

Constipation in children: fibre and probiotics

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ABSTRACT

INTRODUCTION: Prevalence of childhood constipation has been estimated at 1% to 30% in the general population worldwide; most children have no obvious aetiological factors. One third of children with chronic constipation continue to have problems beyond puberty. Half of the children with chronic faecal impaction and faecal incontinence have experienced an episode of painful defecation, and many children with chronic constipation exhibit withholding behaviour. **METHODS AND OUTCOMES:** We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of fibre for children with chronic constipation? What are the effects of probiotics for children with chronic constipation? We searched: Medline, Embase, The Cochrane Library, and other important databases up to May 2014 (BMJ Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). **RESULTS:** We found 12 studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. **CONCLUSIONS:** In this systematic review, we present information relating to the effectiveness and safety of the following interventions: fibre and probiotics.

QUESTIONS

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INTERVENTIONS

FIBRE FOR CHRONIC CONSTIPATION		PROBIOTICS FOR CHRONIC CONSTIPATION	
 Unknown effectiveness		 Unknown effectiveness	
Fibre	4	Probiotics	6

Key points

- Although the use of ROME III criteria is recommended for the definition of functional constipation, diagnostic criteria for functional constipation in children still vary across studies. However, they often involve infrequent and possibly painful passing of large, hard stools, with or without faecal incontinence.
Prevalence of chronic constipation has been estimated at 1% to 5% of children in the UK and US, most of whom have no obvious aetiological factors.
Half of children with chronic faecal impaction and faecal incontinence have experienced an episode of painful defecation, and many children with chronic constipation exhibit withholding behaviour.
Disimpaction may be needed if spontaneous expulsion of the faecal mass is unlikely, or if it is causing discomfort or affecting normal feeding.
- The use of polyethylene glycol (PEG) with or without electrolytes is recommended in clinical guidelines as first-line maintenance pharmacological treatment. However, this review has focused on fibre and probiotics as non-pharmacological interventions for constipation in children.
- Low **fibre** intake is associated with constipation. We found insufficient evidence from RCTs showing that extra fibre intake reduces constipation compared with placebo. We found insufficient evidence on the effects of increased fibre intake compared with lactulose.
- We found insufficient evidence from RCTs on the effects of **probiotics** versus placebo or versus osmotic laxatives at improving symptoms of constipation.
- Overall, many of the studies we found used different definitions and outcome measures, and the quality of evidence was low. There is a need for further large high-quality RCTs in this condition.

Clinical context

GENERAL BACKGROUND

Prevalence of childhood constipation has been estimated at 1% to 30% in the general population worldwide. Aetiological factors are not found in most children. The management of constipation is essentially multifactorial and, along with medical treatment, should address the social and psychological issues that may be associated with it. Guidelines are available that have made recommendations for all general aspects of management. ^{[1] [2]}

FOCUS OF THE REVIEW

This review focuses on the evidence of fibre and probiotics as treatments for functional constipation in children.

COMMENTS ON EVIDENCE

The quality of evidence found for probiotics is low, and very-low for fibre. All studies used different definitions, study design, and outcome measures, which makes it difficult to compare trials with each other.

SEARCH AND APPRAISAL SUMMARY

The update literature search for this review was carried out from the date of the last search, August 2009, to May 2014. For more information on the electronic databases searched and criteria applied during assessment of studies for potential relevance to the review, please see the Methods section. After deduplication and removal of conference abstracts, 59 records were screened for inclusion in the review. Appraisal of titles and abstracts led to the exclusion of 37 studies and the further review of 22 full publications. Of the 22 full articles evaluated, three systematic reviews and four RCTs were included at this update.

ADDITIONAL INFORMATION

It is important to note that every child with constipation should have a normal daily fibre intake. Evidence for extra fibre intake is lacking.

DEFINITION Initially, the Rome II paediatric consortium (1999) defined functional childhood constipation as at least 2 weeks of: scybalous, pebble-like, hard stools for most of the stools; or firm stools two or fewer times per week and no evidence of structural endocrine or metabolic disease.^[3] These criteria were not necessarily comprehensive and were found to be restrictive by some researchers.^[4] In 2004, the Paris Consensus on Childhood Constipation Terminology (PACCT) group defined childhood constipation as the occurrence of two or more of the following six criteria in the previous 8 weeks: frequency of movements fewer than three per week; more than one episode of faecal incontinence per week; large stools in the rectum or palpable on abdominal examination; passing of stools so large that they may obstruct the toilet; retentive posturing and withholding behaviour; and painful defecation.^[5] These criteria were integrated into Rome III criteria (2006).^[6] ^[7] Functional constipation is now defined as the occurrence of two or more of the following six criteria in the previous 2 months in a child with a developmental age of at least 4 years, who has insufficient criteria for the diagnosis of irritable bowel syndrome (including no evidence of an inflammatory, anatomical, metabolic, or neoplastic process): two or fewer defecations in the toilet per week; at least one episode of faecal incontinence per week; history of retentive posturing or excessive volitional stool retention; history of painful or hard bowel movements; presence of a large faecal mass in the rectum; and a history of large diameter stools that may obstruct the toilet. Infants up to 4 years of age have to fulfil two or more criteria for at least 1 month. Many other terms are used in performed studies. Soiling is defined as the involuntary passage of small amounts of stools, resulting in staining of the underwear. The quantity of faecal loss is the main difference between encopresis and soiling. In practice, parents are often unable to accurately estimate the amount of faeces lost in the underwear and, thus, cannot differentiate between encopresis and soiling. Therefore, according to Rome III, the more neutral term of faecal incontinence was adopted, rather than the terms encopresis and soiling. Furthermore, paediatric faecal incontinence is divided into either organic faecal incontinence (e.g., resulting from anorectal malformations or neurological damage) or functional faecal incontinence. Functional faecal incontinence can be subdivided into constipation-associated faecal incontinence and non-retentive faecal incontinence. For this review, we focused on constipation-associated faecal incontinence.^[8] In selecting studies for this review, we did not use a singular definition owing to no clear agreement over the definitions (see Methods). We used the original wording of the authors. Although the use of Rome III criteria are recommended for the definition of functional constipation,^[1] diagnostic criteria for functional constipation in children still vary across studies. However, they often involve infrequent and possibly painful passing of large, hard stools with or without faecal incontinence.

INCIDENCE/ PREVALENCE One systematic review showed a worldwide prevalence of childhood constipation in the general population worldwide ranging from 1% to 30%. Similar prevalence rates were reported for boys and girls.^[9]

AETIOLOGY/ RISK FACTORS Aetiological factors are not found in most children. Hirschsprung's disease, cystic fibrosis, anorectal abnormalities, and metabolic conditions such as hypothyroidism are rare organic causes of childhood constipation. An episode of painful defecation was noted in more than 50% of people who were suffering from faecal soiling or chronic faecal impaction.^[10] **Risk factors** low fibre intake may be associated with childhood constipation.^[11] Prognostic factors could not be identified with one exception; there is strong evidence that the factors of sex or a positive family history have no prognostic value.^[12] ^[13] ^[14] We found no evidence for a difference between bottle-fed and breastfed babies, although it is generally accepted that bottle-fed babies are more at risk of relative water deficiency and breastfed babies frequently have delays of many days between passing normal

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stools. Only more recently, was a significant association found between functional constipation and physical, sexual, and emotional abuse.^[15]

PROGNOSIS

On average, 50% of the children referred to a paediatric gastroenterologist will recover and will be without laxatives after 6 to 12 months, 10% will be well while taking laxatives, and 40% will still be symptomatic despite use of laxatives. After 5 and 10 years, 50% and 80% of the children, respectively, will be recovered, with the vast majority no longer taking laxatives.^{[1] [12] [13] [14]} One follow-up study found that symptom duration of 3 months or less before referral was significantly correlated with better outcome.^[9] **Faecal impaction** disimpaction is necessary if the amount and character of faeces in the colon is of such magnitude that spontaneous expulsion is unlikely, or if it is causing discomfort and affecting normal feeding. Some children with a large rectosigmoid faecaloma may have difficulty passing urine.

AIMS OF INTERVENTION

The management of constipation is essentially multifactorial and, along with medical treatment, should address the social and psychological issues that may be associated with it.^[16] Families, and particularly children, vary considerably in their tolerance of symptoms and treatments. This necessitates a very personal selection and intensity of treatments, making controlled studies very difficult to perform. Medical treatment is aimed at disimpaction of the impacted faeces and restoration of regular bowel habits, which consist of passage of soft, normal stools without discomfort at least once every 3 days and in appropriate places.

OUTCOMES

Treatment success includes lack of pain; defecation three times or more a week; soiling fewer than twice-weekly/frequency of episodes of faecal incontinence; no laxatives for at least 4 weeks; lack of difficulty with defecation; improving constipation. **Quality of life.** **Adverse effects.** We have not reported faecal texture or hardness as an outcome or non-clinical measures such as gut transit time, as measured by the passage of radio opaque pellets.

METHODS

BMJ Clinical Evidence search and appraisal May 2014. The search was limited to infants and children under 16 years of age. Trials with participants up to the age of 18 years were included, as long as the majority were aged under 16 years. Trials were selected for inclusion if they focused on the management of constipation or faecal incontinence with a history of constipation in either the primary health or specialist setting. We included children with idiopathic constipation, but excluded children with a known underlying cause for their constipation (e.g., Hirschsprung's disease [congenital megacolon], operated anorectal malformations, or patients with other pelvic causes). The following databases were used to identify studies for this review: Medline 1966 to May 2014, Embase 1980 to May 2014, and The Cochrane Database of Systematic Reviews, issue 4, 2014 (1966 to date of issue). Additional searches were carried out in the Database of Abstracts of Reviews of Effects (DARE) and the Health Technology Assessment (HTA) database. We also searched for retractions of studies included in the review. An information specialist identified titles and abstracts in an initial search, which an evidence scanner then assessed against predefined criteria. An evidence analyst then assessed full texts for potentially relevant studies against predefined criteria. An expert contributor was consulted on studies selected for inclusion. An evidence analyst then extracted all data relevant to the review. Study design criteria for inclusion in this review were published RCTs and systematic reviews of RCTs in the English language, containing 20 or more individuals (10 in each arm). There was no minimum length of follow-up required for inclusion, and no maximum loss to follow-up. We did not exclude studies described as 'blinded', 'open', 'open label', or not blinded. We included RCTs and systematic reviews of RCTs where harms of an included intervention were assessed, applying the same study design criteria for inclusion as we did for benefits. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the MHRA, which are added to the review as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the *BMJ Clinical Evidence* population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 9).

QUESTION What are the effects of fibre for children with chronic constipation?

OPTION FIBRE

Treatment success

Fibre compared with placebo We don't know whether fibre is more effective than placebo at improving outcomes in children with constipation. It improved some outcomes but not others. Results varied by the specific outcome measured, and the evidence was weak and inconsistent ([very low-quality evidence](#)).

Fibre compared with laxatives (osmotic/bulk-forming/stimulant) We don't know whether fibre and lactulose differ in effectiveness at improving faecal incontinence, abdominal pain, or stool withholding in children with constipation ([very low-quality evidence](#)).

For GRADE evaluation of interventions for constipation in children, [see table, p 9](#).

Benefits:

Fibre versus placebo

We found two systematic reviews (search date 2007; ^[17] 2010 ^[18]), which identified the same two RCTs. ^[19] ^[20] The first review pooled data for one outcome. ^[17] The second review did not pool data. ^[18] We have reported the two RCTs from their original reports ^[19] ^[20] and the pooled data from the first review. ^[17] We found two subsequent RCTs. ^[21] ^[22]

The first, small crossover RCT identified by the reviews (31 children aged 4.5–11.7 years with constipation for 6 months or longer; 18/31 [58%] had [encopresis](#); children were initially disimpacted with phosphate enemas if required before treatment) compared fibre (glucomannan 100 mg/kg up to 5 g/day, with 50 mL of fluid per 500 mg of fibre) with placebo for 4 weeks. ^[19] The initial daily fibre intake was low in 22/31 (71%) children included in the study. Pre-crossover, the RCT found that the proportion of children who had fewer than three bowel movements per week and abdominal pain was significantly smaller with fibre compared with placebo (<3 bowel movements weekly: 19% with fibre v 52% with placebo; P <0.05; abdominal pain: 10% with fibre v 42% with placebo; P <0.05; absolute numbers not reported for either outcome). It also found that the proportion of children who were rated by their physician as having been treated successfully and rated as improved by their parents was significantly larger after treatment with fibre compared with placebo (physician-rated: 45% with fibre v 13% with placebo; P <0.05; parent-rated: 68% with fibre v 13% with placebo; P <0.05; absolute numbers not reported for either comparison). Physician-rated treatment success was defined as more than three bowel movements per week and one or no episodes of encopresis over 3 weeks with no abdominal pain.

The second RCT included in the reviews (56 children aged 3–10 years with chronic idiopathic constipation according to Rome II criteria) compared fibre (cocoa husk supplement, 1 sachet weighted 5.2 g; 3–6 years of age: 2 sachets daily; 7–10 years: 4 sachets daily; dissolved in 200 mL milk) with placebo for 4 weeks. ^[20] Difference in the mean basal dietary fibre intake was not significant and was near to the recommended amount in both groups (12.3 g daily with fibre v 13.4 g daily with placebo; P value not reported). The RCT found no significant difference at 4 weeks between fibre and placebo in subjective improvement in pain (subjective improvement in pain: 16/24 [4%] with fibre v 11/24 [3%] with placebo; P = 0.109). ^[20]

The first review pooled data found no significant difference between fibre and placebo in bowel movements per week (2 RCTs, bowel movements per week: weighted SMD +0.35, 95% CI –0.04 to +0.74, P <0.10; absolute numbers in analysis not reported). ^[17] It described this difference as neither significant nor clinically relevant.

The second review noted that the first RCT ^[19] had no information on blinding of the outcome assessor, no ITT analysis, an unclear definition of constipation, and an unexplained high rate of loss to follow-up (15/46 [32%]). ^[18] It noted that the second RCT ^[20] had adequate randomisation and blinding and a lower loss to follow-up than the first RCT (8/56 [14%]). ^[18]

The first subsequent double-blind RCT (57 children aged 4–12 years, average age about 8 years, functional chronic constipation according to Rome III criteria, previous maintenance therapy with low doses of stool softeners) compared a fibre mixture with placebo (maltodextrin) for 1 month. ^[21] The RCT noted that the fibre mixture also contained some components that were considered pre-biotics, and the stool softeners were discontinued at the start of the trial. The primary outcome was a composite measure of treatment failure (defined as hardened stools, defecation with pain or difficulty, greater intervals between evacuations compared with the previous day, faecal incontinence or impaction, or requiring stool softener). The RCT found no significant difference between fibre and placebo in treatment failure at 4 weeks (9/26 [35%] with fibre v 10/28 [36%] with placebo, RR 0.98, 95% CI 0.54 to 1.75, P = 0.933). The RCT found that fibre significantly increased defecation

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frequency compared with placebo at 4 weeks (change from baseline to end of trial, defecation frequency per day: 0.529 with fibre v 0.232 with placebo, $P = 0.014$). In total, 44/57 (77%) children were included in this analysis. ^[21]

The second subsequent double-blind RCT (80 children, aged 3–16 years, average age 6 years, functional chronic constipation according to Rome III criteria [2 or less stools/week, with soiling and/or withholding behaviours and/or history or painful defecation or hard stools and/or large stools and/or abdominal or faecal mass]) compared glucomannan (a soluble fibre) with placebo (maltodextrine) for 4 weeks. ^[22] The primary outcome was a composite outcome of treatment success (defined as 3 or more bowel movements with no episodes of soiling during the last week of product consumption). Results were based on 72/80 (90%) of children that completed the study. The RCT found no significant difference between groups in treatment success at 4 weeks (20/36 [56%] with glucomannan v 21/36 [58%] with placebo, RR 0.95, 95% CI 0.6 to 1.4, $P > 0.99$). The RCT reported that abdominal pain was reported significantly more frequently with glucomannan compared with placebo at week 1 (median difference 0, 95% CI 0 to 1, $P = 0.04$) and at week 4 (median difference 0, 95% CI 1 to 0, $P < 0.0001$), but there was no significant difference between groups at week 2 ($P = 0.08$) or week 3 ($P = 0.44$). ^[22] Assessment of all outcomes was based on participant's bowel diaries, collected at the final visit.

Fibre versus laxatives (osmotic/bulk-forming/stimulant)

We found two systematic reviews (search date 2010; ^[18] 2012 ^[23]), which identified the same RCT. ^[24] We have reported the RCT from the original report. ^[24] We found one additional RCT. ^[25] Both RCTs compared fibre with lactulose.

The RCT included in the systematic reviews (97 children aged 1–13 years with at least 2 of 4 criteria for constipation: <3 bowel movements weekly; 2 or more faecal incontinence episodes weekly; periodic passage of stool at least once every 7–30 days; or a palpable abdominal or rectal mass) compared fibre (10 g in 125 mL yoghurt drink) with lactulose (10 g in 125 mL yoghurt drink) for 8 weeks followed by 4 weeks of weaning. ^[24] Polyethylene glycol (PEG; macrogol 3350) was added if no clinical improvement was observed after 3 weeks in either group. The RCT found no significant difference in the number of children with one or more faecal incontinence episodes per week (9/42 [4%] with fibre v 5/55 [3%] with lactulose; $P = 0.084$) or in the mean scores (scale: 0 = not at all, 1 = sometimes, 2 = often, and 3 = continuous) of people with abdominal pain or flatulence at weeks 3 and 8 of follow-up (abdominal pain; week 3: 1.58 with fibre v 1.43 with lactulose; $P = 0.33$; week 8: 1.49 with fibre v 1.39 with lactulose; $P = 0.50$; flatulence; week 3: 1.9 with fibre v 2.0 with lactulose; $P = 0.70$; week 8: 2.0 with fibre v 1.9 with lactulose; $P = 0.94$). The RCT also found no significant difference between groups for necessity of step-up medication ($P = 0.99$, absolute numbers not reported). ^[24] It found no significant difference between groups in defecation frequency per week after 8 weeks (7 times per week with fibre v 6 times per week with placebo, $P = 0.481$). Results in the final data set were based on 97/135 (72%) of randomised participants who completed the study (42/65 [65%] with fibre v 55/70 [79%] with lactulose, P value not reported). ^[24] The RCT noted that during the treatment period, 22 people stopped during days 1–56 with fibre compared with 11 who stopped during days 1–51 with lactulose ($P = 0.02$).

The additional RCT (61 children aged 4–16 years confirmed by Rome III criteria with at least 2 criteria for constipation: stool frequency of 2 or fewer per week, at least 1 episode of faecal incontinence per week, history of retentive posturing or excessive volitional stool retention, history of painful or hard bowel movements, presence of large faecal mass in the rectum, and history of large diameter stool that may obstruct the toilet, criteria met at least once per week for at minimum of 2 months before diagnosis) compared partially hydrolysed guar gum as a fibre source with lactulose and reported outcomes at 4 weeks. ^[25] The RCT reported that both groups improved from baseline with regard to bowel movements (from baseline to end of treatment: bowel movement frequency per week, 4 to 5 with fibre v 4 to 6 with lactulose, P value between groups not reported). The RCT found no significant difference between groups in abdominal pain or stool withholding (from baseline to end of treatment: abdominal pain, 49% to 16% with fibre v 51% to 10% with lactulose, $P > 0.05$, absolute numbers not reported; stool withholding 38% to 3% with fibre v 20% to 3% with lactulose, $P > 0.05$, absolute numbers not reported). The RCT reported that 68 participants were enrolled, seven dropped out, and the final data set included 61 participants. The level of blinding was not reported. In addition, the group given fibre were also advised to increase their fluid intake, so co-interventions were not the same between groups, which may have introduced bias.

We found no RCTs comparing fibre with osmotic or bulk-forming or stimulant laxatives other than lactulose.

Harms:

Fibre versus placebo

One review noted that included RCTs reported no adverse effects of fibre. ^[18] The first subsequent RCT reported that no serious adverse events were reported, and the products were well tolerated.

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^[21] The second subsequent RCT reported that the overall rate of adverse effects was similar between groups (total: 5 with glucomannan v 5 with placebo, P value not reported), and that there was one serious adverse event in the glucomannan group but this was unlikely to be related to the study product (1 case of acute rotavirus gastroenteritis). ^[22]

Fibre versus laxatives (osmotic/bulk-forming/stimulant)

One RCT noted that no serious adverse effects were reported in the two study groups, but in three cases (1 with fibre v 2 with lactulose) the study yoghurt intake was decreased because of persistent diarrhoea. ^[24] One RCT reported that, although there was no significant difference between groups, flatulence was recorded more often in the lactulose group than in the fibre group (numerical details not reported). ^[25]

Comment:

One RCT (43 children aged 2–14 years) found that when using a behavioural intervention programme, it was possible to significantly increase the fibre intake of children with constipation. ^[26] However, no significant benefit, in terms of a reduction in laxative use or increased stool frequency, associated with additional fibre intake was demonstrated. ^[26]

All studies used different definitions, and outcome measures and results varied across studies. The overall quality of evidence is very low.

Clinical guide

Low fibre intake is associated with constipation and, therefore, every child with or without constipation needs a normal daily fibre intake. The role of extra fibre on constipation requires further evaluation. Clinical guidelines recommend the use of polyethylene glycol (PEG) with or without electrolytes as first-line maintenance pharmacological treatment for the treatment of functional constipation in children rather than dietary interventions alone. ^[1] ^[2]

QUESTION What are the effects of probiotics for children with chronic constipation?

OPTION PROBIOTICS

Treatment success

Probiotics compared with placebo We don't know whether probiotics are more effective than placebo at improving a composite measure of treatment success or defecation frequency in children with constipation (*low-quality evidence*).

Probiotics compared with laxatives (osmotic/bulk-forming/stimulant) We don't know whether probiotics and osmotic laxatives (magnesium oxide) differ in effectiveness at increasing a composite outcome of treatment success (defined as 3 or more spontaneous defecations per week with no episodes of faecal soiling by the fourth week) at 4 weeks in children with constipation (*low-quality evidence*).

For GRADE evaluation of interventions for constipation in children, see table, p 9.

Benefits:

Probiotics versus placebo

We found three systematic reviews (search date 2007; ^[17] 2010; ^[18] 2013 ^[27]). All three reviews identified the same two RCTs (84 children; 45 children), and the last review included two further RCTs (148 children; 59 children), published after the first two reviews, and pooled data. ^[27] We have, therefore, reported the last review. We found one subsequent RCT. ^[28]

The four RCTs included in the review used different diagnostic criteria (constipation: defined as stools <3 times per week, >12 weeks in 1 RCT; stools <3 times per week, >2 months, and anal fissures or soiling or hard/large stools in 1 RCT; Rome III criteria for constipation in 2 RCTs) and different probiotics (LGG; *Lactobacillus casei* DN; *Bifidobacterium lactis* DN; *Bifidobacterium longum*) for 3 to 12 weeks. It defined treatment success as defecation at least three times per week and no faecal incontinence or less than one episode in 2 weeks. ^[27] The review found no significant difference between probiotics and placebo in treatment success (3 RCTs, 96/132 [73%] with probiotics v 75/123 [61%] with placebo, RR 1.16, 95% CI 0.83 to 1.62, P = 0.37). It also found no significant difference between groups in defecation frequency (3 RCTs, 270 participants, SMD +0.44, 95% CI -0.35 to +1.24). There was significant heterogeneity in this analysis ($I^2 = 87\%$, P for heterogeneity = 0.004), which was not further explained. Both meta-analyses did not include one crossover RCT (59 participants, *B longum*). In addition, in one RCT (84 people), included in both meta-analyses, participants were also given lactulose in both arms of the trial.

The subsequent double-blind RCT compared *Lactobacillus reuteri* with placebo in 44 formula-fed infants aged over 6 months (mean 8.5 months) with functional chronic constipation, as defined by the Rome III criteria. ^[28] The RCT found that *L reuteri* significantly increased the frequency of bowel movements compared with placebo at 2 to 8 weeks (2 weeks, P = 0.042; 4 weeks, P = 0.008;

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8 weeks, $P = 0.27$; results presented graphically, absolute numbers not reported). It found no significant difference between groups with regard to the presence of inconsolable crying episodes at 2 to 8 weeks (2 weeks, $P = 0.64$; 4 weeks, $P = 0.5$; 8 weeks, $P = 0.66$; results presented graphically, absolute numbers not reported).^[28]

Probiotics versus laxatives (osmotic/bulk-forming/stimulant)

We found three systematic reviews (search date 2007;^[17] 2010;^[18] 2013^[27]), which all identified the same small RCT.^[29] We have reported the RCT directly from the original report.^[29]

The RCT (45 children, aged <10 years, with functional constipation for >2 months and at least 1 of the following symptoms: anal fissures with bleeding, faecal soiling, or passage of large and hard stool) compared the osmotic laxative magnesium oxide 50 mg/kg daily (18 children), 8×10^8 colony-forming units of the probiotic *Lactobacillus casei rhamnosus* (18 children), and placebo (9 children), all twice-daily for 4 weeks, in a three-arm trial. We report the comparison of probiotics (*L casei rhamnosus*) with osmotic laxatives (magnesium oxide) here. All outcomes were assessed at 4 weeks. The RCT found that probiotics significantly reduced abdominal pain compared with osmotic laxatives (1.9 episodes with probiotics v 4.8 episodes with osmotic laxatives; $P = 0.04$). However, it found no significant difference in treatment success (defined as 3 or more spontaneous defecations per week with no episodes of faecal soiling by the fourth week) between probiotics and osmotic laxatives (78% with probiotics v 72% with osmotic laxatives; $P = 0.71$; absolute results not reported). The RCT also found similar rates of faecal soiling for probiotics and osmotic laxatives (2.1 episodes with probiotics v 2.7 episodes with osmotic laxatives; statistical significance between groups not assessed).^[29] We found no RCTs comparing probiotics with osmotic or bulk-forming or stimulant laxatives other than magnesium oxide.

Harms:

Probiotics versus placebo

The review reported that one included RCT reported one case of gastroenteritis and three cases of vomiting. A further RCT reported three cases of abdominal pain and one case of vomiting, and that the adverse events were comparable with the placebo groups (further numerical details not reported, P value not reported).^[27] The subsequent RCT found no reported adverse effects.^[28]

Probiotics versus laxatives (osmotic/bulk-forming/stimulant)

The RCT reported no adverse effects associated with probiotics, but reported one case of mild diarrhoea in a child receiving osmotic laxatives.^[29]

Comment:

The results from these RCTs are difficult to compare because they investigated the efficacy of different probiotic agents and used different definitions and outcome measures.

There are many different probiotic micro-organisms with different effects. Currently, evidence is lacking to support use of any probiotic strain in the treatment of constipation in children.

GLOSSARY

Encopresis Faeces that is involuntary passed.

Scybalous A dry, hard mass of faeces.

Faecaloma A large amount of faeces that forms a tumour-like mass.

Low-quality evidence 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 evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Fibre Two systematic reviews added^[18] ^[23] and three RCTs.^[21] ^[22] ^[25] Categorisation unchanged (unknown effectiveness).

Probiotics Two systematic reviews added^[18] ^[27] and one RCT.^[28] Categorisation unchanged (unknown effectiveness)

REFERENCES

1. Tabbers MM, DiLorenzo C, Berger MY, et al. Evaluation and treatment of functional constipation in infants and children: evidence-based recommendations from ESPGHAN and NASPGHAN. *J Pediatr Gastroenterol Nutr* 2014;58:258–274.^[PubMed]
2. National Collaborating Centre for Women's and Children's Health. Constipation in children and young people: diagnosis and management of idiopathic constipation in primary and secondary care. May 2010. Available at <http://www.nice.org.uk/guidance/cg99/evidence/cg99-constipation-in-children-and-young-people-full-guidance3> (last accessed 24 February 2015).
3. Drossman DA, Corazziari E, Talley NJ, et al. *Rome II: the functional gastrointestinal disorders. Diagnosis, pathophysiology and treatment; a multinational consensus*. 2nd ed. McLean, VA: Degnon Associates, 2000.
4. Voskuijl WP, Heijmans J, Heijmans HS, et al. Use of Rome II criteria in childhood defecation disorders: applicability in clinical and research practice. *J Pediatr* 2004;145:213–217.^[PubMed]
5. Benninga M, Candy DC, Catto-Smith AG, et al. The Paris Consensus on Childhood Constipation Terminology (PACCT) group. *J Pediatr Gastroenterol Nutr* 2005;40:273–275.^[PubMed]

6. Hyman PE, Milla PJ, Benninga MA, et al. Childhood functional gastrointestinal disorders: neonate/toddler. *Gastroenterology* 2006;130:1519–1526.[\[PubMed\]](#)
7. Rasquin A, Di Lorenzo C, Forbes D, et al. Childhood functional gastrointestinal disorders: child/adolescent. *Gastroenterology* 2006;130:1527–1537.[\[PubMed\]](#)
8. Bongers ME, Tabbers MM, Benninga MA. Functional nonretentive fecal incontinence in children. *J Pediatr Gastroenterol Nutr* 2007;44:5–13.[\[PubMed\]](#)
9. Mugie SM, Benninga MA, Di Lorenzo C. Epidemiology of constipation in children and adults: a systematic review. *Best Pract Res Clin Gastroenterol* 2011;25:3–18.[\[PubMed\]](#)
10. Partin JC, Hamill SK, Fischel JE, et al. Painful defecation and fecal soiling in children. *Pediatrics* 1992;89:1007–1009.[\[PubMed\]](#)
11. Morais MB, Vitolo MR, Aguirre AN, et al. Measurement of low dietary fiber intake as a risk factor for chronic constipation in children. *J Pediatr Gastroenterol Nutr* 1999;29:132–135.[\[PubMed\]](#)
12. Pijpers M, Bongers M, Benninga M, et al. Functional constipation in children: a systematic review on prognosis and predictive factors. *J Pediatr Gastroenterol Nutr* 2010;50:256–268.[\[PubMed\]](#)
13. Bongers MEJ, van Wijk MP, Reitsma JB, et al. Long-term prognosis for childhood constipation: clinical outcomes in adulthood. *Pediatrics* 2010;126:e156–e162.[\[PubMed\]](#)
14. Borowitz SM, Cox DJ, Kovatchev B, et al. Treatment of childhood constipation by primary care physicians: efficacy and predictors of outcome. *Pediatrics* 2005;115:873–877.[\[PubMed\]](#)
15. Rajindrajith S, Devanarayana NM, Lakmini C, et al. Association between child maltreatment and constipation: a school-based survey using Rome III criteria. *J Pediatr Gastroenterol Nutr* 2014;58:486–490.[\[PubMed\]](#)
16. Baker SS, Liptak GS, Colletti RB, et al. Constipation in infants and children: evaluation and treatment. A medical position statement of the North American Society for Pediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr* 1999;29:612–626. [Erratum in: *J Pediatr Gastroenterol Nutr* 2000;30:109][\[PubMed\]](#)
17. Pijpers MA, Tabbers MM, Benninga MA, et al. Currently recommended treatments of childhood constipation are not evidence based: a systematic literature review on the effect of laxative treatment and dietary measures. *Arch Dis Child* 2009;94:117–131.[\[PubMed\]](#)
18. Tabbers MM, Boluyt N, Berger MY, et al. Nonpharmacologic treatments for childhood constipation: systematic review. *Paediatrics* 2011;128:753–761.[\[PubMed\]](#)
19. Loening-Baucke V, Miele E, Staiano A. Fiber (glucomannan) is beneficial in the treatment of childhood constipation. *Pediatrics* 2004;113:e259–e264.[\[PubMed\]](#)
20. Castillejo G, Bulló M, Anguera A, et al. A controlled, randomized, double-blind trial to evaluate the effect of a supplement of cocoa husk that is rich in dietary fiber on colonic transit in constipated pediatric patients. *Pediatrics* 2006;118:e641–e648.[\[PubMed\]](#)
21. Weber TK, Toporovski MS, Tahan S, et al. Dietary fiber mixture in pediatric patients with controlled chronic constipation. *J Pediatr Gastroenterol Nutr* 2014;58:297–302.[\[PubMed\]](#)
22. Chmielewska A, Horvath A, Dziechciarz P, et al. Glucomannan is not effective for the treatment of functional constipation in children: a double-blind, placebo-controlled, randomized trial. *Clin Nutr* 2011;30:462–468.[\[PubMed\]](#)
23. Gordon M, Naidoo K, Akobeng AK, et al. Osmotic and stimulant laxatives for the management of childhood constipation. In: The Cochrane Library, Issue 4, 2014. Chichester, UK: John Wiley & Sons, Ltd. Search date 2012.[\[PubMed\]](#)
24. Kokke FT, Scholtens PA, Alles MS, et al. A dietary fiber mixture versus lactulose in the treatment of childhood constipation: a double-blind randomized controlled trial. *J Pediatr Gastroenterol Nutr* 2008;47:592–597.[\[PubMed\]](#)
25. Ustundag G, Kuloglu Z, Kirbas N, et al. Can partially hydrolyzed guar gum be an alternative to lactulose in treatment of childhood constipation? *Turk J Gastroenterol* 2010;21:360–364.[\[PubMed\]](#)
26. Sullivan PB, Alder N, Shrestha B, et al. Effectiveness of using a behavioural intervention to improve dietary fibre intakes in children with constipation. *J Hum Nutr Diet* 2012;25:33–42.[\[PubMed\]](#)
27. Kortnerink JJ, Ockeloen L, Benninga MA, et al. Probiotics for childhood functional gastrointestinal disorders: A systematic review and meta-analysis. *Acta Paediatr* 2014;103:365–372.[\[PubMed\]](#)
28. Coccorullo P, Strisciuglio C, Martinelli M, et al. Lactobacillus reuteri (DSM 17938) in infants with functional chronic constipation: a double-blind, randomized, placebo-controlled study. *J Pediatr* 2010;157:598–602.[\[PubMed\]](#)
29. Bu LN, Chang MH, Ni YH, et al. Lactobacillus casei rhamnosus Lcr35 in children with chronic constipation. *Pediatr Int* 2007;49:485–490.[\[PubMed\]](#)

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TABLE	GRADE evaluation of interventions for constipation in children									
Important outcomes					Treatment success					
Number of studies (participants)	Outcome	Comparison	Type of evi- dence	Quality	Consisten- cy	Directness	Effect size	GRADE	Comment	
What are the effects of fibre for children with chronic constipation?										
4 (216) ^{[17] [18] [19] [20] [21] [22]}	Treatment success	Fibre v placebo	4	−2	0	−1	0	Very low	Quality points deducted for weak methods (unclear definitions, no ITT analysis, loss to follow-up) and incomplete reporting of results; directness point deducted for use of co-intervention in 1 RCT	
2 (158) ^{[24] [25]}	Treatment success	Fibre v laxatives (osmotic/bulk-forming/stimulant)	4	−3	0	0	0	Very low	Quality points deducted for sparse data, weak methods, and for incomplete reporting of results	
What are the effects of probiotics for children with chronic constipation?										
5 (at least 309) ^{[27] [28]}	Treatment success	Probiotics v placebo	4	0	−1	−1	0	Low	Consistency point deducted for significant heterogeneity; directness point deducted for inclusion of co-intervention in 1 RCT	
1 (45) ^[29]	Treatment success	Probiotics v laxatives (osmotic/bulk-forming/stimulant)	4	−2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results	
Type of evidence: 4 = RCT; 2 = Observational. Consistency: similarity of results across studies Directness: generalisability of population or outcomes Effect size: based on RR or OR										