

National Institute for Health and Care Excellence

8-year surveillance (2017) – [Constipation in children and young people: diagnosis and management](#) (2010) NICE guideline CG99

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Appendix A: Summary of new evidence from surveillance

History-taking and physical examination

99 – 01	What are the key components of the history-taking and the physical examination that would indicate idiopathic constipation or flag a serious underlying disorder?
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Recommendations derived from this question

- 1.1.1 Establish during history-taking whether the child or young person has constipation. Two or more findings from table 1 indicate constipation.

Table 1 Key components of history-taking to diagnose constipation

Key components	Potential findings in a child younger than 1 year	Potential findings in a child/young person older than 1 year
Stool patterns	<ul style="list-style-type: none"> Fewer than three complete stools per week (type 3 or 4, see Bristol Stool Form Scale – appendix D) (this does not apply to exclusively breastfed babies after 6 weeks of age) Hard large stool 'Rabbit droppings' (type 1, see Bristol Stool Form Scale – appendix D) 	<ul style="list-style-type: none"> Fewer than three complete stools per week (type 3 or 4, see Bristol Stool Form Scale – appendix D) Overflow soiling (commonly very loose [no form], very smelly [smells more unpleasant than normal stools], stool passed without sensation. Can also be thick and sticky or dry and flaky.) 'Rabbit droppings' (type 1, see Bristol Stool Form Scale – appendix D) Large, infrequent stools that can block the toilet

Symptoms associated with defecation	<ul style="list-style-type: none"> • Distress on stooling • Bleeding associated with hard stool • Straining 	<ul style="list-style-type: none"> • Poor appetite that improves with passage of large stool • Waxing and waning of abdominal pain with passage of stool • Evidence of retentive posturing: typical straight legged, tiptoed, back arching posture • Straining • Anal pain
History	<ul style="list-style-type: none"> • Previous episode(s) of constipation • Previous or current anal fissure 	<ul style="list-style-type: none"> • Previous episode(s) of constipation • Previous or current anal fissure • Painful bowel movements and bleeding associated with hard stools

1.1.2 If the child or young person has constipation take a history using table 2 to establish a positive diagnosis of idiopathic constipation by excluding underlying causes. If a child or young person has any 'red flag' symptoms, do not treat them for constipation. Instead, refer them urgently to a healthcare professional with experience in the specific aspect of child health that is causing concern.

Table 2 Key components of history-taking to diagnose idiopathic constipation

Key components	Findings and diagnostic clues that indicate idiopathic constipation	'Red flag' findings and diagnostic clues that indicate an underlying disorder or condition: not idiopathic constipation
Timing of onset of constipation and potential precipitating factors	<p>In a child younger than 1 year:</p> <p>Starts after a few weeks of life</p> <p>Obvious precipitating factors coinciding with the start of symptoms: fissure, change of diet, infections</p> <p>In a child/young person older than 1 year:</p> <p>Starts after a few weeks of life</p> <p>Obvious precipitating factors coinciding with the start of symptoms: fissure, change of diet, timing of potty/toilet training or acute events such as infections, moving house, starting nursery/school, fears and phobias, major change in family, taking medicines</p>	Reported from birth or first few weeks of life

Passage of meconium	Normal (within 48 hours after birth [in term baby])	Failure to pass meconium/delay (more than 48 hours after birth [in term baby])
Stool patterns		'Ribbon stools' (more likely in a child younger than 1 year)
Growth and general wellbeing	In a child younger than 1 year: Generally well, weight and height within normal limits In a child/young person older than 1 year: Generally well, weight and height within normal limits, fit and active	No 'red flag', but see 'amber flag' below.
Symptoms in legs/locomotor development	No neurological problems in legs (such as falling over in a child/young person older than 1 year), normal locomotor development	Previously unknown or undiagnosed weakness in legs, locomotor delay
Abdomen		Abdominal distension with vomiting
Diet and fluid intake	In a child younger than 1 year: Changes in infant formula, weaning, insufficient fluid intake In a child/young person older than 1 year: History of poor diet and/or insufficient fluid intake	
<p>'Amber flag': possible idiopathic constipation</p> <p>Growth and general wellbeing: Faltering growth (see recommendation 1.1.4)</p> <p>Personal/familial/social factors: Disclosure or evidence that raises concerns over possibility of child maltreatment (see recommendation 1.1.5)</p>		

1.1.3 Do a physical examination. Use table 3 to establish a positive diagnosis of idiopathic constipation by excluding underlying causes. If a child or young person has any 'red flag' symptoms do not treat them for constipation. Instead, refer them urgently to a healthcare professional with experience in the specific aspect of child health that is causing concern.

Table 3 Key components of physical examination to diagnose idiopathic constipation

Key components	Findings and diagnostic clues that indicate idiopathic constipation	'Red flag' findings and diagnostic clues that indicate an underlying disorder or condition: not idiopathic constipation
Inspection of perianal area: appearance, position, patency, etc	Normal appearance of anus and surrounding area	Abnormal appearance/position/patency of anus: fistulae, bruising, multiple fissures, tight or patulous anus, anteriorly placed anus, absent anal wink
Abdominal examination	Soft abdomen. Flat or distension that can be explained because of age or excess weight	Gross abdominal distension
Spine/lumbosacral region/gluteal examination	Normal appearance of the skin and anatomical structures of lumbosacral/gluteal regions	Abnormal: asymmetry or flattening of the gluteal muscles, evidence of sacral agenesis, discoloured skin, naevi or sinus, hairy patch, lipoma, central pit (dimple that you can't see the bottom of), scoliosis
Lower limb neuromuscular examination including tone and strength	Normal gait. Normal tone and strength in lower limbs	Deformity in lower limbs such as talipes Abnormal neuromuscular signs unexplained by any existing condition, such as cerebral palsy
Lower limb neuromuscular examination: reflexes (perform only if 'red flags' in history or physical examination suggest new onset neurological impairment)	Reflexes present and of normal amplitude	Abnormal reflexes

- 1.1.4 If the history-taking and/or physical examination show evidence of faltering growth treat for constipation and test for coeliac disease* and hypothyroidism.
- 1.1.5 If either the history-taking or the physical examination show evidence of possible maltreatment treat for constipation and refer to NICE guidance on 'When to suspect child maltreatment', NICE clinical guideline 89 (2009)**.
- 1.1.6 If the physical examination shows evidence of perianal streptococcal infection, treat for constipation and also treat the infection.
- 1.1.7 Inform the child or young person and his or her parents or carers of a positive diagnosis of idiopathic constipation and also that underlying causes have been excluded by the history and/or physical examination. Reassure them that there is a suitable treatment for idiopathic constipation but that it may take several months for the condition to be resolved.

* See also [Coeliac disease: recognition and assessment of coeliac disease](#). NICE clinical guideline 86 (2009).

** See [When to suspect child maltreatment](#). NICE clinical guideline 89 (2009).

Surveillance decision

This review question should not be updated.

Evidence Update 2012

No relevant evidence was identified.

4-year surveillance summary

A chart review and a cross-sectional study indicated that the Rome II criteria are still appropriate for the diagnosis of functional constipation in young children¹ although the paediatric Rome III criteria for functional constipation are less restrictive than the Rome II criteria². The use of a bladder/bowel dysfunction questionnaire in a paediatric urology department was evaluated in one study however, the ICD-9 diagnosis of constipation was not associated with higher scores for constipation related items in the questionnaire³.

One study investigating clinical characteristics of functional constipation at paediatric gastroenterology clinics suggested the following were important: a history of constipation in infancy, picky-eating, lack of exercise, and retentive posturing, greater than 60% rate of hard stools, painful stools, a history of large faecal mass in rectum, and disappearance of constipation symptoms after passing a large stool⁴. Furthermore, a study reporting the development of an algorithm to identify constipation in children with autism spectrum disorders in primary care suggested that subtle or atypical symptoms might indicate the presence of constipation although no specific detail was provided in the abstract⁵.

One study⁶ (n = 305) highlighted by a topic expert post-consultation was a cohort study describing the clinical characteristics and preoperative management of a national cohort of infants with Hirschsprung's Disease. The results indicated that nearly half of the infants with Hirschsprung's Disease passed meconium within 48 hours of birth. Out of the infants who were diagnosed with Hirschsprung's, 92.8% also presented with abdominal distention.

8-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

A topic expert noted that in current practice there appears to be great emphasis on physical examination, even in the absence of red flags and when the history alone gives strong indication of idiopathic constipation. It was suggested that this might lead to treatment delay and also extra cost as children are often being referred on for an 'examination' when the nurse has not undergone specific examination training. It was noted that there was no published evidence on this particular issue.

Impact statement

Evidence was identified on the ROME criteria but it is unlikely to impact on guideline recommendations which focus on key components of history taking and physical examination to diagnose idiopathic constipation.

A topic expert highlighted that new evidence from a national cohort study may impact recommendations on red flags for Hirschsprung's Disease during history taking. The results show that a large proportion of infants with Hirschsprung's Disease pass meconium within 48 hours and that the majority of these infants also presented with abdominal distention. Table 2 in the guideline currently states that any of the following should indicate a 'red flag' for another underlying disorder or condition such as Hirschsprung's disease: delayed passage of meconium (defined as more than 48 hours) and abdominal distention. The new evidence questions the validity of timing of first meconium as a diagnostic clue for Hirschsprung's Disease, however it does not provide any information on what the revised timeframe should be. Furthermore, the majority of infants in the study also presented with abdominal distention symptoms which is listed as a red flag criteria in CG99. For these reasons the study results are considered insufficient to impact the guideline at this point.

However, it is noted that the NICE guideline on [postnatal care](#) (CG37, published June 2006) covers a similar area and that there is a discrepancy across guideline recommendations (see [recommendation 1.4.31](#)). NICE guideline CG37 is scheduled to undergo a full update. The issue around timing of first meconium will therefore be formally considered by the

committee working on the update of CG37. NICE guideline CG99 will be amended accordingly depending on the outcome of this committee discussion.

New evidence is unlikely to change guideline recommendations.

Digital rectal examination

99 – 02 What is the diagnostic value of the DRE in children with chronic idiopathic constipation?

Recommendations derived from this question

- 1.2.1 A digital rectal examination should be undertaken only by healthcare professionals competent to interpret features of anatomical abnormalities or Hirschsprung's disease.
- 1.2.2 If a child younger than 1 year has a diagnosis of idiopathic constipation that does not respond to optimum treatment within 4 weeks, refer them urgently to a healthcare professional competent to perform a digital rectal examination and interpret features of anatomical abnormalities or Hirschsprung's disease.
- 1.2.3 Do not perform a digital rectal examination in children or young people older than 1 year with a 'red flag' (see tables 2 and 3) in the history-taking and/or physical examination that might indicate an underlying disorder. Instead, refer them urgently to a healthcare professional competent to perform a digital rectal examination and interpret features of anatomical abnormalities or Hirschsprung's disease.
- 1.2.4 For a digital rectal examination ensure:
 - privacy
 - informed consent is given by the child or young person, or the parent or legal guardian if the child is not able to give it, and is documented
 - a chaperone is present
 - the child or young person's individual preferences about degree of body exposure and gender of the examiner are taken into account
 - all findings are documented.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Clinical investigations

99 – 03 What is the diagnostic value of the gastrointestinal endoscopy in children with chronic idiopathic constipation?

Recommendations derived from this question

1.3.1 Do not use gastrointestinal endoscopy to investigate idiopathic constipation.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

99 – 04 What is the prevalence of hypothyroidism and coeliac disease in children with chronic constipation?

Recommendations derived from this question

1.3.2 Test for coeliac disease* and hypothyroidism in the ongoing management of intractable constipation in children and young people if requested by specialist services.

* See also [Coeliac disease: recognition and assessment of coeliac disease](#). NICE clinical guideline 86 (2009).

Surveillance decision

This review question should not be updated.

Evidence Update 2012

No relevant evidence was identified.

4-year surveillance summary

The results of a prospective cohort study of children who met the Rome III criteria for constipation indicated that 1.9% of the cohort had biopsy-proven coeliac disease which was considered higher than the prevalence of coeliac disease in the Netherlands⁷. Patients in the study were referred to a paediatrician so it is assumed that the population was children.

8-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The identified new evidence looked at the associations between coeliac disease and symptoms of constipation therefore, it is unlikely that the results would have an impact on the guideline recommendation which states to test for coeliac disease and hypothyroidism in the ongoing management of intractable constipation in children and young people only if requested by specialist services.

New evidence is unlikely to change guideline recommendations.

99 – 05

What is the diagnostic value of the anorectal manometry in children with chronic idiopathic constipation?

Recommendations derived from this question

- 1.3.3 Do not use anorectal manometry to exclude Hirschsprung's disease in children and young people with chronic constipation.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

99 – 06

What is the diagnostic value of plain abdominal radiography to diagnose chronic idiopathic constipation in children?

Recommendations derived from this question

- 1.3.4 Do not use a plain abdominal radiograph to make a diagnosis of idiopathic constipation.
1.3.5 Consider using a plain abdominal radiograph only if requested by specialist services in the ongoing management of intractable idiopathic constipation.

Surveillance decision

This review question should not be updated.

Evidence Update 2012

No relevant evidence was identified.

4-year surveillance summary

One case review evaluated criteria which could be applied to objectively assess constipation status in children based on abdominal radiographs. The study reported that individual parameters on abdominal radiograph included total stool length greater than 33.4 cm and stool length in the rectum greater than 5.9 cm⁸. One case review reported that plain radiographs may be a useful tool for the diagnosis of faecal impaction⁹ whilst a retrospective cohort study indicated that abdominal radiograph was performed more frequently in misdiagnosed children¹⁰. Finally, one systematic review concluded that there was insufficient evidence for a diagnostic

association between clinical symptoms of constipation and faecal loading on abdominal radiographs¹¹.

8-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

It was highlighted that when children are on medication and abdominal palpitation doesn't reveal a faecal mass then abdominal radiography may be useful. However, there was no evidence suggested to support this view.

Impact statement

The guideline recommends that plain abdominal radiograph should not be used to

make a diagnosis of idiopathic constipation and should be considered only if requested by specialist services in the ongoing management of intractable idiopathic constipation. A topic expert noted that plain abdominal radiograph may be a useful tool if other methods fail, which is broadly in line with [recommendation 1.3.5](#). Two case studies highlighted the utility of plain abdominal radiograph in the diagnosis of faecal impaction however results of a systematic

review indicated that there was insufficient evidence to support the use of abdominal radiographs for the diagnosis of constipation. Therefore it is unlikely that new evidence would impact the guideline.

New evidence is unlikely to change guideline recommendations.

99 – 07 What is the diagnostic value of the rectal biopsy in children with chronic idiopathic constipation?

Recommendations derived from this question

- 1.3.6 Do not perform rectal biopsy unless any of the following clinical features of Hirschsprung's disease are or have been present:
- delayed passage of meconium (more than 48 hours after birth in term babies)
 - constipation since first few weeks of life
 - chronic abdominal distension plus vomiting
 - family history of Hirschsprung's disease
 - faltering growth in addition to any of the previous features.

Surveillance decision

This review question should not be updated.

Evidence Update 20112

No relevant evidence was identified.

functional constipation from Hirschsprung's disease¹⁴.

4-year surveillance summary

A retrospective analysis was identified which evaluated infants having a suction rectal biopsy to exclude Hirschsprung's disease¹². The results of the analysis indicated that Hirschsprung's disease occurred less often in premature infants compared with term infants. One retrospective study focusing on clinical signs and symptoms of Hirschsprung's disease in older children reported that recurrent gastrointestinal infection with vomiting and hospitalisation occurred more frequently in children with Hirschsprung's disease whilst rectal biopsy confirmed the diagnosis¹³. Lastly, the results of one study indicated that faecal calprotectin had limited value in differentiating

8-year surveillance summary

A retrospective observational study was identified which evaluated the diagnostic accuracy of a contrast enema in children for Hirschsprung's disease and whether it should be performed before or after rectal biopsies (n = 107)¹⁵. The results indicated that although contrast enema had high diagnostic accuracy in detecting Hirschsprung's disease, it is not as accurate as rectal biopsy. It might therefore only be considered for subsequent surgical planning following histological confirmation of Hirschsprung's disease diagnosis with rectal biopsy. Future diagnostic planning is also suggested as another use however details of which are not reported.

One retrospective study (n = 358) examined the diagnostic accuracy of acetylcholinesterase (AChE) staining to diagnose Hirschsprung's disease¹⁶. Rectal mucosal specimens of children with suspected Hirschsprung's disease were examined and questionnaires were completed to assess final diagnosis from histopathological results. Results indicate that AChE staining has high sensitivity and specificity to accurately diagnose and rule out Hirschsprung's disease.

Impact statement

The new evidence implies there is diagnostic value of rectal biopsy in confirming the diagnosis of Hirschsprung's disease. However, the new evidence does not confirm specific clinical features as being good predictors of Hirschsprung's disease. As such, there is unlikely to be any impact on [recommendation 1.3.6](#).

Topic expert feedback

No topic expert feedback was relevant to this evidence.

New evidence is unlikely to change guideline recommendations.

99 – 08 What is the diagnostic value of transit studies in children?

Recommendations derived from this question

- 1.3.7 Do not use transit studies to make a diagnosis of idiopathic constipation.
- 1.3.8 Consider using transit studies in the ongoing management of intractable idiopathic constipation only if requested by specialist services.

Surveillance decision

No new information was identified at any surveillance review.
This review question should not be updated.

99 – 09 What is the diagnostic value of the abdominal ultrasound in children with chronic constipation?

Recommendations derived from this question

- 1.3.9 Do not use abdominal ultrasound to make a diagnosis of idiopathic constipation.
- 1.3.10 Consider using abdominal ultrasound in the ongoing management of intractable idiopathic constipation only if requested by specialist services.

Surveillance decision

This review question should not be updated.

Evidence Update 2012

No relevant evidence was identified.

4-year surveillance summary

One study was identified which compared digital palpation with transabdominal ultrasound to assess the rectal filling state in children with urological problems¹⁷. Agreement between the two tests for detecting rectal mass was 82.5%.

8-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The identified study did not indicate whether use of abdominal ultrasound adds any useful information over and above that ascertained through thorough physical examination and history taking in the diagnosis of chronic idiopathic constipation. As such, the evidence is unlikely to change the direction of the guideline recommendations which state that abdominal ultrasound should not be used to make a diagnosis of idiopathic constipation and should only be considered in the ongoing management of intractable idiopathic constipation only if requested by specialist services.

New evidence is unlikely to change guideline recommendation

Clinical management

99 – 10 What is the effectiveness of pharmacological and surgical intervention for disimpaction in children with chronic idiopathic constipation?

- 1.4.1 Assess all children and young people with idiopathic constipation for faecal impaction, including children and young people who were originally referred to the relevant services because of 'red flags' but in whom there were no significant findings following further investigations (see tables 2 and 3). Use a combination of history-taking and physical examination to diagnose faecal impaction – look for overflow soiling and/or faecal mass palpable abdominally and/or rectally if indicated.
- 1.4.2 Start maintenance therapy if the child or young person is not faecally impacted.
- 1.4.3 Offer the following oral medication regimen for disimpaction if indicated:
- Polyethylene glycol 3350 + electrolytes, using an escalating dose regimen (see table 4), as the first-line treatment***.
 - Polyethylene glycol 3350 + electrolytes may be mixed with a cold drink.
 - Add a stimulant laxative (see table 4) if polyethylene glycol 3350 + electrolytes does not lead to disimpaction after 2 weeks.
 - Substitute a stimulant laxative singly or in combination with an osmotic laxative such as lactulose (see table 4) if polyethylene glycol 3350 + electrolytes is not tolerated.
 - Inform families that disimpaction treatment can initially increase symptoms of soiling and abdominal pain.

Table 4 Laxatives: recommended doses

Laxatives	Recommended doses
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Macrogols	
Polyethylene glycol 3350 + electrolytes	<p>Paediatric formula: Oral powder: macrogol 3350 (polyethylene glycol 3350)^a 6.563 g; sodium bicarbonate 89.3 mg; sodium chloride 175.4 mg; potassium chloride 25.1 mg/sachet (unflavoured)</p> <p>Disimpaction</p> <p>Child under 1 year: ½–1 sachet daily (non-BNFC recommended dose)</p> <p>Child 1–5 years: 2 sachets on 1st day, then 4 sachets daily for 2 days, then 6 sachets daily for 2 days, then 8 sachets daily (non-BNFC recommended dose)</p> <p>Child 5–12 years: 4 sachets on 1st day, then increased in steps of 2 sachets daily to maximum of 12 sachets daily (non-BNFC recommended dose)</p> <p>Ongoing maintenance (chronic constipation, prevention of faecal impaction)</p> <p>Child under 1 year: ½–1 sachet daily (non-BNFC recommended dose)</p> <p>Child 1–6 years: 1 sachet daily; adjust dose to produce regular soft stools (maximum 4 sachets daily) (for children under 2, non-BNFC recommended dose)</p> <p>Child 6–12 years: 2 sachets daily; adjust dose to produce regular soft stools (maximum 4 sachets daily)</p> <p>Adult formula: Oral powder: macrogol 3350 (polyethylene glycol 3350) 13.125 g; sodium bicarbonate 178.5 mg; sodium chloride 350.7 mg; potassium chloride 46.6 mg/sachet (unflavoured)</p> <p>Disimpaction</p> <p>Child/young person 12–18 years: 4 sachets on 1st day, then increased in steps of 2 sachets daily to maximum of 8 sachets daily (non-BNFC recommended dose)</p> <p>Ongoing maintenance (chronic constipation, prevention of faecal impaction)</p> <p>Child/young person 12–18 years: 1–3 sachets daily in divided doses adjusted according to response; maintenance, 1–2 sachets daily</p>
Osmotic laxatives	
Lactulose	<p>Child 1 month to 1 year: 2.5 ml twice daily, adjusted according to response</p> <p>Child 1–5 years: 2.5–10 ml twice daily, adjusted according to response (non-BNFC recommended dose)</p> <p>Child/young person 5–18 years: 5–20 ml twice daily, adjusted according to response (non-BNFC recommended dose)</p>
Stimulant laxatives	
Sodium picosulfate ^b	Non-BNFC recommended doses

	<p>Elixir (5 mg/5 ml) Child 1 month to 4 years: 2.5–10 mg once a day Child/young person 4–18 years: 2.5–20 mg once a day</p>
	<p>Non-BNFC recommended dose Perles^c (1 tablet = 2.5mg) Child/young person 4–18 years: 2.5–20mg once a day</p>
Bisacodyl	<p>Non-BNFC recommended doses By mouth Child/young person 4–18 years: 5–20 mg once daily By rectum (suppository) Child/young person 2–18 years: 5–10 mg once daily</p>
Senna ^d	<p>Senna syrup (7.5 mg/5 ml) Child 1 month to 4 years: 2.5–10 ml once daily Child/young person 4–18 years: 2.5–20 ml once daily</p>
	<p>Senna (non-proprietary) (1 tablet = 7.5 mg) Child 2–4 years: ½–2 tablets once daily Child 4–6 years: ½–4 tablets once daily Child/young person 6–18 years: 1–4 tablets once daily</p>
Docusate sodium ^e	<p>Child 6 months–2 years: 12.5 mg three times daily (use paediatric oral solution) Child 2–12 years: 12.5–25 mg three times daily (use paediatric oral solution) Child/young person 12–18 years: up to 500 mg daily in divided doses</p>
<p>All drugs listed above are given by mouth unless stated otherwise.</p> <p>Unless stated otherwise, doses are those recommended by the British National Formulary for Children (BNFC) 2009. Informed consent should be obtained and documented whenever medications/doses are prescribed that are different from those recommended by the BNFC.</p> <p>^a At the time of publication (May 2010) Movicol Paediatric Plain is the only macrogol licensed for children under 12 years that includes electrolytes. It does not have UK marketing authorisation for use in faecal impaction in children under 5 years, or for chronic constipation in children under 2 years. Informed consent should be obtained and documented. Movicol Paediatric Plain is the only macrogol licensed for children under 12 years that is also unflavoured.</p> <p>^b Elixir, licensed for use in children (age range not specified by manufacturer). Perles not licensed for use in children under 4 years. Informed consent should be obtained and documented.</p> <p>^c Perles produced by Dulcolax should not be confused with Dulcolax tablets which contain bisacodyl as the active ingredient</p>	

^d Syrup not licensed for use in children under 2 years. Informed consent should be obtained and documented.

^e Adult oral solution and capsules not licensed for use in children under 12 years. Informed consent should be obtained and documented.

- 1.4.4 Do not use rectal medications for disimpaction unless all oral medications have failed and only if the child or young person and their family consent.
- 1.4.5 Administer sodium citrate enemas only if all oral medications for disimpaction have failed.
- 1.4.6 Do not administer phosphate enemas for disimpaction unless under specialist supervision in hospital/health centre/clinic, and only if all oral medications and sodium citrate enemas have failed.
- 1.4.7 Do not perform manual evacuation of the bowel under anaesthesia unless optimum treatment with oral and rectal medications has failed.
- 1.4.8 Review children and young people undergoing disimpaction within 1 week.

*** At the time of publication (May 2010), Movicol Paediatric Plain is the only macrogol licensed for children under 12 years that includes electrolytes. It does not have UK marketing authorisation for use in faecal impaction in children under 5 years, or for chronic constipation in children under 2 years. Informed consent should be obtained and documented. Movicol Paediatric Plain is the only macrogol licensed for children under 12 years that is also unflavoured.

Surveillance decision

This review question should not be updated.

Footnote 'a' in Table 4 will be amended to state that there are a range of paediatric plains available and that not all are licenced for children under 12.

Footnote 'c' will be corrected to state that the manufacturer of Perles is Sanofi.

Evidence Update 2012

An RCT was included which compared disimpaction with rectal enemas versus oral laxatives (PEG) in children aged 4–16 years with severe rectal faecal impaction¹⁸. No difference in successful disimpaction was observed between the enema and PEG groups at follow-up two weeks after disimpaction.

4-year surveillance summary

One RCT compared a single milk and molasses enema in the emergency department with PEG 3350 as paediatric faecal impaction treatment¹⁹. At day 3, more patients in the enema arm reported ideal stool consistency however, at day 5 no difference between groups was noted. Half in the enema arm were reported as upset by emergency department therapy, whereas no children in PEG arm were upset.

8-year surveillance summary

A systematic review of 58 studies (41 clinical trials, 8 observational, 9 systematic review/meta-analysis) (n = not stated) examined the effectiveness of PEG, with or without electrolytes, in the management of functional constipation and the treatment of faecal impaction²⁰. Studies including adults were separated from paediatric studies. Twelve clinical trials evaluated PEG efficacy versus placebo, eight versus lactulose, six were dose studies, five compared polyethylene glycol with and without electrolytes, two compared its efficacy to milk of magnesia, and the rest of the trials evaluate polyethylene glycol with enemas (two), psyllium (one), tegaserod (one), prucalopride (one), paraffin oil (one), fiber combinations (one) and Descurainia sophia (one). Results from the faecal disimpaction trials indicated that PEG is just as effective as enemas, avoiding the need for hospital admissions. However, whether this result applies to children and adults is not reported.

Another systematic review of 2 RCTs (n = 170) compared the effect of PEG to enema for treating faecal impaction in children²¹. The results indicate that those receiving PEG had a significantly reduced chance of treatment success, however this significance was marginal. Treatment with PEG was also associated with increased defecation frequency, but increased risk of watery stools and faecal incontinence. The authors stated that it was not possible to confirm which intervention is more effective due to the limitations of the data.

A systemic review of 45 studies (included 2 RCTs) (n = 1157) evaluated outcomes of different surgical options for the management of idiopathic constipation in children²². Surgical management options included antegrade continence enema, colon resection and pull-through operations, anal dilation, botulinum toxin injection, internal sphincter myectomy, and permanent colostomy. Given the low quality evidence in this area, the authors concluded that it was not possible to confirm which surgical management option was 'best practice'.

Topic expert feedback

Topic expert feedback indicated that there may be variation in dose administration of picolax and sodium picosulfate in clinical practice. However, picolax is not licenced for use in constipation but is used prior to surgery to clean out the bowel. Furthermore, the [NICE Guidelines Manual \(2014\)](#) states that readers of guidelines are expected to refer to the summary of product characteristics for details of drug dosages.

One topic expert highlighted that since the publication of CG99 there are now other commercially available paediatric plain preparations (e.g. Laxido paediatric plain).

It was also noted that although the guideline recommends PEG 3350, some of the evidence concerns the use of PEG 4000. The difference between the PEG varieties is the molecular weight. Systematic reviews identified in the new evidence from surveillance do not distinguish between the two types. It was also noted that PEG 4000 is not listed on the British National Formulary (BNF) or the Monthly Index of Medical Specialities (MIMS) so it is assumed that it is not used in the UK.

Impact statement

New evidence was identified comparing different disimpaction techniques such as enemas and PEG. A large systematic review was identified which supports current recommendations to use PEG as a first line treatment for disimpaction ([recommendation 1.4.3](#)). There were mixed reports on the effectiveness of enemas however the evidence consisted of just two trials of different enemas and a small systematic review. Also, a larger systematic review of surgical management options could not confirm which approach was 'best practice' due to the low quality of the evidence.

In summary, the new evidence is unlikely to change the direction of the guideline recommendation which states that PEG 3350 should be used as first-line treatment of disimpaction and enemas should only be used after oral therapy has failed.

It was also noted that there are two different varieties of PEG (3350 and 4000) appearing in the literature. Currently, the guideline only recommends the use of PEG 3350 and makes no reference to PEG 4000. Given that the original guideline takes into account evidence on both varieties and new systematic reviews do not distinguish between the two, it is unlikely that the recommendations will be impacted. Furthermore, it appears that PEG 4000 is not used in the UK.

Some of the footnotes in Table 4 have been highlighted as needing amendments. A topic expert noted that there are now other paediatric plain preparations available which have the potential to impact footnote 'a'. To account for this change and for any future developments in paediatric plain preparations, the footnote should be changed to state that there are a range of paediatric plain preparations available and that not all are licenced for children under 12. It was noted that footnote 'c' contains incorrect information regarding the manufacturer of Perles, which are in fact produced by Sanofi under the Dulcolax brand. The footnote should be amended to reflect this.

New evidence is unlikely to change guideline recommendations.

99 – 11 **What is the clinical effectiveness of pharmacological interventions for ongoing treatment and maintenance in children with chronic idiopathic constipation?**

99 – 12 **What are the adverse effects of the medium to long term use of laxatives?**

Recommendations derived from these questions

- 1.4.9 Start maintenance therapy as soon as the child or young person's bowel is disimpacted.
- 1.4.10 Reassess children frequently during maintenance treatment to ensure they do not become reimpacted and assess issues in maintaining treatment such as taking medicine and toileting. Tailor the frequency of assessment to the individual needs of the child and their families (this could range from daily contact to contact every few weeks). Where possible, reassessment should be provided by the same person/team.
- 1.4.11 Offer the following regimen for ongoing treatment or maintenance therapy:
- Polyethylene glycol 3350 + electrolytes as the first-line treatment***.
 - Adjust the dose of polyethylene glycol 3350 + electrolytes according to symptoms and response. As a guide for children and young people who have had disimpaction the starting maintenance dose might be half the disimpaction dose (see table 4).
 - Add a stimulant laxative (see table 4) if polyethylene glycol 3350 + electrolytes does not work.
 - Substitute a stimulant laxative if polyethylene glycol 3350 + electrolytes is not tolerated by the child or young person. Add another laxative such as lactulose or docusate (see table 4) if stools are hard.
 - Continue medication at maintenance dose for several weeks after regular bowel habit is established – this may take several months. Children who are toilet training should remain on laxatives until toilet training is well established. Do not stop medication abruptly: gradually reduce the dose over a period of months in response to stool consistency and frequency. Some children may require laxative therapy for several years. A minority may require ongoing laxative therapy.

*** At the time of publication (May 2010), Movicol Paediatric Plain is the only macrogol licensed for children under 12 years that includes electrolytes. It does not have UK marketing authorisation for use in faecal impaction in children under 5 years, or for chronic constipation in children under 2 years. Informed consent should be obtained and documented. Movicol Paediatric Plain is the only macrogol licensed for children under 12 years that is also unflavoured.

Surveillance decision

This review question should not be updated.

Evidence Update 2012

Evidence Update 2012

An RCT examined maintenance treatment with rectal enemas plus oral PEG compared with oral PEG in children aged 8-18 years²³. The results indicated no difference in the primary outcome between the two groups (defined as greater than or equal to three bowel

movements per week). The study was deemed unlikely to impact on the guideline as initial disimpaction was performed with enemas whilst PEG was administered without electrolytes and neither of these practices are recommended in the guideline. Another RCT compared maintenance treatment with PEG 4000 without electrolytes versus milk of magnesia in children

aged 1-4 years with at least one month of functional constipation²⁴. A significant improvement (defined as the proportion of patients with three or more bowel movements per week) was observed in the PEG group.

4-year surveillance summary

PEG

A Cochrane systematic review evaluated the efficacy and safety of osmotic and stimulant laxatives used to treat functional childhood constipation²⁵. The results indicated that PEG preparations may be superior to placebo, lactulose and milk of magnesia for childhood constipation. Furthermore, two reviews^{26, 27}; two RCTs^{28, 29} and a non-randomised study³⁰ indicated a benefit of PEG 4000 preparations for functional constipation in children. Finally, one RCT reported that the number of stools/week was higher in children with constipation randomised to PEG electrolytes whilst PEG-only was better tolerated and accepted³¹.

Domperidone versus PEG

Another RCT (n = 105) compared the effect of oral domperidone to PEG in the treatment of chronic functional constipation in children³². The treatment group received PEG solution for 6 months (0.6g/kg twice a day) followed by domperidone syrup for 3 months (0.15mL three times a day). The control group received the same course of PEG but followed by 3 months of placebo. The results showed no significant difference in response to treatment between the two groups at 1, 3 and 6 months follow-up. The authors report that both groups saw a significant change in symptoms from baseline to follow-up but the direction of the effect is not stated.

Mineral oil

One RCT comparing the laxative effect of cassia fistula emulsion (CFE) with mineral oil (MO) on paediatric functional constipation found the severity of pain during defecation and consistency of stool improved significantly better in CFE group than MO group, but there were not any significant differences between the two groups in faecal incontinence and retentive posturing³³.

Lubiprostone

One non-randomised study assessing the safety and efficacy of different doses of lubiprostone in children and adolescents with functional constipation reported that spontaneous bowel movements increased compared with baseline³⁴. However lubiprostone is not currently licenced for use in children.

Prucalopride

One non-randomised study evaluated the efficacy, safety, and tolerability of prucalopride oral solution in children aged 4 to 12 years with functional constipation³⁵. Prucalopride treatment resulted in a mean bowel movement frequency of 6.8/week and normal stool consistency. However prucalopride is not currently licenced for use in children.

One case series which also incorporated a review of case reports suggested there may be a risk of phosphate toxicity in children and adolescents treated with laxatives³⁶. However, a review outlining the evidence for the safety of laxatives used in chronic paediatric-functional constipation was unable to draw any meaningful conclusions due to a lack of evidence in this population³⁷.

8-year surveillance summary

PEG

One RCT (n = 200) investigated the response and reoccurrence rate after treatment with PEG alone compared to PEG plus lactulose³⁸.

Patients were aged 1-12 years and had a diagnosis of chronic functional constipation. All patients were treated for one month and the responsive patients were followed at 3, 6, and 12 months to assess reoccurrence. Results show that the response rate was significantly higher for those treated with PEG plus lactulose. There was no difference between groups for reoccurrence rates.

Another RCT (n = 92) evaluated the effectiveness and safety of two different doses of PEG for the maintenance treatment of functional constipation in children³⁹. Patients either received a high dose (0.7g/kg) or a low dose (0.3g/kg) of polyethylene 4000 for 6 weeks. Treatment success was defined as more than 3 bowel movements per week and adjustment of the therapy was recommended if the patient experienced less than this. Results

indicated that there was no difference in treatment success between the two doses. However, the low dose group experienced an increase risk of painful defecation, a lower number of stools per week, and lower parental satisfaction (significance not stated).

A systematic review of 58 studies (41 clinical trials, 8 observational, 9 systematic review/meta-analysis) (n = not stated) examined the effectiveness of PEG, with or without electrolytes, in the management of functional constipation and the treatment of faecal impaction²⁰. The reviewed studies included both adults and children, however the results were presented separately. The results showed that PEG with or without electrolytes is more efficacious than placebo or lactulose for treatment of functional constipation in children.

Finally, an updated version of a previously mentioned Cochrane review²⁵ was identified. This review of 25 RCTs evaluated the efficacy and safety of osmotic and stimulant laxatives used to treat functional childhood constipation⁴⁰. A subgroup analysis for each intervention was performed. Results indicated that high dose PEG is significantly more effective than low dose at increasing number of stools per week. This was also the case when compared to lactulose or milk of magnesia treatment. In a comparison of mineral oil treatment and lactulose, number of stools per week was significantly higher in the mineral oil group. There was no difference in the number of stools for the following comparisons: PEG versus enemas, dietary fibre mix versus lactulose, senna versus lactulose, lactitol versus lactulose, hydrolysed guar gum versus lactulose, polyethylene versus D. sophia / dietary fibre/ mineral oil.

Lactulose versus PEG 4000

One RCT (n = 88) compared the efficacy and safety of PEG 4000 to lactulose for the treatment of chronic constipation in children aged 12 to 36 months⁴¹. Results indicate that although both groups experienced increases in stool frequency, the improvement was significantly higher for those treated with PEG. Stool consistency and ease of stool passage was significantly improved in the PEG group.

Cassia fistula's emulsion versus PEG 4000

Another RCT (n = 57) compared the efficacy and safety of cassia fistula's emulsion to PEG

4000 for the treatment of functional constipation in children aged between 2-15 years⁴². Patients received either cassia fistula's emulsion or PEG for 4 weeks and were considered improved if they no longer fulfilled the Rome III criteria for functional constipation. Although the results showed improvement for a proportion of patients receiving each treatment, there was no significant difference between groups. Frequency of defecation was significantly higher in the patients receiving cassia fistula's emulsion.

Flixweed (Descurainia sophia) versus PEG

One RCT (n = 120) compared the efficacy and safety of *Descurainia sophia* (D. sophia) to PEG for the treatment of constipation in children aged 2-12 years⁴³. Patients received either D. sophia seeds (2g for ages 2-4 years, 3g for over 4 years) or PEG for 8 weeks. Improvement was defined as no longer meeting the Rome III criteria for functional constipation. The results indicate patients in both groups improved at follow-up, with no significant difference between the two groups. There was also no significant difference between groups with regards to median weekly stool frequency.

Topic expert feedback

Topic experts indicated that there is poor provision for management of idiopathic constipation in children with additional needs (both learning and physical difficulties) and often these children are excluded from mainstream services. However, the guideline scope covers newborns, infants and children up to their 18th birthday who have idiopathic constipation and no evidence specifically conducted in children with learning or physical difficulties was identified through the surveillance review.

Impact statement

The identified new evidence is supportive of the use of PEG for functional constipation however, it was not clear from an assessment of some of the abstracts if the interventions included PEG alone or in combination with electrolytes which is the first-line maintenance therapy recommended in the guideline. As such, it is not possible to determine the impact of some of this new evidence on the guideline. Promising

benefits of lubiprostone and prucalopride were reported in two studies, but currently these pharmaceuticals are not licensed for use in children or adolescents under 18 years and evidence comparing these treatments with PEG 3350 + electrolytes are necessary to enable their place in the management of idiopathic constipation in children to be established.

There was new evidence to suggest that alternative treatments such as cassia fistula's emulsion, oral domperidone, and D. sophia may be just as effective as PEG alone in the treatment of constipation in children. However this evidence is based on single trials with small sample sizes so until further evidence is available, the recommendations are unlikely to be impacted.

There was new evidence that called into question the use of lactulose for treatment of constipation in children, with a systematic review indicating that both PEG and mineral oil are more effective treatments.

[Recommendation 1.4.11](#) currently advises adding lactulose if stools are hard (only after a stimulant laxative has been substituted if PEG is not tolerated by the child). Recommendations on the use of lactulose therefore provide alternative strategies if first-line treatment is unsuccessful. Furthermore, there are no recommendations on treatment with lactulose alone, so it is unlikely that the new evidence will impact recommendations.

New evidence is unlikely to change guideline recommendations.

99-13 What is the clinical effectiveness of the following complementary therapies for ongoing treatment and/or maintenance in children with chronic idiopathic constipation?

- abdominal massage
- reflexology
- hypnotherapy osteopathy
- cranial osteopathy
- homeopathy

Recommendations derived from this question

No recommendations for this review question.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

NQ – 01 What is the clinical effectiveness of electrical stimulation therapy for ongoing treatment and/or maintenance in children with chronic idiopathic constipation?

This review question was not addressed by the guideline.

New evidence has subsequently been identified and considered for possible addition to the guideline as a new question.

Surveillance decision

This review question should not be added.

Evidence Update 2012

No relevant evidence was identified.

4-year surveillance summary

Three small case series reported that transcutaneous electrical nerve stimulation may improve constipation symptoms in children⁴⁴⁻⁴⁶.

8-year surveillance summary

One systematic review of 6 studies (n = not stated) investigated the effectiveness of electrical stimulation for the treatment of slow transit constipation in children⁴⁷. Results indicated that electrical stimulation therapy was associated with significant improvements in one to four outcome measures in each of the studies: frequency of defecation, soiling, stool consistency, radionuclear transit studies, and quality of life. No further results were reported.

Topic expert feedback

One topic expert noted that there have been a number of mixed reports about the use of electrical nerve stimulation in children with idiopathic constipation.

Impact statement

The guideline does not currently include any recommendations on electrical stimulation therapy. Although the identified systematic review indicated a potential benefit of electrical stimulation therapy for functional constipation, the results are not clearly reported so the effect is unclear. Furthermore, a topic expert raised concerns about the mixed reports on the effectiveness of electrical nerve stimulation. Further data on long-term outcomes are needed before considering electrical stimulation for inclusion in the guideline.

New evidence is unlikely to impact on the guideline.

NQ – 02 What is the clinical effectiveness of physiotherapy for ongoing treatment and/or maintenance in children with chronic idiopathic constipation?

This review question was not addressed by the guideline.

New evidence has subsequently been identified and considered for possible addition to the guideline as a new question.

Surveillance decision

This review question should not be added.

Evidence Update 2012

No relevant evidence was identified.

4-year surveillance summary

One RCT assessed the effect of physiotherapy (muscular training, abdominal massage and diaphragmatic breathing) plus laxatives

compared with laxatives alone in children and adolescents with functional constipation⁴⁸. After 6 weeks of treatment, the frequency of bowel movements was higher in the physiotherapy group although the frequency of faecal incontinence was no different between the groups.

8-year surveillance summary

One RCT (n = 40) examined the effect of connective tissue manipulation (CTM) and Kinesio Taping (KT) on constipation in children with cerebral palsy⁴⁹. Both treatments were compared to control however details of the control group were not reported. Results indicate that there were significant differences between groups with regards to defecation frequency, stool consistency, visual analogue scale, and quality of life. Both CTM and KT were reported to be equally effective physiotherapy approaches to treat constipation in children with cerebral palsy.

One RCT (n = 53) examined the effectiveness of pelvic physiotherapy compared to standard medical care in children aged 5-16 with functional constipation⁵⁰. Standard care was defined as treatment using education, toilet training and laxatives. Pelvic physiotherapy included standard care plus specific physiotherapeutic interventions. Results

showed that overall treatment success was significantly higher in patients receiving pelvic physiotherapy compared to standard care. Significantly more patients receiving pelvic physiotherapy stopped using laxatives. However, there was no difference in quality of life scores between the two groups.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The guideline does not currently include any recommendations on physiotherapy for treatment/maintenance in children with chronic idiopathic constipation. Although the identified RCTs indicated a potential benefit of physiotherapy for functional constipation, these results are based on a limited number of trials with a small sample size. Further data on long-term outcomes and evidence of cost-effectiveness are needed before considering physiotherapy for inclusion in the guideline.

New evidence is unlikely to impact on the guideline.

NQ – 03 What is the clinical effectiveness of anorectal myectomy for ongoing treatment and/or maintenance in children with chronic idiopathic constipation?

This review question was not addressed by the guideline.

New evidence has subsequently been identified and considered for possible addition to the guideline as a new question.

Surveillance decision

This review question should not be added.

Evidence Update 2012

No relevant evidence was identified.

4-year surveillance summary

The role of anorectal myectomy in children with chronic refractory constipation was evaluated in one cohort study⁵¹. Twenty-two patients

improved clinically; 4 patients had a partial response and 2 patients did not respond.

8-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

constipation. Further research in larger studies is needed to determine the long-term benefits and harms of anorectal myectomy before considering for inclusion in the guideline.

Impact statement

The guideline does not currently include any recommendations on anorectal myectomy for treatment of children with chronic idiopathic

New evidence is unlikely to impact on the guideline.

NQ – 04 What is the clinical effectiveness of sacral neuromodulation therapy for ongoing treatment and/or maintenance in children with chronic idiopathic constipation?

This review question was not addressed by the guideline.

New evidence has subsequently been identified and considered for possible addition to the guideline as a new question.

Surveillance decision

This review question should not be added.

Evidence Update 2012

No relevant evidence was identified.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

4-year surveillance summary

A small retrospective review evaluated the use of sacral neuromodulation therapy as a treatment option in adolescents with refractory functional constipation⁵². After implantation, the majority of patients had a normal spontaneous defecation pattern of more than 2 times a week without medication, felt the urge to defecate, and perceived less abdominal pain without relapse of symptoms until 6 months after implantation.

Impact statement

The guideline does not currently include any recommendations on sacral neuromodulation therapy. Further data on long-term outcomes are needed before considering sacral neuromodulation therapy for inclusion in the guideline.

8-year surveillance summary

No relevant evidence was identified.

New evidence is unlikely to impact on the guideline.

NQ – 05 What is the clinical effectiveness of botulinum toxin for ongoing treatment and/or maintenance in children with chronic idiopathic constipation?

This review question was not addressed by the guideline.

New evidence has subsequently been identified and considered for possible addition to the guideline as a new question.

Surveillance decision

This review question should not be added.

Evidence Update 2012

No relevant evidence was identified.

4-year surveillance summary

One RCT evaluated the utility of botulinum toxin injection into the anal sphincter compared with medication as treatment of idiopathic constipation and anal fissure in children⁵³. Botox injection significantly reduced pain on defecation and soiling compared with the control group.

8-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The guideline does not currently include any recommendations on botulinum toxin for treatment/maintenance in children with chronic idiopathic constipation. Further data on long-term outcomes are needed before considering botulinum toxin treatment for inclusion in the guideline.

New evidence is unlikely to impact on the guideline.

NQ – 06 What is the clinical effectiveness of transanal irrigation in children with chronic idiopathic constipation?

This review question was not addressed by the guideline.

New evidence has subsequently been identified and considered for possible addition to the guideline as a new question.

Surveillance decision

This review question should not be added.

Evidence Update 2012

No relevant evidence was identified.

4-year surveillance summary

One retrospective cohort study⁵⁴(n = 13) was highlighted during the consultation period by a stakeholder. Bowel function and social problems were assessed in children with faecal incontinence before and after treatment with Peristeen© transanal irrigation system. The results indicated that all patients experienced a

significant improvement in their faecal continence score with some increase in quality of life scores. It is not clear what proportion of the patients had idiopathic constipation or constipation with a known cause.

8-year surveillance summary

One uncontrolled, non-randomised trial⁵⁵ (n = 42) was highlighted during the consultation period by a stakeholder. The study examined the response rates and quality of life outcomes

for patients aged under 17 years who commenced transanal irrigation for constipation. This was a retrospective database study where 62% of the patients had idiopathic constipation. The median follow-up period was 14 months. Results indicated that quality of life scores were significantly improved after transanal irrigation. Response rates suggested that a larger proportion of patients adopted the treatment (compared to those who stopped within 1 month after commencement). Out of those who adopted the treatment, a larger proportion were classed as responders (defined as totally continent or occasional soiling). The method of analysis is unclear however and significance is not stated for these differences.

One cross-sectional survey⁵⁶ (n = 49) was also highlighted during the consultation period by a stakeholder. The study aimed to assess the treatment efficacy of transanal irrigation and parental satisfaction in children aged 0-18 years with intractable functional constipation treated with Peristeen. Results indicated that out of all children who still used Peristeen at the time of survey, fecal incontinence had resolved completely in 41%, 12% experienced occasional episodes of fecal incontinence (<1 episode per week) and the remaining 47% still experienced episodes of fecal incontinence regularly (≥1 time per week). Despite high parental satisfaction ratings, a large proportion of the children experienced pain during the procedure. Results from a formal statistical analysis were not reported.

Topic expert feedback

One topic expert noted that since the original guideline was produced in 2010, the use of transanal irrigation is becoming more mainstream and a viable option to manage

intractable idiopathic constipation and soiling when standard therapy has failed. A concern was highlighted that some children may be undergoing surgery when the non-surgical option of transanal irrigation may have been a more appropriate option.

Impact statement

New evidence was highlighted on the use of transanal irrigation for the treatment of chronic constipation in children. Although some results indicated that transanal irrigation may have benefit to patients, a cross sectional survey indicated that the procedure was not effective for a large proportion of patients and that many experienced pain during the procedure. Furthermore, all of the studies had small sample sizes and with a retrospective study design and no control group or comparator.

A topic expert highlighted that transanal irrigation is becoming more commonly used in practice and called for the guideline to reflect this. It is noted that this is an area of research that shows promising results for the treatment of constipation in this population, however the findings are considered too preliminary at this point to have an impact on guidance. Until the safety and efficacy of transanal irrigation is confirmed in this population by consistent reports from a reliable evidence base, it is unlikely that the guideline will be impacted. In the meantime NICE are currently developing medical technologies guidance on '[The Peristeen anal irrigation system to manage bowel dysfunction](#)' and we will review this area again at the next surveillance point.

New evidence is unlikely to impact on the guideline.

Diet and lifestyle

99 – 14 **What is the clinical effectiveness of the following for ongoing treatment or maintenance in children with chronic idiopathic constipation?**

- **increasing physical activity**
- **dietary modifications**
- **increasing fluid intake**
- **excluding cows' and goats' milk protein from diet.**

Recommendations derived from this review question

- 1.5.1 Do not use dietary interventions alone as first-line treatment for idiopathic constipation.
- 1.5.2 Treat constipation with laxatives and a combination of:
- Negotiated and non-punitive behavioural interventions suited to the child or young person's stage of development. These could include scheduled toileting and support to establish a regular bowel habit, maintenance and discussion of a bowel diary, information on constipation, and use of encouragement and rewards systems.
 - Dietary modifications to ensure a balanced diet and sufficient fluids are consumed.
- 1.5.3 Advise parents and children and young people (if appropriate) that a balanced diet should include:
- Adequate fluid intake (see table 5).
 - Adequate fibre. Recommend including foods with a high fibre content (such as fruit, vegetables, high-fibre bread, baked beans and wholegrain breakfast cereals) (not applicable to exclusively breastfed infants). Do not recommend unprocessed bran, which can cause bloating and flatulence and reduce the absorption of micronutrients.

Table 5 American dietary recommendations

(Institute of Medicine, 2005). Dietary reference intakes for water, potassium, sodium chloride and sulfate. Washington DC: The National Academies Press

	Total water intake per day, including water contained in food	Water obtained from drinks per day
Infants 0–6 months	700 ml assumed to be from breast milk	
7–12 months	800 ml from milk and complementary foods and beverages	600 ml
1–3 years	1300 ml	900 ml

4–8 years	1700 ml	1200 ml
Boys 9–13 years	2400 ml	1800 ml
Girls 9–13 years	2100 ml	1600 ml
Boys 14–18 years	3300 ml	2600 ml
Girls 14–18 years	2300 ml	1800 ml
<p>The above recommendations are for adequate intakes and should not be interpreted as a specific requirement. Higher intakes of total water will be required for those who are physically active or who are exposed to hot environments. It should be noted that obese children may also require higher total intakes of water.</p>		

- 1.5.4 Provide children and young people with idiopathic constipation and their families with written information about diet and fluid intake.
- 1.5.5 In children with idiopathic constipation, start a cows' milk exclusion diet only on the advice of the relevant specialist services.
- 1.5.6 Advise daily physical activity that is tailored to the child or young person's stage of development and individual ability as part of ongoing maintenance in children and young people with idiopathic constipation.

Surveillance decision

This review question should not be updated.

Increasing physical activity

Evidence Update 2012

No relevant evidence was identified.

4-year surveillance summary

An RCT (conducted in adolescents)⁵⁷ and a cohort study (including pre-school children)⁵⁸ reported that physical activity may be associated with a decreased risk of functional constipation.

8-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence supports the guideline which recommends daily physical activity that is tailored to the child's stage of development and individual ability as part of ongoing maintenance in children and young people with idiopathic constipation ([recommendation 1.5.6](#)).

New evidence is unlikely to change guideline recommendations.

Dietary modifications

Evidence Update 2012

Probiotics

A systematic review and two RCTs evaluating probiotics were included in the Evidence Update. The results of the systematic review indicated that the available data does not currently support the use of probiotics in the treatment of constipation⁵⁹. One RCT comparing *Lactobacillus reuteri* with placebo in infants at least 6 months old reported increased bowel movements in the probiotic group⁶⁰. However no differences between the groups were seen at any follow-up for stool consistency or inconsolable crying. Finally, an RCT examining a fermented milk product containing *Bifidobacterium lactis* in constipated children aged 3–16 years found no significant change in stool frequency from baseline between groups⁶¹.

High fibre

A systematic review examined nonpharmacological treatments for childhood constipation including fibre, prebiotics and probiotics, and fluid⁶². The studies on fibre were mixed with only one out of three showing a significant effect with glucomannan compared with placebo for a number of outcome measures.

4-year surveillance summary

Probiotics / prebiotics

The evidence on the effectiveness of probiotics and prebiotics was mixed with one review indicating that *L. reuteri* DSM 17938 may help infants with constipation⁶³ whilst two systematic reviews^{64, 65}; a follow-up of two RCTs⁶⁶ and a non-randomised trial⁶⁷ reported that probiotics have not proven to be effective for children with functional constipation. In addition, one controlled trial assessed the effect of adding a probiotic to mineral oil in the treatment of functional constipation in children⁶⁸. After the treatment, stool frequency increased in both groups, with greater increase in probiotic + mineral oil group although no difference

between groups was observed for other outcomes such as frequency of hard/very hard stool and frequency of painful defecation.

High fibre

Two systematic reviews^{69,70} and two RCTs^{71,72} reported that there is a lack of evidence to confirm the role of dietary fibre intake on constipation in children. Conversely, one RCT indicated that, compared with placebo, a dietary fibre mixture increased daily bowel movements and frequency of passing non-hardened stools in children with constipation⁷³. Finally, one RCT indicated that an intervention comprising of doctor's dietary advice plus personalised diet management by a registered dietician may improve fibre consumption among children with refractory functional constipation⁷⁴. In addition, one RCT compared general advice on increasing dietary fibre intake with a behavioural intervention tool for children with functional constipation⁷⁵. The results indicated that the behavioural intervention increased the fibre intakes of children with constipation at 3 months compared to standard dietary treatment although no further increase was observed at 6 and 12 months follow-up.

8-year surveillance summary

Probiotics / prebiotics

One RCT (n = 22) examined the effect of daily supplementation of Orafti inulin-type fructans (prebiotic) on stool consistency in constipated children aged 2-5⁷⁶. The treatment lasted 6 weeks and was compared to placebo (maltodextrin). Results indicated that patients supplemented with Orafti inulin-type fructans had significantly softer stools than the control group.

One RCT (n = 56) investigated the effectiveness of probiotics in children aged 4-12 with constipation⁷⁷. Patients received either lactulose plus Protexin or lactulose plus placebo for 4 weeks. Results showed that frequency and consistency of defecation significantly improved in both groups, but there was no difference between them. The

intervention group showed significant improvement in abdominal pain and faecal incontinence after one week but this effect was not significant at the end of the study.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

Regarding the use of prebiotics and probiotics, the impact of the new evidence is limited by conflicting reports from small trials with short follow-up periods. Furthermore, during guideline development the topic experts felt it was not possible to recommend specific probiotics due to a lack of consistent evidence. Further research is needed before considering

prebiotics and probiotics for inclusion in the guideline.

Regarding the use of dietary fibre, there was mixed evidence to support the use of dietary fibre for treatment of constipation. There were also no comparisons made between dietary fibre treatment and laxatives. The guideline currently recommends treating constipation with a combination of laxatives, behavioural interventions and dietary modifications ([recommendation 1.5.2](#)). It also makes recommendations on adequate fibre intake in the diet ([recommendation 1.5.3](#)). As the new evidence does not provide clear direction on whether dietary modifications alone should be used as first-line treatment, it is unlikely that there will be an impact on the guideline.

New evidence is unlikely to change guideline recommendations.

Increasing fluid intake

Evidence Update 2012

A systematic review examined nonpharmacological treatments for childhood constipation including fibre, prebiotics and probiotics, and fluid⁶². No effect was seen with raised fluid intake above normal.

4-year surveillance summary

No relevant evidence was identified.

8-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

There was no new evidence to suggest that increasing fluid intake is an effective treatment for childhood constipation. The guideline currently makes recommendations on adequate fluid intake, however using dietary modifications alone for first-line treatment of childhood constipation is not advised ([recommendation 1.5.1](#)). Therefore the new evidence is unlikely to have an impact on recommendations.

New evidence is unlikely to change guideline recommendations.

Excluding cows' and goats' milk protein from diet.

Evidence Update 2012

No relevant evidence was identified.

4-year surveillance summary

A study which reported the results of two cross-over dietary trials was identified⁷⁸. The results

from the first trial indicated that there was an association between functional constipation and cow's milk consumption. Results from the second trial suggest that this association may not be caused by the type of casein protein in the milk. Furthermore, an RCT was identified which investigated the role of cow's milk allergy as a cause of chronic constipation and effect of cow's milk free diet (CMFD) on its treatment in

children⁷⁹. Significantly more patients in the CMFD group (CMFD for 4 weeks followed by a cow's milk diet for 2 weeks) had decreased signs and symptoms of constipation compared with the control group who received a cow's milk diet for 6 weeks.

8-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The guideline recommends that children and young people with idiopathic constipation should only start a cows' milk exclusion diet on the advice of specialist services and no new evidence was identified through the surveillance review that would change this recommendation.

New evidence is unlikely to change guideline recommendations.

Psychological interventions

99 – 17 **What is the clinical effectiveness of psychological and behavioural interventions in addition to laxatives for ongoing treatment or maintenance in children with chronic idiopathic constipation?**

Recommendations derived from this question

- 1.6.1 Do not use biofeedback for ongoing treatment in children and young people with idiopathic constipation.
- 1.6.2 Do not routinely refer children and young people with idiopathic constipation to a psychologist or child and adolescent mental health services unless the child or young person has been identified as likely to benefit from receiving a psychological intervention.

Surveillance decision

This review question should not be updated.

Evidence Update 2012

A systematic review included two RCTs assessing behavioural interventions⁶². No evidence was found to support the use of behavioural interventions in the treatment of childhood constipation.

4-year surveillance summary

No relevant evidence was identified.

8-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence is consistent with the guideline recommendation not to routinely refer children and young people to a psychologist or child and adolescent mental health services unless the child or young person has been specifically identified as likely to benefit from receiving a psychological intervention. Therefore no impact on the guideline is expected.

New evidence is unlikely to change guideline recommendations.

Antegrade colonic enema procedure

99 – 13 **What is the effectiveness of the antegrade colonic enema (ACE) procedure in children with chronic idiopathic constipation?**

Recommendations derived from this question

- 1.7.1 Refer children and young people with idiopathic constipation who still have unresolved symptoms on optimum management to a paediatric surgical centre to assess their suitability for an antegrade colonic enema (ACE) procedure.
- 1.7.2 Ensure that all children and young people who are referred for an ACE procedure have access to support, information and follow-up from paediatric healthcare professionals with experience in managing children and young people who have had an ACE procedure.

Surveillance decision

This review question should not be updated.

Evidence Update 2012

No relevant evidence was identified.

4-year surveillance summary

Two retrospective reviews^{80,81} and a case series⁸² of children with constipation indicated improvements in outcomes after antegrade continence enemas (ACE). Finally, one retrospective review was identified which assessed the rate of ACE bowel management failure in paediatric refractory constipation, and the management and long term outcome of these patients⁸³. The results indicated that 16% failed successful bowel management after antegrade continence enema requiring additional intervention.

8-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

One topic expert noted that it is current practice to consider rectal irrigation prior to ACE

procedure, highlighting several pieces of evidence to support this. However this evidence includes children with constipation that has a known cause which is outside the scope of this guideline.

Impact statement

No new evidence was identified on choice of washout solution, its type and volume and why ACE works in some children and not in others. The identified new evidence is unlikely to change the direction of the current recommendation which states that children and young people with idiopathic constipation who still have unresolved symptoms on optimum management should be referred to a paediatric surgical centre to assess their suitability for an ACE procedure.

New evidence is unlikely to change guideline recommendations.

99 – 15

What is the effectiveness of the information, support and advice that children and young people and their parents or carers are given regarding the treatment and management of idiopathic constipation?

Recommendations derived from this question

- 1.8.1 Provide tailored follow-up to children and young people and their parents or carers according to the child or young person's response to treatment, measured by frequency, amount and consistency of stools. Use the Bristol Stool Form Scale to assess this (see appendix D). This could include:
- telephoning or face-to-face talks
 - giving detailed evidence-based information about their condition and its management, using, for example, NICE's Information for the public for this guideline
 - giving verbal information supported by (but not replaced by) written or website information in several formats about how the bowels work, symptoms that might indicate a serious underlying problem, how to take their medication, what to expect when taking laxatives, how to poo, origins of constipation, criteria to recognise risk situations for relapse (such as worsening of any symptoms, soiling etc.) and the importance of continuing treatment until advised otherwise by the healthcare professional.
- 1.8.2 Offer children and young people with idiopathic constipation and their families a point of contact with specialist healthcare professionals, including school nurses, who can give ongoing support.
- 1.8.3 Healthcare professionals should liaise with school nurses to provide information and support, and to help school nurses raise awareness of the issues surrounding constipation with children and young people and school staff.
- 1.8.4 Refer children and young people with idiopathic constipation who do not respond to initial treatment within 3 months to a practitioner with expertise in the problem.

Surveillance decision

This review question should not be updated.

Evidence Update 2012

No relevant evidence was identified.

4-year surveillance summary

One study was identified which compared a nurse-led intervention focusing on self-help psychology practice with routine consultant-led care as recommended in CG99⁸⁴. Less 'nurse-led' children were still constipated passing less than 3 stools per week compared with those receiving consultant-led care although the proportion of children, over 4 years, free from soiling accidents was similar in the nurse-led group and with consultant-led care.

8-year surveillance summary

One RCT (n = 235) compared different follow-up strategies for children with functional constipation and whether they improve treatment outcomes⁸⁵. Patients were either assigned to a control group (no scheduled contact), a phone group (2 scheduled phone contacts), or a web group (access to web-based information). Results indicate that after 3 and 6 months, significantly more children in the web group were successfully treated compared to the control and phone groups. There was no difference in treatment success after 12 months. Patients in the web groups opted for significantly more additional phone consultations than the other groups, indicating

that access to web-based information improved self-management behaviour.

Topic expert feedback

Topic experts indicated that the guideline would benefit from including more emphasis on education of health care professionals in how to organise and provide primary and secondary care services for children with constipation.

One topic expert noted that there has been a set of [recommendations](#) published jointly by the Paediatric Continence Forum (PCF) and UK Continence Society (UKCS). The recommendations set out minimum standards of continence care for children and are intended to reduce inequalities in access to services or service provision.

Impact statement

There was new evidence that supported the use of a nurse-led intervention which focussed

on self-help psychology practice. This study addresses one of the research recommendations (RR03) in the guideline. However because it is a service evaluation to determine the appropriateness of developing a nurse-led intervention, further research is needed in a trial setting to formally assess the cost effectiveness of specialist nurse-led services. Therefore no impact on the guideline is expected at this point.

There was new evidence supporting the use of web-based information provision. This is consistent with [recommendation 1.8.1](#) which advises giving verbal information supported by (but not replaced by) written or website information in several formats about constipation. As it supports current recommendations, no impact on the guideline is expected.

New evidence is unlikely to change guideline recommendations.

Editorial and factual corrections identified during surveillance

During surveillance editorial or factual corrections were identified.

- A footnote in CG99 refers to NICE guideline CG86 which has now been replaced by NICE Guideline NG20 [Coeliac disease: recognition, assessment and management](#). This would need updating to refer to the correct guideline.
- Footnote 'a' in Table 4 will be amended to state that there are a range of paediatric plains available and that not all are licensed for children under 12.
- Footnote 'c' in Table 4 will be amended to state that the manufacturer of Perles is Sanofi.

Research recommendations

RR – 01 What is the effectiveness of polyethylene glycol 3350 + electrolytes in treating idiopathic constipation in children younger than 1 year old, and what is the optimum dosage?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 02 Is age-specific information more effective than non-age-specific information in increasing children’s knowledge and understanding of constipation and its treatment, and what information should be given?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 03 This research recommendation will be considered again at the next surveillance point. Do specialist nurse-led children’s continence services or traditional secondary care services provide the most effective treatment for children with idiopathic constipation (with or without faecal incontinence) that does not respond fully to primary treatment regimens? This should consider clinical and cost effectiveness, and both short-term (16 weeks) and long-term (12 months) resolution.

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 04 What is the effectiveness of different volumes and types of solutions used for colonic washouts in children who have undergone an antegrade colonic enema (ACE) procedure for intractable chronic idiopathic constipation?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 05 What is the impact of specific models of service on both clinical and social outcomes to deliver timely diagnosis and treatment interventions in children with chronic idiopathic constipation and their families?

The research recommendation would be answered by a study design that was not included in the search (usually systematic reviews or randomised controlled trials).

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 06 What is the diagnostic and prognostic value of the abdominal ultrasound in children with chronic idiopathic constipation?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 07 What is the clinical effectiveness of increasing physical activity for ongoing treatment/ maintenance in children with chronic idiopathic constipation?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 08 In infants with chronic idiopathic constipation, does changing from one infant milk formula to another improve symptoms? (For example, standard infant formula versus infant formula with oligosaccharides versus standard infant formula + laxative)

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 09 What is the effectiveness of complementary therapies (hypnotherapy) for ongoing treatment/maintenance in children with chronic idiopathic constipation?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 10 What are the experiences of children who have undergone ACE procedure due to intractable chronic idiopathic constipation?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 11 What is the effectiveness of polyethylene glycol 3350 + electrolytes as compared to stimulant laxatives (senna, bisacodyl and sodium picosulfate) in treating idiopathic constipation in children older than 2 years?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

References

1. Osatakul S and Puetpaiboon A. (2014) Use of Rome II versus Rome III criteria for diagnosis of functional constipation in young children. *Pediatrics International* 56:83-88.
2. Burgers R, Levin AD, Di LC et al. (2012) Functional defecation disorders in children: comparing the Rome II with the Rome III criteria. *Journal of Pediatrics* 161:615-620.
3. Drzewiecki BA, Thomas JC, Pope JC et al. (2012) Use of validated bladder/bowel dysfunction questionnaire in the clinical pediatric urology setting. *Journal of Urology* 188:1578-1583.
4. Chang SH, Park KY, Kang SK et al. (2013) Prevalence, clinical characteristics, and management of functional constipation at pediatric gastroenterology clinics. *Journal of Korean Medical Science* 28:1356-1361.
5. Furuta GT, Williams K, Kooros K et al. (2012) Management of constipation in children and adolescents with autism spectrum disorders. *Pediatrics* 130 Suppl 2:S98-105.
6. Bradnock TJ, Knight M, Kenny S et al. (9-3-2017) Hirschsprung's disease in the UK and Ireland: incidence and anomalies. *Archives of Disease in Childhood* .
7. Pelleboer RA, Janssen RL, Deckers-Kocken JM et al. (2012) Celiac disease is overrepresented in patients with constipation. *Jornal de Pediatria* 88:173-176.
8. Marks A, Vasquez E, Moylan S et al. (2013) Definition of reliable, objective criteria by abdominal radiography to identify occult constipation in children with lower urinary tract symptoms. *Journal of Urology* 189:1519-1523.
9. Cunha TB, Tahan S, Soares MF et al. (2012) Abdominal radiograph in the assessment of fecal impaction in children with functional constipation: comparing three scoring systems. *Jornal de Pediatria* 88:317-322.
10. Freedman SB, Thull-Freedman J, Manson D et al. (2014) Pediatric abdominal radiograph use, constipation, and significant misdiagnoses. *J Pediatr* 164:83-88.
11. Berger MY, Tabbers MM, Kurver MJ et al. (2012) Value of abdominal radiography, colonic transit time, and rectal ultrasound scanning in the diagnosis of idiopathic constipation in children: a systematic review. *Journal of Pediatrics* 161:44-50.
12. Sharp NE, Pettiford-Cunningham J, Shah SR et al. (2013) The prevalence of Hirschsprung disease in premature infants after suction rectal biopsy. *Journal of Surgical Research* 184:374-377.
13. Maerzheuser S, Bassir C, and Rothe K. (2012) Hirschsprung disease in the older child: diagnostic strategies. *Clinical Pediatrics* 51:1087-1090.
14. Mahjoub FE, Zahedi N, Ashjai B et al. (2013) Role of fecal calprotectin in differentiating between Hirschsprung's disease and functional constipation. *Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi* 62:288-291.
15. Frongia G, Gunther P, Schenk J et al. (2016) Contrast Enema for Hirschsprung Disease Investigation: Diagnostic Accuracy and Validity for Subsequent Diagnostic and Surgical Planning. *European journal of pediatric surgery : official journal of Austrian Association of Pediatric Surgery ...[et al] = Zeitschrift fur Kinderchirurgie* 26:207-214.
16. Budiarto IR, Obata S, Kinoshita Y et al. (2015) Reevaluation of acetylcholinesterase staining for the diagnosis of Hirschsprung disease and allied disorders. *Journal of pediatric gastroenterology and nutrition* 60:606-612.
17. Burgers R, de Jong TP, and Benninga MA. (2013) Rectal examination in children: digital versus transabdominal ultrasound. *Journal of Urology* 190:667-672.

18. Bekkali NL, van den Berg MM, Dijkgraaf MG et al. (2009) Rectal fecal impaction treatment in childhood constipation: enemas versus high doses oral PEG. *Pediatrics* 124:e1108-e1115.
19. Miller MK, Dowd MD, Friesen CA et al. (2012) A randomized trial of enema versus polyethylene glycol 3350 for fecal disimpaction in children presenting to an emergency department. *Pediatric Emergency Care* 28:115-119.
20. Minguez M, Lopez H, Antonio et al. (2016) Use of polyethylene glycol in functional constipation and fecal impaction. *Revista espanola de enfermedades digestivas : organo oficial de la Sociedad Espanola de Patologia Digestiva* 108:790-806.
21. Dziechciarz P, Wojtyniak K, Horvath A et al. (2015) Enema versus polyethylene glycol for the management of rectal faecal impaction in children with constipation - a systematic review of randomised controlled trials. *Przeglad gastroenterologiczny* 10:234-238.
22. Siminas S and Losty PD. (2015) Current Surgical Management of Pediatric Idiopathic Constipation: A Systematic Review of Published Studies. *Annals of surgery* 262:925-933.
23. Bongers ME, van den Berg MM, Reitsma JB et al. (2009) A randomized controlled trial of enemas in combination with oral laxative therapy for children with chronic constipation. *Clin Gastroenterol Hepatol* 7:1069-1074.
24. Ratanamongkol P, Lertmaharit S, and ongpiputvanich S. (2009) Polyethylene glycol 4000 without electrolytes versus milk of magnesia for the treatment of functional constipation in infants and young children: a randomized controlled trial. *Asian Biomedicine* 3:391-399.
25. Gordon M, Naidoo K, Akobeng AK et al. (2012) Osmotic and stimulant laxatives for the management of childhood constipation. *Cochrane Database of Systematic Reviews* 7:CD009118.
26. Ahmed M, Pai B, and Reynolds T. (2012) Use of polyethylene glycol in children less than 3 years of age. *Jcsp, Journal of the College of Physicians & Surgeons - Pakistan* 22:267-268.
27. Hoekman DR and Benninga MA. (2013) Functional constipation in childhood: current pharmacotherapy and future perspectives. *Expert Opinion on Pharmacotherapy* 14:41-51.
28. Dehghani SM, Askarian M, and Kaffashan HA. (31-8-2013) Oral domperidone has no additional effect on chronic functional constipation in children: A randomized clinical trial. *Indian Journal of Gastroenterology* .
29. Saneian HM. (2012) Comparing the efficacy of polyethylene glycol (PEG), magnesium hydroxide and lactulose in treatment of functional constipation in children. *Journal of Research in Medical Sciences* 17:S145-S149.
30. Wang YW. (2012) Polyethylene glycol 4000 treatment for children with constipation: A randomized comparative multicenter study. *Experimental and Therapeutic Medicine* 3:853-856.
31. Savino F, Viola S, Erasmo M et al. (2012) Efficacy and tolerability of peg-only laxative on faecal impaction and chronic constipation in children. A controlled double blind randomized study vs a standard peg-electrolyte laxative. *BMC pediatrics* 12:178.
32. Dehghani SM, Askarian M, and Kaffashan HA. (2014) Oral domperidone has no additional effect on chronic functional constipation in children: a randomized clinical trial. *Indian journal of gastroenterology : official journal of the Indian Society of Gastroenterology* 33:125-130.
33. Mozaffarpur SA, Naseri M, Esmaeilidooki MR et al. (2012) The effect of cassia fistula emulsion on pediatric functional constipation in comparison with mineral oil: a randomized, clinical trial. *Daru: Journal of Faculty of Pharmacy, Tehran University of Medical Sciences* 20:83.
34. Hyman PE, Di LC, Prestridge LL et al. (2014) Lubiprostone for the treatment of functional constipation in children. *Journal of Pediatric Gastroenterology & Nutrition* 58:283-291.
35. Winter HS, Di LC, Benninga MA et al. (2013) Oral prucalopride in children with functional constipation. *Journal of Pediatric Gastroenterology & Nutrition* 57:197-203.

36. Ladenhauf HN, Stundner O, Spreitzhofer F et al. (2012) Severe hyperphosphatemia after administration of sodium-phosphate containing laxatives in children: case series and systematic review of literature. *Pediatric Surgery International* 28:805-814.
37. van Wering HM, Tabbers MM, and Benninga MA. (2012) Are constipation drugs effective and safe to be used in children? A review of the literature. *Expert Opinion on Drug Safety* 11:71-82.
38. Ala S, Haghghat M, Dehghani SM et al. (2015) Response and recurrence rate after treatment with polyethylene glycol versus polyethylene glycol plus lactulose in children with chronic functional constipation: A randomized controlled trial. *Journal of Comprehensive Pediatrics* 6:no.
39. Dziechciarz P, Horvath A, and Szajewska H. (2015) Polyethylene glycol 4000 for treatment of functional constipation in children. *Journal of pediatric gastroenterology and nutrition* 60:65-68.
40. Gordon M, MacDonald JK, Parker CE et al. (2016) Osmotic and stimulant laxatives for the management of childhood constipation. *The Cochrane database of systematic reviews* CD009118.
41. Treepongkaruna S, Simakachorn N, Pienvichit P et al. (2014) A randomised, double-blind study of polyethylene glycol 4000 and lactulose in the treatment of constipation in children. *BMC pediatrics* 14:153.
42. Esmaeilidooki MR, Mozaffarpur SA, Mirzapour M et al. (2016) Comparison Between the Cassia Fistula's Emulsion With Polyethylene Glycol (PEG4000) in the Pediatric Functional Constipation: A Randomized Clinical Trial. *Iranian Red Crescent medical journal* 18:e33998.
43. Nimrouzi M, Sadeghpour O, Imanieh MH et al. (2015) Flixweed vs. Polyethylene Glycol in the Treatment of Childhood Functional Constipation: A Randomized Clinical Trial. *Iranian journal of pediatrics* 25:e425.
44. Clarke MC, Catto-Smith AG, King SK et al. (2012) Transabdominal electrical stimulation increases colonic propagating pressure waves in paediatric slow transit constipation. *Journal of Pediatric Surgery* 47:2279-2284.
45. Veiga ML, Lordelo P, Farias T et al. (2013) Evaluation of constipation after parasacral transcutaneous electrical nerve stimulation in children with lower urinary tract dysfunction--a pilot study. *Journal of pediatric urology* 9:622-626.
46. Yik YI, Ismail KA, Hutson JM et al. (2012) Home transcutaneous electrical stimulation to treat children with slow-transit constipation. *Journal of Pediatric Surgery* 47:1285-1290.
47. Lu M, He J, and Lu S. (2015) Electrical stimulation therapy for slow transit constipation in children: a systematic review. *International journal of colorectal disease* 30:697-702.
48. Silva CA and Motta ME. (2013) The use of abdominal muscle training, breathing exercises and abdominal massage to treat paediatric chronic functional constipation. *Colorectal Disease* 15:e250-e255.
49. Orhan C, Kaya K, Ozgun et al. (2016) The effects of connective tissue manipulation and Kinesio Taping on chronic constipation in children with cerebral palsy: a randomized controlled trial. *Disability and rehabilitation* 1-11.
50. Lonkhuyzen vE, Marieke L, Bols Esther MJ et al. (2017) Effectiveness of Pelvic Physiotherapy in Children With Functional Constipation Compared With Standard Medical Care. *Gastroenterology* 152:82-91.
51. Redkar RG, Mishra PK, Thampi C et al. (2012) Role of rectal myomectomy in refractory chronic constipation. *African Journal of Paediatric Surgery:AJPS* 9:202-205.
52. van Wunnik BP, Peeters B, Govaert B et al. (2012) Sacral neuromodulation therapy: a promising treatment for adolescents with refractory functional constipation. *Diseases of the Colon & Rectum* 55:278-285.

53. Ahmadi JA. (2013) Intrasphincteric botulinum toxin injection in treatment of chronic idiopathic constipation in children. *Iranian journal of pediatrics* 23:574-578.
54. Nasher O, Hill RE, Peeraully R et al. (2014) Peristeen () transanal irrigation system for paediatric faecal incontinence: a single centre experience. *Int.J.Pediatr.* 2014:954315.
55. Ng J, Ford K, Dalton S et al. (2015) Transanal irrigation for intractable faecal incontinence and constipation: outcomes, quality of life and predicting non-adopters. *Pediatr.Surg.Int.* 31:729-734.
56. Koppen IJ, Kuizenga-Wessel S, Voogt HW et al. (2017) Transanal Irrigation in the Treatment of Children With Intractable Functional Constipation. *J.Pediatr.Gastroenterol.Nutr.* 64:225-229.
57. Huang R, Ho SY, Lo WS et al. (2014) Physical activity and constipation in Hong Kong adolescents. *PLoS ONE [Electronic Resource]* 9:e90193.
58. Driessen LM, Jong Kiefte-de JC, Wijtzes A et al. (2013) Preschool physical activity and functional constipation: the Generation R study. *Journal of Pediatric Gastroenterology & Nutrition* 57:768-774.
59. Chmielewska A and Szajewska H. (7-1-2010) Systematic review of randomised controlled trials: probiotics for functional constipation. *World J Gastroenterol* 16:69-75.
60. Coccorullo P, Strisciuglio C, Martinelli M et al. (2010) *Lactobacillus reuteri* (DSM 17938) in infants with functional chronic constipation: a double-blind, randomized, placebo-controlled study. *Journal of Pediatrics* 157:598-602.
61. Tabbers MM, Chmielewska A, Roseboom MG et al. (2011) Fermented milk containing *Bifidobacterium lactis* DN-173 010 in childhood constipation: a randomized, double-blind, controlled trial. *Pediatrics* 127:e1392-e1399.
62. Tabbers MM, Boluyt N, Berger MY et al. (2011) Nonpharmacologic treatments for childhood constipation: systematic review. *Pediatrics* 128:753-761.
63. Horvath A and Szajewska H. (2013) Probiotics, prebiotics, and dietary fiber in the management of functional gastrointestinal disorders. *World Review of Nutrition & Dietetics* 108:40-48.
64. Korterink JJ, Ockeloen L, Benninga MA et al. (16-11-2013) Probiotics for childhood functional gastrointestinal disorders: a systematic review and meta-analysis. *Acta Paediatrica* .
65. Vandenas Y, De GE, Devreker T et al. (2013) Probiotics and prebiotics in infants and children. *Current Infectious Disease Reports* 15:251-262.
66. Horvath AC. (2013) Functional constipation in children: A follow-up of two randomized controlled trials. *Pediatrica Polska* 88:219-223.
67. Parzecka MJ. (2012) The role of probiotics in the treatment of functional constipation in children and adolescents - Own observations. *Gastroenterologia Polska* 19:162-165.
68. Saneian H, Tavakkol K, Adhamian P et al. (2013) Comparison of *Lactobacillus Sporogenes* plus mineral oil and mineral oil alone in the treatment of childhood functional constipation. *Journal of Research in Medical Sciences* 18:85-88.
69. Kranz S, Brauchla M, Slavin JL et al. (2012) What do we know about dietary fiber intake in children and health? The effects of fiber intake on constipation, obesity, and diabetes in children. *Advances in Nutrition* 3:47-53.
70. Stewart ML and Schroeder NM. (2013) Dietary treatments for childhood constipation: efficacy of dietary fiber and whole grains. *Nutrition Reviews* 71:98-109.
71. Horvath A, Dziechciarz P, and Szajewska H. (28-5-2013) Glucomannan for abdominal pain-related functional gastrointestinal disorders in children: a randomized trial. *World Journal of Gastroenterology* 19:3062-3068.

72. Quitadamo P, Coccorullo P, Giannetti E et al. (2012) A randomized, prospective, comparison study of a mixture of acacia fiber, psyllium fiber, and fructose vs polyethylene glycol 3350 with electrolytes for the treatment of chronic functional constipation in childhood.[Erratum appears in *J Pediatr*. 2012 Dec;161(6):1180]. *Journal of Pediatrics* 161:710-715.
73. Weber TK, Toporovski MS, Tahan S et al. (2014) Dietary fiber mixture in pediatric patients with controlled chronic constipation. *Journal of Pediatric Gastroenterology & Nutrition* 58:297-302.
74. Karagiozoglou-Lampoudi T, Daskalou E, Agakidis C et al. (2012) Personalized diet management can optimize compliance to a high-fiber, high-water diet in children with refractory functional constipation. *Journal of the Academy of Nutrition & Dietetics* 112:725-729.
75. Sullivan PB, Alder N, Shrestha B et al. (2012) Effectiveness of using a behavioural intervention to improve dietary fibre intakes in children with constipation. *Journal of Human Nutrition & Dietetics* 25:33-42.
76. Closa-Monasterolo R, Ferre N, Castillejo-DeVillasante G et al. (2016) The use of inulin-type fructans improves stool consistency in constipated children. A randomised clinical trial: pilot study. *International journal of food sciences and nutrition* 1-11.
77. Sadeghzadeh M, Rabieefar A, Khoshnevisasl P et al. (2014) The effect of probiotics on childhood constipation: a randomized controlled double blind clinical trial. *International journal of pediatrics* 2014:937212.
78. Crowley ET, Williams LT, Roberts TK et al. (2013) Does milk cause constipation? A crossover dietary trial. *Nutrients* 5:253-266.
79. Dehghani SM, Ahmadpour B, Haghghat M et al. (2012) The Role of Cow's Milk Allergy in Pediatric Chronic Constipation: A Randomized Clinical Trial. *Iranian journal of pediatrics* 22:468-474.
80. Peeraully MR, Lopes J, Wright A et al. (2014) Experience of the MACE procedure at a regional pediatric surgical unit: a 15-year retrospective review. *European Journal of Pediatric Surgery* 24:113-116.
81. Rodriguez L, Nurko S, and Flores A. (2013) Factors associated with successful decrease and discontinuation of antegrade continence enemas (ACE) in children with defecation disorders: a study evaluating the effect of ACE on colon motility. *Neurogastroenterology & Motility* 25:140-e81.
82. Har AF, Rescorla FJ, and Croffie JM. (2013) Quality of life in pediatric patients with unremitting constipation pre and post Malone Antegrade Continence Enema (MACE) procedure. *Journal of Pediatric Surgery* 48:1733-1737.
83. Bonilla SF, Flores A, Jackson CC et al. (2013) Management of pediatric patients with refractory constipation who fail cecostomy. *Journal of Pediatric Surgery* 48:1931-1935.
84. Tappin D, Nawaz S, McKay C et al. (2013) Development of an early nurse led intervention to treat children referred to secondary paediatric care with constipation with or without soiling. *BMC pediatrics* 13:193.
85. Modin L, Walsted A, Rittig CS et al. (2016) Follow-up in Childhood Functional Constipation: A Randomized, Controlled Clinical Trial. *Journal of pediatric gastroenterology and nutrition* 62:594-599.