduction in baseline pain episodes and intensity)
Notes	**Study dates:** 2004 to 2008 **Funder:** Not reported **Declarations of interest:** Not reported

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Comment:** Computer-generated randomisation list with permuted block design
Allocation concealment (selection bias)	Low risk	**Comment:** Enrolled children entered sequentially to computer-generated randomisation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Identical-looking/tasting placebo. Group assignment was concealed from participants and investigators
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** Double-blind.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** 4 children dropped out, but 2 each from control and intervention group. Analysis based on 137 children, not 141 allocated

Francavilla 2010 (*Continued*)

Selective reporting (reporting bias)	Low risk	**Comment:** All outcomes reported.
Other bias	Low risk	**Comment:** Well-conducted and reported study.

Gawronska 2007

Methods	RCT with placebo control **Follow-up:** 4 weeks
Participants	**Location**: Poland **Setting:** University department of paediatric gastroenterology **Sample size:** 104 children (52 intervention, 52 control) **Sex:** 48 boys, 56 girls **Dropouts/withdrawals:** None **Diagnosis:** Functional dyspepsia, irritable bowel syndrome, or functional abdominal pain diagnosed using Rome II (Thompson 2000) **Mean age:** 11.9 (SD 3.0) years intervention, 11.2 (SD 2.7) years control
Interventions	**Intervention:** *Lactobacillus rhamnosus* GG (3 x 10^9 CFU) capsules twice daily orally for 4 weeks **Control:** Identical placebo, twice daily orally for 4 weeks
Outcomes	1. Improvement in pain (treatment success) (Faces Pain Scale (Bieri 1990)) 2. Pain intensity and frequency (Faces Pain Scale (Bieri 1990)) 3. Medication for abdominal pain (diary) 4. School absenteeism due to abdominal pain (diary)
Notes	**Study dates:** October 2003 to May 2006 **Funder:** Medical University of Warsaw **Declarations of interest:** Not reported

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Comment:** Computer-generated list with permutated block design.
Allocation concealment (selection bias)	Low risk	**Comment:** Adequate methods for allocation sequence concealment.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** All blinded to assignment.

Gawronska 2007 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** All blinded to assignment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** All participants accounted for.
Selective reporting (reporting bias)	Low risk	**Comment:** All outcomes reported.
Other bias	Low risk	**Comment:** Well-conducted and reported study.

Giannetti 2017

Methods	Cross-over RCT with placebo control **Follow-up:** 6 weeks
Participants	**Location**: Italy **Setting:** Tertiary paediatric clinic **Sample size:** 78 children **Sex:** 32 boys, 41 girls (of those analysed) **Dropouts/withdrawals:** 1 exclusion, 4 lost to follow-up during washout **Diagnosis:** Irritable bowel syndrome or functional dyspepsia diagnosed using Rome III (Rasquin 2006) **Mean age:** Irritable bowel syndrome 11.2 (range 8 to 17.9) years, functional dyspepsia 11.6 (range 8 to 16.6) years
Interventions	**Intervention:** 1 sachet per day of a mixture of 3 *Bifidobacterium* species (namely, 3 billion of *B longum* BB536, 1 billion of *B infantis* M-63, 1 billion of *B breve* M-16V) for 6 weeks, followed by a 2-week washout period **Control:** Identical placebo
Outcomes	1. Improvement in pain defined as being pain-free using validated questionnaire (Walker 2006) 2. Pain frequency measured using validated questionnaire (Walker 2006) 3. Functional Disability Inventory (Claar 2006)
Notes	**Study dates:** January 2014 to December 2014 **Funder:** None reported **Declarations of interest:** The authors declare no conflicts of interest.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Comment:** Computer-generated randomisation.

Giannetti 2017 (*Continued*)

Allocation concealment (selection bias)	Low risk	**Comment:** Independent physician involved in the randomisation.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** All blinded to assignment.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** All blinded to assignment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** All participants accounted for and intention-to-treat analysis carried out
Selective reporting (reporting bias)	Low risk	**Comment:** All outcomes reported, but unable to obtain raw data for pain frequency outcome from authors as they did not respond to our written request (Giannetti 2017).
Other bias	Low risk	**Comment:** Overall a well-conducted trial

Guandalini 2010

Methods	Cross-over RCT with placebo control **Follow-up:** 6 weeks
Participants	**Location**: Italy and India **Setting:** Paediatric tertiary care centres **Sample size:** 67 (cross-over trial) enrolled, 59 completed **Sex:** 31 boys, 28 girls (of those completing study) **Dropouts/withdrawals:** 8 children did not complete the study, 4 from the placebo arm and 4 from the study arm. Reasons for dropouts were inability/unwillingness to complete questionnaires (6 children) and dislike of the preparation given (1 each from study and placebo group) **Diagnosis:** Irritable bowel syndrome diagnosed using Rome II (Thompson 2000) **Mean age:** 12.5 (SD not given; range 5 to 18) years
Interventions	**Intervention:** Patented probiotic preparation VSL#3 (contains live, freeze-dried lactic acid bacteria, at a total concentration of 450 billion lactic acid bacteria per sachet, comprising 8 different strains: *Bifidobacterium breve*, *B longum, B infantis, Lactobacillus acidophilus, L plantarum, L casei, L bulgaris*, and *Streptococcus thermophiles*). 1 sachet once per day for children aged 4 to 11 years and twice a day for children aged 12 to 18 years for 6 weeks **Control:** Identical-looking/tasting placebo taken as above
Outcomes	1. Improvement in pain (Subject's Global Assessment of Relief Child version (SGARC) (Muller-Lissner 2003))

Guandalini 2010 (*Continued*)

	2. Pain frequency and intensity (measure not described) 3. Disruption of daily life (measure not described)
Notes	**Study dates:** Not given **Funder:** Funded by locally available grants. There was no industry support except for providing product and placebo **Declarations of interest:** Not reported

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Comment:** Computer-generated randomisation.
Allocation concealment (selection bias)	Low risk	**Comment:** Separate centre in Chicago, IL, USA managed the data and allocations
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Double-blind, identical-looking/tasting placebo.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** Self reported outcomes, but blinded to treatment group.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** All participants accounted for.
Selective reporting (reporting bias)	Unclear risk	**Comment:** Comparisons made pre/post and not between intervention and control at week 6
Other bias	Low risk	**Comment:** No other major sources of bias identified.

Horvath 2013

Methods	RCT with placebo control **Follow-up:** 4 weeks
Participants	**Location**: Poland **Setting:** University department of paediatric gastroenterology **Sample size:** 84 children (41 intervention, 43 control) **Sex:** 42 boys, 42 girls **Dropouts/withdrawals:** 7 lost to follow-up, 3 withdrawals, 2 protocol violations (all excluded from analysis) **Diagnosis:** Abdominal pain-related functional gastrointestinal disorders diagnosed using Rome III (Rasquin 2006)

Horvath 2013 (*Continued*)

	Mean age: 11.6 (SD 3.0) years intervention, 11.3 (SD 2.5) years control
Interventions	**Intervention:** GNN (glucomannan) polysaccharide of 1,4-D-glucose and D-mannose, 2.52 g per day in 2 doses from sachets dissolved in 125 mL of fluid consumed twice a day (morning and evening) for 4 weeks **Control:** Placebo of maltodextrin at same dosage for 4 weeks
Outcomes	1. Improvement in pain (no pain or decrease of 2 or more points on Faces Pain Scale-Revised (Bieri 1990)) 2. Subjective assessment of pain frequency, abdominal cramps and bloating, nausea, changes in stools (measure not described) 3. School absenteeism, changes in daily activities, rescue therapy, and adverse effects (measure not described)
Notes	**Study dates:** January 2009 to October 2011 **Funder:** Not stated **Declarations of interest:** Not reported

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Comment:** Computer-generated block randomisation.
Allocation concealment (selection bias)	Low risk	**Comment:** Adequate methods described, and sequence was concealed until all data were analysed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Double-blind.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** Double-blind.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** Very basic data reported.
Selective reporting (reporting bias)	Low risk	**Comment:** All outcomes discussed.
Other bias	Low risk	**Comment:** Fairly well-reported study.

Kianifar 2015

Methods	RCT with placebo control **Follow-up:** 4 weeks, immediately postintervention
Participants	**Location**: Iran **Setting:** University department of paediatric gastroenterology **Sample size:** 60 children (30 intervention, 30 control) **Sex:** 27 boys, 25 girls (of those analysed, not given for all included) **Dropouts/withdrawals:** 5 excluded due to lack of follow-up (no breakdown by intervention group given); 3 excluded as took antibiotics during study period **Diagnosis:** Irritable bowel syndrome diagnosed using Rome III (Rasquin 2006) **Mean age:** 7.3 (SD 0.5) years intervention, 6.8 (SD 0.4) years control
Interventions	**Intervention:** *Lactobacillus rhamnosus* GG with a concentration of 1×10^{10} CFU/mL bacteria, 1 capsule twice per day for 4 weeks **Control:** Identical placebo containing inulin at same dosage for 4 weeks
Outcomes	1. Pain severity using 5-point Likert scale 2. Functional changes (disruption of social activities, days of absence from school) rated using 3-point Likert scale
Notes	**Study dates:** August 2012 to September 2012 **Funder:** Mashhad University of Medical Sciences, Iran **Declarations of interest:** Authors declare no conflicts of interest.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Comment:** Randomisation using computer-generated list with permutated block design
Allocation concealment (selection bias)	Low risk	**Comment:** Randomisation using computer-generated list with permutated block design
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Double-blind with identical placebo.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** Double-blind with identical placebo.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** Numbers lost to follow-up not given by group.
Selective reporting (reporting bias)	Low risk	**Comment:** All outcomes reported.

Kianifar 2015 (*Continued*)

Other bias	Low risk	**Comment:** No other major sources of bias identified.

Romano 2010

Methods	RCT with placebo control **Follow-up**: 8 weeks
Participants	**Location**: Italy **Setting:** University department of paediatrics **Sample size:** 56 children (30 intervention, 26 control) **Sex:** 25 boys, 31 girls **Dropouts/withdrawals:** 4 children "lost to completion" (see below) **Diagnosis:** Functional abdominal pain diagnosed using Rome III (Rasquin 2006) **Mean age:** 10.2 (SD 2.5) years intervention, 9.6 (SD 0.4) years control
Interventions	**Intervention:** Oral supplementation with *Lactobacillus reuteri* DSM 17938, 10^8 CFU, twice daily for 4 weeks **Control:** Identical placebo, twice daily for 4 weeks
Outcomes	1. Pain intensity (Wong-Baker FACES Pain Rating Scale; in diary, filled in daily (Wong 1988)) 2. Pain frequency of functional abdominal pain symptoms (Wong-Baker FACES Pain Rating Scale; in diary, filled in daily (Wong 1988))
Notes	**Study dates:** Not given **Funder:** Not stated **Declarations of interest:** Not reported

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Comment:** Randomisation was based on a computer-generated list, which was retained by the dispensing pharmacist at each centre to ensure allocation concealment
Allocation concealment (selection bias)	Low risk	**Comment:** See above.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Double-blind.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** Parent/child reporting, but they are unaware of which treatment they had been allocated to

Romano 2010 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** 4 children "lost to completion" due to non-compliance postrandomisation and were not analysed. Unclear if excluded or lost to follow-up
Selective reporting (reporting bias)	Low risk	**Comment:** All outcomes reported. Authors supplied raw data for pain frequency and intensity outcomes on review authors' request (Romano 2014 [pers comm]), as these were shown in charts only in paper.
Other bias	Low risk	**Comment:** No other sources of bias identified.

Romano 2013

Methods	RCT with placebo control **Follow-up:** 8 weeks
Participants	**Location**: Italy **Setting:** University department of paediatric gastroenterology **Sample size:** 60 children (30 intervention, 30 control) **Sex:** 23 boys, 37 girls **Dropouts/withdrawals:** None **Diagnosis:** Irritable bowel syndrome, diagnosed using Rome III (Rasquin 2006) **Mean age:** 12.3 (SD 2.0) years intervention, 13.1 (SD 1.5) years control
Interventions	**Intervention:** Partially hydrolysed guar gum (PHGG - vegetal, water-soluble, non-viscous, gelling dietary fibre), 5 g/day hidden in 50 mL fruit juice for 4 weeks **Control:** Placebo of 50 mL fruit juice per day for 4 weeks
Outcomes	1. Pain intensity (Wong-Baker FACES Pain Rating Scale (Wong 1988)) 2. Other symptoms of irritable bowel syndrome (Bristol Stool Scale (Lewis 1997), Birmingham IBS Symptom Questionnaire (Roalfe 2008)) 3. Safety and compliance: recorded adverse events
Notes	**Study dates:** November 2010 to May 2011 **Funder:** Not stated **Declarations of interest:** Not reported

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Comment:** Randomisation was based on a computer-generated list.

Romano 2013 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	**Comment:** Insufficient information to judge
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Placebo was used, so participants blinded; states that investigators were also blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** As above
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** All participants accounted for and analysed.
Selective reporting (reporting bias)	Low risk	**Comment:** All outcomes reported.
Other bias	Low risk	**Comment:** No other major sources of bias identified.

Sabbi 2011

Methods	RCT with placebo control **Follow-up:** 10 weeks
Participants	**Location**: Italy **Setting:** Not stated **Sample size:** 61 children **Sex:** Not stated **Dropouts/withdrawals:** Not stated **Diagnosis:** Functional abdominal pain **Mean age:** Not stated
Interventions	**Intervention:** *Lactobacillus rhamnosus* GG (no further details given) for 6 weeks **Control:** Placebo (no further details given)
Outcomes	1. Pain frequency (measure not given) 2. Pain intensity (measure not given)
Notes	**Study dates:** Not stated **Funder:** Not stated **Declarations of interest:** Authors report no conflicts of interest. This was an abstract. We wrote to the author for further details but received no response (Sabbi 2011).

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**

Sabbi 2011 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	**Comment:** Insufficient information to judge.
Allocation concealment (selection bias)	Unclear risk	**Comment:** Insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Double-blind with placebo control.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment:** Double-blind with placebo control, but unclear how outcome was assessed
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** Insufficient information to judge.
Selective reporting (reporting bias)	Unclear risk	**Comment:** Insufficient information to judge.
Other bias	Unclear risk	**Comment:** Insufficient information to judge.

Saneian 2015

Methods	RCT with placebo control **Follow-up:** 12 weeks
Participants	**Location**: Iran **Setting:** Outpatient tertiary clinic of paediatric gastroenterology **Sample size:** 88 children (45 intervention, 43 control) **Sex:** 49 boys, 39 girls **Dropouts/withdrawals:** 21 withdrew (9 intervention, 12 control); 5 discontinued (all from intervention); 1 excluded due to antibiotic use; 9 lost to follow-up (5 intervention, 4 control). All were excluded from analysis **Diagnosis:** Functional abdominal pain diagnosed using Rome III (Rasquin 2006) **Mean age:** 9.0 (SD 2.2) years intervention, 8.5 (SD 2.2) years control
Interventions	**Intervention:** Synbiotic tablets twice daily for a duration of 4 weeks, consisting of the probiotic *Bacillus coagulans* plus fructo-oligosaccharide (100 mg) **Control:** Placebo tablets
Outcomes	Measured at 4 and 12 weeks 1. Improvement in pain defined as at least 2-point reduction in or "no pain" after medication using Wong-Baker FACES Pain Rating Scale (Wong 1988) 2. Clinical Global Impression Severity and Improvement scales (CGI-S; CGI-I) (Guy 1976), physician-rated scales of the global severity of the illness and improvement by the treatment, respectively

Saneian 2015 (*Continued*)

	3. Reported on adverse effects (intervention group (44.4%) experienced more dry mouth compared to control (23.2%))
Notes	**Study dates:** February 2013 to December 2013 **Funder:** Isfahan University of Medical Sciences **Declarations of interest:** Not reported

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Comment:** Computer-generated block randomisation.
Allocation concealment (selection bias)	Low risk	**Comment:** Bottles coded by pharmacist, allocation concealed.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Attending physician, participants, and outcome assessor were unaware of the drug codes until the end of the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** Outcome assessor blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** Paper reports that an intention-to-treat analysis was used, but they did not analyse everyone that had been randomised to each group: 14 in the intervention group and 11 in the control group discontinued medication and were not analysed
Selective reporting (reporting bias)	Low risk	**Comment:** Authors report all stated outcomes, but they do not present raw scores for the continuous data, only the change in score
Other bias	Low risk	**Comment:** No other major sources of bias.

Shulman 2016

Methods	RCT with placebo control **Follow-up:** 6 weeks immediately postintervention
Participants	**Location**: USA **Setting:** Paediatric healthcare network, including both primary and tertiary care **Sample size:** 103 children (51 intervention, 52 control) **Sex:** 55 boys, 48 girls

Shulman 2016 (*Continued*)

	Dropouts/withdrawals: 15 withdrew (12 intervention, 3 control); 1 excluded from intervention group; 3 lost to follow-up (1 intervention, 2 control). All were excluded from analysis. 84 analysed **Diagnosis:** Irritable bowel syndrome diagnosed using Rome III (Rasquin 2006) **Mean age:** 13.1 (SD 0.4) years intervention, 13.5 (SD 0.4) years control
Interventions	**Intervention:** Psyllium fibre. Children 7 to 11 years of age received 6 g, children 12 to 18 years of age received 12 g **Control:** Placebo tablets containing maltodextrin; single daily dose in identical packets
Outcomes	1. Pain severity using Numerical Rating Scale (NRS-11) (von Baeyer 2009) 2. Pain frequency using Numerical Rating Scale (NRS-11) (von Baeyer 2009) 3. Health-related quality of life using Pediatric Quality of Life Generic Core Scales (Varni 2015)
Notes	**Study dates:** January 2009 to March 2014 **Funder:** National Institutes of Health, the Daffy's Foundation **Declarations of interest:** Authors state no conflicts of interest.

Risk of bias ***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Comment:** Block randomisation described.
Allocation concealment (selection bias)	Low risk	**Comment:** Allocation concealment described.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Double-blind study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** Double-blind study.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** 15 withdrew (12 intervention, 3 control); 1 excluded from intervention group; 3 lost to follow-up (1 intervention, 2 control). All were excluded from analysis
Selective reporting (reporting bias)	Low risk	**Comment:** All outcomes reported. Authors supplied raw data for pain frequency and intensity outcomes on review authors' request (Shulman 2016), as these were shown in charts only in paper.
Other bias	Low risk	**Comment:** No other major sources of bias.

Weizman 2016

Methods	RCT with placebo control **Follow-up:** 8 weeks
Participants	**Location**: Israel **Setting:** Paediatric outpatient clinics and community childcare centres **Sample size:** 101 children (52 intervention, 49 control) **Sex:** 53 boys, 40 girls (of those analysed) **Dropouts/withdrawals:** 8 excluded due to poor compliance (5 in intervention, 3 in control group); 93 analysed **Diagnosis:** Functional gastrointestinal disorder diagnosed using Rome III (Rasquin 2006) **Mean age:** 12.2 (SD 2.8) years intervention, 11.7 (SD 3.2) years control
Interventions	**Intervention:** *Lactobacillus reuteri* DSM 17938 10^8 CFU/day once a day as chewable tablets for 4 weeks **Control:** Identical placebo tablets once a day for 4 weeks
Outcomes	1. Pain severity using Hicks Faces Pain Scale-Revised (Hicks 2001) 2. Pain frequency using Hicks Faces Pain Scale-Revised (Hicks 2001) 3. School absenteeism: self report diary
Notes	**Study dates:** March 2011 to October 2013 **Funder:** Study products supplied by BioGaia. No other funding source declared **Declarations of interest:** ZW has served as a speaker for BioGaia. Other authors state no conflicts of interest

Risk of bias ***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Comment:** Adequate methods of randomisation described.
Allocation concealment (selection bias)	Low risk	**Comment:** Allocation concealment was ensured by an independent person
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Double-blind design.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** Double-blind design.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** 8 children (5 control, 3 intervention) excluded due to "poor compliance and violation of the protocol", but states was an intention-to-treat analysis; as these children are not included in the analysis,

Weizman 2016 (*Continued*)

		this was not intention-to-treat
Selective reporting (reporting bias)	Low risk	**Comment:** All outcomes reported.
Other bias	Low risk	**Comment:** No other major sources of bias identified.

Wirth 2014

Methods	RCT with standard/unchanged diet as control **Follow-up:** 2 weeks
Participants	**Location**: Germany **Setting:** Not specified **Sample size:** 103 children (51 intervention, 52 control) **Sex:** 41 boys, 62 girls **Dropouts/withdrawals:** 1 excluded and 6 lost to follow-up in each arm **Diagnosis:** Recurrent abdominal pain for more than 3 months and otherwise healthy condition determined by a standardised evaluation procedure. Pain frequency had to be at least 3 times per week. Does not mention using Rome criteria. Exclusion criteria were positive lactose hydrogen breath test **Mean age:** Not given. Median age 8.8 years (range 3.4 to 16.4 years)
Interventions	**Intervention:** Fructose-restricted diet (fully described in paper) for 2 weeks **Control:** Standard diet, no dietary changes
Outcomes	1. Pain intensity (as measured by questionnaire, no reference given) 2. Pain frequency (as above) 3. "secondary symptoms score" (SSS) was created from 8 parameters (nausea, vomiting, fatigue, sleep disturbance, headache, dizziness, anorexia, and use of pain relievers). No reference given.
Notes	**Study dates:** Not given **Funder:** No details given **Declarations of interest:** The authors declare no conflicts of interest.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	**Comment:** No details given of process.
Allocation concealment (selection bias)	Unclear risk	**Comment:** No details given of process.
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Comment:** Participants could not be blinded as standard diet was the comparator

Wirth 2014 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	High risk	**Comment:** As above, plus outcomes were participant-reported, so subject to bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** No details given regarding loss to follow-up.
Selective reporting (reporting bias)	Low risk	**Comment:** All outcomes reported.
Other bias	Unclear risk	**Comment:** Did not appear to use validated tools. No details given regarding adherence

Young 1997

Methods	Cross-over RCT with placebo control **Follow-up:** 4 weeks
Participants	**Location**: USA **Setting:** Not specified **Sample size:** 11 children **Sex:** Not given **Dropouts/withdrawals:** Not given **Diagnosis:** Chronic recurrent abdominal pain of childhood **Mean age:** Not given. Reported as "school age".
Interventions	**Intervention:** *Lactobacillus plantarum* 299V (LP299V) **Control:** Placebo
Outcomes	Pain severity as measured by index designed for the study (no reference given)
Notes	**Study dates:** Not given **Funder:** No details given **Declarations of interest:** Not given. This was an abstract. The authors of the previous Cochrane review, Huertas-Ceballos 2009, wrote to the author, but there were no further details available

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	**Comment:** Insufficient information to judge.
Allocation concealment (selection bias)	Unclear risk	**Comment:** Insufficient information to judge.

Young 1997 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** Double-blinded study with placebo.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Comment:** Double-blind study with placebo.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** Insufficient information to judge.
Selective reporting (reporting bias)	Unclear risk	**Comment:** Insufficient information to judge.
Other bias	Unclear risk	**Comment:** Insufficient information to judge.

CFU: colony-forming units.
DSM: Deutsche Sammhatg von Mikroorganismen (classification system of micro-organisms).
GP: general practice.
RAP: recurrent abdominal pain.
RCT: randomised controlled trial.
SD: standard deviation.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Agah 2015	Ineligible study design (not randomised)
Christensen 1982	Ineligible study design (not randomised)
Chumpitazi 2014	Ineligible comparator
Dearlove 1983	Ineligible study design (not randomised)
Edwards 1991	Ineligible comparator
Lebenthal 1981	Ineligible study design (not randomised)

Characteristics of studies awaiting assessment *[ordered by study ID]*

Jarocka-Cyrta 2002

Methods	Double-blind, placebo-controlled trial
Participants	Children over 6 years of age with recurrent abdominal pain
Interventions	Not stated
Outcomes	Not stated
Notes	No abstract or full text available as yet for this study, and no contact details available for the author

DATA AND ANALYSES

Comparison 1. Probiotics versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in pain frequency: 0 to 3 months' postintervention	6	523	Std. Mean Difference (IV, Random, 95% CI)	-0.55 [-0.98, -0.12]
2 Change in pain frequency: 0 to 3 months' postintervention. Sensitivity analysis	4	389	Std. Mean Difference (IV, Random, 95% CI)	-0.54 [-0.94, -0.14]
3 Change in pain intensity: 0 to 3 months' postintervention	7	575	Std. Mean Difference (IV, Random, 95% CI)	-0.50 [-0.85, -0.15]
4 Change in pain intensity: 0 to 3 months' postintervention. Sensitivity analysis	5	441	Std. Mean Difference (IV, Random, 95% CI)	-0.68 [-1.05, -0.30]
5 Improvement in pain: 0 to 3 months' postintervention	7	722	Odds Ratio (M-H, Random, 95% CI)	1.63 [1.07, 2.47]
6 Improvement in pain: 0 to 3 months' postintervention. Sensitivity analysis	6	642	Odds Ratio (M-H, Random, 95% CI)	1.95 [1.40, 2.70]
7 Improvement in pain: 0 to 3 months' postintervention. Subgroup analysis (irritable bowel syndrome)	4	344	Odds Ratio (M-H, Random, 95% CI)	3.01 [1.77, 5.13]
8 Improvement in pain: 3 to 6 months' postintervention	2	224	Odds Ratio (M-H, Random, 95% CI)	1.94 [1.10, 3.43]

Comparison 2. Fibre versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in pain intensity: 0 to 3 months' postintervention	2	135	Std. Mean Difference (IV, Random, 95% CI)	-1.24 [-3.41, 0.94]
2 Improvement in pain: 0 to 3 months' postintervention	2	136	Odds Ratio (M-H, Random, 95% CI)	1.83 [0.92, 3.65]

Analysis 1.1. Comparison 1 Probiotics versus placebo, Outcome 1 Change in pain frequency: 0 to 3 months' postintervention.

Review: Dietary interventions for recurrent abdominal pain in childhood

Comparison: 1 Probiotics versus placebo

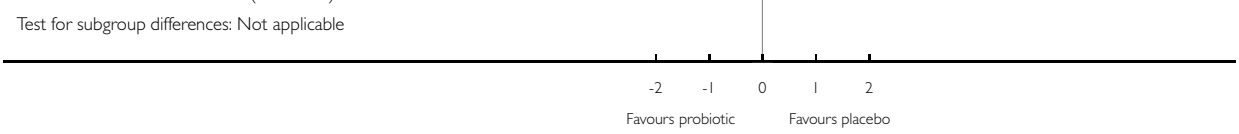
Outcome: 1 Change in pain frequency: 0 to 3 months' postintervention

Study or subgroup	Probiotic N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Asgarshirazi 2015	29	2.14 (0.87)	25	3.4 (1.41)		15.0 %	-1.08 [-1.65, -0.50]
Eftekhari 2015	40	0.7 (0.75)	40	0.53 (0.59)		16.9 %	0.25 [-0.19, 0.69]
Francavilla 2010	67	1.1 (0.8)	69	2.2 (1.2)		17.9 %	-1.07 [-1.43, -0.71]
Gawronska 2007	52	2.2 (1.7)	52	2.6 (1.4)		17.6 %	-0.25 [-0.64, 0.13]
Romano 2010	30	2.12 (0.6)	26	2.6 (0.5)		15.3 %	-0.85 [-1.40, -0.30]
Weizman 2016	47	3.4 (2.6)	46	4.4 (2.9)		17.3 %	-0.36 [-0.77, 0.05]
Total (95% CI)	**265**		**258**			**100.0 %**	**-0.55 [-0.98, -0.12]**

Heterogeneity: $Tau^2 = 0.23$; $Chi^2 = 28.10$, df = 5 (P = 0.00003); $I^2 = 82\%$

Test for overall effect: Z = 2.52 (P = 0.012)

Test for subgroup differences: Not applicable

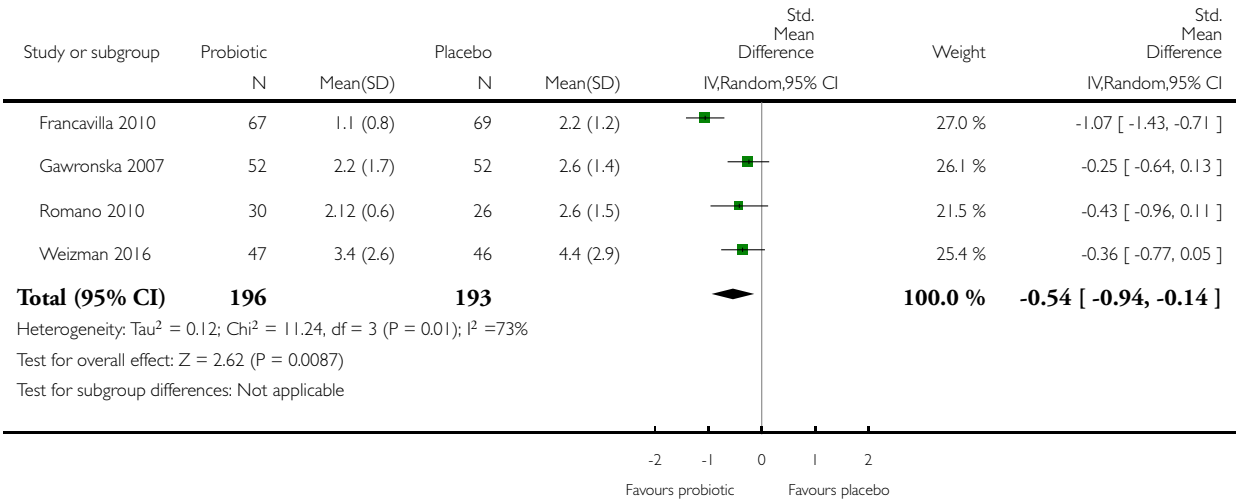


Analysis 1.2. Comparison 1 Probiotics versus placebo, Outcome 2 Change in pain frequency: 0 to 3 months' postintervention. Sensitivity analysis.

Review: Dietary interventions for recurrent abdominal pain in childhood

Comparison: 1 Probiotics versus placebo

Outcome: 2 Change in pain frequency: 0 to 3 months' postintervention. Sensitivity analysis



Analysis 1.3. Comparison 1 Probiotics versus placebo, Outcome 3 Change in pain intensity: 0 to 3 months' postintervention.

Review: Dietary interventions for recurrent abdominal pain in childhood

Comparison: 1 Probiotics versus placebo

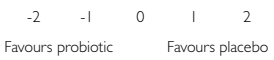
Outcome: 3 Change in pain intensity: 0 to 3 months' postintervention

Study or subgroup	Probiotic N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Asgarshirazi 2015	29	3.93 (1.06)	25	4.24 (1.33)		13.2 %	-0.26 [-0.79, 0.28]
Eftekhari 2015	40	2.53 (1.43)	40	2.25 (1.46)		14.8 %	0.19 [-0.25, 0.63]
Francavilla 2010	67	2.3 (1.3)	69	3.4 (2.1)		16.2 %	-0.62 [-0.97, -0.28]
Gawronska 2007	52	2.5 (1.9)	52	2.9 (1.5)		15.6 %	-0.23 [-0.62, 0.15]
Kianifar 2015	26	0.8 (0.9)	26	1.5 (0.8)		12.8 %	-0.81 [-1.38, -0.24]
Romano 2010	30	1.01 (0.6)	26	2.1 (0.8)		12.3 %	-1.54 [-2.14, -0.93]
Weizman 2016	47	4.8 (3.3)	46	6.4 (4.1)		15.2 %	-0.43 [-0.84, -0.02]
Total (95% CI)	**291**		**284**			**100.0 %**	**-0.50 [-0.85, -0.15]**

Heterogeneity: $Tau^2 = 0.17$; $Chi^2 = 24.95$, df = 6 (P = 0.00035); $I^2 = 76\%$

Test for overall effect: Z = 2.80 (P = 0.0052)

Test for subgroup differences: Not applicable



Analysis 1.4. Comparison 1 Probiotics versus placebo, Outcome 4 Change in pain intensity: 0 to 3 months' postintervention. Sensitivity analysis.

Review: Dietary interventions for recurrent abdominal pain in childhood

Comparison: 1 Probiotics versus placebo

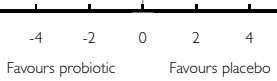
Outcome: 4 Change in pain intensity: 0 to 3 months' postintervention. Sensitivity analysis

Study or subgroup	Probiotic N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Francavilla 2010	67	2.3 (1.3)	69	3.4 (2.1)		23.1 %	-0.62 [-0.97, -0.28]
Gawronska 2007	52	2.5 (1.9)	52	2.9 (1.5)		22.0 %	-0.23 [-0.62, 0.15]
Kianifar 2015	26	0.8 (0.9)	26	1.5 (0.8)		17.3 %	-0.81 [-1.38, -0.24]
Romano 2010	30	1.01 (0.6)	26	2.1 (0.8)		16.4 %	-1.54 [-2.14, -0.93]
Weizman 2016	47	4.8 (3.3)	46	6.4 (4.1)		21.3 %	-0.43 [-0.84, -0.02]
Total (95% CI)	**222**		**219**			**100.0 %**	**-0.68 [-1.05, -0.30]**

Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 14.00$, df = 4 (P = 0.01); $I^2 = 71\%$

Test for overall effect: Z = 3.56 (P = 0.00037)

Test for subgroup differences: Not applicable



Analysis 1.5. Comparison 1 Probiotics versus placebo, Outcome 5 Improvement in pain: 0 to 3 months' postintervention.

Review: Dietary interventions for recurrent abdominal pain in childhood

Comparison: 1 Probiotics versus placebo

Outcome: 5 Improvement in pain: 0 to 3 months' postintervention

Study or subgroup	Probiotic n/N	Placebo n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Bausserman 2005	11/25	10/25		9.7 %	1.18 [0.38, 3.63]
Eftekhari 2015	15/40	21/40		13.1 %	0.54 [0.22, 1.32]
Francavilla 2010	48/67	37/69		16.7 %	2.18 [1.07, 4.45]
Gawronska 2007	25/52	23/52		15.4 %	1.17 [0.54, 2.53]
Giannetti 2017	25/73	15/73		16.0 %	2.01 [0.96, 4.24]
Guandalini 2010	44/59	29/59		15.3 %	3.03 [1.40, 6.60]
Saneian 2015	27/45	17/43		13.8 %	2.29 [0.98, 5.39]
Total (95% CI)	**361**	**361**		**100.0 %**	**1.63 [1.07, 2.47]**

Total events: 195 (Probiotic), 152 (Placebo)

Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 10.89$, df = 6 (P = 0.09); $I^2 = 45\%$

Test for overall effect: Z = 2.27 (P = 0.023)

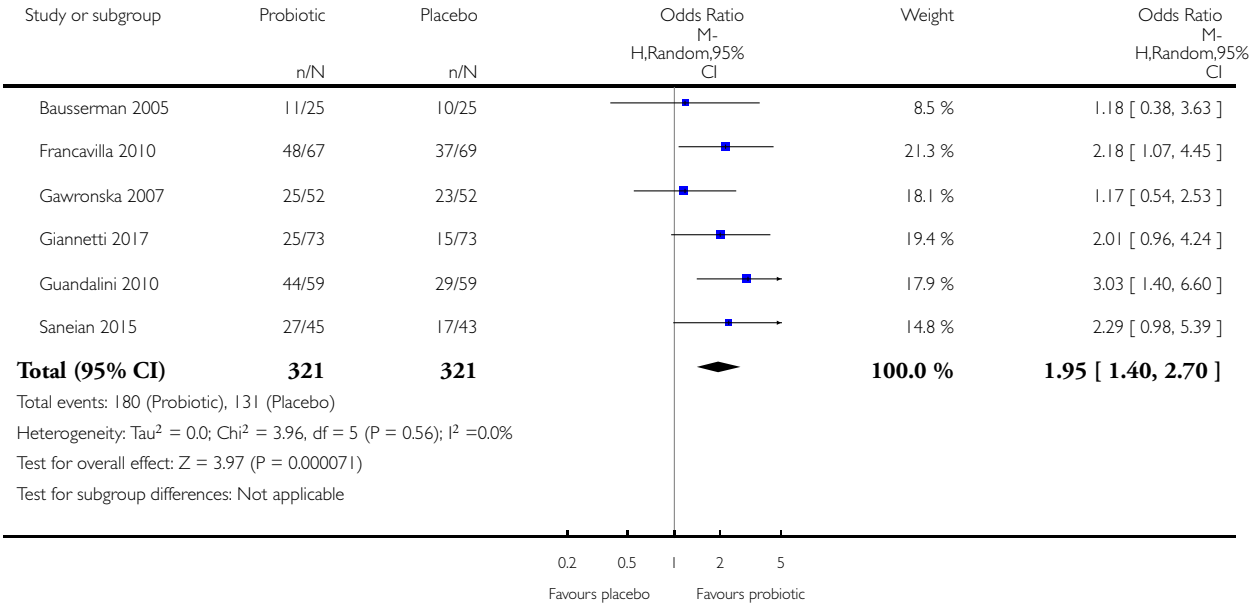
Test for subgroup differences: Not applicable

Analysis 1.6. Comparison 1 Probiotics versus placebo, Outcome 6 Improvement in pain: 0 to 3 months' postintervention. Sensitivity analysis.

Review: Dietary interventions for recurrent abdominal pain in childhood

Comparison: 1 Probiotics versus placebo

Outcome: 6 Improvement in pain: 0 to 3 months' postintervention. Sensitivity analysis



Analysis 1.7. Comparison 1 Probiotics versus placebo, Outcome 7 Improvement in pain: 0 to 3 months' postintervention. Subgroup analysis (irritable bowel syndrome).

Review: Dietary interventions for recurrent abdominal pain in childhood

Comparison: 1 Probiotics versus placebo

Outcome: 7 Improvement in pain: 0 to 3 months' postintervention. Subgroup analysis (irritable bowel syndrome)

Study or subgroup	Probiotic n/N	Placebo n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Bausserman 2005	11/25	10/25		18.9 %	1.18 [0.38, 3.63]
Francavilla 2010	33/42	17/38		23.9 %	4.53 [1.71, 12.02]
Giannetti 2017	20/48	7/48		23.5 %	4.18 [1.56, 11.21]
Guandalini 2010	44/59	29/59		33.8 %	3.03 [1.40, 6.60]
Total (95% CI)	**174**	**170**		**100.0 %**	**3.01 [1.77, 5.13]**
Total events: 108 (Probiotic), 63 (Placebo)					
Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 3.77$, df = 3 (P = 0.29); $I^2 = 21\%$					
Test for overall effect: Z = 4.06 (P = 0.000049)					
Test for subgroup differences: Not applicable					

Analysis 1.8. Comparison 1 Probiotics versus placebo, Outcome 8 Improvement in pain: 3 to 6 months' postintervention.

Review: Dietary interventions for recurrent abdominal pain in childhood

Comparison: 1 Probiotics versus placebo

Outcome: 8 Improvement in pain: 3 to 6 months' postintervention

Study or subgroup	Probiotic n/N	Placebo n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Francavilla 2010	53/67	43/69		55.6 %	2.29 [1.07, 4.92]
Saneian 2015	29/45	23/43		44.4 %	1.58 [0.67, 3.71]
Total (95% CI)	**112**	**112**		**100.0 %**	**1.94 [1.10, 3.43]**

Total events: 82 (Probiotic), 66 (Placebo)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.41$, df = 1 (P = 0.52); $I^2 = 0.0\%$

Test for overall effect: Z = 2.28 (P = 0.023)

Test for subgroup differences: Not applicable

Analysis 2.1. Comparison 2 Fibre versus placebo, Outcome 1 Change in pain intensity: 0 to 3 months' postintervention.

Review: Dietary interventions for recurrent abdominal pain in childhood

Comparison: 2 Fibre versus placebo

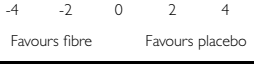
Outcome: 1 Change in pain intensity: 0 to 3 months' postintervention

Study or subgroup	Fibre N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Romano 2013	30	1.63 (0.16)	30	2.05 (0.19)		49.4 %	-2.36 [-3.03, -1.69]
Shulman 2016	33	3.24 (1.58)	42	3.46 (1.55)		50.6 %	-0.14 [-0.60, 0.32]
Total (95% CI)	**63**		**72**			**100.0 %**	**-1.24 [-3.41, 0.94]**

Heterogeneity: $Tau^2 = 2.38$; $Chi^2 = 28.91$, df = 1 (P<0.00001); $I^2 = 97\%$

Test for overall effect: Z = 1.11 (P = 0.27)

Test for subgroup differences: Not applicable

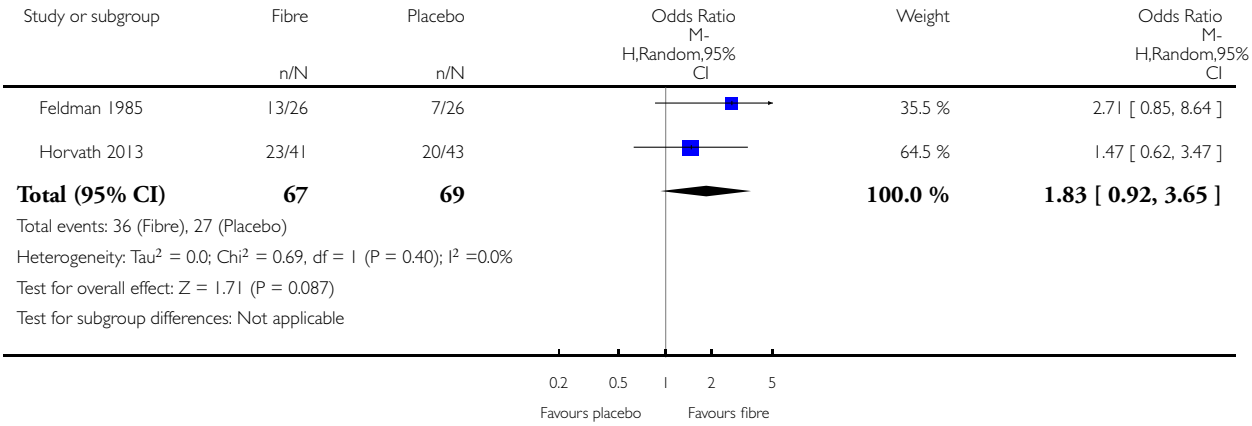


Analysis 2.2. Comparison 2 Fibre versus placebo, Outcome 2 Improvement in pain: 0 to 3 months' postintervention.

Review: Dietary interventions for recurrent abdominal pain in childhood

Comparison: 2 Fibre versus placebo

Outcome: 2 Improvement in pain: 0 to 3 months' postintervention



ADDITIONAL TABLES

Table 1. Assessment of risk of bias in included studies

Domain	'Risk of bias' judgement		
	Low	**High**	**Unclear**
Selection bias			**Selection bias**
Random sequence generation	If the study details any of the following methods: simple randomisation (such as coin-tossing, throwing dice, or dealing previously shuffled cards, a list of random numbers, or com-	If the study details no randomisation or other inadequate method such as alternation, assignment based on date of birth, case record number, and date of presentation. These may be re-	If there is insufficient detail to judge the risk of bias.

Table 1. Assessment of risk of bias in included studies (*Continued*)

	puter-generated random numbers) or restricted randomisation (blocked, ideally with varying block sizes or stratified groups, provided that within-groups randomisation is not affected)	ferred to as 'quasi-random'	
Allocation concealment	If the study details concealed allocation sequence in sufficient detail to determine that allocations could not have been foreseen in advance of or during enrolment	If the study details a method where the allocation is known prior to assignment	If there is insufficient detail to judge the risk of bias.
Performance bias			**Performance bia**
Blinding of participants and personnel	If the study details a method of blinding the participants and personnel. This requires sufficient detail to show they were unable to identify the therapeutic intervention from the control intervention	Considering the nature of the interventions, it may not be possible to blind the participants and therapists. The effect of this will be addressed in the Discussion	If there is insufficient detail to judge the risk of bias.
Detection bias			**Detection bias**
Blinding of outcome assessment	If the study details a blinded outcome assessment. This may only be possible for outcomes that are externally assessed	If the outcome assessment is not blinded. We expect this may be unavoidable for self rated outcomes of unblinded interventions	If there is insufficient detail to judge the risk of bias.
Attrition bias			**Attrition bias**
Incomplete outcome data	If the study reports attrition and exclusions, including the numbers in each intervention group (compared with total randomised participants), reasons for attrition or exclusions, and any re-inclusions. Also, the impact of missing data is not believed to alter the conclusions, and there are acceptable reasons for the missing data	We may judge the risk of attrition bias to be high due to the amount, nature, or handling (such as per-protocol analysis) of incomplete outcome data	If there is insufficient detail to judge the risk of bias, e.g. if the number of people randomised to each treatment is not reported
Reporting bias			**Reporting bias**

Table 1. Assessment of risk of bias in included studies (*Continued*)

Selective outcome reporting	If there is judged to be complete reporting, which will be found on comparison of the published study and protocol, if available	If the reporting is selective, so that some outcome data are not reported	If there is insufficient detail to judge the risk of bias, such as the protocol is not available
Other sources of bias			**Other sources o**
Assessment of other sources of bias in other domains not covered by the tool, including validity of outcome measures utilised	If there is judged to be no other factors that would be likely to introduce major potential bias	If other factors are identified that are judged to represent a high risk of bias	If there is insufficient detail to judge the risk of other bias

APPENDICES

Appendix 1. Search strategies

Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 5) in t*he Cochrane Library*

Search dates: 19 April 2013 (990 records); 11 April 2014 (1271 records); 26 March 2015 (49 records); 10 June 2016 (81 records).
#1 Pain*:ti,ab
#2 Ache*:ti,ab
#3 Sore*:ti,ab
#4 Discomfort*:ti,ab
#5 Distress*:ti,ab
#6 Cramp*:ti,ab
#7 Disorder:ti,ab
#8 Disorders:ti,ab
#9 Symptom:ti,ab
#10 Symptoms:ti,ab
#11 Migraine:ti,ab
#12 Migraines:ti,ab
#13 Epilep*:ti,ab
#14 Colic*:ti,ab
#15 Syndrome:ti,ab
#16 Syndromes:ti,ab
#17 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16
#18 Stomach*:ti,ab
#19 Abdom*:ti,ab
#20 Intestin*:ti,ab
#21 Viscera*:ti,ab
#22 Tummy:ti,ab
#23 Bowel*:ti,ab
#24 Belly:ti,ab

#25 Gastrointestinal:ti,ab
#26 GI:ti,ab
#27 Gastric:ti,ab
#28 #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27
#29 #17 and #28
#30 Colonic disease*:ti,ab
#31 Irritable bowel:ti,ab
#32 IBS:ti,ab
#33 Functional dyspepsia:ti,ab
#34 MeSH descriptor: [Irritable Bowel Syndrome] explode all trees
#35 MeSH descriptor: [Colonic Diseases, Functional] explode all trees
#36 MeSH descriptor: [Abdominal Pain] explode all trees
#37 MeSH descriptor: [Dyspepsia] explode all trees
#38 MeSH descriptor: [Colic] explode all trees
#39 MeSH descriptor: [Abdomen, Acute] explode all trees
#40 #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39
#41 Recurr*:ti,ab
#42 Chronic*:ti,ab
#43 Intermittent*:ti,ab
#44 Episode*:ti,ab
#45 Bout:ti,ab
#46 Bouts:ti,ab
#47 Spasm*:ti,ab
#48 Transitory:ti,ab
#49 Transient:ti,ab
#50 Functional:ti,ab
#51 Continu*:ti,ab
#52 Paroxysmal:ti,ab
#53 Persistent:ti,ab
#54 Idiopathic:ti,ab
#55 Unspecifi*:ti,ab
#56 Non specifi*:ti,ab
#57 Nonspecific*:ti,ab
#58 Motility:ti,ab
#59 MeSH descriptor: [Recurrence] explode all trees
#60 #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59
#61 #40 and #60
#62 irritable bowel syndrome*:ti,ab
#63 #61 or #62
#64 Child*:ti,ab
#65 Adolescen*:ti,ab
#66 Boy*:ti,ab
#67 Girl*:ti,ab
#68 teen*:ti,ab
#69 Schoolchild*:ti,ab
#70 Young adult*:ti,ab
#71 Youth*:ti,ab
#72 Pediatric*:ti,ab
#73 Paediatric*:ti,ab
#74 Student*:ti,ab
#75 Pupil*:ti,ab
#76 Juvenile*:ti,ab

#77 Young person*:ti,ab
#78 MeSH descriptor: [Child] explode all trees
#79 MeSH descriptor: [Adolescent] explode all trees
#80 MeSH descriptor: [Young Adult] explode all trees
#81 MeSH descriptor: [Students] explode all trees
#82 #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80 or #81
#83 #63 and #82

Ovid MEDLINE In-Process & Other Non-Indexed Citations and Ovid Medline (1946 to current)

Search dates: 11 April 2013 (6238 records); 11 April 2014 (5957 records); 25 March 2015 (223 records); 9 June 2016 (300 records).
1 stomach*.tw.
2 abdom*.tw.
3 intestin*.tw.
4 viscera*.tw.
5 tummy.tw.
6 bowel*.tw.
7 belly.tw.
8 gastrointestinal.tw.
9 gi.tw.
10 gastric.tw.
11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12 pain*.tw.
13 Ache*.tw.
14 Sore*.tw.
15 Discomfort*.tw.
16 Distress*.tw.
17 Cramp*.tw.
18 Disorder$1.tw.
19 Symptom$1.tw.
20 Migraine$1.tw.
21 Epilep*.tw.
22 syndrome$1.tw.
23 colic*.tw.
24 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25 irritable bowel$.tw.
26 ibs.tw.
27 functional dyspepsia.tw.
28 25 or 26 or 27
29 ((stomach* or abdom* or intestin* or viscera* or tummy or bowel* or belly or gastrointestinal or gi or gastric) adj3 (pain* or Ache* or Sore* or Discomfort* or Distress* or Cramp* or Disorder$1 or Symptom$1 or Migraine$1 or Epilep* or syndrome$1 or colic*)).tw.
30 exp Irritable Bowel Syndrome/
31 exp Colonic Diseases/
32 exp Abdominal Pain/
33 exp Dyspepsia/
34 exp Colic/
35 exp Abdomen, Acute/
36 30 or 31 or 32 or 33 or 34 or 35
37 28 or 29 or 36
38 Recurr*.tw.
39 Chronic*.tw.
40 Intermittent*.tw.
41 Bout$1.tw.

42 spasm*.tw.
43 Transitory.tw.
44 Transient.tw.
45 Functional.tw.
46 Continu*.tw.
47 Paroxysmal.tw.
48 Persistent.tw.
49 Idiopathic.tw.
50 unspecifi*.tw.
51 Non specifi*.tw.
52 nonspecifi*.tw.
53 motility.tw.
54 episod*.tw.
55 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54
56 exp Recurrence/
57 55 or 56
58 37 and 57
59 irritable bowel syndrome*.tw.
60 58 or 59
61 randomized controlled trial.pt.
62 controlled clinical trial.pt.
63 randomi#ed.ab.
64 placebo$.ab.
65 randomly.ab.
66 trial.ab.
67 groups.ab.
68 exp animals/ not humans.sh.
69 or/61-67
70 69 not 68
71 60 and 70
72 exp Child/
73 exp Adolescent/
74 exp Young Adult/
75 exp Students/
76 Child*.tw.
77 Adolescen*.tw.
78 Young person*.tw.
79 Boy*.tw.
80 Girl*.tw.
81 teen*.tw.
82 Schoolchild*.tw.
83 Young adult*.tw.
84 Youth*.tw.
85 P*ediatric*.tw.
86 Student*.tw.
87 Pupil*.tw.
88 Juvenile*.tw.
89 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88
90 71 and 89

Embase Ovid (1974 to current)

Search dates: 11 April 2013 (2272 records); 11 April 2014 (2523 records); 25 March 2015 (250 records); 9 June 2016 (345 records).

1 recurr*.tw.
2 chronic*.tw.
3 intermittent*.tw.
4 bout$1.tw.
5 spasm*.tw.
6 transitory.tw.
7 transient.tw.
8 functional.tw.
9 continu*.tw.
10 paroxysmal.tw.
11 persistent.tw.
12 idiopathic.tw.
13 unspecifi*.tw.
14 non specifi*.tw.
15 nonspecifi*.tw.
16 motility.tw.
17 episod*.tw.
18 or/1-17
19 exp recurrent disease/
20 18 or 19
21 stomach*.tw.
22 abdom*.tw.
23 intestin*.tw.
24 viscera*.tw.
25 tummy.tw.
26 bowel*.tw.
27 belly.tw.
28 gastrointestinal.tw.
29 gi.tw.
30 gastric.tw.
31 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32 pain*.tw.
33 Ache*.tw.
34 Sore*.tw.
35 Discomfort*.tw.
36 Distress*.tw.
37 Cramp*.tw.
38 Disorder$1.tw.
39 Symptom$1.tw.
40 Migraine$1.tw.
41 Epilep*.tw.
42 syndrome$1.tw.
43 colic*.tw.
44 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43
45 irritable bowel$.tw.
46 ibs.tw.
47 functional dyspepsia.tw.
48 45 or 46 or 47
49 ((stomach* or abdom* or intestin* or viscera* or tummy or bowel* or belly or gastrointestinal or gi or gastric) adj3 (pain* or Ache* or Sore* or Discomfort* or Distress* or Cramp* or Disorder$1 or Symptom$1 or Migraine$1 or Epilep* or syndrome$1 or colic*)).tw.
50 48 or 49
51 exp colic/
52 exp irritable colon/

53 exp abdominal pain/
54 exp dyspepsia/
55 colon disease/
56 50 or 51 or 52 or 53 or 54 or 55
57 20 and 56
58 irritable bowel syndrome*.tw.
59 57 or 58
60 Clinical trial/
61 Randomized controlled trial/
62 Randomization/
63 Single blind procedure/
64 Double blind procedure/
65 Crossover procedure/
66 Placebo/
67 Randomi?ed controlled trial$.tw.
68 Rct.tw.
69 Random allocation.tw.
70 Randomly allocated.tw.
71 Allocated randomly.tw.
72 (allocated adj2 random).tw.
73 Single blind$.tw.
74 Double blind$.tw.
75 ((treble or triple) adj blind$).tw.
76 Placebo$.tw.
77 Prospective study/
78 or/60-77
79 Case study/
80 Case report.tw.
81 Abstract report/ or letter/
82 or/79-81
83 78 not 82
84 59 and 83
85 exp Child/
86 exp Adolescent/
87 exp Young Adult/
88 exp Students/
89 Child*.tw.
90 Adolescen*.tw.
91 Young person*.tw.
92 Boy*.tw.
93 Girl*.tw.
94 teen*.tw.
95 Schoolchild*.tw.
96 Young adult*.tw.
97 Youth*.tw.
98 P*ediatric*.tw.
99 Student*.tw.
100 Pupil*.tw.
101 Juvenile*.tw.
102 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101
103 84 and 102

CINAHL Healthcare Databases Advanced Search (Cumulative Index to Nursing and Allied Health Literature; 1981 to current)

Search dates: 18 April 2013 (175 records); 11 April 2014 (195 records); 26 March 2015 (21 records); 9 June 2016 (11 records).
1. CINAHL; recurr*.ti,ab;
2. CINAHL; chronic*.ti,ab;
3. CINAHL; intermittent*.ti,ab;
4. CINAHL; (bout OR bouts).ti,ab;
5. CINAHL; spasm*.ti,ab;
6. CINAHL; transitory.ti,ab;
7. CINAHL; transient.ti,ab;
8. CINAHL; functional.ti,ab;
9. CINAHL; continu*.ti,ab;
10. CINAHL; paroxysmal.ti,ab;
11. CINAHL; persistent.ti,ab;
12. CINAHL; idiopathic.ti,ab;
13. CINAHL; unspecifi*.ti,ab;
14. CINAHL; "non specifi*".ti,ab;
15. CINAHL; nonspecifi*.ti,ab;
16. CINAHL; motility.ti,ab;
17. CINAHL; episod*.ti,ab;
18. CINAHL; exp RECURRENCE/;
19. CINAHL; 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18;
20. CINAHL; stomach*.ti,ab;
21. CINAHL; abdom*.ti,ab;
22. CINAHL; intestin*.ti,ab;
23. CINAHL; viscera*.ti,ab;
24. CINAHL; tummy.ti,ab;
25. CINAHL; bowel*.ti,ab;
26. CINAHL; belly.ti,ab;
27. CINAHL; gastrointestinal.ti,ab;
28. CINAHL; gi.ti,ab;
29. CINAHL; gastric.ti,ab;
30. CINAHL; 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29;
31. CINAHL; pain*.ti,ab;
32. CINAHL; Ache*.ti,ab;
33. CINAHL; Sore*.ti,ab;
34. CINAHL; Discomfort*.ti,ab;
35. CINAHL; Distress*.ti,ab;
36. CINAHL; Cramp*.ti,ab;
37. CINAHL; (Disorder OR Disorders).ti,ab;
38. CINAHL; (Symptom OR Symptoms).ti,ab;
39. CINAHL; (Migraine OR Migraines).ti,ab;.
40. CINAHL; Epilep*.ti,ab;
41. CINAHL; (syndrome OR syndromes).ti,ab;
42. CINAHL; colic*.ti,ab;
43. CINAHL; 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42;
44. CINAHL; 30 AND 43;
45. CINAHL; "irritable bowel*".ti,ab;
46. CINAHL; ibs.ti,ab;
47. CINAHL; "functional dyspepsia".ti,ab;
48. CINAHL; exp COLIC/;
49. CINAHL; exp IRRITABLE BOWEL SYNDROME/;

50. CINAHL; exp COLONIC DISEASES, FUNCTIONAL/;
51. CINAHL; exp ABDOMINAL PAIN/;
52. CINAHL; exp DYSPEPSIA/;
53. CINAHL; 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52;
54. CINAHL; 44 OR 53;
55. CINAHL; 19 AND 54;
56. CINAHL; (irritable AND bowel AND syndrome*).ti,ab;
57. CINAHL; 55 OR 56;
58. CINAHL; Child*.ti,ab;
59. CINAHL; Adolescen*.ti,ab;
60. CINAHL; "Young person*".ti,ab;
61. CINAHL; Boy*.ti,ab;
62. CINAHL; Girl*.ti,ab;
63. CINAHL; teen*.ti,ab;
64. CINAHL; Schoolchild*.ti,ab;
65. CINAHL; "Young adult*".ti,ab;
66. CINAHL; Youth*.ti,ab;
67. CINAHL; Student*.ti,ab;
68. CINAHL; Pupil*.ti,ab;
69. CINAHL; Juvenile*.ti,ab;
70. CINAHL; exp CHILD/;
71. CINAHL; exp STUDENTS/;
72. CINAHL; 70 OR 71;
73. CINAHL; Pediatric*.ti,ab;
74. CINAHL; Paediatric*.ti,ab;
75. CINAHL; 67 OR 68 OR 69 OR 72 OR 73 OR 74;
76. CINAHL; 63 OR 64 OR 65 OR 66;
77. CINAHL; 58 OR 59 OR 60 OR 61 OR 62;
78. CINAHL; 70 OR 73 OR 74 OR 75;
79. CINAHL; 57 AND 78;
80. CINAHL; exp RANDOMIZED CONTROLLED TRIALS/;
81. CINAHL; random*.ti,ab;
82. CINAHL; "clin* trial*".ti,ab;
83. CINAHL; (singl* OR doubl* OR tripl* OR trebl*).ti,ab;
84. CINAHL; (mask* OR blind*).ti,ab;
85. CINAHL; 83 AND 84;
86. CINAHL; "random* allocate*".ti,ab;
87. CINAHL; "random assign*".ti,ab;
88. CINAHL; exp RANDOM ASSIGNMENT/;
89. CINAHL; exp CLINICAL TRIALS/;
90. CINAHL; exp META ANALYSIS/;
91. CINAHL; 88 OR 89 OR 90;
92. CINAHL; 80 OR 81 OR 82 OR 85 OR 86 OR 87;
93. CINAHL; 91 OR 92;
94. CINAHL; 79 AND 93;

PsycINFO Ovid (1806 to current)

Search dates: 18 April 2013 (238 records); 11 April 2014 (757 records); 25 March 2015 (47 records); 9 June 2016 (87 records).
1 stomach*.tw.
2 abdom*.tw.
3 intestin*.tw.
4 viscera*.tw.

5 tummy.tw.
6 bowel*.tw.
7 belly.tw.
8 gastrointestinal.tw.
9 gi.tw.
10 gastric.tw.
11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12 pain*.tw.
13 Ache*.tw.
14 Sore*.tw.
15 Discomfort*.tw.
16 Distress*.tw.
17 Cramp*.tw.
18 Disorder$1.tw.
19 Symptom$1.tw.
20 Migraine$1.tw.
21 Epilep*.tw.
22 syndrome$1.tw.
23 colic*.tw.
24 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25 irritable bowel$.tw.
26 ibs.tw.
27 functional dyspepsia.tw.
28 25 or 26 or 27
29 ((stomach* or abdom* or intestin* or viscera* or tummy or bowel* or belly or gastrointestinal or gi or gastric) adj3 (pain* or Ache* or Sore* or Discomfort* or Distress* or Cramp* or Disorder$1 or Symptom$1 or Migraine$1 or Epilep* or syndrome$1 or colic*)).tw.
30 exp Irritable Bowel Syndrome/
31 exp Dyspepsia/
32 recurr*.tw.
33 chronic*.tw.
34 intermittent*.tw.
35 bout$1.tw.
36 spasm*.tw.
37 transitory.tw.
38 transient.tw.
39 functional.tw.
40 continu*.tw.
41 paroxysmal.tw.
42 persistent.tw.
43 idiopathic.tw.
44 unspecifi*.tw.
45 non specifi*.tw.
46 nonspecifi*.tw.
47 motility.tw.
48 episod*.tw.
49 or/32-48
50 irritable bowel syndrome*.tw.
51 exp Students/
52 Child*.tw.
53 Adolescen*.tw.
54 Young person*.tw.
55 Boy*.tw.
56 Girl*.tw.

57 teen*.tw.
58 Schoolchild*.tw.
59 Young adult*.tw.
60 Youth*.tw.
61 P*ediatric*.tw.
62 Student*.tw.
63 Pupil*.tw.
64 Juvenile*.tw.
65 28 or 29 or 30 or 31
66 49 and 65
67 50 or 66
68 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64
69 67 and 68

ERIC ProQuest (Education Resources Information Center; 1966 to current)

Search dates: 19 April 2013 (276 records); 11 April 2014 (294 records); 26 March 2015 (no records); 9 June 2016 (2 records).
(ab,ti(Pain*) OR ab,ti(Ache*) OR ab,ti(Sore*) OR ab,ti(Discomfort*) OR ab,ti(Distress*) OR ab,ti(Cramp*) OR ab,ti(Disorder) OR ab,ti(Disorders) OR ab,ti(Symptom*) OR ab,ti(Migraine*) OR ab,ti(Epilep*) OR ab,ti(Colic*) OR ab,ti(Syndrome*))
AND
(Ab,ti(Recurr*) OR ab,ti(Chronic*) OR ab,ti(Intermittent*) OR ab,ti(Episode*) OR ab,ti(Bout) OR ab,ti(Bouts) OR ab,ti((Spasm*) OR ab,ti(Transitory) OR ab,ti(Transient) OR ab,ti(Functional) OR ab,ti(Continu*) OR ab,ti(paroxysmal) OR ab,ti(Persistent) OR ab,ti (Idiopathic) OR ab,ti(Unspecifi*) OR ab,ti(Non specifi*) OR ab,ti(motility) OR SU.EXACT.EXPLODE("Recurrence"))
AND
(Ab,ti(Stomach*) OR ab,ti(Abdom*) OR ab,ti(Sore*) OR ab,ti(Intestin*) OR ab,ti(Viscera*) OR ab,ti(Tummy) OR ab,ti(Bowel*) OR ab,ti(Belly) OR ab,ti(Gastrointestinal) OR ab,ti(GI) OR ab,ti(Epilep*) OR ab,ti(Gastric))
OR
(Ab,ti(irritable bowel*) OR ab,ti(ibs) OR ab,ti(colonic disease*) OR ab,ti(functional dyspepsia))

British Education Index ProQuest (1975 to current)

Search dates: 19 April 2013 (46 records); 11 April 2014 (48 records); 26 March 2015 (no records); 9 June 2016 (5 records).
((ab,ti(Stomach*) OR ab,ti(Abdom*) OR ab,ti(Intestin*) OR ab,ti(Viscera*) OR ab,ti(Tummy) OR ab,ti(Bowel*) OR ab,ti(Belly) OR ab,ti(Gastrointestinal) OR ab,ti(GI) OR ab,ti(Gastric))
AND
((ab,ti(Pain*) OR ab,ti(Ache*) OR ab,ti(Sore*) OR ab,ti(Discomfort*) OR ab,ti(Distress*) OR ab,ti(Cramp*) OR ab,ti(Disorder) OR ab,ti(Disorders) OR ab,ti(Symptom) OR OR ab,ti(Symptoms) OR ab,ti(Migraine) OR ab,ti(Migraines) OR ab,ti(Epilep*) OR ab,ti(Colic*) OR ab,ti(Syndrome) OR ab,ti(Syndromes))
OR
(Ab,ti(irritable bowel*) OR ab,ti(ibs) OR ab,ti(Functional dyspepsia))

ASSIA (Applied Social Sciences Index and Abstracts ProQuest; 1987 to current)

Search dates: 19 April 2013 (179 records); 11 April 2014 (545 records); 26 March 2015 (27 records); 9 June 2016 (48 records).
((ab,ti(Stomach*) OR ab,ti(Abdom*) OR ab,ti(Intestin*) OR ab,ti(Viscera*) OR ab,ti(Tummy) OR ab,ti(Bowel*) OR ab,ti(Belly) OR ab,ti(Gastrointestinal) OR ab,ti(GI) OR ab,ti(gastric)
AND
(ab,ti(Pain*) OR ab,ti(Ache*) OR ab,ti(Sore*) OR ab,ti(Discomfort*) OR ab,ti(Distress*) OR ab,ti(Cramp*) OR ab,ti(Disorder) OR ab,ti(Disorders) OR ab,ti(Symptom*) OR ab,ti(Symptoms) OR ab,ti(Migraine*) OR ab,ti(Epilep*) OR ab,ti(Syndrome) OR ab,ti(Syndromes) OR ab,ti(colic*)
AND
(ab,ti(Recurr*) OR ab,ti(Chronic*) OR ab,ti(Intermittent*) OR ab,ti(Episode*) OR ab,ti(Bout) OR ab,ti(bouts) OR ab,ti(Spasm*) OR ab,ti(Transitory) OR ab,ti(Transient) OR ab,ti(Functional) OR ab,ti(Continu*) OR ab,ti(Paroxysmal) OR ab,ti(Persistent) OR ab,ti(Idiopathic) OR ab,ti(Unspecifi*) OR ab,ti(Non specifi*) OR ab,ti(motility))

OR
(ab,ti(irritable bowel) OR ab,ti(ibs) OR ab,ti(functional dyspepsia))

Allied and Complementary Medicine Healthcare Databases Advanced Search (AMED; 1985 to current)

Search dates: 18 April 2013 (63 records); 11 April 2014 (74 records); 25 March 2015 (1 record); 9 June 2016 (1 record).
1. AMED; Recurr*.ti,ab;
2. AMED; Chronic*.ti,ab;
3. AMED; Intermittent*.ti,ab;
4. AMED; Episod*.ti,ab;
5. AMED; (Bout OR Bouts).ti,ab;
6. AMED; Spasm*.ti,ab;
7. AMED; Transitory.ti,ab;
8. AMED; Transient.ti,ab;
9. AMED; Functional.ti,ab;
10. AMED; Continu*.ti,ab;
11. AMED; Paroxysmal.ti,ab;
12. AMED; Persistent.ti,ab;
13. AMED; Idiopathic.ti,ab;
14. AMED; Unspecifi*.ti,ab;
15. AMED; "Non specifi*".ti,ab;
16. AMED; Nonspecific*.ti,ab;
17. AMED; Motility.ti,ab;
18. AMED; exp RECURRENCE/;
19. AMED; 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18;.
20. AMED; Pain*.ti,ab;
21. AMED; Ache*.ti,ab;
22. AMED; Sore*.ti,ab;
23. AMED; Discomfort*.ti,ab;
24. AMED; Distress*.ti,ab;
25. AMED; Cramp*.ti,ab;
26. AMED; (Disorder OR Disorders).ti,ab;
27. AMED; (Symptom OR Symptoms).ti,ab;
28. AMED; (Migraine OR Migraines).ti,ab;
29. AMED; Epilep*.ti,ab;
30. AMED; Colic*.ti,ab;
31. AMED; (Syndrome OR Syndromes).ti,ab;
32. AMED; 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31;
33. AMED; Stomach*.ti,ab;
34. AMED; Abdom*.ti,ab;
35. AMED; Intestin*.ti,ab;
36. AMED; Viscera*.ti,ab;
37. AMED; Tummy.ti,ab;
38. AMED; Bowel*.ti,ab;
39. AMED; Belly.ti,ab;
40. AMED; Gastrointestinal.ti,ab;
41. AMED; GI.ti,ab;
42. AMED; Gastric.ti,ab;
43. AMED; 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42;
44. AMED; 32 AND 43;
45. AMED; "Colonic disease*".ti,ab;
46. AMED; "Irritable bowel".ti,ab;
47. AMED; IBS.ti,ab; 86

48. AMED; "Functional dyspepsia".ti,ab;
49. AMED; exp IRRITABLE BOWEL SYNDROME/;
50. AMED; exp COLONIC DISEASE/;
51. AMED; exp ABDOMINAL PAIN/;
52. AMED; exp DYSPEPSIA/;
53. AMED; 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52;
54. AMED; 44 OR 53;
55. AMED; 19 AND 54;
56. AMED; (irritable AND bowel AND syndrome*).ti,ab;
57. AMED; Child*.ti,ab;
58. AMED; Adolescen*.ti,ab;
59. AMED; Boy*.ti,ab;
60. AMED; Girl*.ti,ab;
61. AMED; teen*.ti,ab;
62. AMED; Schoolchild*.ti,ab;
63. AMED; "Young adult*".ti,ab;
64. AMED; Youth*.ti,ab; 767 results.
65. AMED; (Pediatric* OR Paediatric*).ti,ab;
66. AMED; Student*.ti,ab;
67. AMED; Pupil*.ti,ab;
68. AMED; Juvenile*.ti,ab;
69. AMED; "Young person*".ti,ab;
70. AMED; exp CHILD/;
71. AMED; exp ADOLESCENT/;
72. AMED; exp STUDENTS/;
73. AMED; 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69 OR 70 OR 71 OR 72;
74 AMED; 55 OR 56;
75. AMED; 74 AND 73;

LILACS (Latin American and Caribbean Health Science Information database; lilacs.bvsalud.org/en/)

Search dates: 19 April 2013 (11 records); 11 April 2014 (13 records); 26 March 2015 (no records); 9 June 2016 (no records).
((Pt randomized controlled trial OR Pt controlled clinical trial OR Mh randomized controlled trials OR Mh random allocation OR Mh double-blind method OR Mh single-blind method) AND NOT (Ct animal AND NOT (Ct human and Ct animal)) OR (Pt clinical trial OR Ex E05.318.760.535$ OR (Tw clin$ AND (Tw trial$ OR Tw ensa$ OR Tw estud$ OR Tw experim$ OR Tw investiga$)) OR ((Tw singl$ OR Tw simple$ OR Tw doubl$ OR Tw doble$ OR Tw duplo$ OR Tw trebl$ OR Tw trip$) (trial$ OR ensa$ OR estud$ OR experim$ OR investiga$ OR singl$ OR simple$ OR Tw doubl$ OR Tw doble$ OR Tw duplo$ OR Tw trebl$ OR Tw trip$) AND (Tw blind$ OR Tw cego$ OR Tw ciego$ OR Tw mask$ OR Tw mascar$)) OR Mh placebos OR Tw placebo$ OR (Tw random$ OR Tw randon$ OR Tw casual$ OR Tw acaso$ OR Tw azar OR Tw aleator$) OR Mh research design) AND NOT (Ct animal AND NOT (Ct human and Ct animal)) OR (Ct comparative study OR Ex E05.337$ OR Mh follow-up studies OR Mh prospective studies OR Tw control$ OR Tw prospectiv$ OR Tw volunt$ OR Tw volunteer$) AND NOT (Ct animal AND NOT (Ct human and Ct animal))) [Palavras]
and ((recurr$ or chronic$ or intermittent$ or bout or bouts or spasm$ or transitory or transient or functional or continu$ or Paroxysmal or Persistent or Idiopathic or unspecifi$ or Non specifi$ or nonspecific$ or motility or episode$) [Palavras] and (pain$ or ache$ or sore$ or discomfort$ or distress$ cramp$ or colic$ or disorder or disorders or symptom or symptoms or Migraine$ or Epilep* or syndrome$) and (stomach$ or abdom$ or intestin$ or viscera$ or tummy$ or bowel$ or belly or gastrointestinal or gi or gastric)) [Palavras]

OpenGrey (www.opengrey.eu)

Search dates : 19 April 2013 (1 record); 11 April 2014 (1 record); 26 March 2015 (no records); 9 June 2016 (no records).
Irritable bowel syndrom*
Ibs
functional dyspepsia

Chronic* AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
Recurr* AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
Intermittent* AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
Bout* AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
spasm* AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
Transitory AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
Transient AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
Functional AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
Continu* AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
Paroxysmal AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
Persistent AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
Idiopathic AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
unspecifi* AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
Non specifi* AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
nonspecifi* AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
motility AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))
episod* AND (abdom* OR stomach* OR intestin* OR viscera* OR tummy OR bowel* OR belly or gastrointestinal OR gi OR gastric))

ClinicalTrials.gov (clinicaltrials.gov/)

Search dates: 11 April 2014 (69 records); 26 March 2015 (35 records); 9 June 2016 (62 records).
"irritable bowel" OR "abdominal pain" in the condition field. Limited to children.

World Health Organization International Clinical Trials Registry Platform (WHO ICTRP; apps.who.int/trialsearch)

Search dates: 11 April 2014 (106 records); 26 March 2015 (4 records); 9 June 2016 (32 records).
"irritable bowel" OR "abdominal pain" in the condition field. Limited to children and interventional studies.

Appendix 2. Additional methods

The table below provides details of analyses that had been planned and described in the protocol (Martin 2014b), but were not employed as they were not required.

Method planned for data analysis		Reason for non-use
Unit of analysis issues	**Cluster-randomised trials** Cluster-randomised trials randomise groups of people rather than individuals. For each cluster-randomised trial, we will first determine whether or not the data incorporates sufficient controls for clustering (such as robust standard errors or hierarchical linear models). If data do not have proper controls, we will then attempt to obtain an appropriate estimate of the data's intracluster correlation coefficient. If we cannot find an estimate in the report of the trial, then we will request an estimate from the trial report authors. If the authors do not provide an estimate, if possible, we will obtain one from a similar study and conduct a sensitivity analysis to determine if the results are robust when different values are imputed. We will do this according to procedures described in Higgins 2011b.	No cluster-randomised trials of dietary interventions were located
	Trials with multiple intervention groups This is a common scenario. To avoid any unit of analysis errors in the meta-analysis, we will use the following approach for a study that could contribute multiple comparisons 1. The interventions will only be analysed together if they are clinically similar. In this situation, the control group will not be split, but the intervention groups will be combined to enable a single pair-wise comparison for the meta-analysis. If the interventions are similar enough to be in a single meta-analysis but not able to be combined, then the control group will be split. If the interventions are not similar, the data will be used in separate meta-analyses.	No multiple intervention group trials were located.
Assessment of reporting biases	**Publication bias** If we identify sufficient trials (at least 10) , we will use the outcome data to produce a funnel plot to investigate the likelihood	We did not identify 10 or more trials for any single outcome within any particular type of dietary intervention

(*Continued*)

	of overt publication bias (Sutton 2000). Any asymmetry of the funnel plot may indicate possible publication bias. We will explore other reasons for asymmetry such as poor methodological quality or heterogeneity. We will look for publication bias by comparing the results of the published and unpublished data	
Subgroup analysis and investigation of heterogeneity	We will undertake subgroup analysis by the duration of follow-up: immediate outcome measurement (less than three months), medium term (three to 12 months), and long term (greater than 12 months)	We were able to perform analyses for immediate outcome measurement. However, due to a lack of trials reporting longer durations of follow-up, we could only perform one analysis at medium-term follow-up
Sensitivity analyses	Where data allow, we will perform sensitivity analyses to assess the robustness of conclusions in relation to two aspects of study design: 1. the effect of inadequate allocation concealment, by the removal of studies judged as high or unclear risk of bias for this domain; and 2. the effect of inadequate blinding to treatment allocation by outcome assessors, by the removal of studies judged as high or unclear risk of bias for this domain.	We were only able to perform sensitivity analyses for three probiotic intervention outcomes. There were insufficient data to perform any sensitivity analyses for fibre-based intervention outcomes

WHAT'S NEW

Last assessed as up-to-date: 9 June 2016.

Date	Event	Description
12 December 2016	New citation required and conclusions have changed	The inclusion of 15 new studies changed the conclusions from those of the previous 2009 review, which found no evidence to support any intervention. We found moderate-quality evidence to support the use of probiotics in recurrent abdominal pain
12 December 2016	New search has been performed	Updated following a new search in April 2013 and updated searches in April 2014, March 2015, and June 2016

CONTRIBUTIONS OF AUTHORS

Review design: AEM, SL

Review co-ordination: AEM

Data collection:

- Search strategy design: AEM, AB
- Searches: AEM, AB
- Search results screening: TVN, AEM, RAA, AB, RW. JTC resolved disagreements.
- Retrieval of papers: AEM, AB
- Paper screening and appraisal, and extraction of data: TVN, AEM, RAA, AB, JTC, RW
- Writing to authors for additional information: TVN, AEM, AB, RW
- Entering the data into Review Manager 5: TVN, AEM, RAA, AB, JTC

Analysis of the data: TVN, AEM, RAA, AB, JTC, SL

Interpretation of the data: TVN, AEM, RAA, SL

- Methodological perspective: TVN, AEM, RAA, AB, JTC, RW
- Clinical perspective: TVN, AEM, SL

DECLARATIONS OF INTEREST

The work of the evidence synthesis team is funded by the National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care South West Peninsula (PenCLAHRC). However, the Funder had no role in the review itself.

Tamsin V Newlove-Delgado: none known.

Alice E Martin: none known.

Rebecca A Abbott: none known.

Alison Bethel: none known.

Joanna Thompson-Coon: none known.

Rebecca Whear: none known

Stuart Logan: none known.

The authors who practice clinical paediatrics are Alice E Martin and Stuart Logan. Alice is a Paediatric Trainee and works under the guidance of various Consultant Paediatricians. Stuart is a Consultant Paediatrician and treats children according to current best evidence, in light of their preference. There are therefore no conflicts of interest with this review.

SOURCES OF SUPPORT

Internal sources

- None, Other.

External sources

- None, Other.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Rebecca Whear was added to the review team after registration of the protocol (Martin 2014b). She was involved in screening abstracts and full texts, data extraction, writing to authors, and contributed to discussions pertaining to methods.

Due to the varying definitions of duration of follow-up used in some studies, we classified when outcomes were measured into three groups: postintervention (immediately or the earliest data available following the end of treatment), medium-term follow-up (three to six months' postintervention), and long-term follow-up (six months or longer). This is a slight change from the protocol (Martin 2014b), in which we planned to use four groups: immediate outcome measurement, short term (less than three months), medium term (three to 12 months), and long term (greater than 12 months).

We reported adverse effects, in line with advice in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011c).

As requested by the editors, we also reported Tau² when using the random-effects model, which provides an estimate of the between-study variance.

NOTES

This is a new review, which supersedes a previously published review (Huertas-Ceballos 2009).