

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Clinical Practice – Surveillance Programme

Surveillance review consultation document

4-year surveillance review of CG99: Diagnosis and management of idiopathic childhood constipation in primary and secondary care

Background information

Guideline issue date: May 2010

4-year review: May 2014

Surveillance review recommendation

Surveillance review proposal for consultation:

The Constipation in children guideline should not be considered for an update at this time.

Main findings of the current 4 year surveillance review

An [Evidence Update](#) was produced for the guideline in 2012 and was used as a source of evidence for the review proposal. The Evidence Update indicated that there is currently insufficient new evidence to invalidate the guideline recommendations. The search strategy for this 4 year surveillance review was slightly different from that of other clinical guidelines due to the large proportion of diagnostic questions covered in the guideline. As such, a search was carried out between 3 February 2012 (the end of the search period for the Evidence Update) and 2 March 2014 to identify observational studies in addition to randomised clinical trials (RCTs) and systematic reviews and relevant abstracts were assessed. Clinical feedback was also obtained from members of the guideline development group (GDG) through a questionnaire survey.

New evidence was identified for the current 4 year surveillance review relating to the following clinical areas within the constipation in children guideline.

Clinical area: Assessment and diagnosis		
Q: What is the diagnostic value of the history-taking and the physical examination in diagnosing chronic idiopathic constipation in newborns, infants and children?		
Evidence summary	GDG/clinical perspective	Impact
<p><u>Evidence Update 2012</u> A systematic review indicated that early intervention for constipation may be associated with improved recovery.¹ The results were considered to be consistent with a statement in the introduction of the guideline that early identification and effective treatment can improve outcomes.</p> <p><u>4-year surveillance review (2014)</u> A retrospective chart review and a cross-sectional study indicated that the Rome II criteria are still appropriate for the diagnosis of functional constipation in young children although the paediatric Rome III criteria for functional constipation are less restrictive than the Rome II criteria.^{2,3} 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 questionnaire.⁴</p> <p>One study investigating clinical characteristics of functional constipation at paediatric gastroenterology clinics suggested the following: 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 stool.⁵ Furthermore, a study reporting the development of an algorithm to identify constipation in children with autism spectrum disorders</p>	<p>None identified.</p>	<p>The majority of the clinical characteristics described in the identified new evidence are in-line with the key components of history-taking to diagnose constipation in children outlined in the guideline.</p>

<p>in primary care suggested that subtle or atypical symptoms might indicate the presence of constipation although no specific detail was provided in the abstract.⁶</p>		
Clinical area: Clinical investigations		
Q: What is the prevalence of hypothyroidism and coeliac disease in children with chronic constipation?		
Evidence summary	GDG/clinical perspective	Impact
<p><u>Evidence Update 2012</u> None identified.</p> <p><u>4-year surveillance review (2014)</u> 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 Netherlands.⁷</p>	<p>None identified.</p>	<p>The identified new evidence looked at the associations between coeliac disease and symptoms of constipation therefore, it is unlikely that the results would 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.</p>
Clinical area: Clinical investigations		
Q: What is the diagnostic value of plain abdominal radiography to diagnose chronic idiopathic constipation in children?		
Evidence summary	GDG/clinical perspective	Impact
<p><u>Evidence Update 2012</u> None identified.</p> <p><u>4-year surveillance review (2014)</u> One systematic review concluded that there was insufficient evidence for a diagnostic association between clinical symptoms of constipation and faecal loading on abdominal radiographs.¹¹</p>	<p>It was highlighted that when children are on medication and abdominal palpitation doesn't reveal a faecal mass then abdominal radiography may be useful.</p>	<p>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 and no new consistent evidence was identified which would impact on these recommendations.</p>
Clinical area: Clinical investigations		
Q: What is the diagnostic value of the rectal biopsy in children with chronic idiopathic constipation?		
Evidence summary	GDG/clinical perspective	Impact

<p><u>Evidence Update 2012</u> None identified.</p> <p><u>4-year surveillance review (2014)</u> A retrospective analysis was identified which evaluated infants having a suction rectal biopsy to exclude Hirschsprung disease.¹² The results of the analysis indicated that Hirschsprung disease occurred less often in premature infants compared with term infants. One retrospective study focusing on clinical signs and symptoms of Hirschsprung disease in older children reported that recurrent gastrointestinal infection with vomiting and hospitalisation occurred more frequently in children with Hirschsprung disease whilst rectal biopsy confirmed the diagnosis.¹³ Lastly, the results of one study indicated that faecal calprotectin had limited value in differentiating functional constipation from Hirschsprung's disease.¹⁴</p>	<p>None identified.</p>	<p>Taken together, the new evidence implies the 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 disease. As such, there is unlikely to be any impact on the guideline recommendation which states that rectal biopsy should not be performed unless any of the following clinical features of Hirschsprung's disease are or have been present:</p> <ul style="list-style-type: none"> • 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.
<p>Clinical area: Clinical investigations</p>		
<p>Q: What is the diagnostic value of the abdominal ultrasound in children with chronic constipation?</p>		
<p>Evidence summary</p>	<p>GDG/clinical perspective</p>	<p>Impact</p>
<p><u>Evidence Update 2012</u> None identified.</p> <p><u>4-year surveillance review (2014)</u> One study was identified which compared digital with transabdominal ultrasound to assess the rectal filling state in children with urological problems.¹⁵ Agreement between the two tests for detecting rectal mass was 82.5%.</p>	<p>None identified.</p>	<p>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 new 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.</p>
<p>Clinical area: Clinical management</p>		
<p>Q: What is the effectiveness of pharmacological and surgical intervention for disimpaction in children with chronic idiopathic constipation?</p>		
<p>Evidence summary</p>	<p>GDG/clinical perspective</p>	<p>Impact</p>

<p><u>Evidence Update 2012</u> An RCT was included which compared disimpaction with rectal enemas versus oral laxatives in children aged 4–16 years with severe rectal faecal impaction.¹⁶ No difference in successful disimpaction was observed between the enema and PEG groups at follow-up two weeks after disimpaction. The Evidence Update concluded that the results of this study are unlikely to impact on the guideline which currently recommends first-line treatment of impaction with PEG 3350 plus electrolytes.</p> <p><u>4-year surveillance review (2014)</u> One RCT compared a single milk and molasses enema in the emergency department with PEG 3350 as paediatric faecal impaction treatment.¹⁷ 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.</p>	<p>GDG feedback indicated that there may be variation in dose administration of picolax and sodium picosulfate in clinical practice. However, the Guidelines Manual (2012) states that readers of guidelines are expected to refer to the summary of product characteristics for details of drug dosages.</p>	<p>This 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.</p>
<p>Clinical area: Clinical management</p>		
<p>Q: What is the clinical effectiveness of pharmacological interventions for ongoing treatment/maintenance in children with chronic idiopathic constipation?</p>		
<p>Evidence summary</p>	<p>GDG/clinical perspective</p>	<p>Impact</p>
<p><u>Evidence Update 2012</u> An RCT examined maintenance treatment with rectal enemas plus oral PEG compared with oral PEG in children aged 8-18 years.¹⁸ 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.</p>	<p>The GDG 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.</p> <p>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 review to substantiate these concerns.</p>	<p>The identified new evidence is supportive of the use of PEG for functional constipation however, it was not clear from an assessment 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 this new evidence on the guideline. Promising benefits of lubiprostone and prucalopride were reported in two studies however, currently these pharmaceuticals are not licensed for use in children or adolescents under 18 years and evidence comparing these treatments</p>

<p>Another RCT by Ratanamongkol et al. (2009) 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 constipation.¹⁹ A significant improvement (defined as the proportion of patients with three or more bowel movements per week) was observed in the PEG group. The Evidence Update concluded that this evidence reinforces current recommendations on maintenance therapy with PEG in the guideline.</p> <p><u>4-year surveillance review (2014)</u> <i>Polyethylene glycol</i> A Cochrane systematic review evaluated the efficacy and safety of osmotic and stimulant laxatives used to treat functional childhood constipation.²⁰ The results indicated that polyethylene glycol (PEG) preparations may be superior to placebo, lactulose and milk of magnesia for childhood constipation. Furthermore, two reviews, two RCTs and a non-randomised study indicated a benefit of PEG preparations for functional constipation in children.²¹⁻²⁵ 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 accepted.²⁶</p> <p><i>Mineral oil</i> 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 posturing.²⁷</p> <p><i>Lubiprostone</i> One non-randomised study assessing the safety and efficacy of different doses of lubiprostone in children</p>		<p>against PEG 3350 + electrolytes are necessary to enable their place in the management of idiopathic constipation in children to be established.</p>
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<p>and adolescents with functional constipation reported that spontaneous bowel movements increased compared with baseline.²⁸</p> <p><i>Prucalopride</i> One non-randomised study evaluated the efficacy, safety, and tolerability of prucalopride oral solution in children, ages 4 years or older to 12 years or younger, with functional constipation.²⁹ Prucalopride treatment resulted in a mean bowel movement frequency of 6.8/week, normal stool consistency, and reduced frequency of faecal incontinence.</p>		
Clinical area: Clinical management		
Q: What are the adverse effects of the medium- to long-term use of laxatives?		
Evidence summary	GDG/clinical perspective	Impact
<p><u>Evidence Update 2012</u> None identified.</p> <p><u>4-year surveillance review (2014)</u> 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 laxatives.³⁰ 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 population.³¹</p>	None identified.	Laxatives are currently recommended as maintenance therapy as soon as a child or young person's bowel is disimpacted and no new evidence was identified which would change the direction of this recommendation.
Clinical area: Clinical management		
Q: What is the effectiveness of the Antegrade Colonic Enema (ACE) procedure in children with chronic idiopathic constipation?		
Evidence summary	GDG/clinical perspective	Impact
<p><u>Evidence Update 2012</u> None identified.</p> <p><u>4-year surveillance review (2014)</u></p>	None identified.	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

<p>Two retrospective reviews and a case series of children with constipation indicated improvements in outcomes after antegrade continence enemas (ACE).³²⁻³⁴ 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 patients.³⁵ The results indicated that 16% did not experience improvement in symptoms after antegrade continence enema and required additional intervention.</p>		<p>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.</p>
<p>Clinical area: Clinical management</p>		
<p>Q: What is the clinical effectiveness of the following complementary therapies for ongoing treatment/maintenance in children with chronic idiopathic constipation?</p> <ul style="list-style-type: none"> • abdominal massage • reflexology • hypnotherapy • osteopathy • cranial osteopathy • craniosacral therapy • homeopathy. 		
<p>Evidence summary</p>	<p>GDG/clinical perspective</p>	<p>Impact</p>
<p><u>Evidence Update 2012</u> None identified.</p> <p><u>4-year surveillance review (2014)</u> 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 constipation.³⁶ 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.</p>	<p>None identified.</p>	<p>The guideline does not currently include any recommendations on complementary therapies for treatment/maintenance in children with chronic idiopathic constipation due to a lack of available evidence. Although the identified RCT indicated a potential a benefit of physiotherapy over medication for functional constipation, further data on long-term outcomes and evidence of cost effectiveness is needed before considering for inclusion in the guideline. Furthermore, as the study included the use of physiotherapy in conjunction with pharmacological treatment it is not clear what benefit physiotherapy has in children with chronic constipation that has not resolved with usual treatment.</p>

Clinical area: Clinical management		
<p>Q: What is the clinical effectiveness of the following for ongoing treatment/maintenance in children with chronic idiopathic constipation?</p> <ul style="list-style-type: none"> • increasing physical activity • dietary modifications • increasing fluid intake • excluding cows' and goats' milk protein from diet. 		
Evidence summary	GDG/clinical perspective	Impact
<p><u>Evidence Update 2012</u> <i>Probiotics</i> A systematic review and two RCTs evaluating probiotics were included in the Evidence Update.³⁷⁻³⁹ Overall, the Evidence Update concluded that the evidence is limited and a robust assessment of probiotics in the management of constipation was not possible. As such, the identified new evidence was unlikely to impact on the guideline.</p> <p><i>Non-pharmacological treatments</i> A systematic review examined non-pharmacological treatments for childhood constipation including fibre, prebiotics and probiotics, and fluid.⁴⁰ The evidence from this review was considered to be consistent with current guideline recommendations.</p> <p><u>4-year surveillance review (2014)</u> <i>Excluding cows' milk</i> The results of two cross-over dietary trials demonstrated conflicting results with one suggesting an association between functional constipation and cow's milk consumption whilst a second trial did not show an effect from type of casein.⁴¹ 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 children.⁴² 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</p>	<p>Feedback from the GDG indicated that there needs to be a change in emphasis relating to diet and constipation in the guideline as there may be a view among parents that they are being blamed for the constipation because they have provided their child with a poor diet.</p>	<p>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 which would change the direction of this recommendation.</p> <p>New evidence was identified which supports the guideline recommendation that daily physical activity tailored to the child's stage of development and individual ability should be included as part of ongoing maintenance in children and young people with idiopathic constipation.</p> <p>During guideline development the GDG felt it was not possible to recommend specific probiotics due to a lack of consistent evidence and the new evidence identified for the surveillance review still does not give a clear and consistent view on the benefits and harms of probiotics for management of constipation. Further research is needed before considering for inclusion in the guideline.</p> <p>The guideline recommends that dietary interventions alone should not be used as first-line treatment of idiopathic constipation as the GDG felt there was insufficient evidence to recommend the use of fibre supplements in the treatment or ongoing management of constipation in children. Similarly, no evidence was found to suggest that increasing fibre-rich foods was effective in treating or managing constipation however,</p>

<p>constipation compared with the control group who received a cow's milk diet for 6 weeks.</p> <p><i>Physical activity</i> An RCT (conducted in adolescents) and a cohort study (including pre-school children) reported that physical activity may be associated with a decreased risk of functional constipation.^{43,44}</p> <p><i>Dietary modifications</i> <u>Probiotics / prebiotics</u> The evidence on the effectiveness of probiotics and prebiotics was mixed with one review⁴⁵ indicating that <i>L. reuteri</i> DSM 17938 may help infants with constipation whilst two systematic reviews^{46,47}; a follow-up of two RCTs⁴⁸ and a non-randomised trial⁴⁹ reported that probiotics have not proved 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 children.⁵⁰ After the treatment, stool frequency increased in both groups, with greater increase in synbiotic + 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.</p> <p><u>High fibre</u> Two systematic reviews^{51,52} and two RCTs^{53,54} 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 nonhardened stools in children with constipation.⁵⁵ 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</p>		<p>the GDG felt that children should be advised to eat a healthy diet, including fibre containing foods and no new evidence was identified which would change the direction of this recommendation.</p>
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<p>constipation.⁵⁶ In addition, one RCT compared general advice on increasing dietary fibre intake with a behavioural intervention tool for children with functional constipation.⁵⁷ 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.</p>		
<p>Clinical area: Clinical management</p>		
<p>Q: What is the clinical effectiveness of psychological and behavioural interventions in addition to laxatives for ongoing treatment/maintenance in children with chronic idiopathic constipation?</p>		
<p>Evidence summary</p>	<p>GDG/clinical perspective</p>	<p>Impact</p>
<p><u>Evidence Update 2012</u> A systematic review included two RCTs assessing behavioural interventions.⁴⁰</p> <p><u>4-year surveillance review (2014)</u> None identified.</p>	<p>None identified.</p>	<p>The new evidence was considered to be 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.</p>
<p>Clinical area: Information and support</p>		
<p>Q: What is the effectiveness of the information, support and advice that children/young people and their parents / carers are given regarding the treatment/management of idiopathic constipation?</p>		
<p>Evidence summary</p>	<p>GDG/clinical perspective</p>	<p>Impact</p>
<p><u>Evidence Update 2012</u> None identified.</p> <p><u>4-year surveillance review (2014)</u> One study was identified which compared a nurse-led intervention focusing on self-help psychology practice with routine consultant-led care as recommended in CG99.⁵⁸ 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</p>	<p>The GDG 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.</p>	<p>One study was identified which aimed to answer one of the research recommendations in the guideline but, as this was a service evaluation to determine the appropriateness of developing a nurse-led intervention it is unlikely to impact on the guideline recommendations. Further research is need in a trial setting to formally assess the cost effectiveness of specialist nurse-led services.</p>

consultant-led care.		
Area not currently covered by the guideline: Additional management options for constipation in children		
Evidence summary	GDG/clinical perspective	Impact
<p><u>Evidence Update 2012</u> None identified.</p> <p><u>4-year surveillance review (2014)</u></p> <p><i>Anorectal myectomy</i> The role of anorectal myectomy in children with chronic refractory constipation was evaluated in one study.⁵⁹ Twenty-two patients improved clinically; 4 patients had a partial response and 2 patients did not respond.</p> <p><i>Sacral neuromodulation therapy</i> A small retrospective review evaluated the use of sacral neuromodulation therapy as a treatment option in adolescents with refractory functional constipation.⁶⁰ After implantation, the majority of patients had a normal spontaneous defecation pattern of > 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.</p> <p><i>Transcutaneous electrical nerve stimulation</i> Three small case series reported that transcutaneous electrical nerve stimulation may improve constipation symptoms in children.⁶¹⁻⁶³</p> <p><i>Botulinum toxin</i> 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 children.⁶⁴ Botox injection significantly reduced defecation of painful stools and soiling compared with the control group.</p>	None identified.	Further research in larger studies is needed to determine the long-term benefits and harms of these management options in children with constipation before considering for inclusion in the guideline.

For the following areas of the guideline no new evidence was identified:

- The diagnostic value of the digital rectal examination in children with chronic idiopathic constipation
- The diagnostic value of the gastrointestinal endoscopy in children with chronic idiopathic constipation
- The diagnostic value of the anorectal manometry in children with chronic idiopathic constipation
- The diagnostic value of transit studies in children

Ongoing research

None identified.

Anti-discrimination and equalities considerations

The GDG 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 all newborns, infants and children up to their 18th birthday who have idiopathic constipation and no evidence on management of idiopathic constipation specifically conducted in children with learning or physical difficulties was identified through the review.

Conclusion

Through the 4 year surveillance review of CG99 no new evidence was identified which may potentially change the direction of current guideline recommendations. The proposal is not to update the guideline at this time.

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