Constipation in children:

The diagnosis and management of idiopathic childhood constipation in primary and secondary care

National Collaborating Centre for Women's and Children's Health

Commissioned by the National Institute for Health and Clinical Excellence

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Implementation of this guidance is the responsibility of local commissioners and/or providers

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Contents

Contents iv
Guideline Development Group membership and acknowledgements 1
Acknowledgements 2
1 Guidance summary 3
1.1 Key priorities for implementation 3
1.2 Recommendations 8
1.3 Research recommendations 15
1.4 Care pathway 18
2 Introduction 19
2.1 Idiopathic constipation in children 19
2.2 Aim and scope of the guideline 20
2.3 Abbreviations and Glossary 21
2.4 For whom is the guidance intended? 23
2.5 Other relevant documents 23
2.6 Who has developed the guidance? 24
2.7 Guideline development methodology 24
2.8 Schedule for updating the guidance 28
3 Assessment and diagnosis 29
3.1 History taking and physical examination 29
3.2 Digital rectal examination 35
4 Clinical investigations 38
4.1 Introduction 38
4.2 Endoscopy 38
4.3 Hypothyroidism and coeliac disease 39
4.4 Manometry 42
4.5 Radiography 47
4.6 Rectal Biopsy 50
4.7 Transit Studies 56
4.8 Ultrasound 67
5 Clinical Management 71
5.1 Disimpaction 71
5.2 Maintenance therapy 80
5.3 Adverse effects of laxative use 96
5.4 Diet and lifestyle 109
5.5 Psychological and behavioural interventions 128
5.6 Complementary therapies 142
5.7 Antegrade colonic enema procedure 144

6 Information and support 151
Appendix A 162
Scope of the guideline 162
Appendix B 169
Declarations of interest 169
Appendix C 172
Registered stakeholder organisations 172
Appendix D 176
Clinical questions 176
Appendix E 178
Health Economics 178
Appendix F 200
Involving children in guideline development 200
Appendix G 214
Bristol Stool Form Scale 214
Appendix H 215
References 215
Appendix I 223
Search strategies 223
Evidence tables 224
Appendix K 225
Excluded studies 225

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1 Guidance summary

1.1 Key priorities for implementation

History taking and physical examination

Establish during history taking whether the child has constipation. Two or more findings from table 1, with symptoms lasting for more than 1 month, indicate constipation:

Table 1 Key components of history taking

Key components of history taking	Potential findings child under 1 year of age	Potential findings in child/young person over 1 year of age
Stool patterns	Fewer than 3 complete stools per week (see Bristol Stool Form Scale: 3 & 4 – Appendix G) Hard large stool “Rabbit droppings” (see Bristol Stool Form Scale – Appendix G)	Fewer than 3 complete stools per week (see Bristol Stool Form Scale: 3 & 4 – Appendix G) Overflow soiling (that is, very loose, very smelly stool passed without sensation) “Rabbit droppings” (see Bristol Stool Form Scale – Appendix G) Large, infrequent stools that can block the toilet
Symptoms associated with defecation	Distress on stooling Bleeding associated with hard stool Straining	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
History	Previous episode(s) of constipation Previous or current anal fissure	Previous episode(s) of constipation Previous or current anal fissure Painful bowel movements and bleeding associated with hard stools

History taking and physical examination

If the child has constipation take a history using table 2 to establish a positive diagnosis of idiopathic constipation by excluding underlying causes. If a child has any “red flags” symptoms do not treat for constipation. Instead, refer them urgently to a health care professional experienced in child health.

Table 2 History taking

Key components of history taking	Potential findings and diagnostic clues in a child younger than 1 year	Potential findings and diagnostic clues in a child/young person older than 1 year
Timing of onset of constipation and potential precipitating factors	Starts after a few weeks of life Obvious precipitating factors coinciding with the start of symptoms: fissure, change of diet, infections	Starts after a few weeks of life Obvious precipitating factors coinciding with the start of symptoms: fissure, change of diet, timing of potty/toilet training and acute event such as infections, moving house, starting nursery/school, fears and phobias, major change in family
	Reported from birth or first few weeks of life	Reported from birth or first few weeks of life
Passage of meconium	Normal, that is within 24 hours after birth (in term baby)	Normal, that is within 24 hours after birth (in term baby)
	Failure to pass/delay, that is more than 24 hours after birth (in term baby)	Failure to pass/delay, that is more than 24 hours after birth (in term baby)
Growth and general well being	Generally well, weight and height within normal limits	Generally well, weight and height within normal limits, fit and active
	Faltering growth	Faltering growth
Symptoms in legs /locomotor development	No neurological problems in legs, normal locomotor development	No neurological problems in legs (such as falling over), normal locomotor development
	Previously unknown or undiagnosed weakness in legs, locomotor delay	Previously unknown or undiagnosed weakness in legs, locomotor delay
Abdomen	Abdominal distension and vomiting	Abdominal distension and vomiting
Diet and fluid intake	Changes in formula, weaning, insufficient fluid intake	History of poor diet and/or insufficient fluid intake
Personal/familial/social factors	Disclosure or evidence that raises concerns over possibility of child maltreatment (see 'When to suspect maltreatment in children' NICE clinical guideline 89 for examples of evidence and subsequent management)	Disclosure or evidence that raises concerns over possibility of child maltreatment (see 'When to suspect maltreatment in children' NICE clinical guideline 89 for examples of evidence and subsequent management)

Green cells: indicative of idiopathic constipation.
Amber cells: 'amber flag', possible idiopathic constipation.
Red cells: 'red flag' for underlying disorder/condition, exclude idiopathic constipation.

History taking and physical examination

Do a physical examination. Use table 3 to establish positive diagnosis of idiopathic constipation by excluding underlying causes. If a child has any "red flag" symptoms do not treat them for constipation. Instead refer them urgently to a health care professional experienced in child health.

Table 3 Physical examination

Key components of the physical examination	Potential findings and diagnostic clues
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 overweight child
	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
	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
Red cells: 'red flag' for underlying disorder/condition, exclude idiopathic constipation Green cells: indicative of idiopathic constipation	

History taking and physical examination

Inform the child 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.

Digital rectal examination

Do not perform a digital rectal examination in children older than 1 year unless there is a 'red flag' (see tables 2 and 3) in the history-taking and/or physical examination that might indicate an underlying disorder.

Disimpaction

Assess all children with idiopathic constipation for faecal impaction, including children who were referred because of "red flags" but in whom there were no significant findings following further investigations (see tables 2 and 3).

Disimpaction

Use the following oral medication regimen for disimpaction if indicated:

- Use polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain) using an escalating dose regimen (see table 4) as the first-line treatment. Movicol Paediatric Plain may be mixed with a cold drink.
- Add a stimulant laxative using table 4 if polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain) 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 (Movicol Paediatric Plain) is not tolerated.

Table 4 Laxatives recommended doses

Laxatives	Recommended doses
Macrogols	

Movicol	Movicol Paediatric Plain (Norgine)* Oral powder, macrogol '3350' (polyethylene glycol '3350') 6.563 g, sodium bicarbonate 89.3 mg, sodium chloride 175.4 mg, potassium chloride 25.1 mg/sachet, Disimpaction By mouth: Child under 1 year: half to 1 sachet daily (non-BNFC recommended dose) Child 1–5 years: treat until impaction resolves or for maximum 7 days. 2 sachets on 1st day, then 4 sachets daily for 2 days, then 6 sachets daily for 2 days, then 8 sachets daily for 2 days Child 5–12 years: treat until impaction resolves or for maximum 7 days. 4 sachets on 1st day, then increased in steps of 2 sachets daily to maximum of 12 sachets daily Ongoing maintenance (chronic constipation, prevention of faecal impaction) By mouth: Child under 1 year: half to 1 sachet daily (non-BNFC recommended dose) Child 1–6 years: 1 sachet daily; adjust dose to produce regular soft stools (maximum 4 sachets daily) Child 6–12 years: 2 sachets daily; adjust dose to produce regular soft stools (maximum 4 sachets daily)
Osmotic laxatives	
Lactulose	By mouth: Child 1 month to 1 year: 2.5 ml twice daily, adjusted according to response Children 1–5 yrs: 2.5–10 ml twice daily, adjusted according to response (non-BNFC recommended dose) Children 5 -18 yrs: 5–20 ml twice daily, adjusted according to response (non-BNFC recommended dose)
Stimulant Laxatives	
Sodium picosulphate**	Non-BNFC recommended doses: By mouth: Child 1 month to 4 years: 2.5–10 mg once a day Child 5 -18 years: 2.5–20 mg once a day
Bisacodyl	Non-BNFC recommended doses: By mouth: Child 4 -18 years: 5 -20 mg once daily By rectum (suppository): Child 2–18 years: 5 -10 mg once daily
Senna ***	Sennokot syrup By mouth: Child 1 month to 4 years: 2.5–10 ml once daily

[*] At the time of publication (October, 2009), Movicol Paediatric Plain did 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 which is also unflavoured.

[**] Elixir, licensed for use in children (age range not specified by manufacturer). Perles not licensed for use in children under 4 years

[***] Syrup not licensed for use in children under 2 years

	Child 5-18 years: 2.5 -20ml once daily Senna (non-proprietary) By mouth: Child 6-18 years: 1-4 tablets once daily
Docusate Sodium****	By mouth: Child 6 months-2 years: 12.5 mg 3 times daily (use paediatric oral solution) Child 2-12 years: 12.5-25 mg 3 times daily (use paediatric oral solution) Child 12-18 years: up to 500 mg daily in divided doses

(Note: unless otherwise stated, doses are those recommended by the British National Formulary for Children-BNFC 2009)

Maintenance therapy

Use the following regimen for ongoing treatment or maintenance therapy:

- Use polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain*) as the first line treatment.
- Adjust the dose of polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain) according to symptoms and response. As a guide for children 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 (Movicol Paediatric Plain) does not work.
- Substitute a stimulant laxative if polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain) is not tolerated by the child. 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. 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.

Diet and lifestyle

Do not use dietary interventions alone as first-line treatment for childhood constipation.

Diet and lifestyle

Treat constipation with laxatives and a combination of:

- Negotiated and non-punitive behavioural interventions suited to the child's stage of development. This 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

**** Adult oral solution and capsules not licensed for use in children under 12 years

* At the time of publication (October, 2009), Movicol Paediatric Plain did 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 which is also unflavoured

Information and support

Offer children with idiopathic constipation and their families a point of contact with specialist health professionals who can give ongoing support.

1.2 Recommendations

History taking and physical examination

Establish during history taking whether the child has constipation. Two or more findings from table 1, with symptoms lasting for more than 1 month, indicate constipation:

Table 1 Key components of history taking to diagnose constipation

Key components of history taking	Potential findings child under 1 year of age	Potential findings in child/young person over 1 year of age
Stool patterns	Fewer than 3 complete stools per week (see Bristol Stool Form Scale: 3 & 4 – Appendix G) Hard large stool "Rabbit droppings" (see Bristol Stool Form Scale – Appendix G)	Fewer than 3 complete stools per week (see Bristol Stool Form Scale: 3 & 4 – Appendix G) Overflow soiling (that is, very loose, very smelly stool passed without sensation) "Rabbit droppings" (see Bristol Stool Form Scale – Appendix G) Large, infrequent stools that can block the toilet
Symptoms associated with defecation	Distress on stooling Bleeding associated with hard stool Straining	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
History	Previous episode(s) of constipation Previous or current anal fissure	Previous episode(s) of constipation Previous or current anal fissure Painful bowel movements and bleeding associated with hard stools

If the child has constipation take a history using table 2 to establish a positive diagnosis of idiopathic constipation by excluding underlying causes. If a child has any "red flags" symptoms do not treat for constipation. Instead refer them urgently to a health care professional experienced in child health.

If the history-taking and/or physical exam show evidence of faltering growth test for coeliac disease and hypothyroidism.

If either the history taking or the physical examination show evidence of possible maltreatment refer to 'When to suspect child maltreatment', NICE clinical guideline 89 (2009).

Table 2 Key components of history taking to diagnose idiopathic constipation

Key components of history taking	Potential findings and diagnostic clues in a child younger than 1 year	Potential findings and diagnostic clues in a child/young person older than 1 year
Timing of onset of constipation and potential precipitating factors	Starts after a few weeks of life Obvious precipitating factors coinciding with the start of symptoms: fissure, change of diet, infections	Starts after a few weeks of life Obvious precipitating factors coinciding with the start of symptoms: fissure, change of diet, timing of potty/toilet training and acute event such as infections, moving house, starting nursery/school, fears and phobias, major change in family
	Reported from birth or first few weeks of life	Reported from birth or first few weeks of life
Passage of meconium	Normal, that is within 24 hours after birth (in term baby)	Normal, that is within 24 hours after birth (in term baby)
	Failure to pass/delay, that is more than 24 hours after birth (in term baby)	Failure to pass/delay, that is more than 24 hours after birth (in term baby)
Growth and general well being	Generally well, weight and height within normal limits	Generally well, weight and height within normal limits, fit and active
	Faltering growth	Faltering growth
Symptoms in legs /locomotor development	No neurological problems in legs, normal locomotor development	No neurological problems in legs (such as falling over), normal locomotor development
	Previously unknown or undiagnosed weakness in legs, locomotor delay	Previously unknown or undiagnosed weakness in legs, locomotor delay
Abdomen	Abdominal distension and vomiting	Abdominal distension and vomiting
Diet and fluid intake	Changes in formula, weaning, insufficient fluid intake	History of poor diet and/or insufficient fluid intake
Personal/familial/ social factors	Disclosure or evidence that raises concerns over possibility of child maltreatment (see 'When to suspect maltreatment in children' NICE clinical guideline 89 for examples of evidence and subsequent management)	Disclosure or evidence that raises concerns over possibility of child maltreatment (see 'When to suspect maltreatment in children' NICE clinical guideline 89 for examples of evidence and subsequent management)
Green cells: indicative of idiopathic constipation. Amber cells: 'amber flag', possible idiopathic constipation. Red cells: 'red flag' for underlying disorder/condition, exclude idiopathic constipation.		

Do a physical examination. Use table 3 to establish positive diagnosis of idiopathic constipation by excluding underlying causes. If a child has any "red flag" symptoms do not treat them for constipation. Instead refer them urgently to a health care professional experienced in child health.

Table 3 Key components of physical examination to diagnose idiopathic constipation

Key components of the physical examination	Potential findings and diagnostic clues
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 overweight child

	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
	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
Red cells: 'red flag' for underlying disorder/condition, exclude idiopathic constipation Green cells: indicative of idiopathic constipation	

Inform the child 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.

Digital rectal examination

Perform a digital rectal examination in all children younger than 1 year with a diagnosis of idiopathic constipation that does not respond to adequate treatment within 4 weeks.

Do not perform a digital rectal examination in children older than 1 year unless there is a 'red flag' (see tables 2 and 3) in the history-taking and/or physical examination that might indicate an underlying disorder.

A digital rectal examination should only be undertaken by healthcare professionals competent to interpret features of anatomical abnormalities or Hirschsprung's disease.

For a digital rectal examination ensure:

- informed consent is given by the child, or the parent or legal guardian if the child is not able to give it, and is documented
- a chaperone is present
- individual preferences about degree of body exposure and sex of the examiner are taken into account
- all findings are documented.

Endoscopy

Do not use gastrointestinal endoscopy to investigate idiopathic constipation.

Hypothyroidism and coeliac disease

Test for coeliac disease in the ongoing management of intractable constipation in children when requested by specialist services.

Manometry

Do not use anorectal manometry to exclude Hirschsprung's disease in children with chronic constipation

Radiography

Do not use a plain abdominal radiograph to make a diagnosis of idiopathic constipation

Consider using a plain abdominal radiograph only if requested by specialist services in the ongoing management of intractable idiopathic constipation.

Rectal Biopsy

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 (>24 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

Transit studies

Do not use transit studies to make a diagnosis of idiopathic constipation.

Consider using transit studies in the ongoing management of intractable idiopathic constipation only if requested by specialist services.

Ultrasound

Do not use abdominal ultrasound to make a diagnosis of idiopathic constipation.

Consider using abdominal ultrasound in the ongoing management of intractable idiopathic constipation only if requested by specialist services.

Disimpaction

Assess all children with idiopathic constipation for faecal impaction, including children who were referred because of "red flags" but in whom there were no significant findings following further investigations (see tables 2 and 3).

Use the following oral medication regimen for disimpaction if indicated:

- Use polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain) using an escalating dose regimen (see table 4) as the first-line treatment*. Movicol Paediatric Plain may be mixed with a cold drink.
- Add a stimulant laxative using table 4 if polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain) 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 (Movicol Paediatric Plain) is not tolerated.

Do not use rectal medications for disimpaction unless all oral medications have failed.

Administer sodium citrate enemas only if all oral medications for disimpaction have failed.

* At the time of publication (October, 2009), Movicol Paediatric Plain did 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 which is also unflavoured.

Do not administer phosphate enemas for disimpaction unless under specialist supervision in hospital, and only if all oral medications and sodium citrate enemas have failed.

Do not perform manual evacuation of the bowel under anaesthesia unless optimal treatment with oral and rectal medications has failed.

Review children undergoing disimpaction within 1 week.

Table 4 Laxatives recommended doses

Laxatives	Recommended doses
Macrogols	
Movicol	Movicol Paediatric Plain (Norgine)* Oral powder, macrogol ‘3350’ (polyethylene glycol ‘3350’) 6.563 g, sodium bicarbonate 89.3 mg, sodium chloride 175.4 mg, potassium chloride 25.1 mg/sachet, Disimpaction By mouth: Child under 1 year: half to 1 sachet daily (non-BNFC recommended dose) Child 1-5 years: treat until impaction resolves or for maximum 7 days. Two sachets on 1st day, then 4 sachets daily for 2 days, then 6 sachets daily for 2 days, then 8 sachets daily for 2 days Child 5-12 years: treat until impaction resolves or for maximum 7 days. Four sachets on 1st day, then increased in steps of 2 sachets daily to maximum of 12 sachets daily Ongoing maintenance (chronic constipation, prevention of faecal impaction) By mouth: Child under 1 year: half to 1 sachet daily (non-BNFC recommended dose) Child 1-6 years: 1 sachet daily; adjust dose to produce regular soft stools (max. 4 sachets daily) Child 6-12 years: 2 sachets daily; adjust dose to produce regular soft stools (max. 4 sachets daily)
Osmotic laxatives	
Lactulose	By mouth: Child 1 month to 1 year: 2.5 ml twice daily, adjusted according to response Children 1-5 yrs: 2.5-10 ml twice daily, adjusted according to response (non-BNFC recommended dose) Children 5 -18 yrs: 5-20 ml twice daily, adjusted according to response (non-BNFC recommended dose)
Stimulant Laxatives	
Sodium picosulphate**	Non-BNFC recommended doses: By mouth: Child 1 month to 4 years: 2.5-10 mg once a day

[*] At the time of publication (October, 2009), Movicol Paediatric Plain did 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 which is also unflavoured

[**] Elixir, licensed for use in children (age range not specified by manufacturer). Perles not licensed for use in children under 4 years

	Child 5 -18 years: 2.5-20 mg once a day
Bisacodyl	Non-BNFC recommended doses: By mouth: Child 4 -18 years: 5 -20 mg once daily By rectum (suppository): Child 2-18 years: 5 -10 mg once daily
Senna ***	Sennokot syrup By mouth: Child 1 month to 4 years: 2.5-10 ml once daily Child 5-18 years: 2.5 -20ml once daily Senna (non-proprietary) By mouth: Child 6-18 years: 1-4 tablets once daily
Docusate Sodium****	By mouth: Child 6 months-2 years: 12.5 mg 3 times daily (use paediatric oral solution) Child 2-12 years: 12.5-25 mg 3 times daily (use paediatric oral solution) Child 12-18 years: up to 500 mg daily in divided doses

(Note: unless otherwise stated, doses are those recommended by the British National Formulary for Children-BNFC 2009)

Maintenance therapy and adverse effects of laxative use

Start maintenance therapy as soon as the child's bowel is disimpacted.

Reassess children frequently during maintenance treatment to ensure they do not become reimpacted.

Use the following regimen for ongoing treatment or maintenance therapy:

- Use polyethylene glycol ‘3350’ + electrolytes (Movicol Paediatric Plain*) as the first-line treatment
- Adjust the dose of polyethylene glycol ‘3350’ + electrolytes (Movicol Paediatric Plain) according to symptoms and response. As a guide for children 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 (Movicol Paediatric Plain) does not work.
- Substitute a stimulant laxative if polyethylene glycol ‘3350’ + electrolytes (Movicol Paediatric Plain) is not tolerated by the child. 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. 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.

*** Syrup not licensed for use in children under 2 years

**** Adult oral solution and capsules not licensed for use in children under 12 years

* At the time of publication (October, 2009), Movicol Paediatric Plain did 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 which is also unflavoured

Diet and lifestyle

Do not use dietary interventions alone as first-line treatment for childhood constipation.

Advise 60 minutes of physical activity per day as part of ongoing treatment or maintenance in children with idiopathic constipation. This activity should be tailored to the child's stage of development and individual ability.

Treat constipation with laxatives and a combination of:

- Negotiated and non-punitive behavioural interventions suited to the child's stage of development. This 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.

Advise parents and children (where appropriate) that a balanced diet should include:

- Adequate fibre. Recommend including foods with a high fibre content (such as fruit, vegetables, baked beans and wholegrain breakfast cereals). Do not recommend unprocessed bran, which can cause bloating and flatulence and reduce the absorption of micronutrients.
- Adequate fluid intake (see table 5)

Provide children with idiopathic constipation and their families with written information about diet and fluid intake.

In children with idiopathic constipation, start a cow's milk exclusion diet only on the advice of specialist services.

Table 5 UK dietary reference values for fluid requirements by age groups

Age	Fluid requirements (ml per kg per day)
0–3 months	150
4–6 months	130
7–9 months	120
10–12 months	110
1–3 years	95
4–6 years	85
7–10 years	75
11–14 year	55
15–18 years	50

Psychological and behavioural interventions

Do not use biofeedback for ongoing treatment in children with idiopathic constipation.

Do not routinely refer children with idiopathic constipation to a psychologist or child and adolescent mental health services unless they have identified psychological needs.

Antegrade colonic enema procedure

Refer children with idiopathic constipation who still have symptoms on optimum specialist management to a specialist surgical centre to assess their suitability for an antegrade colonic enema (ACE) procedure.

Ensure that all children who are referred for ACE procedure have access to support, information and follow-up from paediatric health professionals with experience in managing children who have had ACE procedure.

Information and support

Provide tailored follow-up to children and their parents or carers according to a child's response to treatment, measured by frequency, amount and consistency of stools (use the Bristol Stool Form Scale to assess this – Appendix G). This could include:

- telephoning or face-to-face talks
- giving detailed evidence-based information about their condition, for example the 'Understanding NICE guidance' leaflet 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.

Offer children with idiopathic constipation and their families a point of contact with specialist health professionals who can give ongoing support.

Refer children with idiopathic constipation who do not respond to initial treatment within 3 months to a practitioner with expertise in the problem.

1.3 Research recommendations

Disimpaction

What is the effectiveness of polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain) in treating idiopathic constipation in children younger than 1 year old, and what is the optimum dosage?

Why this is important?

There is some evidence that treatment of constipation is less effective if faecal impaction is not dealt with first. Disimpaction with oral macrogols is recommended for children and their use avoids the need for rectal treatments.

Rectal treatments, especially in hospital, are more common than oral treatments at home. Although relatively few infants are admitted to hospital, there would be savings if initially all children were disimpacted at home.

Polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain), an oral macrogol, is licensed for disimpaction in children older than 5 years. Increasing experience has shown that it is effective in infants younger than 1 year old, but evidence is limited to small case series. If dosage guidelines and evidence on macrogol use in infants were obtained and published, more healthcare professionals might be encouraged to try macrogols in this age group. It would also allow the guideline to be applicable across the whole paediatric age group.

Information and Support

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?

Why this is important?

When treating idiopathic constipation it is helpful if children understand how the bowel works, what can go wrong and what they can do about it. Younger children (pre toilet training) need to allow stools to come out. Older children have a more active role and need to develop a habit of sitting on the toilet each day, pushing stools out and taking any medication. Volition from the child is vital to establish and sustain a regular toilet habit. Intended learning outcomes are similar for all age groups.

Theory-based research has led to the development of some materials such as 'Sneaky-poo' that are not appropriate for young children. To help clinicians and parents motivate children to fully participate in managing their constipation it is important to discover how best to communicate information to them, what materials are most effective and, specifically, what works at different ages.

Information and Support

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.

Why this is important?

Findings from one trial [1] have suggested that children referred to a tertiary gastroenterology service and diagnosed as having idiopathic constipation are managed as effectively by nurse-led follow-up as by a consultant paediatric gastroenterology service. Parent satisfaction was improved by the nurse-led service. However the nurse-led service may require increased resources because many more contacts are made. Several services with a similar model of care have been established but cost effectiveness has not been formally assessed.

By the time children reach tertiary care they have often suffered years of constipation with or without faecal incontinence and have intractable constipation.

For coherent services to develop across the UK, the cost effectiveness of specialist nurse-led services provided as first referral point if primary treatment regimens have not worked needs to be examined.

Antegrade colonic enema

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?

Why this is important?

The ACE procedure has a role in the management of people with treatment-resistant symptoms. Close follow-up is integral to the effectiveness of this technique to allow safe and effective administration of washout solutions.

The choice of washout solutions and frequency of administration differs between centres. Outcomes may be improved by evaluating how experienced centres choose washout solutions and by comparing techniques.

Centres offering the ACE procedure as treatment for children with chronic idiopathic constipation should be surveyed for their choice of washout solution. To determine the perceived strengths and weaknesses of each solution, the survey should cover enema, choice of washout fluid, volumes and frequency of administration.

Information and support

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?

Why this is important?

There has been no research to explore the social impact on children with constipation and their families, and many of the clinical studies have been of mediocre quality. A comprehensive study is needed that investigates the effectiveness of specific models of care, and that takes into consideration both the clinical and social impact of this complex condition.

1.4 Care pathway

See attached document

2 Introduction

2.1 Idiopathic constipation in children

Constipation is common in childhood. It is prevalent in around 5-30% of the child population, depending on the criteria used for diagnosis. Symptoms become chronic in more than one third of patients and constipation is a common reason for referral to secondary care [2], [3], [4], [5]. Morbidity may be under-reported because people may not seek advice because they are embarrassed.

The exact cause of constipation is not fully understood but factors that may contribute include pain, fever, dehydration, dietary and fluid intake, psychological issues, toilet training and familial history of constipation. Constipation is referred to as 'idiopathic' if it cannot be explained by anatomical or physiological abnormalities.

Many people don't recognise the signs and symptoms of constipation and few relate the presence of soiling to constipation. The signs and symptoms of childhood idiopathic constipation include: poor appetite, lack of energy, irregular bowel activity, foul smelling wind and stools, excessive flatulence, irregular stool texture, passing occasional enormous stools or frequent small pellets, withholding or straining to stop passage of stools, soiling or overflow, abdominal pain, distension or discomfort, unhappy, angry or irritable mood and general malaise[6].

Painful defecation is an important factor in constipation but it is not always recognised; 'withholding' behaviours to prevent passage of painful stools are often confused with straining to pass stools. Families may delay seeking help for fear of a negative response from healthcare professionals. It has been suggested that some healthcare professionals underestimate the impact of constipation on the child and family [7]. This may contribute to the poor clinical outcomes often seen in children with constipation.

Soiling is debilitating but rarely life threatening so it might be expected to have little impact on healthcare provision. But many children experience social, psychological and educational consequences that require prolonged support.

Some children with physical disabilities, such as cerebral palsy, are more prone to idiopathic constipation as a result of impaired mobility. Children with Down's syndrome are also more prone to the condition. It is important that assessment and ongoing management for these children happen in the same way as is recommended for all children.

Without early diagnosis and treatment, an acute episode of constipation can lead to anal fissure and become chronic. By the time the child is seen they may be in a vicious cycle. Children and families are often given conflicting advice and practice is inconsistent, making treatment potentially less effective and frustrating for all concerned. Early identification of constipation and effective treatment can improve outcomes for children [8], [9], [10]. This guideline provides strategies based on the best available evidence to support early identification, positive diagnosis and timely, effective management. Implementation of this guideline will provide a consistent, coordinated approach and will improve outcomes for children.

2.2 Aim and scope of the guideline

This guideline aims to provide guidance in the following areas:

- Diagnosis of idiopathic constipation, including:
  - Patient history
  - Clinical examination, including the role of digital rectal examination
  - Diagnostic criteria (for example ROME III criteria)
  - The following investigations to rule out alternative diagnoses such as Hirschsprung's disease or coeliac disease:
    - Blood tests
    - Radiological investigations
    - Gastrointestinal endoscopy
    - Manometry
    - Rectal biopsy
- Management, including:
  - Dietary manipulation, including role of water and milk intake, fruits, vegetables (fibres and roughage), fruit juices and cereals
  - Exclusion of cows' milk protein
  - Physical activity
  - Pharmacological treatments, specifically bulk-forming laxatives, stimulant laxatives and osmotic laxatives
  - Psychological and behavioural management including toilet training, behavioural modification, maintaining toilet diaries, rewarding, psychosocial counselling including biofeedback therapy and intense psychotherapy
  - Complementary and alternative interventions, specifically abdominal massage, reflexology and hypnotherapy
  - Surgical management, including manual evacuation under general anaesthetic and antegrade colonic enema (ACE procedure)
- Indications for referral to specialist services
- Information and support needs for children and families.

The following areas are specifically excluded from the guideline:

- Diagnosis and treatment of another disease identified during the diagnosis of childhood idiopathic constipation
- Management and diagnosis of comorbidity
- Care received in specialist services after referral
- The additional management for children with an underlying, congenital, genetic, metabolic, endocrine or neurological disorder who also have constipation.

Further information about the areas that are covered by the guideline is available in the scope of the guideline (reproduced in Appendix A).

2.3 Abbreviations and Glossary

Abbreviations

A&E	accident and emergency department
ACE	antegrade colonic enema
AGA	antigliadin antibodies
ALPASC	Avon longitudinal study of parents and children
AP	allergic proctitis
ARM	anorectal manometry
CD	coeliac disease
CFU	colony forming unit
CI	confidence interval
CTT	colonic transit time
HD	Hirschsprung's disease
IGA	immunoglobulin
IND	intestinal neuronal dysplasia
EMA	antiendomysium antibodies
ESPGHAN	European Society of Paediatric Gastroenterology, Hepatology and Nutrition
FAP	functional abdominal pain
FNRFI	functional non-retentive faecal incontinence
LR	likelihood ratio
NCC-WCH	National Collaborating Centre for Women's and Children's Health
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
RAIR	rectoanal inhibitory reflex
ROC	receiver operator charateristic
tTG	tissue transglutaminase

Glossary of terms

Acute constipation	Self-limiting constipation
Allergic proctitis	Proctitis is an inflammation of the rectum. Allergic proctitis is inflammation attributed to allergic causes. The causes of the allergies have been attributed mostly to dietary proteins
Anal stenosis	A narrowing of the anus which results in a reduced lumen and particularly a loss of the capacity to dilate with passage of faeces. Straining, passage of ribbon-like faeces and constipation result.
Anal wink	The reflex contraction of the external anal sphincter
Antegrade colonic enema (ACE) procedure	A surgical procedure in which a channel is created into the caecum in the large intestine. This allows a catheter to be inserted and the bowel to be washed out. Sometimes known as Malone antegrade colonic enema (MACE) procedure
Anteriorly placed anus	A congenital malformation in which the anus is malpositioned
Biofeedback	Treatment method involving teaching the individual how to relax the external anal sphincter during straining. Treatment modalities include manometric and electromyographic biofeedback
Chronic constipation	Constipation lasting longer than 8 weeks

Colony-forming unit (CFU)	A measure of viable (living) bacterial or fungal cells numbers. Results are given as CFU/mL (colony-forming units per milliliter) for water, and CFU/g (colony-forming units per gram) for soil or other porous material
Constipation	A term to describe the subjective complaint of passage of abnormally delayed or infrequent passage of dry, hardened faeces often accompanied by straining and/or pain
Diarrhoea	The frequent passage of loose or watery stools, usually accompanied by abdominal cramping and urgency
Disimpaction	The evacuation of impacted faeces
Encopresis	Deliberate defecation in an inappropriate place. This is not to be confused with soiling
Faecal impaction	Severe constipation with a large faecal mass in either the rectum or the abdomen, and/or overflow soiling
Faecal incontinence	The involuntary leakage of faeces
Functional constipation	See idiopathic constipation
Hirschsprung's disease	A congenital abnormality in which the nerve cells in a section of the bowel are not present. As a result, faeces can become trapped in the bowel
Idiopathic constipation	Constipation is termed idiopathic when it cannot (currently) be explained by any anatomical, physiological, radiological or histological abnormalities. The exact aetiology is not fully understood but it is generally accepted that a combination of factors may contribute to the condition.
Intractable constipation	Constipation which does not respond to sustained, optimum medical management
Kerckring folds	Circular folds projecting into the lumen of the the small bowel composed of reduplications of the mucous membrane.
Macrogols	A form of osmotic laxative. PEG 3350 and PEG 4000 are examples of macrogols
Megacolon	An abnormally enlarged colon that can be congenital (as in Hirschsprung's disease) or acquired (as in chronic constipation)
Megarectum	A large rectum as a result of underlying nerve supply abnormalities or muscle dysfunction, often as a result of chronic faecal loading which remains after disimpaction of the rectum. The cause of the megarectum is unknown, but onset in childhood may be the result of chronic stool holding by the child, leading to progressive distension of the rectum and eventual loss of awareness of rectal distension. Once this has occurred the patient can no longer recognize when stool is present in the rectum; the distension of the rectum causes chronic inhibition of the resting tone of the internal anal sphincter. This leads to the loss of control of liquid or semisolid stool that passes by the fecal impaction without the patient being aware of it.
Organic constipation	Constipation is termed organic when there is an identifiable physiological or anatomical cause
Osmotic laxatives	Laxatives which increase the amount of water in the faeces thereby making them softer

Patulous anus	Widely patent anal orifice
Rectoanal inhibitory reflex (RAIR)	Relaxation of the internal anal sphincter in response to increased pressure of stool, gas or liquid entering the rectum. If voluntary muscle action occurs, the rectum empties through the anal canal. This reflex is absent in cases of congenital megacolon.
Retentive posturing	Typical straight legged, tiptoed, back arching posture
ROME (II & III) criteria	The Rome criteria is a system developed to classify functional gastrointestinal disorders (FGIDs): disorders of the digestive system in which symptoms cannot be explained by the presence of structural or tissue abnormality, based on clinical symptoms. Some examples of FGIDs include irritable bowel syndrome, functional dyspepsia, functional constipation, and functional heartburn. The most recent revision of the criteria, the Rome III criteria, were published in 2006 Further details can be found on the website: *www.romecriteria.org*
Side effects/adverse effects	An undesired effect resulting from treatment
Smearing	The intentional spreading of faeces
Soiling	Involuntary passage of fluid or semi solid stool into clothing as a result of overflow from a faecally loaded bowel
Specialist services/ specialist advice/ specialist care/specialist management	Services/advice/care/management provided by health care professionals with expertise in constipation management in children and young people
Stimulant laxatives	Laxatives which increase bowel motility

2.4 For whom is the guidance intended?

This guidance is of relevance to those who work in or use the National Health Service (NHS) in England and Wales, in particular:

- GPs, primary care and child health teams
- Professional groups who are routinely involved in the care of children and families
- Professionals who may encounter children in the course of their professional duties, for example radiographers, mental health professionals, surgeons
- Those responsible for commissioning and planning healthcare services, including primary care trust commissioners, Health Commission Wales commissioners, and public health and trust managers.
- Professionals working in social services and education/childcare settings.

2.5 Other relevant documents

This guideline is intended to complement other existing and proposed works of relevance, including the following guidance published by NICE.

- ‘Coeliac Disease’, NICE clinical guideline 86 [11]
- ‘Urinary tract infection in children’, NICE clinical guideline 54 [12]

- 'Nocturnal enuresis' NICE clinical guideline 79 (expected publication date October 2010)

2.6 Who has developed the guidance?

The guidance was developed by a multi-professional and lay working group (the Guideline Development Group or GDG) convened by the National Collaborating Centre for Women's and Children's Health (NCC-WCH). Membership included:

- One specialist paediatric nurse (Chair)
- Two general practitioners
- Two paediatricians
- One dietician
- One psychologist
- One paediatric surgeon
- One gastrointestinal nurse
- One community nurse
- One health visitor
- Two patient/carer members.

Staff from the NCC-WCH provided methodological support for the guidance development process, undertook systematic searches, retrieved and appraised the evidence and wrote successive drafts of the guidance.

One external advisor was appointed by the GDG to advise on pharmacological interventions

All GDG members' and external advisers' potential and actual conflicts of interest were recorded on declaration forms provided by NICE (summarised in Appendix B). None of the interests declared by GDG members constituted a material conflict of interest that would influence recommendations developed by the GDG.

2.7 Guideline development methodology

This guidance was commissioned by NICE and developed in accordance with the guideline development process outlined in the NICE *Guidelines Manual (2009)*.[13] Table 2.1 summarises the key stages of the process and which version of the guidelines manual was followed at each stage.

In accordance with NICE's Equality Scheme, ethnic and cultural considerations and factors relating to disabilities have been considered by the GDG throughout the development process and specifically addressed in individual recommendations where relevant. Further information is available from: www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp.

Table 2.1 Stages in the NICE guideline development process and versions of `The guidelines manual' followed at each stage

Stage	2007 version	2009 version
Scoping the guideline (determining what the guideline would and would not cover)	✓	
Preparing the work plan (agreeing timelines, milestones, guideline development group constitution, etc.)	✓	
Forming and running the guideline development group	✓	
Developing clinical questions	✓	

Identifying evidence	✓	
Reviewing and grading evidence	✓	
Incorporating health economics	✓	
Making group decisions and reaching consensus	✓	
Linking guidance to other NICE guidance	✓	
Creating guideline recommendations	✓	
Writing the guideline	✓	
Stakeholder consultation on the draft guideline		✓
Finalising and publishing the guideline (including pre-publication check)		✓
Declaration of interests	✓	✓

Forming clinical questions and search strategies

The GDG formulated clinical questions based on the scope (see Appendix D). These formed the starting point for subsequent evidence reviews. Relevant published evidence to answer the clinical questions was identified by applying systematic search strategies (see Appendix J) to the following databases: Medline (1950 onwards), Embase (1980 onwards), Cumulative Index to Nursing and Allied Health Literature (CINAHL; 1982 onwards), and three Cochrane databases (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and the Database of Abstracts of Reviews of Effects). Searches to identify economic studies were undertaken using the above databases and the NHS Economic Evaluation Database (NHS EED). None of the searches was limited by date or language of publication (although publications in languages other than English were not reviewed). Generic and specially developed search filters were used to identify particular study designs, such as randomised controlled trials (RCTs). There was no systematic attempt to search grey literature (conferences, abstracts, theses and unpublished trials), nor was hand searching of journals not indexed on the databases undertaken.

Towards the end of the guideline development process, the searches were updated and re-executed, to include evidence published and indexed in the databases by 20th July 2009. Full details of the systematic searches, including the sources searched and the search strategies for each review question are presented in Appendix D.

Reviewing and grading the evidence

Evidence relating to clinical effectiveness was reviewed and graded using the hierarchical system presented in Table 2.2. This system reflects the susceptibility to bias inherent in particular study designs.

The type of clinical question dictates the highest level of evidence that may be sought. In assessing the quality of the evidence, each study receives a quality rating coded as '++', '+' or '−'. For issues of therapy or treatment, the highest possible evidence level (EL) is a well-conducted systematic review or meta-analysis of randomised controlled trials (RCTs; EL = 1++) or an individual RCT (EL = 1+). Studies of poor quality are rated as '−'. Usually, studies rated as '−' should not be used as a basis for making a recommendation, but they can be used to inform recommendations.

Table 2.2 Levels of evidence for intervention studies

Level	Source of evidence
1++	High-quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1−	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case-control or cohort studies; high-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2−	Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	Non-analytical studies (for example, case reports, case series)
4	Expert opinion, formal consensus

For each clinical question, the highest available level of evidence was sought. Where appropriate, for example, if a systematic review, meta-analysis or RCT was identified to answer a question, studies of a weaker design were not considered. Where systematic reviews, meta-analyses and RCTs were not identified, other appropriate experimental or observational studies were sought. For diagnostic tests, test evaluation studies examining the performance of the test were used if the effectiveness (accuracy) of the test was required, but where an evaluation of the effectiveness of the test in the clinical management of patients and the outcome of disease was required, evidence from RCTs or cohort studies was optimal. For studies evaluating the accuracy of a diagnostic test, sensitivity, specificity, positive predictive values (PPVs) and negative predictive values (NPVs) were calculated or quoted where possible (see Table 2.3).

The hierarchical system described above covers studies of treatment effectiveness. However, it is less appropriate for studies reporting accuracy of diagnostic tests. In the absence of a validated ranking system for this type of test, NICE has developed a hierarchy of evidence that takes into account various factors likely to affect the validity of such studies (see Table 2.4).

Table 2.3 '2 × 2' table for calculation of diagnostic accuracy parameters

	Reference standard positive	**Reference standard negative**	**Total**
Test positive	a (true positive)	b (false positive)	a+b
Test negative	c (false negative)	d (true negative)	c+d
Total	a+c	b+d	a+b+c+d = N (total number of tests in study)

Sensitivity = a/(a+c), specificity = d/(b+d), PPV = a/(a+b), NPV = d/(c+d)

Table 2.4 Levels of evidence for studies of the accuracy of diagnostic tests

Level	**Type of evidence**
Ia	Systematic review (with homogeneity)[a] of level-1 studies [b]
Ib	Level-1 studies [b]
II	Level-2 studies [c]; systematic reviews of level-2 studies
III	Level-3 studies [d]; systematic reviews of level-3 studies

IV	Consensus, expert committee reports or opinions and/or clinical experience without explicit critical appraisal; or based on physiology, bench research or 'first principles'

a Homogeneity means there are minor or no variations in the directions and degrees of results between individual studies that are included in the systematic review.
b Level-1 studies are studies that use a blind comparison of the test with a validated reference standard (gold standard) in a sample of patients that reflects the population to whom the test would apply.
c Level-2 studies are studies that have only one of the following:

- narrow population (the sample does not reflect the population to whom the test would apply)
- use a poor reference standard (defined as that where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference')
- the comparison between the test and reference standard is not blind
- case-control studies.

d Level-3 studies are studies that have at least two or three of the features listed above.

Summary results and data are presented in the text. More detailed results and data are presented in the evidence tables provided in Appendix X. Where possible, dichotomous outcomes are presented as relative risks (RRs) with 95% confidence intervals (CIs), and continuous outcomes are presented as mean differences with 95% CIs or standard deviations (SDs).

The body of evidence identified for each clinical question was synthesised qualitatively in clinical evidence statements. Quantitative synthesis (meta-analysis) was undertaken for two clinical questions in this guideline (psychological and behavioural interventions, and maintenance) as it was felt that there were a sufficient number of similar studies to merit such analysis.

Health economics

The aims of the health economic input to the guideline were to inform the GDG of potential economic issues relating to the management of idiopathic constipation, and to ensure that recommendations represented a cost-effective use of healthcare resources. Health economic evaluations aim to integrate data on benefits (ideally in terms of quality adjusted life years (QALYs), harms and cost of alternative options.

The GDG prioritised a number of clinical questions where it was thought that economic considerations would be particularly important in formulating recommendations. Systematic searches for published economic evidence were undertaken for these questions. For economic evaluations, no standard system of grading the quality of evidence exists and included papers were assessed using a quality assessment checklist based on good practice in economic evaluation. [14] Reviews of the (very limited) relevant published economic literature are presented alongside the clinical effectiveness reviews or as part of appendices detailing original economic analyses (see below).

For this guideline an economic evaluation was conducted to support the following area

- cost effectiveness of methods of disimpaction and maintenance of idiopathic constipation in children

Evidence to recommendations

For each clinical question, recommendations for clinical care were derived using, and linked explicitly to, the evidence that supported them. In the first instance, informal consensus methods were used by the GDG to agree clinical and, where appropriate, cost effectiveness evidence statements. Statements summarising the GDG's interpretation of the evidence and any extrapolation from the evidence used to form recommendations were also prepared to ensure transparency in the decision-making process.

In areas where no substantial clinical research evidence was identified, the GDG made consensus statements and used their collective experience to identify good practice. The health economics justification in areas of the guideline where the use of NHS resources (interventions) was considered was based on GDG consensus in relation to the likely cost-effectiveness implications of the recommendations. The GDG also identified areas where evidence to answer their clinical questions was lacking and used this information to formulate recommendations for future research.

Towards the end of the guideline development process, formal consensus methods were used to consider all the clinical care recommendations and research recommendations that had been drafted previously. The GDG identified ten 'key priorities for implementation' (key recommendations) and five high-priority research recommendations. The key priorities for implementation were those recommendations likely to have the biggest impact on patient care and patient outcomes in the NHS as a whole; they were selected through two rounds of formal voting. The priority research recommendations were selected in a similar way.

Stakeholder involvement in the guideline development process

Registered stakeholder organisations were invited to comment on the draft scope of the guideline and the draft guideline. Stakeholder organisations were also invited to undertake a pre-publication check of the final guideline to identify factual inaccuracies. The GDG carefully considered and responded to all comments received from stakeholder organisations. The comments and responses, which were reviewed independently for NICE by a Guidelines Review Panel, are published on the NICE website. [This paragraph will apply to the final guideline]

A full list of the stakeholders for this guideline can be found in Appendix C.

In addition, children were consulted on the content (scope) of the guideline using a questionnaire survey and on the guideline recommendations via a stakeholder meeting. See Appendix F for further details of this work.

2.8 Schedule for updating the guidance

Clinical guidelines commissioned by NICE are published with a review date 3 years from date of publication. Reviewing may begin earlier than 3 years if significant evidence that affects guideline recommendations is identified sooner.

3 Assessment and diagnosis

3.1 History taking and physical examination

Introduction

Idiopathic constipation is often seen as a minor problem which will either spontaneously resolve or respond to extra fibre and fluids in the diet. Parents often feel that it is their fault and that the significance of idiopathic constipation is overlooked. They also find difficult to accept that constipation could be idiopathic and worry that is an indicator of a more serious underlying health problem. For the child or young person, as well as for their families, the impact of idiopathic constipation on all aspects of their lives should not be underestimated.

A thorough and complete history taking is the most essential part of the initial process of diagnosis and treatment of idiopathic constipation. The first step in this process is to exclude other medical conditions and to facilitate a speedy diagnosis of idiopathic constipation. Careful history taking alongside the physical examination should identify the "red flags" which would suggest that the constipation is from an organic cause which requires further investigation. A positive diagnosis of idiopathic constipation will allow for correct and timely interventions and will prevent repetitive and often unnecessary investigations.

Accurate record keeping will allow this history to accompany the child on the patient journey to avoid unnecessary duplication of questioning and to facilitate a clear and holistic picture of the presenting condition.

Health professionals need to be aware of the social consequences of what may seem to be a trivial condition and the importance of their role in the early recognition of idiopathic constipation. In doing so they will benefit children and their families and help prevent the long term effects of idiopathic constipation.

Clinical Question

What are the key components of the history taking and the physical examination that would indicate idiopathic constipation or flag a serious underlying disorder?

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation
- included key components of the history taking and the physical examination that would indicate idiopathic constipation or flag a serious underlying

disorder such as: Hirschsprung's' disease, coeliac disease, hypothyroidism, anorectal malformations, neurological conditions, abdominal tumours

- included the following outcomes: changes in frequency of bowel movements, changes in stools consistency/appearance, changes in pain/difficulty on passing stools, changes in frequency of episodes of soiling, reduction in laxatives use, parent/child views or quality of life
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

A total of 487 articles were identified from the searches and 16 articles were retrieved for detailed assessment. Of these, 3 studies were identified for inclusion in this review

Narrative summary

One retrospective case-control study performed in the USA[3] (2003) [EL=III] determined the precipitants of constipation in early childhood. One hundred and twenty-five children (age 44 months ± 13, 49% male) were recruited for the patient group from 26 primary care centres after visiting their primary care physician with a chief complaint of constipation for the first time. Ninety-five children who had no history of constipation were chosen as controls (mean age 46 months ± 18, 54% male), 22 non-constipated patient siblings were recruited at the time that their constipated siblings were recruited, and 73 non-sibling control children were recruited though advertisements. Constipation was defined as the passage of fewer than 3 bowel movements each week for at least 2 consecutive weeks. Parents of both patients and controls were asked to fill out a questionnaire about the child's bowel habits. Parents indicated how difficult toilet training had been using a Likert scale (0-not at all difficult, to 4-extremely difficult). Parents of the constipated children indicated which events (from a list of 18) occurred in the 3 months prior to onset of constipation, and which of these they felt had contributed to the child becoming constipated. Results of the questionnaires showed no statistically significant differences for either family history of constipation or initial age of toilet training between constipated children and healthy controls. A high degree of difficulty with toilet training (mean score 2.1 ± 1.3 vs. 1.4 ± 1.1, $p<0.001$), a degree of difficulty and pain in passing bowel movements and the child expressing worry about passing bowel movement (% children: 75 vs. 8, $p<0.001$) were more likely to have occurred in the constipated children than in the healthy controls. Children were grouped according to whether they became constipated before or after their second birthday. The events parents reported having occurred in the 3 months before the onset of constipation were similar in the two groups, with the exception of toilet training having occurred more often before constipation in the older children (40% vs. 20%), and making the dietary transition from breast to bottle and from liquid to solid diets having occurred more often before constipation in the younger children (30% vs. 0%). Large or painful bowel movements were seen by far the most frequent precipitating event for both age groups. Toilet training was seen as more of a precipitant for older onset children (20% vs. 10%), whereas transition from breast to bottle and from liquid to solid foods was seen to be more of a problem for younger-onset children (25% vs. 0%). No attrition or loss to follow up was reported.

One retrospective case series performed in a tertiary referral centre in Canada[15] (2009) [EL=III] determined what proportion of children evaluated in an emergency department (ED) because of crying had a serious underlying etiology as well as the individual contributions of history, physical examination and laboratory investigations in determining diagnosis. Of 37,549 ED visits that occurred during a 9 month eligibility period, 238 children (males 124 (52%), median age 2.3 months (1.0–5.4)) met the inclusion criteria of ≤12 months old, being afebrile (<38°C) and presenting with a chief complaint of crying. Charts were reviewed retrospectively by searching the electronic database using a chief complaint family word root search for: "cry", "irritable", "fuss", "scream" and "colic". The relevant histories were analysed for the final diagnosis, and the contribution of history, examination and investigations to the final diagnosis. The final diagnosis was found by positive findings on history and/or physical examination alone in 66.4% (158 of 238) of children. Constipation was diagnosed in 11 children, all of which were diagnosed by history and examination alone. The features in history and physical examination considered to be helpful in diagnosis of constipation were: a history of difficult, infrequent, hard stools and palpation of small pellets on abdominal examination. Within the sample, abdominal radiograph was performed 14 times with no positive findings. Abdominal ultrasound was performed 16 times with two positive findings (12.5%), which contributed to the diagnosis of intussusception and acute cholecystitis in two cases, but no constipation. It should be noted that due to the lack of a uniform testing protocol these results may not be generalisable to other settings.

A retrospective cohort conducted in the USA[16] (2003) [EL=II] tested the hypothesis in 2 cohorts of 315 children that key features in the history, physical examination and radiographic evaluation would enable the avoidance unnecessary rectal biopsies. Cohort 1 comprised 265 children presenting with constipation who had undergone rectal biopsy to diagnose Hirschsprung's disease (HD). Cohort 2 comprised a concurrent selected cohort of 50 children with idiopathic constipation (IC). Only patients with definite information were included therefore the number of patients in each analysis varies due to missing data. Delayed passage of meconium was defined as failure to pass meconium in the first 48 hours of life. These data were available in 59% of cases. Abdominal distension was determined from parental response to questionnaire or data noted during patients visits. Enterocolitis was defined as diarrhoea associated with fever. In the group where onset of constipation occurred when they were <1 year old, significantly more children with HD reported delayed passage of meconium as compared to children with IC (65% vs. 13%, $p<0.05$). Abdominal distension and vomiting were also reported in significantly more children with HD as compared to children with IC (80 % vs. 42%, $p<0.05$ and 72% vs. 21%, $p<0.05$). Faecal impaction requiring manual evacuation occurred in significantly more children with IC as compared to children with HD (30% vs. 6%, $p<0.05$). There were no significant differences between children with HD and children with IC regarding enterocolitis. In the group where onset of constipation occurred after 1 year of age significantly more children with HD reported delayed passage of meconium as compared to children with IC (81% vs. 1%, $p<0.05$) and also significantly more children with HD reported abdominal distension as compared to children with IC (53% vs. 7%, $p<0.05$). No children with IC experienced vomiting as compared to 23% of children with HD ($p<0.05$). There were no significant differences between children with HD and children with IC regarding enterocolitis or faecal impaction requiring manual evacuation.

Evidence statement

One retrospective case-control study [EL=III] showed that a high degree of difficulty with toilet training, difficulty and pain in passing bowel movement and the child expressing worry about passing bowel movement were significantly more likely to have occurred in the constipated children than in the healthy controls. There were no significant differences for either family history of constipation or initial age of toilet training the constipated children and the healthy controls. Toilet training was seen as more of a precipitant in the children who became constipated after their second birthday and transition from liquid to solids was seen as more of a precipitant in children who became constipated before their second birthday. Large or painful bowel movements were seen by far the most frequent precipitating event for both age groups.

One retrospective case series [EL=III] showed that in a group of children evaluated in an emergency department because of crying all children diagnosed with constipation were diagnosed by history and examination alone. Criteria to diagnose constipation were a history of difficult, infrequent, hard stools and palpation of small pellets on abdominal examination.

One retrospective cohort study [EL=II] showed that significantly more children with Hirschsprung's disease reported delayed passage of meconium, abdominal distension and vomiting as compared to children with idiopathic constipation. In children younger than 1 year old faecal impaction requiring manual evacuation occurred in significantly more children with idiopathic constipation as compared to children with Hirschsprung's disease, but there were no significant differences between the two groups for children older than 1 year regarding this clinical feature. There were no significant differences between children with Hirschsprung's disease and children with idiopathic constipation regarding enterocolitis. The average age at onset of symptoms for patients with Hirschsprung's disease was 8 months (range 1 day to 9 years) and for patients with idiopathic constipation it was 15 months (range 7 days to 16 years)

GDG interpretation of the evidence

It is the GDG's view that both history taking and physical examination constitute an essential step in the diagnosis of any medical condition in general and of idiopathic constipation in particular. This is supported by the GDG's professional experience and also evidence obtained from the review. The GDG noted that there is insufficient evidence that allows for identification of all the specific key components that would make up a comprehensive history taking and physical examination that would indicate idiopathic constipation or flag a serious underlying disorder.

In order to complete identification of all key components of history taking and physical examination formal consensus methodology was employed amongst the GDG members asking them first to identify what they thought these components might be and then undertaking 2 rounds of consensus voting in order to agree which ones should be included in the guideline as key components.

Recommendations

Establish during history taking whether the child has constipation. Two or more findings from table 1, with symptoms lasting for more than 1 month, indicate constipation:

Table 1 Key components of history taking to diagnose constipation

Key components of history taking	Potential findings child under 1 year of age	Potential findings in child/young person over 1 year of age

Stool patterns	Fewer than 3 complete stools (see Bristol Stool Form Scale: 3 & 4 – Appendix G) per week Hard large stool “Rabbit droppings” (see Bristol Stool Form Scale – Appendix G)	Fewer than 3 complete stools per week (see Bristol Stool Form Scale: 3 & 4 – Appendix G) Overflow soiling (i.e. very loose, very smelly stool passed without sensation) “Rabbit droppings” (see Bristol Stool Form Scale – Appendix G) Large, infrequent stools which can block the toilet
Symptoms associated with defecation	Distress on stooling and bleeding associated with hard stool Straining	Poor appetite improving 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
History	Previous episode (s) of constipation Previous/current anal fissure	Previous episode (s) of constipation Previous/ current anal fissure Painful bowel movements and bleeding associated with hard stool

If the child has constipation take a history using table 2 to establish a positive diagnosis of idiopathic constipation by excluding underlying causes. If a child has any “red flags” symptoms do not treat for constipation. Instead refer them urgently to a health care professional experienced in child health.

If the history-taking and/or physical exam show evidence of faltering growth test for coeliac disease and hypothyroidism.

If either the history taking or the physical examination show evidence of possible maltreatment refer to ‘When to suspect child maltreatment’, NICE clinical guideline 89 (2009).

Table 2 Key components of history taking to diagnose idiopathic constipation

Key components of history taking	**Potential findings and diagnostic clues in a child younger than 1 year**	**Potential findings and diagnostic clues in a child/young person older than 1 year**
Timing of onset of constipation and potential precipitating factors	Starts after a few weeks of life Obvious precipitating factors coinciding with the start of symptoms: fissure, change of diet, infections	Starts after a few weeks of life Obvious precipitating factors coinciding with the start of symptoms: fissure, change of diet, timing of potty/toilet training and acute event such as infections, moving house, starting nursery/school, fears and phobias, major change in family
	Reported from birth or first few weeks of life	Reported from birth or first few weeks of life
Passage of meconium	Normal, that is within 24 hours after birth (in term baby)	Normal, that is within 24 hours after birth (in term baby)
	Failure to pass/delay, that is more than 24 hours after birth (in term	Failure to pass/delay, that is more than 24 hours after birth (in term

	baby)	baby)
Growth and general well being	Generally well, weight and height within normal limits	Generally well, weight and height within normal limits, fit and active
	Faltering growth	Faltering growth
Symptoms in legs /locomotor development	No neurological problems in legs, normal locomotor development	No neurological problems in legs (such as falling over), normal locomotor development
	Previously unknown or undiagnosed weakness in legs, locomotor delay	Previously unknown or undiagnosed weakness in legs, locomotor delay
Abdomen	Abdominal distension and vomiting	Abdominal distension and vomiting
Diet and fluid intake	Changes in formula, weaning, insufficient fluid intake	History of poor diet and/or insufficient fluid intake
Personal/familial/ social factors	Disclosure or evidence that raises concerns over possibility of child maltreatment (see 'When to suspect maltreatment in children' NICE clinical guideline 89 for examples of evidence and subsequent management)	Disclosure or evidence that raises concerns over possibility of child maltreatment (see 'When to suspect maltreatment in children' NICE clinical guideline 89 for examples of evidence and subsequent management)
Green cells: indicative of idiopathic constipation. Amber cells: 'amber flag', possible idiopathic constipation. Red cells: 'red flag' for underlying disorder/condition, exclude idiopathic constipation.		

Do a physical examination. Use table 3 to establish positive diagnosis of idiopathic constipation by excluding underlying causes. If a child has any "red flag" symptoms do not treat them for constipation. Instead refer them urgently to a health care professional experienced in child health.

Table 3 Key components of physical examination to diagnose idiopathic constipation

Key components of the physical examination	**Potential findings and diagnostic clues**
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 overweight child
	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
	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
Red cells: 'red flag' for underlying disorder/condition, exclude idiopathic constipation Green cells: indicative of idiopathic constipation	

Inform the child 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.

3.2 Digital rectal examination

Introduction

The digital rectal examination (DRE) is recommended by a number of national and international guidelines as part of the routine examination of children with chronic constipation. [17], [18], [19]

However there is doubt as to its value in the assessment of children with chronic constipation. It is an investigation that is often not well tolerated by children or their parents.

Rarely, it may be necessary to perform a DRE to exclude an anatomical cause of constipation, for example anal stenosis.

In this section we shall look at the evidence base regarding the value of this examination in children with chronic constipation.

Clinical Question

What is the diagnostic value of the digital rectal examination in children with chronic idiopathic constipation?

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation undergoing digital rectal examination
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

A total of 79 articles were identified from the searches and 11 articles were retrieved for detailed assessment. Of these, two case-series were identified for inclusion in this review.

Narrative summary

One prospective case series conducted in USA[20] (2001) [EL=3] aimed to determine whether clinical variables accurately identify children with radiologically proven constipation. The study involved 251 children aged 2-12 years old who presented to the Emergency Department (ED) with abdominal pain and underwent an abdominal radiograph. Clinical variables (as a model) showed a sensitivity of 77%, a specificity of 35%, a positive predictive value of 60% and a negative predictive value of 55%. Only the following clinical variables were significantly different between the groups of children who were shown to be constipated as per abdominal radiography and those who were not: history of normal/hard stool consistency (Group 1: 74% (100/135), Group 2: 61% (61/99), p=0.016); absence of rebound tenderness (Group 1: 98% (138/141), Group 2: 90% (99/110), p=0.007); presence of left lower quadrant tenderness (Group 1: 20% (19/96), Group 2: 9% (6/69) p=00499) and stool present in rectal vault as per rectal exam (Group 1: 69% 70/102, Group 2: 43% (29/68), p=0.008). No clinical variable, either as a single variable or in a model, accurately identified patients with abdominal pain and radiographically proven constipation. One single variable, stool present on rectal exam, was the best discriminator between patients with and without constipation. The model accurately predicted 77% of patients with radiographically proven constipation; however 35% of the patients predicted by the model as radiographically constipated actually had other diagnosis. It should be noted that 32% of the enrolled subjects did not undergo a rectal examination.

A retrospective case series also conducted in the USA[21] (1995) [EL=3] aimed to determine if the presence of faecal retention in encopretic children on presentation could be assessed objectively using a plain abdominal radiography, and whether faecal retention so determined correlated with findings at initial clinical assessment. The total population sample comprised 60 children aged 4-18 diagnosed with encopresis as defined by the DSM Revised Third Edition: “repeated involuntary (or, much more rarely, intentional) passage of faeces into places not appropriate for that purpose (e.g. clothing or floor)…the event must occur at least once a month for at least 6 months, the chronological and mental age of the child must be at least 4 years, and physical disorders that can cause faecal incontinence, such as aganglionic megacolon, must be ruled out”. Forty-seven encopretic children were diagnosed with faecal retention by radiography criteria on presentation, whereas 13 encopretic children showed no evidence of faecal retention by radiographic criteria on presentation. When the diagnosis of retention by abdominal radiography (systematic reading) was done by agreement of at least two radiologists the diagnosis of retention by rectal examination showed a sensitivity of 88.6%, a specificity of 41.6% a positive predictive value of 84.8% and a negative predictive value of 50%. When the diagnosis of retention by abdominal radiography (systematic reading) was done by agreement of the three radiologists the diagnosis of retention by rectal examination showed a sensitivity of 91.7%, a specificity of 71.4% a positive predictive value of 94.3% and a negative predictive value of 62.5%. There were no significant differences between encopretic children whose abdominal radiography were reviewed for the study and those who did not have radiography or whose radiography could not be retrieved. Children with retention (as per radiography) were significantly more likely to have stool in the rectum on presentation (p=0.015) and were significantly less likely to have parents report a difficult toilet training (p=0.018). There were no other significant differences between the two groups regarding the rest of the variables measured. (Not all data were available for every child).

Evidence statement

One prospective case series [EL=3] showed that stool present on rectal examination as diagnosed per DRE was the best discriminator between patients with and without radiographically diagnosed constipation.

One retrospective case series [EL=3] showed good sensitivity and positive predictive value of the DRE in children diagnosed with faecal retention by radiography, but its specificity and negative predictive value were poor.

GDG interpretation of the evidence

The GDG concluded that DRE is not useful for the diagnosis of chronic idiopathic constipation but it is useful to help diagnose other serious problems e.g. anal stenosis, Hirschsprung's disease. The younger the child is, the more important it is that a DRE is carried out as these serious problems are more frequently diagnosed in younger children, particularly children under 1 year old. However, older children who have other relevant clinical features may also require these diagnoses to be excluded.

The GDG concluded that faecal retention/impaction can be diagnosed by taking an appropriate history, asking the parents about the presence of overflow soiling and bowel habits and by the detection of palpable faeces on abdominal examination.

It is the GDG's view that a DRE should only be undertaken for diagnosis of constipation in children by healthcare professionals who are competent to do so.

Ideally, if indicated, a DRE should be performed only once for an individual child. For this reason the GDG believes it is very important to maintain good communication between primary and secondary care and/or between different health care professionals to ensure that unnecessary repeats do not happen.

Recommendations

Perform a digital rectal examination in all children younger than 1 year with a diagnosis of idiopathic constipation that does not respond to adequate treatment within 4 weeks.

Do not perform a digital rectal examination in children older than 1 year unless there is a 'red flag' (see tables 2 and 3) in the history-taking and/or physical examination that might indicate an underlying disorder.

A digital rectal examination should only be undertaken by healthcare professionals competent to interpret features of anatomical abnormalities or Hirschsprung's disease.

For a digital rectal examination ensure:

- informed consent is given by the child, or the parent or legal guardian if the child is not able to give it, and is documented
- a chaperone is present
- individual preferences about degree of body exposure and sex of the examiner are taken into account
- all findings are documented.

4 Clinical investigations

4.1 Introduction

As with many difficult clinical problems, various investigations are performed with little evidence that they help with diagnosis or treatment. Investigations cost money and therefore have an opportunity cost as the money may well be better spent providing further support for families. Investigations are not always painless and so unless they can be shown to either aid diagnosis or enhance the efficacy of treatment they should not be performed. Waiting for the results of investigations can add extra worry and delay parents and children from taking charge of the constipation problem and thus postpone effective treatment and recovery.

This section looks at the evidence for the use of commonly and less commonly employed investigations: abdominal ultrasound; plain abdominal radiography; transit studies; blood tests (thyroid function tests and coeliac disease tests); gastrointestinal endoscopy; anorectal manometry and rectal biopsy

4.2 Endoscopy

Clinical question

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

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation undergoing gastrointestinal endoscopy
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

A total of 139 articles were identified from the searches but no articles were retrieved for detailed assessment.

GDG interpretation of the evidence

No published evidence was found for the diagnostic value of the gastrointestinal endoscopy in children with chronic idiopathic constipation. Gastrointestinal endoscopy is an invasive procedure with associated morbidity and mortality. In the very rare circumstances when this test will be indicated because of suspicion of organic pathology, this will happen only after less invasive tests have shown positive results e.g. positive blood tests for coeliac disease. Therefore the GDG concluded that gastrointestinal endoscopy should not be used to investigate children with idiopathic constipation.

Recommendations

Do not use gastrointestinal endoscopy to investigate idiopathic constipation.

4.3 Hypothyroidism and coeliac disease

Clinical Question

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

Previous NICE Guidelines

A similar clinical question was looked at in the NICE clinical guideline for Coeliac disease [11] where the question addressed was:

"What are the signs and symptoms which indicate a diagnosis of coeliac disease?

– gastrointestinal symptoms

– non-gastrointestinal symptoms

The guideline recommended:

–"Consider offering serological testing for coeliac disease to children and adults with any of the following:

persistent or unexplained constipation" (other conditions not related to constipation were also listed)

–"Offer serological testing for coeliac disease to children and adults with any of the following signs and symptoms:

failure to thrive or faltering growth (in children)" (other conditions not related to constipation were also listed)

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

A total of 92 articles were identified from the searches (50 on coeliac disease, 42 on hypothyroidism) and 18 articles were retrieved for detailed assessment (12 on coeliac disease, six on hypothyroidism). Of these, four studies on coeliac disease were identified for inclusion in this review: two prospective cohorts and two retrospective case series. None of these studies investigated the prevalence of coeliac disease in children with idiopathic constipation but rather looked at the associations between coeliac disease and symptoms of constipation in a variety of populations of children. No studies were identified for inclusion that considered the prevalence of hypothyroidism in children with idiopathic constipation.

Narrative summary

A prospective cohort conducted in Italy [22] (2001) [EL=2+] estimated the prevalence of coeliac disease (CD) in patients with Down syndrome and defined the clinical characteristics of CD among 1202 (609 males) Down syndrome patients. One thousand one hundred and ten patients were children (age range: 15 months to 18 years) and 92 were adults (age range 18 to 46 years). CD was diagnosed according the Revised European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) criteria. Patients were selected for intestinal biopsy on the basis of antiendomysium antibodies (EMA) positivity, antigliadin antibodies immunoglobulin (AGA IgA) positivity, or both in children younger than 2 years of age. Down syndrome was confirmed by karyotype in all cases. All patients were receiving a gluten-containing diet.

Fifty-five patients, including 47 children (36 males, aged 4 to 46 years) were diagnosed with CD and constituted Group 1. Their clinical features were compared with those observed in 55 IgA AGA-positive/EMA-negative patients (Group 2: 33 males, aged 3 to 40 years) and in 57 IgA AGA-negative/EMA-negative Down syndrome patients (Group 3: 34 males, aged 4 to 38 years)). Group 2 and Group 3 patients were selected randomly from among the screened patients to be age and gender matched to Group 1. A detailed questionnaire was completed to obtain information about familial gastroenterologic history with special attention to feeding habits (breast milk or formula, age of introduction of gluten-containing foods); gastrointestinal function, particularly the features of CD, such as chronic diarrhoea, vomiting, failure to thrive, and anorexia; presence of autoimmune or neoplastic conditions. Weight and height were evaluated using Down syndrome percentile charts. Constipation was present in significantly more patients in Group 1 (29.1%) when compared to patients in Groups 2 (14.5%) and 3 (8.8%), ($p<0.05$). However other signs and symptoms were also present in significantly more patients in Group 1 when compared to patients in groups 2 and 3 (growth failure: 52.7 vs. 10.9 vs. 7, $p<0.001$; diarrhoea 41.8 vs. 1.8 vs. 6.9, $p<0.001$; vomiting 20 vs. 1.8 vs. 1.7, $p<0.001$ and anorexia 18.2 vs. 1.8 vs. 3.4, $p<0.01$). It should be noted that the parents of eight EMA-positive children and two EMA-positive adults did not give permission for intestinal biopsy to be performed and were not included among the 55 CD patients.

A prospective cohort study conducted in the UK [23] (2004) [EL=2+] established the prevalence of undiagnosed coeliac disease in the general population at age seven and looked for any associated clinical features in 5470 children aged 7.5 years (gender not reported) participating in the Avon Longitudinal Study of Parents and Children (ALPASC) (a population based birth cohort study established in 1990). CD was diagnosed based on a two stage screening: first a sensitive initial radioimmunoassay for antibodies to tissue transglutaminase (endomysial antigen; (tTG antibodies) was conducted. If positive to previous, serum IgA antiendomysial antibodies (IgA-EMA) by indirect inmunofluorescence were measured. Children with tTG antibodies <97.5th centile were defined as antibody negative. Details of gastrointestinal symptoms including constipation were collected by routine questionnaire at age 6.75 years. Four thousand three hundred and twenty four children (79%) returned questionnaires. Five thousand three hundred and thirty three children were tTG antibody negative controls whereas 54 children were IgA-EMA positive (1.0%; 95% confidence interval 0.8 to 1.4). An additional 137 children were tTG antibody positive, but IgA-EMA negative. Of 4285 tTG antibody negative controls who returned their questionnaires, 435 (10 %) reported any constipation at age 6.75 years. Of 42 IgA-EMA positive children who returned their questionnaires, six (14%) reported any constipation at age 6.75 years (odds ratio (95% CI): 1.48 (0.62 to 3.52)). Aside from constipation other symptoms reported at age 6.75 years were not significantly more frequent in IgA-EMA positive children than in tTG antibody negative controls (any diarrhoea (number, %): 21 (50) vs. 1450 (34), (OR: 1.96 (95% CI: 1.06 to 3.59); any vomiting: 23 (55) vs. 1933 (45), (OR: 1.47 (95% CI: 0.80 to 2.71); any stomach pains: 28 (66) vs. 2557 (60), (OR: 1.35 (95% CI: 0.71 to 2.57)). However, significantly more IgA-EMA positive children than tTG antibody negative controls reported multiple (≥3) gastrointestinal symptoms (17 (40) vs. 931 (22), (OR: 2.45 (95% CI: 1.33 to 4.5). IgA-EMA were more common in girls (OR 2.12; 95% CI: 1.20 to 3.75). IgA-EMA positive children were shorter and weighed less than those who tested negative for tTG antibody (p<0.0001). It should be noted that since ALPASC is an observational study based on analysis of anonymous samples, confirmatory biopsy for coeliac disease was not possible. No data regarding clinical symptoms at 6.75 years were available for 21% of the total sample. It is unclear how the symptom "constipation" was defined.

A multicentre hospital based retrospective case series [24] conducted in Italy (2004) [EL=3], evaluated the prevalence of CD in immigrant children, the clinical findings in these patients and the possible relationship between immigration, dietary habits and CD in childhood. One thousand eight hundred and eighty one Italian (891 males, age range 6 months to 16 years (mean 7.9)) and 36 immigrant children (15 males, age range 6 months to 15 years (mean 7.3)) consecutively diagnosed as having CD between January 1999 and December 2001 were included. CD was diagnosed based on the revised criteria of the European Society of Paediatric Gastroenterology and Nutrition (ESPGAN). Clinical pattern and presenting symptoms at diagnosis were classified and grouped in three categories: "classical forms" included the following symptoms: chronic diarrhoea, weight loss, abdominal distension and vomiting; "atypical forms" included: iron-deficiency anaemia, short stature, delayed puberty, and recurrent oral aphtae; and "silent forms" included serological screening of first degree relative and loss of Kerckring folds at endoscopy. Two out of nine children (25%) presenting with atypical forms of CD had abdominal pain with constipation. None of the children diagnosed with "classical forms" (n=25; 69.4%) or with "silent forms" (n=2; 5.5%) was reported to having experienced constipation. Clinical patterns in Italian children were similar to those of immigrant children but presenting symptoms at diagnosis were not reported for Italian children. It is unclear how the symptom "constipation" was defined in the first place.

One retrospective case series conducted in Ireland [25] (1972) [EL=3] assessed the incidence of constipation in 112 children diagnosed with CD. Of the total population 12 children had constipation (six males, age range 6 to 102 months). CD was diagnosed based on clinical variables (undernutrition and retarded growth) and jejunal biopsy (grade 2/3 or grade 3 jejunal mucosal damage). Growth retardation was assessed using the graphs of Tanner and Whitehouse (1959) and subsequently confirmed by catch-up growth following treatment with gluten-free diets. Jejunal mucosal damage was assessed according to authors' classification: normal mucosa grade 0; mild non-specific change grade 1; grade 2 and 3 correspond to moderate and severe villous atrophy. Constipation was defined as the passage of stools of harder consistency than normal, or the clinical observation of impaction of abnormal amounts of hard (usually pale) faeces in colon and rectum. Twelve children (10.7%) had been constipated at some stage before diagnosis; 66.7% of those children had had constipation alternating with diarrhoea and 25% additionally presented anorexia and failure to thrive. It is unclear whether the authors used a validated classification system for jejunal mucosal damage.

Evidence statement

There is no published evidence on the prevalence of hypothyroidism and coeliac disease in children with idiopathic constipation

One prospective cohort study [EL=2+] showed that the prevalence of constipation as a symptom in patients, both adults and children, with Down syndrome and subsequently diagnosed with CD was 29.1%. Constipation was present in significantly more patients diagnosed with CD as compared to controls. Faltering growth, diarrhoea, vomiting and anorexia were also present in significantly more patients diagnosed with CD when compared to controls.

One prospective cohort [EL=2+] showed that 14% of children who tested positive to serum IgA antiendomysial antibodies had constipation. However, constipation was not associated with positivity to serum IgA antiendomysial antibodies, and neither were diarrhoea, vomiting or stomach pains. Having multiple (≥3) gastrointestinal symptoms was associated with positivity to serum IgA antiendomysial antibodies.

One retrospective case series [EL=3] showed that the prevalence of constipation as a symptom in children with CD was 10.7% and that 66.7% of those children had constipation alternating with diarrhoea and 25% presented with constipation, anorexia and faltering growth.

One retrospective case series [EL=3] showed that 25% of children presenting with atypical forms of coeliac disease had abdominal pain with constipation. This corresponded to 5.6% of the total sample of children with CD.

GDG interpretation of the evidence

The GDG believes that there is no evidence to support the routine testing of children with chronic constipation for CD and hypothyroidism. However if other symptoms e.g. faltering growth, are present in the history, this may suggest an underlying disorder like hypothyroidism as the cause of the constipation, and in that case testing would be justified.

In some children who do not respond to sustained optimal medical management it is the GDG's experience that an atypical presentation of CD could be the cause of the constipation therefore testing would be justified.

Recommendations

Test for coeliac disease in the ongoing management of intractable constipation in children when requested by specialist services.

4.4 Manometry

Clinical Question

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

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation undergoing anorectal/rectal manometry and also undergoing rectal biopsy as the gold standard method to diagnose Hirschsprung's disease
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

A total of 480 articles were identified from the searches and 27 articles were retrieved for detailed assessment. Of these 5 studies were identified for inclusion in this review: 2 prospective case series and 3 retrospective case series

Narrative summary

A retrospective case series conducted in Finland[26] (2009) [EL=3] reported on the value of anorectal manometry (ARM) with reference to operative rectal biopsy in the diagnosis/exclusion of Hirschsprung's disease (HD) in children under 1 year of age, and on the prognostic significance of a normal rectoanal inhibitory reflex (RAIR) in these patients. Eighty-one patients (49 male, median age at time of ARM and biopsy: 2 months (range 0.1 to 11 months) under 1 year of age who presented with delayed passage of meconium, abdominal distension and vomiting or constipation who underwent ARM were included. The records of all patients who met the inclusion criteria were reviewed. All children underwent both ARM and operative rectal biopsy. The RAIR was present in 40 children. None of those children had HD. Thirty-nine children had normal histology and one child had hypoganglionosis. The RAIR was absent in 41 children, 33 of those had HD and eight had normal histology. The operative rectal biopsy was 100% accurate in diagnosing HD for all variables (sensitivity, specificity, positive predictive value and negative predictive value). Both the sensitivity and the negative predictive value was 100% for the ARM, but its specificity was 83% and its positive predictive value was 80%. Patients who had HD were significantly younger at the time of investigation than those who did not. The operative rectal biopsy was adequate and diagnostic in all cases. There was one case of rectal bleeding following biopsy which required suturing in theatre. In the case of patients diagnosed with HD the histology from bowel resected at pull-through operation was consistent with pre-operative diagnosis in all cases.

A retrospective case series conducted in Korea [27] (2007) [EL=3] evaluated the incidence and clinical aspects of allergic proctitis (AP) in patients with symptoms that mimic HD. In addition, the authors determined the sensitivity and specificity of ARM and suction rectal biopsy used for evaluation of HD. One hundred and five infants younger than 6 months of age (61 boys, mean age: 2.1 $\pm$ 0.9 months) with severe abdominal distension that mimicked HD referred to department of paediatrics and division of paediatric surgery and underwent all triple tests including barium enema, ARM and rectal suction biopsy. Some patients had associated symptoms like constipation, poor oral intake, vomiting, poor weight gain and diarrhoea. HD was finally diagnosed with full thickness biopsy. The RAIR was absent in 48 children, 34 of whom had HD and ten had normal histology. In this group 4 children were diagnosed with other pathologies (two with AP and two with intestinal neuronal dysplasia (IND)). The RAIR was present in 57 children, five of whom had HD and 43 had normal histology. In this group nine children were diagnosed with other pathologies (five with AP and four with IND). The diagnostic variables for the ARM in HD were as follows: sensitivity: 87.18% (CI: 73.29 to 94.90), specificity: 78.79% (CI: 67.49 to 86.92), positive predictive value 70.83% and negative predictive value 91.23%. The diagnostic variables for the rectal suction rectal biopsy in HD were as follows: sensitivity 92.31% (CI: 76.68 to 97.35), specificity: 100% (94.50 to 100.00), positive predictive value 100% and negative predictive value: 95.65%.

A prospective case series conducted in Singapore [28] (1989) [EL=3] assessed the accuracy of ARM in the diagnosis of Hirschsprung's disease (HD) using histological aganglionosis as the reference point for final diagnosis. Fifty children referred consecutively to one of the authors for anorectal manometric studies were included. All children underwent both manometry and biopsy. Fourty-five patients had concordant results (both on manometry and biopsy) and only for those demographic data are reported: 31 were male and age ranged from birth to 11 months. Specimens not including the submucosal layer were considered inadequate and repeat full-thickness operative rectal biopsies were taken. The RAIR was absent in 16 children, 15 of whom had HD and one had normal histology. The RAIR was present in 34 children, four of whom had HD and 30 had normal histology. Diagnostic variables for the ARM in the total sample (n=50) were as follows: accuracy 90%, sensitivity 79%, specificity 97%, positive predictive value 94% and negative predictive value 88%. Diagnostic variables for the ARM in neonates (n=10) were as follows: accuracy 90%, sensitivity 86%, specificity 100%, positive predictive value 100% and negative predictive value 75%. Diagnostic variables for the ARM in infants (n=18) were as follows: accuracy 94.4%, sensitivity 90%, specificity 100%, positive predictive value 100% and negative predictive value 89%. Five children (10%) required repeat full-thickness biopsy for inadequate sampling. No complications were encountered with manometry in all 50 children studied.

A retrospective case series conducted in Taiwan [29] (1993)[EL=3] evaluated the possibility of using ARM for screening for HD. Thirty-nine patients (age range: 3 days to 9 years) with constipation or suspected HD were included. All children underwent both anorectal manometry and rectal suction biopsy. The RAIR was absent in eight patients, 15 of whom had HD and three normal histology. The final diagnosis of HD was made by the patient's clinical history, barium enema and rectal suction biopsy. Three children showed inconclusive results with manometry due to poor tracing of internal sphincter contraction as a result of oversedation (n=2) and to anal stenosis (n=1). Diagnostic variables for the ARM were as follows: accuracy 90%, sensitivity 100%, specificity 86%, positive predictive value 83% and negative predictive value 100%.

A prospective case series conducted in Belgium [30] (1990) [EL=3] ascertained the traps and limitations of testing the RAIR, how frequently they occur and the possible explanations for equivocal or false results. Two hundred and sixty one patients referred for ARM in order to confirm or exclude HD were included. All patients had presented with constipation varying from slight to intractable, with highly differing durations ranging from neonatal ileus to chronic constipation in adults. Ninety-four patients (36%) were <6 months, 106 (41%) were aged between 6 months to 6 years, 47 (18%) between 6 to 15 years and 5% comprised two adolescents and 12 adults (gender not reported for all patients). All children underwent ARM. A confident interpretation of the RAIR occurred in 232 children (RAIR present (n=207), RAIR absent (n=25)). The result of this first manometric evaluation was verified either by biopsy or by repeated manometry in 54 cases. In other cases the clinical evolution did not warrant further investigation. This review only includes children who underwent both manometry and biopsy. In these, the RAIR was present in two children who had HD and was absent in four children who had a normal histology. The RAIR was equivocal ("?absent") in nine children, four of whom had HD and five who had normal histology. The RAIR was equivocal ("?present") in eight children, two of whom had HD and six who had a normal histology. The incidence of false results at first manometry was significantly higher in neonates as compared to children older than 1 month (5/22 (22.7.8%) vs. 4/239 (1.7%)). The incidence of equivocal results at first manometry was also higher in neonates as compared to children older than 1 month (4/22 (18.2%) vs. 25/239 (10.4%)). In no case was the result of a rectal biopsy known at the time of manometry. Authors reported that the following factors prevented the examiners from reaching a definite conclusion when measuring the RAIR: low anal tone (n=8), restlessness of patient (n=7), reflex external sphincter contraction partially or completely masking possible RAIR (n=4), presence of megarectum (n=3), artefacts (n=1), unstable RAIR (n=6). Details of both the manometry and biopsy results were reported only in cases where the RAIR was equivocal in the first manometry and in those children where the result proved to be false (either negative or positive). Considering this, it is not possible to calculate the sensitivity, specificity, positive and negative predictive values of the ARM. The incidence of false results in manometry performed by different examiners is reported in the paper, but there are missing data not accounted for and therefore we do not report it here.

Evidence statement

A retrospective case series [EL=3] showed that the anorectal manometry (ARM) had the same sensitivity and negative predictive value (100%) as the operative rectal biopsy in diagnosing Hirschsprung's Disease (HD) but its specificity and positive predictive value were lower (83 % vs. 100% and 80 % vs. 100% respectively)

A retrospective case series [EL=3] showed that the ARM performed worse in all diagnostic variables than the suction rectal biopsy in diagnosing HD (sensitivity: 87.18% (CI: 73.29 to 94.90) vs. 92.31% (CI: 76.68 to 97.35), specificity: 78.79% (CI: 67.49 to 86.92) vs. 100% (94.50 to 100.00), positive predictive value 70.83% vs. 100% and negative predictive value 91.23% vs. 95.65%)

A prospective case series [EL=3] showed that the diagnostic variables for the ARM in diagnosing HD were as follows: accuracy 90%, sensitivity 79%, specificity 97%, positive predictive value 94% and negative predictive value 88 %. ARM was less accurate and less sensitive in neonates when compared to infants and its negative predictive value was also lower. Specificity and positive predictive value were the same for both age groups (100%)

A retrospective case series [EL=3] showed that the diagnostic variables for the ARM in diagnosing HD were as follows: accuracy 90%, sensitivity 100%, specificity 86%, positive predictive value 83% and negative predictive value 100%.

A prospective case series [EL=3] showed that the incidence of both false and equivocal results for ARM were significantly higher in neonates as compared to children older than 1 month. Different factors prevented the examiners from reaching a definite conclusion when measuring the RAIR: low anal tone, restlessness of patient, reflex external sphincter contraction partially or completely masking possible, presence of megarectum, artefacts and unstable RAIR.

Table 4.1 Rectoanal Inhibitory Reflex (RAIR) in children with and without Hirschsprung's disease (HD)

Study	Manometry	Biopsy	
		HD (number of children)	No HD (number of children)
Jarvi, 2009	RAIR +	0	40
	RAIR –	33	8
Lee, 2007	RAIR +	5	52

	RAIR –	34	14
Low, 1989	**RAIR +**	4	30
	RAIR –	15	1
Kong, 1993	**RAIR +***	0	8
	RAIR –	15	3
	Inconclusive/failure	0	3
Penninckx, 1990	**RAIR +**	2	Not reported
	RAIR –	Not reported	4
	Equivocal-present?	2	6
	Equivocal-absent?	4	5

RAIR + means that the reflex was present
RAIR – means that the reflex was absent
Numbers in blue represent "false positive" and "false negatives" for the RAIR

Table 4.2 Diagnostic variables for the anorectal manometry and the rectal biopsy in children with Hirschsprung's disease

Study	Test	Accuracy	Sensitivity	Specificity	PPV	NPV
Jarvi 2009	ARM	–	100	83	80	100
	Biopsy*	100	100	100	100	100
Lee 2007	ARM	–	87.18	78.79	70.83	91.23
	Biopsy	–	92.31	100	100	95.65
Low 1989	ARM	90	79	97	94	88
	Biopsy	Unclear but 5 children (10%) required repeat full-thickness biopsy for inadequate sampling				
Kong 1993	ARM	90	100	86	83	100
	Biopsy	Unclear whether or not all patients underwent rectal biopsy but it looks as this was probably the case				
Penninckx 1990	ARM	Not possible to calculate				
	Biopsy					

ARM: anorectal manometry
PPV: positive predictive value
NNP: negative predictive value

* Unclear whether biopsy was actually performed, but it seems that it was the case
* Apart from this study in which operative rectal biopsy was performed, suction rectal biopsy was performed in all the others

GDG interpretation of the evidence

The GDG understands from the evidence that ARM is not a reliable test to diagnose HD and that there are many factors which can confound its results. The GDG is aware that ARM is used as a research tool in some centres. However, if there is a strong clinical suspicion for HD then a rectal biopsy should be performed without delay, because this is the gold standard test to diagnose HD.

Recommendations

Do not use anorectal manometry to exclude Hirschsprung's disease in children with chronic constipation

4.5 Radiography

Clinical Question

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

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation
- were not case-reports
- were published in English

No restrictions were applied on the publication date.

Overview of available evidence

One search was conducted for all radiological investigations (plain abdominal radiography, abdominal ultrasound and transit studies). A total of 646 articles were identified and 72 articles were retrieved for detailed assessment. Of these, one systematic review (including six studies), two case control studies and one retrospective case series were identified for inclusion in this review.

Narrative summary

One robust systematic review conducted in the Netherlands[31] (2005) [EL=III] evaluated the additional diagnostic value of the plain abdominal radiography in the diagnosis of constipation in children. Six studies (three case series, two case-control studies, and one retrospective re-examination of abdominal radiographs) were included. All studies were hospital-based, controlled, observational studies investigating the relationship between faecal loading on plain abdominal radiography and symptoms and signs related to constipation, in otherwise healthy children aged from 1 to 18 years old. Some studies included children with soiling or encopresis, while others excluded this group. In the six studies included, three different scoring systems for assessing impaction on abdominal radiography were used: three studies, Barr-score; two studies, revised Barr-score (Blethyn) and one study, authors' own scoring system (Leech). The ability of the abdominal radiography to discriminate between clinically constipated and non constipated children was evaluated in four studies with variable results (sensitivity (%): 76 (95% CI: 58 to 89) vs. 60 (95% CI: 46 to 72) vs. 80 (95% CI: 65 to 90); specificity (%): 75 (95% CI: 63 to 85) vs. 43 (95% CI: 18 to 71) vs. 90 (95% CI: 74 to 98); likelihood ratio (LR) 1.0 (95% CI: 0.5 to 1.6) vs. LR: 3.0 (95% CI: 1.6 to 4.3) vs. LR: 8.0 (95% CI: 0.7 to 17.1). One study reported an accuracy of 80% (95% CI: 50 to 100). The ability of the clinical examination to discriminate between radiographically constipated and non constipated children was evaluated in one study and reported a sensitivity of 77% (95% CI: 70 to 84) a specificity of 35% (95% CI: 27 to 44) and a LR of 1.2 (95% CI: 1.0 to 1.4). One study found a significant association between a history of hard stool and faecal impaction on abdominal radiography: LR: 1.2 (95% CI: 1.0 to 1.4), whereas another study found a significant association between a finding of absent rebound tenderness and faecal impaction on abdominal radiography: LR: 1.1 (95% CI: 1.0 to 1.2). The association between stool present on rectal examination and faecal impaction on abdominal radiography was significant in one study (LR: 1.6 (95% CI: 1.2 to 2.0)) but not in a second one LR: 1.5 (95% CI: 0.8 to 2.3). The interobserver reliability ranged from moderate to excellent (k range, 0.63 to 0.95) in five studies and from poor to moderate (k=0.28 to 0.60) in one study. The intraobserver reliability was evaluated in three studies only and ranged from moderate (k=0.52) to excellent (k≥0.85).

A diagnostic case control study conducted in the Netherlands [32] (2006) [EL=III] assessed the intra- and interobserver variability and determined diagnostic accuracy of the Leech method in identifying children with functional constipation. 89 non selected consecutive children (median age: 9.8 years) were included in the study, carried out at a tertiary gastroenterology outpatient's clinic. Fifty-two constipated children comprised the patients group. Control children (n=37) fulfilled the criteria for functional abdominal pain (FAP, n=6) and for "functional non-retentive faecal incontinence" (FNRFI, n=31)). The mean Leech score (using the first score) was significantly higher in constipated children than in the control group (10.1 vs. 8.5; p=0.002). The mean colonic transit time (CTT) was significantly longer in constipated children than in the control group (92 hours vs. 37 hours; p<0.0001). The Leech method showed a sensitivity of 75% and a specificity of 59%. The positive predictive value and the negative predictive value were 72% and 63% respectively. The CTT showed a sensitivity of 79% and a specificity of 92% (cut-off point 54 hours as per study). Using a cut-off point of 62 hours (as per literature) the sensitivity decreased (71%) whereas the specificity improved (95%). The positive predictive value was 69% and the negative predictive value was 97%. The area under the curve ROC (Receiving Operator Characteristic) was significantly smaller for the Leech method as compared to the CTT (0.68, 95% CI: 0.58 to 0.80 vs. 0.90, 95% CI: 0.83 to 0.96; p=0.00015). Two scorers produced significantly higher or lower scores in their repeat scoring of the same radiograph using the Leech method (intraobserver variability). Scorer 3 produced the largest difference (-1.6 (-2.0 to -1.3); p<0.0001) while the second score of scorer 2 was on average 0.7 points lower (0.03 (-0.4 to -0.5); p=0.0005). The two scores of scorer 1 were not systematically different (0.7 (0.2 to 1.2); p=0.89). Differences between repeated scores of the same scorer showed large variability (SD), even after accounting for a systematic error (scorer 1: 2.2, Limits of agreement: -6.0 to 5.0; scorer 2: 2.2 Limits of agreement: -7.0 to 7.0 and scorer 3: 1.5 Limits of agreement: -5.0 to 3.0). These "limits of agreement" are large in comparison to the scale on which the Leech score is measured. Analysis of interobserver variability of the Leech method showed that scorer 3 scored consistently lower than scorer 1 (Mean of differences 2.7; p<0.000) and scorer 2 (mean of differences 2.9; p<0.0001). No systematic differences were found between scorer 2 and scorer 1. In 5% of cases the Leech scores of the same patient produced by different scorers could differ by four points or more.

A diagnostic retrospective case series conducted in the Netherlands[33] (2006) [EL=III] assessed the reproducibility of three scoring systems (Barr, Leech and Blethyn) for plain abdominal radiography, in order to determine which one is most useful in clinical practice. Clinical records of 40 consecutive patients (mean age 7 years) referred to hospital for assessment of constipation were reviewed. Patients complained of infrequent defecation, soiling, encopresis, or abdominal pain. Masked abdominal radiographs of the children were independently evaluated by two observers, both experienced paediatric radiologists. Observers assessed each radiograph on two separate occasions, 6 weeks apart. The Leech score showed the highest reproducibility with high intraobserver agreement for both observers (k=0.88 and k=1.00 respectively), and high interobserver agreement (k=0.91 in the first round and k=0.84 in the second round). The Barr score showed a fair intraobserver agreement for both observers (k=0.75 and k=0.66 respectively) but a moderate interobserver agreement in the first round (k=0.45). Interobserver agreement improved in the second round (k=0.71). The Blethyn score showed the lowest reproducibility with low intraobserver agreement for both observers (k=0.61 and k=0.65 respectively), and also low interobserver agreement (k=0.31 in the first round and k=0.43 in the second round). All k values were statistically significant ($p<0.05$).

One diagnostic case control conducted in the USA [34] (2005) [EL=III] evaluated the relationship between a history of constipation, faecal loading on X-rays and a history of urinary tract infections (UTIs) in an office practice. One hundred and thirty three children (mean age: 5.6 years) were included in the study. Patients (n=100) were children with a history of UTIs who were already undergoing a voiding cystourethrogram whereas controls (n=33) were children undergoing a plain film of the abdomen for reasons that did not include constipation/UTIs. Faecal load on abdominal radiograph was compared to clinical variables: number of bowel movements/week and stools consistency. The correlation between symptoms of constipation and faecal load on abdominal X-ray was poor (correlation coefficient=0.08)

Evidence statement

One systematic review [EL=III] of 6 studies found conflicting evidence for the association between a clinical diagnosis of constipation and a radiographic diagnosis of constipation.

One case control study [EL=III] found that the Leech scoring method showed poor diagnostic accuracy and reproducibility.

One retrospective case series [EL=III] showed that the Leech scoring was highly reproducible.

One case control study [EL=III] showed poor correlation between symptoms of constipation and faecal load on abdominal X-ray.

GDG interpretation of the evidence

The GDG is aware that most of the children attending hospital with symptoms of constipation would have a plain abdominal radiography as a routine test to confirm idiopathic constipation and that subsequent treatment is based on the result. However, the evidence shows that the plain abdominal radiography has little or no value to either confirm or refute a diagnosis of idiopathic constipation.

It is the GDG's view that a plain abdominal radiography should only be performed if absolutely necessary and in the majority of cases of children with chronic constipation it is not. Clinical features obtained from the history taking and the physical examination would usually allow diagnosis of chronic idiopathic constipation.

The GDG concluded that there may be occasional situations when a plain abdominal radiography is indicated and could be valuable. These include situations when a child has been treated for some time with little success, when there is suspicion that something else is going on that is not functional constipation, in specialist services to track progress in certain circumstances and when a child has been on large doses of laxatives and faecal matter turns soft and with no edges that can be felt on abdominal palpation.

Even when the dose of radiation given per radiography may be small, the GDG believes that it is not necessary to expose children to it when repetitive radiographies are performed, and overuse seems to be common practice. The GDG understands that abdominal radiography appearances are open to misinterpretation, usually over-estimating faecal loading or missing rectal impaction. It is the GDG's view that if radiographies will be performed at all a transit study may be more valuable.

It is the GDG's view that when a plain abdominal radiography needs to be performed the reasoning has to be clear and the best possible methodology used with minimal risk.

Recommendations

Do not use a plain abdominal radiograph to make a diagnosis of idiopathic constipation

Consider using a plain abdominal radiograph only if requested by specialist services in the ongoing management of intractable idiopathic constipation.

4.6 Rectal Biopsy

Clinical Question

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

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation undergoing rectal biopsy
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

A total of 199 articles were identified from the searches and 26 articles were retrieved for detailed assessment. Of these, four studies were identified for inclusion in this review: two retrospective cohort studies and two retrospective case series.

Narrative summary

A retrospective cohort conducted in the USA [16] (2003) [EL=II] tested the hypothesis in two cohorts of 315 children that key features in the history, physical examination and radiographic evaluation would enable the avoidance of unnecessary rectal biopsies. Cohort 1 were 265 children presenting with constipation who had undergone rectal biopsy to diagnose Hirschsprung's disease (HD). Cohort 2 was a concurrent selected cohort of 50 children with idiopathic constipation (IC). Only patients with definite information were included therefore the number of patients in each analysis varies due to missing data. Delayed passage of meconium was defined as failure to pass meconium in the first 48 hours of life. These data were available in 59% of cases. Abdominal distension was determined from parental response to questionnaire or data noted during patients visits. Enterocolitis was defined as diarrhoea associated with fever. In the group where onset of constipation occurred when they were less than one year old, significantly more children with HD reported delayed passage of meconium as compared to children with IC (65% vs. 13%, $p<0.05$). Abdominal distension and vomiting were also reported in significantly more children with HD as compared to children with IC (80 % vs. 42%, $p<0.05$ and 72% vs. 21%, $p<0.05$). Faecal impaction requiring manual evacuation occurred in significantly more children with IC as compared to children with HD (30% vs. 6%, $p<0.05$). There were no significant differences between children with HD and children with IC regarding enterocolitis. In the group where onset of constipation occurred after 1 year of age significantly more children with HD reported delayed passage of meconium as compared to children with IC (81% vs. 1%, $p<0.05$) and also significantly more children with HD reported abdominal distension as compared to children with IC (53% vs. 7%, $p<0.05$). No children with IC experienced vomiting as compared to 23% of children with HD ($p<0.05$). There were no significant differences between children with HD and children with IC regarding enterocolitis or faecal impaction requiring manual evacuation.

Data on the onset of symptoms was available for 46 patients with HD and 40 patients with IC. The average age at onset of symptoms for patients with HD was 8 months (range 1 day to 9 years). A detailed distribution of the age of onset of symptoms is as follows: 60% at 1st week of life, 70% at 1st month of life, 87% at 1st year of life and 13% after 1 year of life. The average age at onset of symptoms for patients with IC was: 15 months (range 7 days to 16 years). A detailed distribution of the age of onset of symptoms is as follows: 15% at 1st week of life, 55% at 1st month of life, 68% at 1st year of life and 32% after 1 year of life. At least 34% of HD patients had the classic triad (delayed passage of meconium + vomiting + abdominal distension). At least one feature of the triad was noted in 98% of patients with HD. Only 60% of patients with IC had a history of delayed passage of meconium, vomiting or abdominal distension. 100% HD patients vs. 64% IC patients had one or more of the following: delayed passage of meconium, vomiting, abdominal distension and a transition zone on contrast enema. Thirty-six percent of patients with constipation had none of these features.

A retrospective cohort conducted in Italy[35] (2007) [EL=II] described the clinical features of a group patients with intestinal dysganglionoses (ID) (HD and intestinal neuronal dysplasia (IND)) along with a group of consecutive patients with IC, to compare them and to find out if the clinical criteria to indicate rectal suction biopsy (RSB) in constipated children do exist. One hundred and forty-one patients (median age: 20 months, mean 44 months ± 67 with ID were included. A total of 1118 biopsies were performed on 429 patients (mean of 2.6 each). In 63 patients (14.7%) biopsies were inadequate for a reliable diagnosis of absent submucosal layer. One hundred and forty three patients (33.3%) received a diagnosis of ID. Ninety-six out of one hundred and forty three fulfilled inclusion criteria, being 49 IND and 47 HD. Forty-five consecutive patients with a diagnosis of IC (out of the remaining 286 patients) fulfilled inclusion criteria and were consequently included, for a total sample of 141. In case of a negative RSB, idiopathic constipation was diagnosed according to Rome II criteria. Clinical variables (meconium passage, symptoms onset, intestinal obstruction, abdominal distension, reported enterocolitis, failure to thrive, palpable faecal masses and soiling) were retrospectively extracted from patients' notes. There was failure/delay in the passage of meconium in 87% of children diagnosed with HD as compared to 7% of children with IC ($p<0.001$). Symptoms onset occurred at <1 year old in 80% of children with IC as compared to 96% of children with HD ($p<0.02$). No child with IC experienced intestinal obstruction as compared to 49% of children with HD ($p<0.001$). Significantly more children with HD experienced abdominal distension and failure to thrive as compared to children with IC (85% vs. 20%, $p<0.001$ and 27.5% vs. 11%, $p<0.045$, respectively). Significantly more children with IC experienced soiling as compared to children with HD (46.5% vs. 4%, $p<0.001$). There were no significant differences between children with HD and children with IC regarding reported enterocolitis and presence of palpable faecal masses.

A retrospective case series conducted in the UK [36] (1998) [EL=III] developed criteria that would reliably and consistently identify children with HD and thereby avoid the trauma and expense of unnecessary rectal biopsies in the others. One hundred and forty one children (aged 1 day to 13 years, gender not reported) who had rectal biopsy to exclude HD were included. Clinical variables (age at diagnosis, bleeding per rectum, anal fissures, severe behavioural/emotional problems, soiling and enterocolitis) were retrospectively extracted from patients' case notes. Constipation was defined as a decreased frequency of bowel movements (<3/week), or a difficulty in defection which is perceived by the parents as a problem, requiring medication (oral or rectal) or manual intervention by the parents. Seventeen out of one hundred and forty two children were diagnosed with HD. The age at diagnosis ranged between 1 day and 3 years, but most children were diagnosed when they were neonates (14 children: <4 weeks, 1 child: 4 to 12 weeks, 1 child: 12 weeks to 1 year and 1 child: >1 year). Ten children (58.8%) had a history of delayed passage of meconium (>48h after birth). The age of onset of constipation was less than 4 weeks in all 17 children with HD. Eight children (47%) had a history of enterocolitis but no children had experienced bleeding per rectum, anal fissures, severe behavioural/emotional problems or soiling. One hundred and twenty four out of one hundred and forty two children were diagnosed with constipation. The age at diagnosis ranged between 1 day and 13 years, but most children were diagnosed when they were >1 year old (20 children: <4 weeks, 12 children: 4 to 12 weeks, 14 children: 12 weeks to 1 year and 78 children: >1 year). Seventeen children (13.7%) had a history of delayed passage of meconium (>48h after birth). The age of onset of constipation was <4 weeks in 40 children, between 4 to 12 weeks in 32 children, between 12 weeks to 1 year in 22 children and >1 year in 25 children. Thirty-seven children (30%) had experienced bleeding per rectum, 14 children (11%) anal fissures, ten children (8%) severe behavioural/emotional problems and 16 (13%) had experienced soiling. No child with constipation had a history of enterocolitis. History of onset of constipation was available in 136 of the 141 children (96%). The five children in whom this history could not be obtained from the notes were all older than 1 year (three teenagers) and none had HD.

A retrospective case series conducted in the UK [37] (2003) [EL=III] aimed to review the author's experience of rectal biopsy to exclude HD and the author's clinical criteria to perform rectal biopsy in these children. One hundred and eighty two patients (118 males mean age 2.9 years (range 2 days to 16 years)) who presented with chronic constipation or intestinal obstruction and had rectal biopsy to exclude HD were included. All children underwent either suction rectal biopsy (SRB) (n=104) or full-thickness rectal biopsy (n=78). Clinical variables obtained were: meconium passage, constipation since birth, intestinal obstruction, failure to thrive and chronic abdominal distension. Twenty-five patients (14%) were diagnosed with HD (mean age: 3.64 months (range 2 days to 4 years)). One hundred and eighty two patients who had rectal biopsies provided 355 specimens in which 79% of suctions biopsies and 97% of full-thickness biopsies were adequate, including rectal mucosa and submucosal. In 20 children with HD the diagnosis was made at the first attempt by suction rectal biopsy. Repeat biopsies were performed on 14 (8%) of 182 patients because of inadequate initial biopsy, clarification of atypical inervation and confirmation of negative results. Nineteen out of one hundred and four patients who underwent SRB were >1 year old. Because five children (12 specimens) who were older than 1 year had inadequate suction biopsies at the beginning of the series, it was decided that SRB was not suitable for children >1 year old. Three patients with HD (aged 6 days, 12 days and 6 weeks) had a false negative in acetylcholinesterase staining. In these the diagnosis were later established from repeated biopsies: 1 full thickness biopsy, 1 laparotomy and 1 suction biopsy. Thirty-nine percent of the children (16/41) who passed meconium >48h after birth but only 5% of the children (6/114) who passed meconium <24 h after birth were diagnosed with HD. Six percent of the children (3/46) for whom data on passage of meconium was unknown were diagnosed with HD. Thirty-two percent of the children (17/53) who had constipation since birth were diagnosed with HD. Sixty-nine percent of the children (9/13) who presented with intestinal obstruction were diagnosed with HD. Twenty-two percent of the children (4/18) who reported failure to thrive were diagnosed with HD. Twenty-three percent of the children (3/13) who reported chronic abdominal distension were diagnosed with HD. Figures for patients who may have had more than one symptom were not reported in the paper.

Evidence statement

One retrospective cohort [EL=II] showed that significantly more children with HD reported delayed passage of meconium, abdominal distension and vomiting as compared to children with IC. In children <1 year old faecal impaction requiring manual evacuation occurred in significantly more children with IC as compared to children with HD, but there were no significant differences between the two groups for children >1 year regarding this clinical feature. There were no significant differences between children with HD and children with IC regarding enterocolitis. The average age at onset of symptoms for patients with HD was 8 months (range 1 day to 9 years) and for patients with IC it was 15 months (range 7 days to 16 years).

One retrospective cohort [EL=II] showed that significantly more children with HD reported failure/delay in the passage of meconium, intestinal obstruction, abdominal distension and failure to thrive as compared to children with IC. Significantly more children with IC experienced soiling as compared to children with HD. Symptoms onset occurred at <1 year old in significantly more children with HD as compared to children with IC. There were no significant differences between children with HD and children with IC regarding reported enterocolitis and presence of palpable faecal masses.

One retrospective case series [EL=III] showed that most children were diagnosed with HD when they were neonates as compared to most children with IC who were diagnosed when they were >1 year old. The age of onset of constipation was less than 4 weeks in all children with HD. Significantly more children with HD had a history of delayed passage of meconium (>48h after birth) as compared to children with constipation. Forty-seven percent of children with HD had a history of enterocolitis but no children had experienced bleeding per rectum, anal fissures, severe behavioural/emotional problems or soiling. No child with constipation had a history of enterocolitis, but symptoms like bleeding per rectum, anal fissures, severe behavioural/emotional problems or soiling were reported in most of them.

One retrospective case series [EL=III] showed that delayed passage meconium (>48h after birth), constipation since birth, intestinal obstruction, failure to thrive chronic abdominal distension were present in significantly more children diagnosed with HD as compared to children diagnosed with constipation.

Table 4.3 Clinical features in children with Hirschsprung's disease and children with Idiopathic Constipation

Clinical signs and symptoms	Lewis et al., 2003		Pini-Prato et al., 2007		Khan et al., 2003		Gosh et al., 1998	
	HD	**IC**	**HD**	**IC**	**HD**	**IC**	**HD**	**IC**
Number of children	46	40	47	45	25	157	17	124
Failure / delayed passage of meconium	<1y: 65 >1y: 81*	<1y: 13 >1y: 1	87	7	64	16	58.8	13.7
Abdominal distension	<1y: 80 >1y: 53	<1y: 42 >1y: 7	85	20	23	6		
Enterocolitis	<1y: 13 >1y: 13	<1y: 15 >1y: 14	10.5	9			47	0
Vomiting	<1y: 72 >1y: 23	<1y: 21 >1y: 0						
Intestinal obstruction			49	0	69	2		
Failure to thrive			27.5	11	22	8		
Faecal impaction requiring man evacuation	<1y: 6 >1y: 46	<1y: 30 >1y: 30						
Palpable faecal masses			17	22				
Soiling			4	46.5			0	13
Bleeding per rectum							0	30
Anal fissures							0	11
Severe behavioural /emotional problems							0	8
Classic triad: delayed passage of meconium + vomiting + abdominal distension	At least 34 98: at least 1 feature	Full triad: 0 60: at least 1 feature						
≥ 1 of the following: delayed passage of meconium, vomiting, abdominal distension and a transition zone on contrast enema	100	64						

All figures for clinical signs and symptoms are %
HD: Hirschsprung's disease, C: Constipation, y: year old
Cells shaded in blue: statistically significant comparisons
Non-shaded cells: non-statistically significant comparisons
Cells shaded in grey: variables not measured

* Data available for 59% of total sample including both HD and IC

Table 4.4 Age at onset of constipation/diagnosis in children with Hirschsprung's disease and children with Idiopathic Constipation

Study	Age at onset of constipation/diagnosis	
Lewis et al., 2003[*]	HD	age of onset of constipation: Mean: 8 months (range 1 day to 9 years) 1rst week of life: 60 % 1rst month of life: 70% 1rst year of life: 87% after 1 year of life: 13%
	IC	age of onset of constipation: Mean: 15 months (range 7 days to 16 years) 1rst week of life: 15% 1rst month of life: 55% 1rst year of life: 68% after 1 year of life: 32%
Pini-Prato et al., 2007	HD	age of onset of constipation: at < 1year old (n=47): 96% at > 1 year old (n=47): 4%
	IC	age of onset of constipation: at < 1year old (n=45): 80% at > 1 year old (n=45): 20%
Khan et al., 2003	HD	mean age of patients diagnosed with HD: 3.64 months (range 2 days to 4 years)
	IC	Unclear
Gosh et al., 1998	HD	age at diagnosis: 1 day to 3 years 14 children: < 4 weeks 1 child: 4 to 12 weeks 1 child: 12 weeks to 1 year 1 child: > 1 year age of onset of constipation: all 17 children: < 4 weeks
	IC	age at biopsy: 1 day to 13 years 20 children: < 4 weeks 12 children: 4 to 12 weeks 14 children: 12 weeks to 1 year 78 children: > 1 year age of onset of constipation: 40 children: < 4 weeks 32 children: 4 to 12 weeks 22 children: 12 weeks to 1 year 25 children: > 1 year

HD: Hirschsprung's disease, C: Constipation, y: year old
Non-shaded cells: non-statistically significant comparisons

GDG interpretation of the evidence

The GDG is aware that many children are undergoing rectal biopsies which have been inappropriately requested from a clinical point of view. The GDG believes that one reason for this is that sometimes both parents and clinicians get very anxious because they want to find a cause for the child's constipation "at all cost", particularly when the child's symptoms do not improve with medical treatment. The

[*] data available for 46 patients with HD and 40 patients with IC

GDG understands from the evidence that there are clear features in the child's history that are good predictors of Hirschsprung's disease and, if discovered, would increase the chances of a positive biopsy result. Clinicians should take time to elicit these features when taking a history and also make sure that there are no issues of treatment adherence that could explain why the child is not getting better.

Recommendations

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 (>24 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

4.7 Transit Studies

Clinical Question

What is the diagnostic value of transit studies in children?

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation undergoing transit studies to aid diagnosis
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

One search was conducted for all radiological investigations (plain abdominal radiography, abdominal ultrasound and transit studies). A total of 646 articles were identified and 72 articles were retrieved for detailed assessment. Of these a total of 20 studies were identified for inclusion in this review: 11 diagnostic case control studies, 4 diagnostic prospective case series and 5 diagnostic retrospective case series.

Narrative summary

Studies using radiopaque markers

A diagnostic case control study (2006) conducted in the Netherlands[32] (2006) [EL=III] assessed the intra- and interobserver variability and the diagnostic accuracy of the Leech method of identifying children with functional constipation. Eighty-nine consecutive children (median age: 9.8 years) were included in the study. Fifty-two constipated children comprised the patients group. Children in the control group (n=37) fulfilled the criteria for functional abdominal pain (FAP, n=6) and for functional non-retentive faecal incontinence (FNRFI, n=31)). The Leech method to diagnose constipation in plain abdominal radiography was compared to the colonic transit time (CTT) with radiopaque markers. The mean Leech score (using the first score) was significantly higher in constipated children than in the control group (10.1 vs. 8.5; p=0.002). The mean CTT was significantly longer in constipated children than in the control group (92 hours vs. 37 hours; p<0.0001). The Leech method showed a sensitivity of 75% and a specificity of 59%. The positive predictive value and the negative predictive value were 72% and 63% respectively. The CTT showed a sensitivity of 79% and a specificity of 92% (cut-off point 54 hours as per study). Using a cut-off point of 62 hours (as per literature) the sensitivity decreased (71%) whereas the specificity improved (95%). The positive predictive value was 69% and the negative predictive value was 97%. The area under the curve ROC (Receiving Operator Characteristic) was significantly smaller for the Leech method as compared to the CTT (0.68, 95% CI: 0.58 to 0.80 vs. 0.90, 95% CI: 0.83 to 0.96; p=0.00015).

A diagnostic case control study conducted in China [38] (2005) [EL=III] investigated the difference of CTT between constipated children and normal healthy controls to elicit its significance in assessing the dynamics of the whole gastro-intestine and each segment. Ninety-six children were included in the study. Patients were 28 children (38 boys, mean age: 6 years (range 3 to 14)) with confirmed functional constipation whereas controls were 68 children (38 boys, mean age: 6 years (range 3 to 13)) with normal frequency and character of evacuation. All children underwent CTT with radiopaque markers. No other tests/variables were used as a reference/comparator. Total CTT was significantly longer in patients as compared to controls (hours, mean ± SD) (59.9 ± 2.3 vs. 14.8 ± 0.8; p<0.01). All segmental transit times were also significantly longer in patients as compared to controls (hours, mean ± SD) (Right colon: 20.3 ± 1.2 vs. 7.3 ± 1.1; p<0.01); (Left colon: 12.8 ± 1.7 vs. 3.4 ± 0.8; p<0.01); (Rectosigmoid: 26.8 ± 1.4 vs. 4.1 ± 1.2; p<0.01).

A diagnostic prospective case series conducted in the Netherlands [39] (2004) [EL= III] investigated the relation between symptoms of chronic constipation and CTT and evaluated the possible relation between symptoms and CTT and outcome after one year of follow up. One hundred and sixty nine consecutive patients (65% boys, median age 8.4 years) with chronic idiopathic constipation underwent CTT and the following clinical variables were also recorded: defecation frequency, encopresis frequency, night-time encopresis and presence of a rectal mass on physical examination. The total CTT (hours, median, 25 to 75th centiles) was 58 (37 to 92). Forty-seven percent of the children had a delayed total CTT (>62 hours). Transit times (hours) for ascending colon, descending colon and rectosigmoid were 10 (5 to 16), 10 (5 to 18) and 32 (18 to 63) respectively. Twenty-one percent of the children had delayed transit in the ascending colon (>18 hours), 22% in the descending colon (>20 hours) and 48% in the rectosigmoid (>34hours). There were no significant differences in any of the outcomes between boys and girls. Children with a defection frequency of 0 to1/week (n=79) had a significantly longer CTT and rectosigmoid transit time (RSTT) (hours, median), as compared to children with defecation frequencies of >1 to 3/week (n=55) and ≥3/week (n=35), (CTT: 74 vs. 50 and 49, p=0.001); (RSTT: 38 vs. 30 and 28, p=0.009). Children with an encopresis frequency (day and night) of ≥2/day (n=79) had significantly longer CTT and RSTT (hours, median) as compared to children with an encopresis frequency of 1 to 2/day (n=48), children with an encopresis frequency of <1/day (n=24) and children with no encopresis at all (CTT: 70 vs. 50, 52 and 49 respectively, P= 0.003); (RSTT: 38 vs. 30, 31 and 24 respectively, p=0.03). Children with night time encopresis (n=63) had significantly longer CTT and RSTT (hours, median) as compared with children without night time encopresis (n=106), (CTT: 74 vs. 47, p<0.0001); (RSTT: 46 vs. 28, p<0.0001). Children with a rectal mass present on physical examination (n=51) had significantly longer CTT and RSTT (hours, median) as compared to children with no rectal mass (n=118); (CTT: 86 vs. 48, p<0.0001);

(RSTT: 64 vs. 28, p<0.0001). There were significant baseline differences between boys and girls: median defecation frequency at intake was lower in girls than boys (1.0 vs. 2.0 times/week; p=0.03); encopresis frequency more than twice weekly was reported more often in boys (94% vs. 73%; p=0.0002). More girls than boys reported no encopresis at all (20% vs. 6% p<0.05).

A diagnostic case control study conducted in Brazil [40] (2004) [EL=III] evaluated symptoms and clinical findings in a prospective series of adolescents with functional constipation and aimed to identify colonic disorders by measuring total and segmental colonic transit times with radiopaque markers. Sixty-one adolescents were included in the study. Patients were 48 children (mean age 14 years (range 12 to 18), 13 boys) with complaints of constipation for 1 year or longer. Controls were 13 children (nine boys, age not reported) with no digestive complaints who participated in a previous study by the same authors. All children underwent CTT with radiopaque markers and this was related to clinical variables. Seventeen percent of the children were diagnosed with normal colonic transit, 60% with slow colonic transit, 13% with pelvic floor dysfunction and 10% with slow colonic transit and pelvic floor dysfunction. Total CTT was significantly longer in constipated children as compared to the healthy controls (hours, mean ± SD; median and range) (62.9 ± 12.6; 69 (62.9 to 12.6) vs. 30.2 ± 13.2; 27.5 (10.8 to 50.4); p<0.001). Segmental transit time were also significantly longer in constipated children as compared to the healthy controls for both the right and the left colon (hours, mean ± SD, range) (right colon: 18.6 ± 15; 13.2 (12 to 54) vs. 6.7 ± 3.9; 4.8 (1.2 to 12); p=0.001); (left colon: 24.3 ± 13.7; 22.8 (2.4 to 51.6) vs. 7.9 ± 7.8; 7.2 (0 to 28.8); p<0.001). There were no significant differences between constipated and non constipated children for the rectosigmoid segment. The interval (days) between evacuations was significantly longer for children with slow colonic transit as compared to children with pelvic floor dysfunction (mean, SD) (7.7 ± 6.6 days vs. 3.7 ± 2.4 days; p<0.003). A faecal mass palpable at initial examination was statistically associated with slow colonic transit (p=0.03). Other clinical variables were not statistically associated with a delay in either colon or rectosigmoid transit: onset of constipation, scybalous faeces, large volume, faecaloma, anal bleeding, soiling, previous use of laxative/suppositories/enemas, history of constipation in family, anal fissure, daily ingestion of fibre, sex, age and skin colour.

A diagnostic case control study conducted in Spain [41] (2002) [EL=III] evaluated the use of a colonic motility study easily applied in daily clinical practice to more clearly define patients with this disorder. Sixty-eight children aged 2 to 14 years were included. Patients were 38 children with a history of chronic idiopathic constipation >6 months, with/without secondary encopresis, refractory to conventional treatment. Controls were 30 children with normal bowel habits who underwent abdominal radiography as part of a clinical study with normal results. All children underwent CTT with radiopaque markers. No reference test was used but results were related to the frequency of defecation. Patients had a significantly longer CTT than controls (hours, mean ± SD, ranges) (49.57 ± 25.38 (15.6 to 122.4) vs. 29.08 ± 8.30 (14.4 to 50); p<0.001). Patients also had a significantly longer transit time in both the left colon and the rectosigmoid as compared to controls (Left colon: 15.41 ± 13.13 (2.4 to 32) vs. 6.60 ± 6.20 (2.4 to 24); p=0.01); (Rectosigmoid: 24.20 ± 16.77 (4.8 to 69.6) vs. 14.96 ± 8.70 (2.4 to 19.2); p=0.01). There were no significant differences in segmental transit time for the right colon between patients and controls. Patients with a prolonged total CTT (n=19) were significantly younger at onset of constipation when compared to patients with a total CTT within reference values (n=19); (1.77 (0.88) vs. 2.54 (1.18); p<0.05) (years, mean (SD)). Significantly more patients with a prolonged total CTT (n=19) had a family history of constipation when compared to patients with a total CTT within reference values (n=19); (79% vs. 21%, p<0.01). An abdominal mass was found in significantly more patients with a prolonged total CTT (n=19) as compared to patients with a total CTT within reference values (n=19): (93.8% vs. 60%, p<0.05). Encopresis (episodes/night, mean, SD) was significantly more frequent in patients with a prolonged total CTT (n=19) as compared to patients with a total CTT within reference values (n=19); (0.60 (0.91) vs. 0.10 (0.44), p<0.05). No significant differences between patients and controls were found for age, age at diagnosis, sex, defecations/week, pain at defecation, enuresis, anal fissure, rectal mass or encopresis episodes/day, mean daily fibre intake and calorie consumption. A statistically significant inverse correlation was observed between total CTT and the number of weekly defecations (correlation coefficient, r=0.68, p<0.001). Two children from the patients group did not complete the study.

A diagnostic case control study conducted in Brazil [42] (1998) [EL=III] measured total and segmental colonic transit time in constipated adolescents and to compare the results with those in non-constipated children. Twenty-six adolescents aged 12-18 years were included in the study. Patients were 13 children with a history of constipation of at least one year of duration and controls were 13 children with no digestive complaints. There were nine boys in each group. All children underwent total and segmental CTT with radiopaque markers. Clinical variables were recorded. The total CTT (hours) was significantly longer in constipated children as compared to non constipated children (mean ± SD; median and range) (58.25 ± 17.46; 68.4 (27.6 to 72) vs. 30.18 ± 13.15; 27.5 (10.8 to 50.4); p<0.001). Segmental transit times (hours) for the right and left colon were also significantly longer in constipated children as compared to non constipated children (mean ± SD, median and range) (right colon: 15.97 ± 12.48; 13.7 (2.4 to 43.2) vs. 6.74 ± 3.91; 7.2 (1.2 to 12); p=0.03); (left colon: 24.74 ± 13.39; 25.7 (7.2 to 51.6) vs. 7.94 ± 7.82; 7.2 (0 to 28.8); p<0.001). There were no significant differences between the two groups for the transit time in rectosigmoid. The interval between stools was significantly longer for constipated children as compared to non-constipated children (5.8 ± 2.3 days vs. daily, p<0.01). There were no significant differences between the two groups regarding: age, weight and height, bulky or small stools, encopresis, rectal mass, intense use of laxatives, bowel movements/week and mean daily intake of fibres.

A diagnostic case control study conducted in Poland [43] (2007) [EL=III] determined whether a new method of ultrasound (US) assessment of stool retention could be used as a method of identifying children with functional chronic constipation, and whether children with an enlarged rectum and colon (as seen on US) should be referred for further procedures such as proctoscopy and assessment of CTT. The study was conducted at a gastroenterology outpatient clinic and 225 children were enrolled. One hundred and twenty children (mean age 6.25 years) with chronic constipation were compared to 105 children with a normal defecation pattern (mean age 8.25 years). Chronic constipation was diagnosed based on history and physical examination. In all patients the defecation disorders had persisted longer than 6 months. All patients fulfilled the Rome II criteria for defecation disorders. The control group did not differ from the patients regarding gender; but the comparison regarding age is not clearly reported. Children underwent abdominal US. Children with a US diagnosis of megarectum, faecal impaction and enlarged colon were referred for proctoscopy and measurement of colonic transit time. Children with faecal impaction (as per US) had significantly longer average segmental transit time for the rectum, sigmoid and left colon (p<0.001, p=0.0015 and p=0.0104 respectively). There was no statistically significant difference for the right side of the colon. Children with an overfilled splenic flexure on US had a significantly longer transit time in the left side of the colon (p=0.0029).

A diagnostic case control study conducted in The Netherlands [44] (1996) [EL=III] investigated the presence of slow colonic transit in children with constipation using radiopaque markers. One hundred and forty-eight children were included in the study. Patients were 94 children (63 boys, mean age 8 years (range 5-14)) with complaints of constipation with/without encopresis, encopresis alone or recurrent abdominal pain, whereas controls were 54 healthy children (10 boys, mean age 11 years (range 7-15). All children underwent CTT with radiopaque markers and their results were related to the presence of clinical symptoms. Based on the CTT results 24 children were diagnosed with paediatric slow transit constipation (PSTC) and 70 children with normal delayed transit constipation (NDTC). The total CTT (hours) was (median, and range) 189 104.4 to 380.4) for children with PSTC and 46.8 (3.6 to 99.6) for children with NDTC (n=70). Segmental transit time (hours, median, and range) in the right colon was 27.0 (3.6 to 60) for children with PSTC (n=24) and 8.4 (0 to 32.4) for children with NDTC (n=70). Values for the left colon were 37.2 (0 to 110.4). In children with PSTC (n=24) and 7.2 (0 to 36.0) in children with NDTC (n=70) whereas values for the rectosigmoid were 116.4 (49.2 to 226.8) for PSTC children (n=24) and 27.0 (0 to 90.0) for NDTC children (n=70). Daytime soiling was present in significantly more children with PSTC (n=24) as compared to children with NDTC (n=70); (92% vs. 69%, p=0.05). Night-time soiling was also present in significantly more children with PSTC (n=24) as compared to children with NDTC (n=70); (17 (71) vs. 8 (11), p<0.01). Daytime soiling episodes/week (median, range) were significantly more frequent in children with PSTC (n=24) as compared to children with NDTC (n=70); (14.0 (0 to 7) vs. 5.0 (0 to 56), p<0.01). Night-time soiling episodes/week (median, range) were also significantly more frequent in children with PSTC (n=24) as compared to children with NDTC (n=70); (7 (0 to 7) vs. 0 (0 to 7), p<0.01). Stools were normal in significantly more children with PSTC as compared to children with NDTC (75% vs. 49%; p=0.03). Pain during defecation was present in significantly more children with NDTC as compared to children with PSTC (60% vs. 33%; p=0.01). Significantly more children with PSTC complained of no rectal sensation as compared to children with NDTC (33 % vs. 14%, p=0.03). A palpable abdominal mass was present in significantly more children with PSTC as compared to children with NDTC (71% vs. 39%; p=0.02). A palpable rectal mass was present in significantly more children with PSTC as compared to children with NDTC (71% vs. 13%; p<0.01). There were no significant differences between the two groups regarding: sex, age, toilet training status, age at which toilet training started, bowel movements/week, large amounts of stools every 7-30 days, encopresis episodes/week, abdominal pain, poor appetite, daytime or night-time urinary incontinence. The proportion of children with PSTC and rectal palpable mass, night time soiling or both was 0.34, 0.39 and 0.82 respectively. Only 7% of children without any of these characteristics had PSTC. Further analysis of the NDTC group after separation into a group with total CTT<63h and one with total CTT between 63 and 100h showed the same significant differences when compared with PSTC children as did the total NDTC group allowing the merge of these children.

A case control study conducted in the Netherlands [45] (1995) [EL=III] investigated the presence or absence of faecal retention in each child using CTT and compared these findings to the Barr score. Two hundred and eleven children with complaints of infrequent defecation (paediatric constipation, n=129, 64% boys, median age: 8 years (5-14)), encopresis and/or soiling (ES, n=54, 81% boys, median age: 9 years (5-17)) or recurrent abdominal pain (RAP, n=23, 39% boys, median age: 9 years (5-16)) were included. Two hundred and six children underwent CTT with radiopaque markers assessed with the Metcalf method and these were compared to a plain abdominal radiograph read using the Barr score. Data on assessment of plain abdominal radiographs using Barr score was available for 101 children only. The total CTT (hours, mean and range) was significantly longer for children with encopresis only as compared to children with RAP (41.4 (16.6 to 104.4) vs. 32.5 (4.8 to 69.6; p=0.03). There were no significant differences for the CTT between children with PC (79.3 (2.4 to 384)) and the other two groups. Transit time in the right colon (hours, mean and range) was significantly longer in children with PC as compared to children with encopresis only (13.2 (<1.2 to 60) vs. 7.9 (<1.2 to 26.4); p<0.01) and to children with RAP (13.2 (<1.2 to 60) vs. 7.7 (1.2 to 21.6; p<0.01). There were no significant differences between children with encopresis only and children with RAP. Transit time in the left colon/hours was significantly longer in children with PC as compared to children with encopresis only (mean and range) (16.1 (<1.2 to 110.4) vs. 6.8 (<1.2 to 25.2); p<0.01) and to children with RAP (16.1

(<1.2 to 110.4) vs. 7.0 (1.2 to 25.2); p<0.01). There were no significant differences between children with encopresis only and children with RAP. Transit time in the rectosigmoid/hours was significantly longer in children with PC as compared to children with encopresis only (mean and range) (49.7 (<1.2 to 226.8) vs. 26.7 (4.8 to 93.6); p<0.01) and to children with RAP (49.7 (<1.2 to 226.8) vs. 8.9 (1.2 to 49.2); p<0.01). It was also significantly longer in children with encopresis only as compared to children with RAP (26.7 (4.8 to 93.6); p<0.01 vs. 8.9 (1.2 to 49.2); p<0.01; p=0.05). The interobserver agreement for the CTT was perfect in 62% of the readings of the first radiograph and a difference of one marker was present in 25%. For the second radiograph a perfect agreement was achieved in 92% of the readings and a difference of one marker was present in 6%. Sixty percent of children with PC (n=57) had mean Barr scores ≥10 (mean of two observers) in the first radiograph and 63% in the second one. Forty-seven percent of children with isolated ES (n=30) had mean Barr scores ≥10 in the first radiograph and 60% in the second one. Forty-seven percent of children with RAP (n=14) had mean Barr scores ≥10 (mean of two observers) in the first radiograph and 63% in the second one. The interobserver agreement for the Barr score (agreement between the two observers for the different segments on the same radiograph) varied from fair (k=0.28) to moderate (k=0.60). The intraobserver agreement (regarding the difference in quantity and quality of stool between radiograph I and II as scored by the same radiologist) varied from poor (k=0.05) to moderate (k=0.47) for both observers. The intraobserver agreement (regarding the existence of constipation as measured by a Barr-score of 10 or more points between radiographs I and II) was fair for both observers (k=0.22 and 0.25 respectively). The correlation between a positive Barr score (≥10) and a delayed total CTT (>62h) was fair (k=0.22) for all children. K values on a separated analysis for each group were: 0.20 (PC group: 0.20), 0.02 (ES group) and 0.46 (RAP group). Abnormal Barr scores were found in at least 46% of patients with normal transit times, whereas positive Barr scores correlated only with a total CTT exceeding 100 hours. Five patients of the 211 originally recruited were excluded from the study: 4 were not able to swallow the capsules and 1 had an "uninterpretable" abdominal radiography.

A diagnostic prospective case series conducted in the UK [46] (1994) [EL=III] assessed the reliability of interpretation and the clinical value of solid marker transit studies in children with soiling and spurious diarrhoea (otherwise known as overflow incontinence). Fifty-two children (median age: 8 years (range 2-13.5 years)) with constipation and/or soiling underwent CTT with radiopaque markers. No reference tests were used but outcomes of CTT were related to the frequency of bowel movements and soiling. In relation to the patterns of transit time 21 children (40%) were diagnosed with normal transit, 4 children (8%) with mild delay, 9 children (17%) with moderate delay and 18 children (35%) with severe delay. In relation to the patterns of marker distribution 15 children (29%) were diagnosed with pancolonic transit delay, 5 children (10%) with segmental transit delay and 11 children (21%) with outlet obstruction. Significantly more children with severe transit delay (n=18) had fewer than two bowel movements/week when compared to children with normal transit (n=21); (87% vs. 27%, p<0.001). Significantly more children with severe transit delay (n=18) had more than 3 soiling episodes/week when compared to children with normal transit (n=21); (92% vs. 35%, p<0.005). No correlation was found between the duration of the symptoms and the severity of transit delay. Thirty-nine percent of the children with severe delay (n=18) had outlet obstruction, 56% pancolonic transit delay and 5% segmental transit delay (in descending colon). Significantly more children with mild delay (n=4) had segmental transit delay (in rectosigmoid) than pancolonic transit delay (75% vs. 25%, p<0.005). Significantly more children with outlet obstruction had fewer than two bowel movements/week as compared to children with segmental transit delay (100% vs. 83%, p<0.05). Significantly more children with pancolonic transit delay had fewer than two bowel movements/week as compared to children with segmental transit delay (83% vs. 33%, p<0.05). There were no significant differences between children with outlet obstruction and children with pancolonic transit delay. Significantly more children with outlet obstruction had more than three soiling episodes/week as compared to children with segmental transit delay (100%, vs. 0%, $p<0.05$). Significantly more children with pancolonic transit delay had more than 3 soiling episodes/week as compared to children with segmental transit delay (57% vs. 0%, $p<0.05$). The interobserver coefficient of variation was 2.1% and the intraobserver coefficient of variation was 3.1%.

A diagnostic case control study conducted in Italy[47] (1994) [EL=III] studied colonic transit and anorectal motility in children with severe brain damage, looking for differences from asymptomatic children and from patients with functional faecal retention and normal neurologic development. Forty-two children were included in the study. Patients were 16 children with brain damage referred for gastroenterologic evaluation of constipation (10 boys; mean age 5.1 ± 3.5 years (range 1.5 to 12 years). Controls were 15 children diagnosed with idiopathic constipation (IC) (termed functional faecal retention in the paper) (9 boys; mean age 6.0 ± 2.9 years (range 2 to 11 years) and 11 children with no gastrointestinal problems (7 boys; mean age 5.6 ± 3.9 years (range 2 to 12 years)). All children underwent total gastrointestinal transit time (TGTT)[*] with radiopaque markers. The TGTT/hours was not significantly different in children with brain damage as compared to children with functional faecal retention (mean ± SD) (106.4 ± 6.1 vs. 98.6 ± 5.1). The total number of markers at 48 hours and 72 hours (mean, standard error of the mean (SEM)) in the left colon was significantly larger in brain damaged children as compared to children with IC (at 48 hrs: 7.3 ± 1.3 vs. 3.0 ± 1.0, $p< 0.05$), (at 72 hrs: 3.3 ± 0.8 vs. 0.5 ± 0.3, $p<0.01$). The distribution of the markers in both right colon and rectum was not significantly different between the two groups at anytime. Twenty-nine of the children originally undergoing evaluation for severe brain damage were found to have constipation, but only 16 were included in the study. It is not clear why the other 13 were excluded. Exact values for all segmental transit times in the two groups were not reported.

A multicentre retrospective case series conducted in Switzerland [48] (1993) [EL=III] investigated the relationship between clinical, manometric, and histological findings in a group of children with chronic constipation in order to evaluate the role of anorectal manometry in the diagnosis of neuronal intestinal dysplasia (NID) and the relationship of histological and manometric findings to clinical severity of constipation and outcome. Forty-eight children (25 boys, mean age: 6.4 ± 5.2 years) with initial symptoms of chronic constipation or soiling, or obstructive symptoms in early life suggestive of Hirschsprung's disease were included in the study. Thirty children underwent CTT with radiopaque markers. The total transit time/hours for children with normal histology (n=15) was (mean ± SD) 70.0 ± 42.6. Segmental transit times' results were not reported and it is not clear whether they were measured in the first instance. CTT results for children diagnosed with abortive and classic neuronal intestinal dysplasia are not reported for the purposes of this review as they are considered organic causes of constipation.

A diagnostic retrospective case series conducted in France[49] (1998) [EL=III] analysed epidemiologic, manometric and radiologic data in a large population of young patients presenting in a paediatric tertiary care hospital in order to classify different types of idiopathic constipation according to age of onset, sex and pelvic floor function. One thousand one hundred and eighty two children (63% boys) diagnosed with constipation with/without encopresis were included in the study. Children were divided into two different subgroups: constipated children without encopresis (C patients, n=855) and constipated children with encopresis (C+E patients, n=327). Sixty-five percent of the C patients were younger than 4 years old (C-4 patients) whereas 35% were more than 4 years old (C+4 patients). Three hundred and seventy

[*] Italian papers included in this review measured "total gastrointestinal transit time (TGITT)". Because of the similarity in the figures with the other studies' CTTs we assumed that TGITT is the name by which CTT known in Italy.

eight children underwent CTT with radiopaque markers. No other test was used as a comparator. The total CTT/hours was significantly longer in C+E patients (n=168), C+4 patients (n=112), and C-4 patients (n=77) when compared to controls (n=21) (median, range) (67.2 (2 to 168), 54.6 (9 to 168) and 49.6 (8 to 161) vs. 22.8 (9.4 to 56.4); p<0.0001). C+E patients had significantly longer total CTT when compared to C+4 patients (67.2 (2 to 168) vs. 54.6 (9 to 168); p<0.05). Transit time in the right colon/hours was significantly longer in both C+4 and C-4 patients when compared to controls (median, range) (12 (0 to 48) and 14.8 (0 to 96) vs. 7.2 (0.6 to 19.2), p<0.0005) and also when comparing C+E patients with controls (14 (0 to 144) vs. 7.2 (0.6 to 19.2), p<0.0001). Transit time in the left colon/hours was significantly longer in both C+4 and C+E patients when compared to controls (median, range) (12 (0 to 96) and 13.6 (0 to 96) vs. 7.4 (1.2 to 22.8), p<0.005) and also when comparing C-4 patients with controls (12.4 (0 to 72) vs. 7.4 (1.2 to 22.8), p<0.0005). Transit time in the rectosigmoid/hours was significantly longer in both C+4 and C+E patients when compared to controls (median, range) (26.4 (0 to 108) and 30.2 (0 to 142) vs. 10.4 (1.21 to 34.2), p<0.0001) and also when comparing C-4 patients with controls (18.4 (0 to 106) vs. 10.4 (1.21 to 34.2), p<0.005). Transit time in the total colon + rectum/hours was significantly longer in all patients groups when compared to controls (median, range) (49.6 (8 to 161), 54.6 (9 to 168) and 67.2 (2 to 168) vs. 22.8 (9.4 to 56.4), p<0.0001). Transit time in the total colon + rectum/hours was significantly longer in C+E patients when compared to C+4 patients (median, range) (67.2 (2 to 168) vs. 54.6 (9 to 168), p<0.05). Twenty-nine percent of the total sample was diagnosed with normal transit. Significantly more C+E patients were diagnosed with normal transit when compared to C-4 patients (38 (22.5%) vs. 33 (43), p<0.001). Thirty-six percent of the total sample was diagnosed with terminal constipation (defined as delay in the rectosigmoid site with/without delay in the right or left colon). Significantly more C+4 patients were diagnosed with terminal constipation as compared to C-4 patients (42 (37.5) vs. 17 (22), p<0.05). Significantly more C+E patients were diagnosed with terminal constipation as compared to C-4 patients (70 (41.5) vs. 17 (22), p<0.005). Twenty-three percent of the total sample was diagnosed with non terminal constipation and 12% with pancolic constipation.

A diagnostic case control conducted in Italy[50] (1985) [EL=III] quantified bowel function in healthy children in regard to frequency of defecation, gastrointestinal transit time and manometric characteristics of the anorectal tract and to compare variables of bowel function in children with chronic constipation with those in the normal population. One hundred and sixty six children were included in the study. Patients were 63 children (mean age 5.4 ± 4.1 years (2 months to 4 years)) with long-standing constipation, whereas controls were 103 healthy children free of bowel complaints. All children underwent TGITT with radiopaque markers and this was related to the frequency of defecation. The TGITT/hours for the healthy controls was (mean ± SD, range) 25.0 ± 3.7 (19 to 33). Fifty-three patients had a TGITT >33 hours and 10 patients a TGITT <33 hours. Segmental transit time was measured in 39 out of 53 children with prolonged transit time and it was lowest in the colon for three patients, in the rectum for 24 patients and in the colon and rectum for 12 patients. The stool frequency and the TGITT were significantly correlated in patients with prolonged transit time (mean, SD) (patients with TGITT >33 hours (n=53): 2.5 ± 0.9; r=0.75; p<0.001) and in healthy controls (healthy controls (n=78): 6.3 ± 1.3; r=0.78; p<0.001). In 7 of 53 patients with TGITT >33 hours, the bowel frequency overlapped the range observed in the control subjects. Segmental colonic transit times (right and left colon and rectosigmoid) were evaluated but results were not reported.

A diagnostic case-control study conducted in Italy [51] (1984) [EL=III] determined the motility characteristics of the anorectum and measured total gastrointestinal transit time (TGITT) in children with chronic constipation, with/without faecal overflow. Ninety-nine children were included in the study. Patients were 53 children (40 boys, mean age 8.3 years (range 4.8 to 12.9)) with constipation of several months of duration with/without soiling. Controls were 46 healthy children (24 boys, mean age 8.1 years (range 4.2 to 12) without gastrointestinal complaints. Controls were matched for age and weight but not for sex with the constipated children. All children underwent TGITT with radiopaque markers. No test was used as a comparator. The TGITT/hours was significantly longer in patients with soiling (n=32) as compared to the healthy controls (mean ± SD, range) (58 ± 14.3 (36 to 86) vs. 25.6 ± 3.7 (19 to 33); p<0.001) and was also significantly longer in patients without soiling (n=21) as compared to the healthy controls (61.1 ± 15 (36 to 96) vs. 25.6 ± 3.7 (19 to 33); p<0.001. Segmental transit times were not measured.

A diagnostic prospective case series conducted in France [52] (1983) [EL= III] described the clinical presentation of children with idiopathic disorders of faecal continence and aimed to demonstrate that they have functional abnormalities of large-bowel motility. One hundred and seventy six patients aged 2 to 15 years (64% boys) with idiopathic disorders of bowel function other than Hirschsprung's disease were included in the study. All patients underwent CTT with radiopaque markers. The transit time of one radiopaque marker in all three colonic segments were significantly longer in constipated children (with/without spina bifida occulta) as compared to normal children (hours, minutes; mean ± SD) (ascending colon: 13:24 ± 1:5 vs. 7:10 ± 1:4, p<0.05); (descending colon: 13:49 ± 1:37 vs. 7:37 ± 1:3, p<0.05) and (rectum: 30:22 ± 2:42 vs. 11:4 ± 1:5, p<0.05). There were no significant differences regarding segmental transit times between children with and without spina bifida occulta. Total transit times were not reported.

Studies using radio-isotope markers

A retrospective case series conducted in Australia [53] (2005) [EL=III] reviewed the authors' results of scintigraphic studies on children with severe chronic constipation and assessed the use of the geometric centre (GC) and visual interpretation of images in categorising these children. Nuclear transit times were performed on 101 consecutive children (mean age 7.3 ± 3.7 years) with severe constipation. All had symptoms of severe chronic constipation and/or encopresis that had not responded to at least six months of medical therapy with laxatives, dietary alterations and behaviour modification. Colonic transit time was estimated by analysis of the images acquired between 6 and 48 hours. The mean sum of the geometric centre was calculated for four imaging periods (mean ± SD, range): 6, 24, 30 and 48h. Twenty four children were classified as having normal transit time (15.7±3.3 (7.3 to 19.1), 50 children as having slow transit constipation (11.2±1.9 (7.5 to 16.3)) p<0.001 as compared to normal transit time and Idiopathic constipation (IC) (termed functional faecal retention in the paper) groups. Twenty-two children were considered to have IC (15.1±1.5 (12.7-18.2)). Five children were classified as "borderline" but their results were not reported. The GC at each of the four imaging periods was significantly smaller at all four imaging periods in children with slow transit constipation as compared to normal transit and IC groups (mean ± SD, range) (p<0.05 at 6 hours and p<0.001 at 24, 30 and 48 hours). No significant difference in the GC at any imaging time was found when comparing patients with normal transit with those with IC.

A diagnostic retrospective case series conducted in the USA [54] (2004) [EL=III] examined the symptoms and pelvic floor function by anorectal manometry (ARM) and balloon expulsion test (BET) in adolescents ≤18 years of age referred to a tertiary care centre for symptoms of refractory constipation, and to describe the results of scintigraphic colonic transit measurements in the patients who also underwent this test. Sixty-seven adolescents (mean age: 14.7± 3.3 yr, 67% female) with constipation unresponsive to first line, symptomatic treatments were included in the study. Sixteen children were diagnosed with functional constipation (FC) (defined in the paper as "prolonged symptoms of hard or infrequent stools with no evidence of structural, endocrine or metabolic disease"), 18 children with functional faecal retention (FFR)(defined in the paper as "passage of large diameter stools at infrequent intervals, with both purposeful retentive posturing and involuntary faecal soling as judged by the clinician") and 33 children with constipation-predominant irritable bowel syndrome IBS(C-IBS) (defined in the papers as "primarily abdominal pain, either relived by defecation or associate with a change in the frequency or form osfstools with symptoms of constipation"). Only results for children with FC and children with FFR are reported here. 61% of the total population underwent colonic transit time (CTT) with radioisotope markers. A geometric centre at 24h of ≤ 1.6 was classified as slow colonic transit and > 3.8 considered fast colonic transit. Clinical symptoms (nausea, vomiting, bloating, weight loss and incomplete rectal evacuation) were recorded. The geometric centre at 24 hours (mean, SD?) was 2.03 ± 0.99 (n=41, including C-IBS children). Values for children with FC and children with FFR were 1.73 ± 0.29 and 2.04 ± 0.38 respectively. 30 % of the total sample undergoing CTT (n=41, including C-IBS children) were diagnosed with slow colonic transit. 42% of children with FC and 14% of children with FFR were diagnosed with slow colonic transit. 7.5% of the total sample undergoing CTT (n=41, including C-IBS children) were diagnosed with fast colonic transit. None of the children with FC and FFR were diagnosed with fast colonic transit. There was no significant association of abnormal GC at 24 hours (fast or slow) and individual gastrointestinal symptoms (no further details reported).

A diagnostic retrospective case series conducted in Australia [55] (2002) [EL=III] correlated symptoms, signs, transit times and immunohistochemistry to determine the diagnostic differences between slow transit constipation (STC) and functional faecal retention (FFR). One hundred and eighty children (mean ages: 10.5 years (STC); 6 years (FFR)) were included in the study. All children suffered from severe, intractable constipation which did not respond to at least 6 months of medical therapy instituted by a general practitioner or paediatrician. All children underwent nuclear colonic transit time (CTT) and clinical variables, including stool characteristics were assessed. According to the CTT results, 19 children were diagnosed with STC and 161 FFR. There were no gender differences between both groups and children from both groups reported a similar incidence of major symptoms: constipation, soiling, abdominal pain, bloating, anal pain, vomiting, poor appetite and behavioural problems. The frequency of prematurity was similar between both groups, as well as the number of children who passed meconium more than 24 hours after birth and those who had a family history of constipation. Significantly more SCT patients had soft/variably soft stools as compared to FFR patients (39% vs. 16%, (p<0.001). More patients with SCT had a stool frequency of less 1/week as compared to FFR (28% vs. 11%). Constipation was present from a few weeks birth in more children with STC as compared to children with FFR (26% vs. 11%) but this was not statistically significant.

A diagnostic prospective case series conducted in Italy [56] (1993) [EL=III] presented the results of children referred for constipation who underwent total and segmental transit time by scintigraphy with 111In-DTPA. Thirty-nine children (age range: 2-13 years) were included in the study. Constipation was defined as two or fewer bowels motions/week or straining for more than 25% of the defecating time. All children underwent total and segmental CTT with radio-isotope markers. The interval between defecations was recorded. Thirty-two children were found to have normal colon morphology whereas 7 children were diagnosed with dolichocolon. Only results for children with normal colon morphology are reported here. Children with normal colon morphology were classified in four different subgroups according to the results of their total and segmental CTT: children with normal transit time (n=13), children with mainly rectosigmoid retention (n=5), children with prolonged transit time in all segments (n=14) and children with more prolonged transit time in rectosigmoid tract (n=7). Children with normal transit time (n=13) had a total transit time (hours, mean ± SD) of 27.79 ± 4.10. Children with mainly rectosigmoid retention (n=5) had a total transit time (hours, mean ± SD) of 53.36 ± 29.66. Children with prolonged transit time in all segments (n=14) had a total transit time (hours, mean ± SD) of 62.09 ± 7.23. Children with more prolonged transit time in rectosigmoid tract (n=7) had a total transit time (hours, mean ± SD) of 92.36 ± 24.16. The interval between defecations/hours was significantly longer in patients with more prolonged transit time in rectosigmoid tract (n=7) as compared to patients with prolonged transit time in all segments (n=14), patients with mainly rectosigmoid retention (n=5), and patients with normal transit time (n=13), (mean ± SD) (85.71 ± 32.25 vs. 53.00 ± 15.97, 35.60 ± 14.54 and 23.38 ± 5.42 respectively).

Evidence statement

One diagnostic case control study [EL=II] showed that the colonic transit time with radiopaque markers was more accurate at detecting children with functional constipation compared to the plain abdominal radiography read using the Leech score. One diagnostic case control [EL=III] showed a better reproducibility for the colonic transit time with radiopaque markers in detecting the presence of faecal retention as compared to the plain abdominal radiography read using the Barr score.

Seven diagnostic case controls [EL=III] and one diagnostic prospective case series [EL=III] showed that collectively children with constipation have longer colonic transit times compared to children without constipation.

One diagnostic case control [EL=III] showed that colonic transit time was not significantly different in children with severe brain damage and constipation as compared with children with no bran damage and functional faecal retention

Four diagnostic case controls, three diagnostic prospective case series [EL=III] and one diagnostic retrospective case series [EL=III] showed an association between clinical variables and length of colonic transit time. One diagnostic retrospective case series [EL=II] showed no significant association between clinical variables and length of colonic transit time.

GDG interpretation of the evidence

The GDG concluded that transit studies may be of value to inform clinical and surgical decision making in a small number of children with intractable constipation following referral to specialist services. It is the GDG's view that transit studies can help in demystifying constipation as a "psychological" problem and facilitate communication with the parents.

There is not clear evidence of what is "normal" and the fact that the test comes back as "normal" does not necessarily mean that the child is not constipated. The GDG believes that the results of the transit studies should be interpreted in the context of the clinical picture, the population and the clinical setting.

Different methods to measure transit time are used in different centres and there is no evidence to confirm which one is better.

Recommendations

Do not use transit studies to make a diagnosis of idiopathic constipation.

Consider using transit studies in the ongoing management of intractable idiopathic constipation only if requested by specialist services.

4.8 Ultrasound

Clinical Question

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

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation undergoing abdominal ultrasound
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

One search was conducted for all radiological investigations (plain abdominal radiography, abdominal ultrasound and transit studies). A total of 646 articles were identified and 72 articles were retrieved for detailed assessment. Of these, four diagnostic case control studies and one diagnostic prospective case series were identified for inclusion in this review on abdominal ultrasound.

Narrative summary

A diagnostic case control study conducted in the UK[57] (2004) [EL=III] investigated the accuracy of the transverse diameter of the rectum on ultrasonography as an additional parameter for diagnosing constipation in children with lower urinary tract dysfunction. Forty-nine children aged between 5-13 years were enrolled in the study. Cases were 23 patients with a positive history of voiding dysfunction and constipation whereas controls were 26 urological patients without lower urinary tract dysfunction and a normal defecation pattern. The study was conducted at a hospital clinic. The rectal diameter (mean) was significantly larger in constipated children than in children with a normal defecation pattern (4.9 cm (SD 1.01; 95% CI: 4.4 to 5.3) vs. 2.1 cm (SD 0.64; 95% CI: 1.8 to 2.4); $p<0.001$). There was no significant difference in age between the two groups ($p=0.20$) or in the period between the last time a stool was passed prior to the rectal measurement ($p=0.16$). In all patients with voiding dysfunction and faecal constipation the rectal examination confirmed stool in the rectum. It should be noted that none of the patients had a sensation to defecate during the investigation.

A diagnostic case control study conducted in the UK[58] (2005) [EL=III] established normal values for the rectal crescent (diameter) in healthy children, compared them with the rectal crescent in children with constipation and explored whether pelvic ultrasound can help in establishing a diagnosis of megarectum. The study was conducted at a tertiary referral centre and a total of 177 children were enrolled. Ninety-five children (median age 6.5 years) with a history of constipation of at least 6 months duration were compared to 82 children (median age 5.5 years) with no history of constipation or other anorectal or gastrointestinal problems and no previous anorectal surgery. The median rectal crescent was significantly larger in children with constipation as compared to healthy children (3.4 cm (range 2.10 to 7.0; IQR 1.0) vs. 2.4 cm (range 1.3 to 4.2; IQR 0.72); $p<0.001$). A receiver operating characteristic analysis indicated good discrimination between rectal diameters of children with constipation and healthy children (area under the curve: 0.847; 95% CI: 0.791 to 0.904). The cut-off point for establishing the diagnosis of megarectum was set at 3.0cm. There were no significant differences between the two groups in terms of age, weight and height (p values 0.114, 0.198 and 0.131 respectively). Results were adjusted for confounders (age, height and weight). Age and rectal diameter were significantly related ($p<0.0001$): the older the child the bigger the rectal diameter. It should be noted that time to last evacuation was not ascertained and authors acknowledged that this may influence the size of the rectal crescent.

A diagnostic case control study conducted in Poland [43] (2007) [EL=III] determined whether a new method of ultrasound (US) assessment of stool retention could be used as a method of identifying children with functional chronic constipation, and to determine whether children with an enlarged rectum and colon (as seen on US) should be referred for further procedures such as proctoscopy and assessment of colonic transit time. The study was conducted at a gastroenterology outpatient clinic and 225 children were enrolled. One hundred and twenty children (mean age 6.25 years) with chronic constipation were compared to 105 children with normal defecation pattern (mean age 8.25 years). The diameter of the rectal ampulla measured by US was significantly larger in constipated children than in the control group (mean/mm ± SD) (43.06 ± 9.68 vs. 31.83 ± 8.24). The diagnosis of megarectum was based on the measurement of the rectopelvic ratio. The rectopelvic ratio for all ages was significantly bigger for the constipated children as compared to the control group (mean ± SD) (0.22 ± 0.05 vs. 0.15 ± 0.04). The cut-off value to diagnose megarectum was 0.189. Children with faecal impaction (as per US) had significantly longer average segmental transit time for the rectum, sigmoid and left colon ($p<0.001$, $p=0.0015$ and $p=0.0104$ respectively). There was no statistically significant difference for the right side of the colon. Children with an overfilled splenic flexure on US had a significantly longer transit time in the left side of the colon ($p=0.0029$). A sensitivity of 88.3% was reported for the US as compared with proctoscopy in the diagnosis of faecal impaction. No value for specificity was reported.

A diagnostic case control study conducted in Denmark[59] (2008) [EL=III] looked into a possible correlation between a dilated rectum measured by ultrasound and a faecal mass detected by digital rectal examination; and evaluated whether this method could diagnose constipation according to Rome III criteria. Fifty-one children aged 4-12 years were enrolled in the study. Twenty-seven children (mean age 7.0 years) diagnosed with chronic constipation were compared to 24 healthy children (mean age 9.1 years). Constipated children had been referred to an outpatient clinic with either constipation or faecal incontinence, with or without urinary incontinence and a history of urinary tract infection. All constipated children fulfilled Rome III criteria. The rectal diameter (mm; mean ± 2SD) was significantly larger in children with rectal impaction as compared to children without rectal impaction as per digital rectal examination (40.5 ± 7.9 vs. 21.0 ± 4.2; $p<0.001$). The cut-off value for the presence of rectal impaction was 29.4 mm. The rectal diameter (mm, mean ± 2SD) was significantly larger in the constipated children as compared to the healthy controls (39.6 ± 8.2 vs. 21.4 ± 6.00; $p<0.001$). The rectal diameter decreased significantly in children from the constipated group who responded to the laxative treatment ((n=15) 39.6 ± 8.2 vs. 26.9 ± 5.6; $p<0.01$); but still remained significantly greater than in the healthy children ($p<0.05$). Eleven children did not respond to treatment and no significant differences were observed in their rectal diameter as compared to pre-treatment. Seven of the constipated children (26%) had a rectal diameter smaller than the established cut-off point for rectal impaction, despite the fact that they fulfilled the Rome III criteria for constipation. Two healthy children with rectal impaction had a markedly larger rectal diameter (38 and 31 mm) than the other healthy controls. No correlation was found between the rectal diameter and the age or sex of the children in either group. There was no significant difference in height and weight distribution between the two groups, but the healthy children were significantly older than the constipated children. The intraobserver variability was small, as shown by a low coefficient of variation of the three consecutive measurements (5.8% ± 4.3%). There was no significant correlation between bladder volume at the time of measurement and rectal diameter (r=0.04). It should be noted that all investigations were performed by the same observer, a paediatric intern, who had no prior radiological experience.

A diagnostic prospective case series conducted in the UK[60] (2008) [EL=III] assessed the correlation between severity of constipation and US findings, the correlation between clinical examination and US findings and the correlation between findings at serial out-patient follow-up visits to assess clinical improvements and US findings. Five hundred children (317 male, median age: 8 years (age range 8 months to 18 years)) both new referrals and follow-up, attending a constipation outpatient clinic were included. There was a significant correlation between the mean severity symptom score (SSS) score and the mean US total score in all four visits (first visit (n=500), mean SSS: 23.5 (SD 11.6), mean US total score: 4.02 (SD 2.8), Pearson's correlation: 0.39, p<0.001; second visit (n=226), mean SSS: 19.9 (SD 12.6), mean US total score: 3.49 (SD 2.6), Pearson's correlation: 0.49, p<0.001; third visit (n=62), mean SSS: 23.02 (SD 13.7), mean US total score: 3.66 (SD 2.6), Pearson's correlation: 0.26, p=0.04; fourth visit (n=12), mean SSS: 28.5 (SD 16.8), mean US total score: 4.9 (SD 3.2), Pearson's correlation: 0.70, p=0.01). There was a significant correlation between the US score and the clinical examination of palpable faeces in all four visits (first visit (n=500), mean palpable faeces score: 1.42 (SD 1.6), mean US total score: 4.02 (SD 2.8), Pearson's correlation: 0.89 p<0.001; second visit (n=226), mean palpable faeces score: 1.10 (SD 1.6), mean US total score: 3.49 (SD 2.6), Pearson's correlation: 0.845 p<0.001; third visit (n=62), mean palpable faeces score: 1.10 (SD 1.6), mean US total score: 3.66 (SD 2.6), Pearson's correlation: 0.77 p<0.001; fourth visit (n=12), mean palpable faeces score: 1.92 (SD 1.7), mean US total score: 4.9 (3.2), Pearson's correlation: 0.91 p<0.001). It should be noted that no control group was included in the study and that the population size became very small at the fourth visit.

Evidence statement

Four case control studies [EL=III] showed that the rectal diameter as measured by abdominal ultrasound was significantly larger in constipated children than in children with a normal defecation pattern.

Two case control studies [EL=III] showed that abdominal ultrasound made a good discrimination between rectal diameters of children with constipation and healthy children.

One case control study [EL=III] showed that the rectal diameter as measured by abdominal ultrasound was significantly larger in children with rectal impaction as compared to children without rectal impaction as diagnosed per DRE.

One case control study [EL=III] showed that the rectal diameter as measured by abdominal ultrasound decreased significantly in constipated children who responded to laxative treatment; but still remained significantly greater than in healthy children.

One case control study [EL=III] showed a good reproducibility for the abdominal ultrasound in measuring the rectal diameter in constipated and healthy children.

One diagnostic prospective case series [EL=III] showed a significant correlation between the severity of constipation and abdominal ultrasound findings, and between clinical examination and abdominal ultrasound findings

GDG interpretation of the evidence

There is no evidence that the abdominal US adds any useful information over and above that ascertained through thorough physical examination and history-taking in the diagnosis of chronic idiopathic constipation. The GDG is aware that the US is used in practice and it is their view that further research may demonstrate its usefulness in follow-up to indicate response to therapy and facilitate prognosis.

Recommendations

Do not use abdominal ultrasound to make a diagnosis of idiopathic constipation.

Consider using abdominal ultrasound in the ongoing management of intractable idiopathic constipation only if requested by specialist services.

Research Recommendation

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

Why this is important

Evidence is emerging which suggests that abdominal ultrasound may be used reliably to identify children with chronic constipation by measuring rectal diameter; constipated or impacted children have a larger rectal diameter when compared to normal controls. Whilst clinical evaluation alone is sufficient to diagnose the majority of patients, it is possible that this modality has a further role in the evaluation of response to treatment. Given that symptoms of chronic constipation are notoriously subjective, a reliable technique to measure the success of treatment would be valuable not only to guide therapy for individual patients but also to identify recurrence whilst symptoms are sub-clinical. The evidence-base for the use of many medications remains limited and ultrasound may also have a role in allowing comparison of the efficacy of different medications to inform future guideline development. Whilst ultrasound is both safe and non-invasive, and access to facilities across the country is widespread, it is operator dependent. Reliability in a clinical setting must be established.

A multicentre double-blind trial is required to compare the clinical and cost effectiveness of the use of transabdominal ultrasound versus clinical assessment in the management of children with chronic constipation. The trial should enrol children with chronic constipation achieving the Rome III Paediatric criteria referred to specialist services for treatment. In each centre, an investigator independent to the clinical team should perform ultrasound as part of follow-up, using a standardised technique. Children should be randomised into two groups; for one group, the results of the ultrasound should be made available to the clinical team to allow therapy to be adjusted. For the other group, clinical assessment alone should be used. Assessment will continue for a period of time after patients have become asymptomatic in order to examine the rates of recurrence. Time taken for resolution of symptoms should be the primary outcome measure. Secondary outcome measures should include rate of recurrence, patient and clinician satisfaction and cost-effectiveness.

5 Clinical Management

5.1 Disimpaction

Introduction

Faecal impaction is a severe constipation with a large faecal mass in either the rectum or the abdomen, and/or overflow soiling. Disimpaction involves the evacuation of impacted faeces using different treatment regimes.

There is no one treatment regime which will suit all children and a variety of approaches are in evidence throughout the NHS in England and Wales as well as differences in practice between clinicians regarding management of constipation, including disimpaction.

Optimal medical management of children with chronic idiopathic constipation will tend to reduce the number requiring surgical intervention. However, patients who remain impacted despite pharmacological regimes may require manual evacuation under general anaesthetic.

In this section, the available evidence for disimpaction will be reviewed and recommendations made based on the GDG's expert interpretation of that evidence.

Clinical Question

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

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation
- included the following pharmacological and surgical interventions: stimulant laxatives (both oral and rectal medications), osmotic laxatives (both oral and rectal medications) and manual evacuation of the bowel under general anaesthesia
- included the following outcomes: changes in frequency of bowel movements, changes in stools consistency/appearance, changes in pain/difficulty on passing stools, changes in frequency of episodes of soiling, reduction in laxatives use, parent/child views/satisfaction or quality of life
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

One single search was performed on pharmacological and surgical interventions for disimpaction and ongoing maintenance in children with chronic idiopathic constipation. A total of 986 articles were identified from this search and 143 articles were retrieved for detailed assessment. Of these, 5 studies were identified for inclusion in this review: 2 RCTs, 1 retrospective cohort (multicentre) and 2 prospective case series.

Narrative summary

One RCT conducted in the USA[61] (2002) [EL=1–] investigated the efficacy and safety of four different doses of PEG 3350 without electrolytes in the treatment of childhood faecal disimpaction. Forty-one children (27 male, median age 7.5 years (range 3.3 to 13.1)) with functional faecal retention and with evidence of faecal impaction at physical examination were included in the study. Children were randomized into 4 groups and each group received a different dose of PEG 3350: group I (n=10) 0.25 g/kg per day, group II (n=10) 0.5 g/kg per day, group III (n=10) 1.0 g/kg per day and group IV (n=10)1.5 g/kg per day. Medication was taken for 3 consecutive days at breakfast, premixed with a solution flavoured with orange (maximum dose 100g daily). Outcomes were measured 5 days after starting treatment (48 hours after last drug use). Clearance of faecal impaction was achieved in 30 patients (75%) of the total population. Significantly more children on higher doses of laxatives were disimpacted as compared to children on lower doses (note: values for each group are estimates taken from a bar chart); ((number of patients, %), a) 0.25 g/kg per day (n=10): 5; b) 0.5 g/kg per day (n=10): 4; c) 1.0 g/kg per day (n=10): 9; d) 1.5 g/kg per day (n=9): 10; $p<0.05$ c and d (95%) vs. a and b (55%)). Thirty-three children (83% of the total sample) had more than 3 bowel movements during the 5-day study. The time of the first bowel movement after initiation of treatment (mean ± SD) was 1.89 ± 0.46 days for the total sample. Children on higher doses had significantly higher number of bowel movements as compared to baseline than children on lower doses of laxative (values for each group are estimates taken from a bar chart, baseline value is less than 2 for all groups): (number of bowel movements: (0.25 g/kg per day, n=10): 6, (0.5 g/kg per day, n=10): 8, (1.0 g/kg per day, n=10): 11, (1.5 g/kg per day, n=9): 12; $p<0.005$ for each group compared to the others). No significant differences were found in any of the following parameters among the 4 groups: straining, stool consistency, stool amount, gas and cramping. Ninety-five percent of children took PEG 3350 on the first attempt. Mean daily volumes required to take the appropriate study dose were not significantly different between groups. At baseline the duration of constipation was significantly longer for the group receiving 1.5 g/kg per day as compared to the group receiving 0.5 g/kg per day ($p<0.03$).

An RCT conducted in the USA [62] (1993) [EL=1–] compared the efficacy and acceptability of the treatment of faecal impaction using either mineral oil or pineapple isotonic intestinal lavage solution containing PEG 3350 (unclear from paper whether this contained electrolytes or not). Forty-eight children aged >2 years with idiopathic constipation were included in the study. Children were randomised into 2 groups: group I (n=17) received 2-8 tablespoons of mineral oil in 2 divided doses for 2 days, whereas group II (n=19) received a pineapple flavoured balanced oral lavage solution (sweetened with Nutra-Sweet®) 20ml/kg/h to drink for 4 hours once daily on 2 consecutive days. Children were reassessed two days after completing treatment. The number of bowel movements after treatment (>5 / 1 to 5 /none) increased significantly in children treated with lavage solution (n=19) as compared to children treated with mineral oil (n=17) (% children per category : 9/8/2 vs. 2/10/5, $p<0.005$). The first bowel movement after treatment

(<1 day / >1 day / none) occurred significantly quicker in children taking lavage solution (n=19) as compared to those taking mineral oil (n=17), (%children per category: 14/3/2 vs. 6/6/5, p<0.01). Palpable abdominal masses (none/a few/many) were found in significantly more children taking lavage solution (n=19) as compared to children taking mineral oil (n=17) (% children per category: 17/1/1 vs. 10/4/3, p<0.005). No children treated with mineral oil (n=17) experienced vomiting (none/occasional/a lot) as compared to children treated with lavage solution (n=19), (% children per category: 17/0/0 vs. 12/6/1, p<0.005). Compliance was significantly better (good/fair/poor) in children taking mineral oil (n=17) than in those taking lavage solution (n=19), (%children per category: 14/3/0 vs. 6/7/6, p<0.01). There were no significant post-treatment differences between the two groups regarding cramps/bloating, abdominal distension, consistency of stools, anal fissure, anal sphincter tone, perineal soiling and willingness to consider the same treatment in case of recurrence of impaction. There were no significant differences at baseline between the 2 groups regarding: duration of constipation, frequency of stooling, associated encopresis, rectal bleeding, previous treatments with enemas/fibre diet, palpable abdominal masses, abdominal distension, anal fissure, perineal soiling, sphincter tone and consistency of stool. Significantly more patients in the lavage group gave a history of previous treatment with mineral oil (p<0.05). Twelve patients failed to return for the two days post-treatment reassessment.

A multicentre retrospective cohort study conducted in the UK[63] (2007) [EL= 2-] estimated the clinical and economic impact of using PEG 3350 plus electrolytes (macrogol 3350; Movicol, Movicol Paediatric Plain) in an outpatient setting compared to enemas and suppositories and manual evacuation to treat paediatric faecal impaction. Two hundred and twenty-four children aged between 2 and 11 years, suffering from intractable constipation from 5 different centres were included in the study. A total of 112 children at the 5 centres had received PEG 3350 plus electrolytes. These were compared to 101 children in the 5 centres who received enemas and suppositories and with 11 children in 2 of the centres who underwent manual evacuation of the bowel under anaesthesia. Significantly more patients who received PEG 3350 plus electrolytes (n=5 centres) were disimpacted within 5 days when compared to patients who received enemas and suppositories (n=5 centres) and those who underwent manual evacuation of the bowel under anaesthesia (n=2 centres); (97% (CI: 94%, 100%) vs. 73% (CI: 58%, 89%) vs. 89% (CI: 67%, 100%) respectively; p<0.001). No significant differences were found between the 3 groups for time to initial disimpaction and time to disimpaction for those who did not disimpact within 3 days. The doses required for successful disimpaction within 5 days (mean, 95% CI) were 29 (13 to 44) sachets for PEG 3350 plus electrolytes, 2 (1 to 3) units for enemas and 1 (1 to 2) units for suppositories. Significantly more children who underwent manual evacuation of the bowel under anaesthesia (n=11 patients) suffered from vomiting as an adverse effect of the intervention when compared to children who received PEG 3350 plus electrolytes (n=112 patients) or enemas and suppositories (n=101 patients); (18% vs. 2% and 2%; p<0.01). There were no significant differences among 3 groups for: urinary tract infection, dermatitis around anus, thrush and gastric illness.

A prospective case series (phase 1 of the study; phase 2 is an RCT) conducted in the UK [64] [EL=3] assessed the efficacy of polyethylene glycol 3350 plus electrolytes (PEG+E; Movicol) as oral monotherapy in the treatment of faecal impaction in children and compared PEG+E with lactulose as maintenance therapy in a randomised trial. Sixty-five constipated children (mean age: 5.7 years, 68% boys) with intractable constipation that had failed to respond to conventional treatment (prior to enrolment 37% children reported taking at least 1 laxative medication, the most common of which was lactulose) and would require hospital admission for disimpaction were included. Children received PEG+E (Movicol) (13.8g powder dissolved in at least 125ml water per sachet) plus electrolytes, administered orally in hospital according to an escalating dosing regime, until disimpaction was achieved (up to 7 days). Successful disimpaction was indicated by the passage of watery stools. Disimpaction was successful in 58 children (92%) of the total population (25 children aged 2 to 4 years (89%) and 33 children aged 5 to 11 years (94%)). Disimpaction was achieved at 5.7 ± 1.2 days (mean, SD) (median, range: 6.0 (3 to 7)) for the total sample (n=63). Disimpaction was achieved at 5.8 ± 1.2 days (6.0 (3 to 7) in children aged 2 to 4 (n=28) and in 5.6 ± 1.1 days (6.0 (3 to 7)) in children aged 5 to 11 (n=35).The maximum dose required (sachets/day) to achieve disimpaction was 6 for the total population (4 for children aged 2 to 4 and 6 for children aged 5 to 11). The mean number (SD) of sachets required to achieve disimpaction was 19.6 (7.5) for the total sample (n=63) (14.3 (4.5) for children aged 2 to 4 years (n=28) and 23.6 (6.8) for children aged 5 to 11 (n=35)). Five children (8%) did not complete the phase 1: 3 children withdrew before receiving any study medication and 2 children failed to disimpact within the time allowed. The two children who failed to disimpact in the 7 days specified in the study protocol were continued on PEG+E administration and eventually disimpacted.

A prospective case series conducted in the USA [65] (2001) [EL=3] examined the efficacy and dosing of PEG 3350 without electrolytes (Miralax®) in children with constipation. Twenty-four constipated children between ages of 18 months and 12 years were included in the study. Data were available for only 20 children who completed study (9 boys, mean age 6.09 ± 4.2 years). Eleven children had constipation alone whereas 9 children had constipation and soiling. Children received a PEG solution, at an initial dose ~1g/kg body weight per day (14 ml/kg/d solution) given in 2 divided doses for 8 weeks. PEG powder was dissolved in water, juice or other clear-liquid beverage. For determination of best dose for each child, parents asked to increase or decrease volume of PEG solution by 20% every 3 days as required to yield 2 soft-to-loose stools per day. Children of appropriate developmental status were advised to sit on the toilet for 5 minutes after each meal. Patients were examined on enrolment and at the end of 8 weeks of therapy for the presence or absence of a palpable faecal mass, faecal impaction and rectal dilatation. Soiling frequency, painful defecation and fear of defecation/stool withholding at enrolment were compared with that recorded on diary forms during the last 2 weeks (weeks 7 and 8) of treatment. Soiling frequency decreased significantly (n=9) (mean ± SEM) after treatment when compared to baseline (10.0 ± 2.4 vs. 1.3 ± 0.7, p=0.003) and total resolution of soiling occurred in 4 patients (44.4%). Painful defecation (n=20) was completely resolved with treatment as compared to its presence in 75% of children at baseline (p<0.0001). Fear of defecation/stool withholding decreased significantly during treatment as compared to baseline (5% vs. 70%; p<0.0001). No abdominal faecal mass was found in any children (n=18) after treatment, this was significant when compared to findings at baseline (abdominal mass present in 44%, p<0.0029). Faecal rectal impaction was present in significantly more children (n=18) before than during treatment (83% vs. 22%, p<0.0006). Dilated rectal vault was found in significantly less children after treatment (n=18) than at baseline (11% vs. 78%, p<0.0001). The final effective dose during the last 2 weeks of treatment (mean ± SEM) (g/kg/day) was 0.84 ± 0.27 (range 0.27 to 1.42). Four subjects dropped from study because of failure to return required symptoms diaries: two of these had an excellent response to therapy by parent report and two were lost to follow up.

Evidence statement

*Osmotic laxatives (oral medications)**

* We are following the BNFC classification of laxatives.

A prospective case series [EL=3] showed that PEG 3350+E (Movicol) administered orally in hospital for up to 7 days was effective in achieving disimpaction in constipated children.

One prospective case series [EL=3] showed that a solution of PEG 3350 without electrolytes (Miralax®), at an initial dose ~1g/kg body weight per day (14 ml/kg/d solution) given in 2 divided doses for 8 weeks was effective in decreasing soiling frequency, painful defecation, fear of defecation /stool withholding, faecal rectal impaction, and dilated rectal vault after 6 weeks of treatment. It was also effective in resolving completely abdominal rectal masses after treatment.

One RCT [EL=1-] showed that PEG 3350 administered orally in 4 different doses (0.25, 0.5, 1.0 and 1.5 g/kg per day) for 3 consecutive days was effective in achieving disimpaction in constipated children. It also showed that higher doses of PEG 3350 were more effective than lower doses in achieving disimpaction in constipated children.

One RCT [EL=1-] showed that a pineapple isotonic intestinal lavage solution containing PEG 3350 administered during 2 consecutive days, was more effective than mineral oil administered as 2-8 tablespoons in 2 divided doses for 2 days, in producing the first bowel movement and in increasing bowel movements after treatment but less effective in resolving palpable abdominal masses. PEG 3350 also showed better compliance and fewer side effects in children taking mineral oil as compared to children taking lavage solution.

One multicentre retrospective cohort study [EL=2-] showed that PEG 3350 plus electrolytes was more effective in achieving disimpaction within 5 days in children with constipation when compared to children who received enemas and suppositories and those who underwent manual evacuation of the bowel under anaesthesia.

Faecal softeners:

One RCT [EL= 1-] showed that a pineapple isotonic intestinal lavage solution containing PEG 3350 administered during 2 consecutive days, was more effective than mineral oil administered as 2-8 tablespoons in 2 divided doses for 2 days, in producing the first bowel movement and in increasing bowel movements after treatment but less effective in resolving palpable abdominal masses. It also showed better compliance and fewer side effects in children taking mineral oil as compared to children taking lavage solution.

Osmotic laxatives and stimulant laxatives (rectal medications)

One multicentre retrospective cohort study [EL=2-] showed that enemas and suppositories were less effective in achieving disimpaction within 5 days in children with constipation when compared to children who received PEG + E 3350.

Manual evacuation of the bowel under general anaesthesia:

One multicentre retrospective cohort study [EL=2-] showed that manual evacuation of the bowel under general anaesthesia was less effective in achieving disimpaction within 5 days in children with constipation when compared to children who received PEG + E 3350. It also showed that children who underwent manual evacuation of the bowel under general anaesthesia experienced more vomiting when compared to children who received macrogol 3350 plus electrolytes and those who received enemas and suppositories.

Stimulant laxatives (oral medications)

There is no evidence for the effectiveness of stimulant laxatives (oral medications) for treating disimpaction in children with constipation.

Health economic consideration

Given the lack of evidence of difference in effectiveness, the health economic analysis for this guideline was undertaken with the a priori assumption that all first line pharmacological strategies had the same level of effectiveness, although different assumptions provided by the GDG were used for some of the second and third line treatments where first line treatments failed. Failure is defined as on-going constipation requiring further treatment. The GDG were interested in finding out the difference in cost for a range of strategies for disimpaction and maintenance and whether the cost of a high-priced drug would be off-set by the lower cost of failure if that high-priced drug was more effective, leading to overall savings. The economic analysis also compared the total costs per patient (including the cost of failure) of various pharmacological strategies, and considered the effect of different doses of treatment where these clinical data were available.

The economic analysis also calculated thresholds of cost-effectiveness of treatment. Where one treatment or group of treatments was more effective than the alternative, there would need to be some additional therapeutic benefit of the more expensive option in order for it to be the preferred option on cost-effectiveness grounds. This additional therapeutic benefit was converted into quality adjusted life years in order to apply the NICE threshold of £20,000 per QALY to this analysis. Data on QALY weights were obtained from the published literature reviewed above.

The only data identified which estimated the effectiveness of different doses of treatment was one small study based on treatment with Movicol. An economic analysis of the cost-effectiveness of treatment by dose was undertaken using this clinical effectiveness data.

The results strongly indicated that effectiveness is the dominant factor in determining the overall cost-effectiveness of treatment for disimpaction. Since success is determined by effectiveness and adherence to treatment, the treatment with the greatest chance of overall success should be the preferred option on cost-effectiveness grounds. (see appendix E for a full description of the health economic models).

GDG interpretation of the evidence

The GDG noted the evidence of the effectiveness of PEG 3350 in disimpaction and this reflects their clinical experience.

The GDG noted the absence of evidence for the effectiveness of stimulant laxatives in disimpaction. However, from clinical experience the GDG concluded that they can be useful as a second-line intervention. In the light of this, the GDG collated the information into a table so that clinicians can select the most appropriate second-line doses of each laxative (or combination of laxatives) for their patients.

The GDG concluded that children need to be assessed to diagnose and treat faecal impaction in the first place; otherwise not even the best maintenance treatment will work if children do not receive treatment for disimpaction beforehand. Giving maintenance treatment without disimpacting first could worsen the symptoms of constipation. The GDG noted that families should be informed that initial disimpaction treatment can increase symptoms of soiling and abdominal pain.

The GDG noted from the health economic analysis that successful disimpaction is the most cost effective treatment for any child regardless of the initial price.

The GDG understands from the evidence that PEG (Movicol) is effective, well tolerated and safe. It can be used at home with low supervision. The GDG's experience is that PEG is safe and effective to use in the under 1s. However, it is off-license for this age group and the GDG recognise the importance of further research in this area.

The health economic evidence is that the most cost-effective intervention is the one that works for the individual child since any difference in price of an individual laxative is outweighed by the downstream savings of even small changes in effectiveness of treatment (that is, avoiding unnecessary future treatment including hospitalisation (see appendix E).

The GDG concluded that enemas are effective for disimpaction, but the administration route is uncomfortable for the children. Sodium citrate enema should be the first choice only if all other oral therapies have failed, because it produces fewer adverse effects than phosphate enemas. The GDG noted that phosphate enemas should only be used under specialist supervision with the appropriate consideration of the risk of toxicity.

Manual evacuation is effective but it requires hospital admission and general anaesthesia with the associated economic cost and disruption in the child's and family life therefore should only be used as the last resource and only when other oral and rectal treatments have failed.

Health economic considerations

A health economic model was developed for this guideline to assess the cost-effectiveness of different strategies for disimpaction. Given the lack of evidence of differences in efficacy, the baseline assumption was that all first line pharmacological strategies had the same level of effectiveness, although different assumptions provided by the GDG were used for some of the second and third line treatments where first line treatments failed (see appendix E for a more comprehensive discussion of the health economic model). Failure was defined as on-going constipation requiring further treatment. The GDG were interested in finding out the difference in cost for a range of strategies for disimpaction and for maintenance and whether the cost of a high-priced drug would be off-set by the lower cost of failure if that high-priced drug was more effective, leading to overall savings. The economic analysis also compared the total costs per patient (including the cost of failure) of various pharmacological strategies, and considered the effect of different doses of treatment where these clinical data were available.

The economic analysis also calculated thresholds of cost-effectiveness of treatment. Where one treatment or group of treatments was more effective than the alternative, there would need to be some additional therapeutic benefit of the more expensive option in order for it to be the preferred option on cost-effectiveness grounds. This additional therapeutic benefit was converted into quality adjusted life years in order to apply the NICE threshold of £20,000 per QALY to this analysis. Data on QALY weights were obtained from the published literature reviewed above.

The modelling was based on the available clinical data and on GDG consensus for parameters where data could not be identified. The modelling showed that treatments with a high chance (80%) of success cost less than treatment with a low chance of success (20%), regardless of the price of drugs used or the dose provided. Also, the cost of failure (changing doses, combining drugs, and manual evacuation as a last resort) was a far greater determinant of overall cost than the cost of initial treatment.

The analysis by dose of Movicol Paediatric Plain showed that highly effective strategies will lead to cost savings due to the high downstream costs of invasive treatment requiring hospitalisation that are saved. Effectiveness is determined both by the type of drug used and by the dose given. The data we have been able to identify on doses of treatment suggest that higher doses of Movicol that lead to effectiveness levels of 95% compared with 55% for lower doses would be cost saving to the NHS.

The disimpaction model based on a consensus of treatment pathways developed by the GDG showed that oral pharmacological alternatives were more than ten times cheaper than enemas which were assumed to be less effective and require hospitalisation. At a 20% failure rate, oral pharmacological treatment provided a mean benefit of 0.23 QALYs per child. The threshold analysis showed Movicol Paediatric Plain would need to increase be 2.6% more effective than the nearest alternative (in this case Senna) in order for it to be the preferred option on cost-effectiveness grounds.

Given the lack of head to head comparisons of treatment alternatives, the health economic analysis provided transparency to the GDG's clinical judgement that treatment failure plays a major role in determining the total cost per child of disimpaction and maintenance so that the cheapest priced option is not the most cost-effective overall.

Recommendations

Assess all children with idiopathic constipation for faecal impaction, including children who were referred because of "red flags" but in whom there were no significant findings following further investigations (see tables 2 and 3).

Use the following oral medication regimen for disimpaction if indicated:

- Use polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain) using an escalating dose regimen (see table 4) as the first-line treatment*. Movicol Paediatric Plain may be mixed with a cold drink.
- Add a stimulant laxative using table 4 if polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain) 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 (Movicol Paediatric Plain) is not tolerated.

Do not use rectal medications for disimpaction unless all oral medications have failed.

Administer sodium citrate enemas only if all oral medications for disimpaction have failed.

Do not administer phosphate enemas for disimpaction unless under specialist supervision in hospital, and only if all oral medications and sodium citrate enemas have failed.

Do not perform manual evacuation of the bowel under anaesthesia unless optimal treatment with oral and rectal medications has failed.

Review children undergoing disimpaction within 1 week.

* At the time of publication (October, 2009), Movicol Paediatric Plain did 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 which is also unflavoured

Table 4 Laxatives recommended doses

Laxatives	Recommended doses
Macrogols	
Movicol	Movicol Paediatric Plain (Norgine)* Oral powder, macrogol ‘3350’ (polyethylene glycol ‘3350’) 6.563 g, sodium bicarbonate 89.3 mg, sodium chloride 175.4 mg, potassium chloride 25.1 mg/sachet, Disimpaction By mouth: Child under 1 year: half to 1 sachet daily (non-BNFC recommended dose) Child 1-5 years: treat until impaction resolves or for maximum 7 days. Two sachets on 1st day, then 4 sachets daily for 2 days, then 6 sachets daily for 2 days, then 8 sachets daily for 2 days Child 5-12 years: treat until impaction resolves or for maximum 7 days. Four sachets on first day, then increased in steps of 2 sachets daily to maximum of 12 sachets daily Ongoing maintenance (chronic constipation, prevention of faecal impaction) By mouth: Child under 1 year: half to 1 sachet daily (non-BNFC recommended dose) Child 1-6 years: 1 sachet daily; adjust dose to produce regular soft stools (max. 4 sachets daily) Child 6-12 years: 2 sachets daily; adjust dose to produce regular soft stools (max. 4 sachets daily)
Osmotic laxatives	
Lactulose	By mouth: Child 1 month to 1 year: 2.5 ml twice daily, adjusted according to response Children 1-5 yrs: 2.5-10 ml twice daily, adjusted according to response (non-BNFC recommended dose) Children 5 -18 yrs: 5-20 ml twice daily, adjusted according to response (non-BNFC recommended dose)
Stimulant Laxatives	
Sodium picosulphate**	Non-BNFC recommended doses: By mouth: Child 1 month to 4 years: 2.5-10 mg once a day Child 5 -18 years: 2.5-20 mg once a day
Bisacodyl	Non-BNFC recommended doses: By mouth: Child 4 -18 years: 5 -20 mg once daily By rectum (suppository): Child 2-18 years: 5 -10 mg once daily

* At the time of publication (October, 2009), Movicol Paediatric Plain did 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 which is also unflavoured

** Elixir, licensed for use in children (age range not specified by manufacturer). Perles not licensed for use in children under 4 years

Senna ***	Sennokot syrup By mouth: Child 1 month to 4 years: 2.5-10 ml once daily Child 5-18 years: 2.5 -20ml once daily Senna (non-proprietary) By mouth: Child 6-18 years: 1-4 tablets once daily
Docusate Sodium****	By mouth: Child 6 months-2 years: 12.5 mg 3 times daily (use paediatric oral solution) Child 2-12 years: 12.5-25 mg 3 times daily (use paediatric oral solution) Child 12-18 years: up to 500 mg daily in divided doses

(Note: unless otherwise stated, doses are those recommended by the British National Formulary for Children-BNFC 2009)

Research Recommendation

What is the effectiveness of polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain) in treating idiopathic constipation in children younger than 1 year old, and what is the optimum dosage?

Why this is important

There is some evidence that treatment of constipation is less effective if faecal impaction is not dealt with first. Disimpaction with oral macrogols is recommended for children and their use avoids the need for rectal treatments.

Rectal treatments, especially in hospital, are more common than oral treatments at home. Although relatively few infants are admitted to hospital, there would be savings if initially all children were disimpacted at home.

Polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain), an oral macrogol, is licensed for disimpaction in children older than 5 years. Increasing experience has shown that it is effective in infants younger than 1 year old, but evidence is limited to small case series. If dosage guidelines and evidence on macrogol use in infants were obtained and published, more healthcare professionals might be encouraged to try macrogols in this age group. It would also allow the guideline to be applicable across the whole paediatric age group.

5.2 Maintenance therapy

Introduction

There is little published evidence to guide health professionals about the pharmacological management of chronic constipation. There is no one treatment regime which will suit all children and a variety of approaches are in evidence throughout the NHS in England and Wales as well as differences in practice between clinicians regarding management of constipation, including disimpaction.

In this section, the available evidence for ongoing treatment/maintenance will be reviewed and recommendations made based on the GDG's expert interpretation of that evidence.

*** Syrup not licensed for use in children under 2 years

**** Adult oral solution and capsules not licensed for use in children under 12 years

Clinical Question

What is the clinical effectiveness of pharmacological interventions for ongoing treatment/maintenance in children with chronic idiopathic constipation?

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation
- included the following pharmacological and surgical interventions: stimulant laxatives (both oral and rectal medications), osmotic laxatives (both oral and rectal medications) and bulk forming laxatives
- included the following outcomes: changes in frequency of bowel movements, changes in stools consistency/appearance, changes in pain/difficulty on passing stools, changes in frequency of episodes of soiling, reduction in laxatives use, parent/child views/satisfaction or quality of life
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

One single search was performed on pharmacological and surgical interventions for disimpaction and ongoing maintenance in children with chronic idiopathic constipation. A total of 986 articles were identified from this search and 143 articles were retrieved for detailed assessment. Of these, 15 studies were identified for inclusion in this review: 14 RCTs (7 open label, 6 double blind and 1 single blind) and 1 prospective cohort study.

Narrative summary

Laxatives vs. laxatives

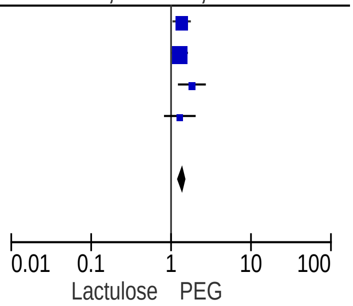
Osmotic laxatives vs. osmotic laxatives: Polyethylene glycol (PEG) vs. lactulose

One meta-analysis of 4 RCTs comparing polyethylene glycol (PEG) vs. lactulose showed that treatment success was significantly higher for PEG as compared to lactulose (fig 1).

Fig 1. Polyethylene glycol (PEG) vs. lactulose in the ongoing treatment/maintenance of idiopathic constipation in children

	PEG		Lactulose			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Candy 2006	27	27	19	26	32.6%	1.36 [1.07, 1.73]
Dupont, 2005	44	47	29	40	44.4%	1.29 [1.05, 1.58]
Gremse, 2002	31	37	17	37	13.1%	1.82 [1.25, 2.66]
Voskuijl, 2004	25	46	19	45	10.0%	1.29 [0.84, 1.98]
Total (95% CI)		**157**		**148**	**100.0%**	**1.37 [1.20, 1.57]**
Total events	127		84			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.75$, df = 3 (P = 0.43); $I^2 = 0\%$
Test for overall effect: Z = 4.56 (P < 0.00001)



It should be noted that different types of PEG, different definitions of treatment success as well as different assessment points were used in the studies.

The following are the narratives summaries with details of the individual studies included in the metanalysis:

A double-blind RCT* conducted in the UK [64] (2006) [EL=1+] assessed the efficacy of PEG 3350 plus electrolytes (PEG 3350+E; Movicol) as oral monotherapy in the treatment of faecal impaction in children and to compare PEG 3350+E with lactulose as maintenance therapy in a randomised trial. Sixty-five children (mean age: 5.7 years (56% children 5 to 11 years), 68% boys) with intractable constipation that had failed to respond to conventional treatment were included in the study. All children received PEG 3350+E (13.8g powder dissolved in at least 125ml water per sachet) administered orally in hospital according to an escalating dosing regime until disimpaction was achieved (up to 7 days). Fifty-eight children (67% boys, mean age: 5.7 ± 2.6 years (range 2 to 11 years)) entered phase 2 of the study and were randomised to receive PEG 3350+E (13.8g powder dissolved in at least 125ml water per sachet) or lactulose (10g powder dissolved in at least 125ml water) for 12 weeks. For both medications children received oral maintenance doses commencing with half of the numbers of sachets required for disimpaction/day. Additional laxative treatment with senna was allowed as rescue medication if the response to a single agent alone was judged inadequate by the investigator. There were no significant differences at baseline between the two treatment groups regarding age, sex, height and weight. Children taking PEG 3350+E had significantly more successful defecations/week (last on-treatment value) as compared to children taking lactulose (mean, SD, range: PEG 3350+E (n=27): 9.4 (4.56; 2 to 24); lactulose (n=26): 5.9 (4.29; 2 to 23); difference in means: 3.5; 95% CI: 1.0 to 6.0; p=0.007). No children taking PEG 3350+E reimpacted whereas seven children taking lactulose did (23%; p=0.011. No children taking PEG 3350+E needed to use senna as rescue medication whereas eight children taking lactulose did (31%; p=0.002). The number of sachets used each day (mean, SD) for children taking PEG 3350+E (n=27) was 0.91 (0.41) whereas for children taking lactulose (n=26) it was 2.41 (0.91). There were no significant post-treatment differences in mean values per patient between the two groups with respect to: predominant bowel movement form, pain, straining, soiling and overall assessment of treatment. Sixty-four percent of children on PEG 3350+E (n=27) experienced adverse effects as compared to 83% of children on lactulose. There was a similar incidence of adverse effects in each age group. The most commonly reported events were gastrointestinal and resolved during the study. No clinically significant abnormal values were observed in urine and plasma electrolytes after 12 weeks of maintenance therapy in either group.

* This is phase 2 of the study. Phase 1 was a prospective case series already discussed in the review on disimpaction

A double-blind RCT conducted in France [66] (2005) [EL=1+] assessed the safety of a PEG 4000 laxative without additional salts in paediatric patients. Ninety-six children (51 male) aged 6 months to 3 years with constipation despite their usual dietary treatment for at least 1 month were included. Children were randomised to receive either PEG 4000 (starting dose: 1 sachet (4g) and 1 placebo to be taken at breakfast) or lactulose (starting dose: 1 sachet (3.33g) and 1 placebo to be taken at breakfast) for 3 months. For both drugs, the dose could be doubled if it was ineffective in children aged 13 months to 3 years. If the maximum authorised dose was unsuccessful, one micro-enema of glycerol per day could be prescribed for a maximum of 3 consecutive days. If the child did not produce stools after treatment, two enemas could be administered at a 48 hour interval. This procedure was only allowed twice during the study. If the child produced liquid stools for more than 1 day or more than 2 or 3 stools/day depending on age, the dose could be decreased by 1 pair of sachets/day to a minimum of 1 pair of sachets every other day and possibly to transitory interruption. Outcomes were assessed at day 42 and day 84 after initiating treatment. There were no clinically relevant differences between the two treatment groups at baseline for clinical or biological parameters. At day 42 the stool frequency (number of stools/week, median (interquartile range)) was not significantly different for babies (aged 6 months to 12 months) taking PEG 4000 as compared to babies taking lactulose. However, for toddlers (aged 13 months to 3 years) taking PEG 4000 (n=51) the stool frequency increased significantly more than for toddlers taking lactulose (n=45) (8 (6-10) vs. 6 (5-7); p=0.013). At day 84 there were no significant differences in either babies or toddlers for both treatments groups regarding stool frequency. At day 42 significantly more children taking lactulose (14/41, 34%) reported a higher frequency of hard stools as compared to children taking PEG 4000 (4/46, 9%; p=0.003). This remained the case at day 84 (PEG 4000: 3/47, 6% vs. lactulose: 11/40, 28%; p=0.008). At day 42 significantly more children taking lactulose (19/44, 43%) reported using enemas as compared to children taking PEG 4000 (14/48, 30%). This remained the case at day 84 (PEG 4000: 8/48, 17% vs. lactulose: 17/42, 41%; p=0.012). Faecal impaction was diagnosed in significantly more patients taking lactulose as compared to children taking PEG 4000 (PEG 4000: 1/51, 2% vs. lactulose 6/45, 13%; p=0.049). There were no significant differences in the doses used (sachets/day) (median (interquartile range)) for both medications in either babies or toddlers (babies: PEG 1 (0.9 to 1) vs. lactulose 1 (1 to 1.3); toddlers: PEG 1 (1 to 3) vs. lactulose 1.1 (0.9 to 1.5)). Treatment was stopped in 1 child in the lactulose group because of lack of efficacy.

A double-blind RCT conducted in the Netherlands [67] (2004) [EL=1+] compared the clinical efficacy and safety of PEG 3350+E (Transipeg®; PEG with electrolytes) and lactulose in paediatric idiopathic constipation. Ninety-one children (49 male) aged 6 months to 15 years with constipation were included. During the run-in phase (1 week before treatment) no laxatives were allowed and at the end all patients received 1 enema daily for 3 days. Children ≤6 years received 60 ml of Klyx (sodium dioctylsulfosuccinate and sorbitol) and children >6 years received 120ml Klyx. During the initial phase children were randomised to receive either PEG 3350+E (children aged 6 months to 6 years (inclusive): 1 sachet (2.95g) per day; children older than 6 years: 2 sachets (5.9g) per day) or lactulose for 8 weeks (children aged 6 months to 6 years (inclusive): 1 sachet (6g) per day; children older than 6 years: 2 sachets (12g) per day). Overall treatment success defined as 3 or more bowel movement per week and 1 encopresis episode or less every 2 weeks. After 8 weeks there were no significant differences regarding both defecation frequency/week and encopresis frequency/week for children taking PEG 3350+E as compared with children taking lactulose. Success percentages were significantly greater for children taking PEG 3350+E as compared to children taking lactulose (56 (95% CI 39 to 70) vs. 29 (95% CI 16 to 44); p=0.02). Significantly more sachets a day were taken by children on lactulose as compared to children on PEG 3350+E (mean, SD: 2.4 (0.4) vs. 1.99 (0.3); p=0.03). No serious or significant side effects were recorded.

Significantly more adverse effects (abdominal pain, pain at defecation and straining at defecation) were seen in patients taking lactulose as compared to PEG 3350+E ($p<0.05$). There were no significant differences between the two groups regarding: bloating, diarrhoea, flatulence, nausea, hard stool consistency and vomiting. Significantly more children complained of bad palatability of PEG 3350+E compared to lactulose and this caused the premature withdrawal of one patient. There were no significant differences at baseline between the two groups with respect to: age, sex, defecation frequency, encopresis, large amounts of stool and faecal impaction. Nine children dropped out the study: four children in the PEG 3350+E group and five in the lactulose group. Two children in each group were lost to follow-up. Overall treatment success was independent of age (<6 years and ≥6 years) and use of laxatives for more than 1 year prior to the start of the study. In children treated for less than 1 year a significant difference in success was found between those treated with PEG 3350 and those treated with lactulose (63% vs. 1% respectively; $p=0.02$).

An open label RCT (crossover) conducted in the USA[68] (2002) [EL=1-] compared the efficacy of PEG 3350 and lactulose in the treatment of chronic constipation in children. Forty-four children aged 2 to 16 years (mean 7.8 ± 3.7), referred for evaluation of constipation were included. Children were randomised to receive either PEG 3350 (Miralax®) 10g/m2/day orally for 2 weeks (mean weight adjusted dose: 0.3 g/kg/day (range 0.2 to 0.5)) or lactulose 1.3g/kg/day orally for 2 weeks. There was no washout period in between the two medications. Outcome measures were stool frequency, stool form, easy of passage, effectiveness (global assessment, as reported by parent or guardian) and laxative preference (based on efficacy, ease of administration and side effects). The mean number of bowel movements, the stool form (mean sum of scores) and the easy of stool passage (mean sum of scores) were not significantly different in children taking PEG 3350 as compared to children taking lactulose. PEG 3350 was significantly more effective than lactulose (% effective, PEG 3350 (n=37): 84 vs. lactulose (n=37): 46; $p=0.002$). Seventy-three percent of patients said they preferred PEG 3350 as compared to 27% who said they preferred lactulose. Seven patients withdrew during the first 2-week treatment period due to lack of efficacy of the assigned intervention: six of these patients were taking lactulose at the time of withdrawal.

Osmotic laxatives vs. osmotic laxatives: Polyethylene glycol (PEG) 3350 without added electrolytes vs. magnesium oxide (milk of magnesia (MOM))

A prospective cohort study conducted in the USA[69] (2002) [EL=2+] determined the efficiency, acceptability, and treatment dosage of PEG 3350 without electrolytes (MiraLax®) during a 12-month treatment period in children with idiopathic constipation and encopresis. Forty-nine children ≥4 years of age referred for idiopathic constipation and encopresis of more than 1 year duration were included. Twenty-eight children (20 boys, mean age ± SD: 8.7 ± 3.6 years, range 4.1 to 17.5 years) received PEG 3350 17g dissolved in 240 ml of a beverage such as juice or Kool-Aid at an initial dose of 0.5 to 1g/kg/daily. Twenty-one children (17 boys mean ± SD: 7.3 ± 3.0 years; range: 4.0 to 13.9 years) received MOM at an initial dose of 1 to 2.5 ml/kg. Large laxative dosages could be divided into two daily doses. Parents were told to adjust the dose of medication by 30ml for PEG 3350 and by 7.5ml (one-half tablespoon) for MOM every 3 days to a dosage that resulted in 1 to 2 soft bowel movements/day and prevented soiling and abdominal pain. If the child retained stools despite compliance with assigned laxative, daily senna was added to treatment. Treatment lasted 12 months. Children were assessed at 1, 3, 6, and 12 months after initiating treatment. Bowel movement frequency was not significantly different between the 2 treatment groups at any of the 4 assessment points. The frequency of soiling (mean, results are estimates taken form bar chart as not reported in text) decreased significantly more in children taking MOM as compared to children taking PEG 3350 at 1 and 12 months (1 month PEG: 3.0 vs. MOM: 0.5; 12 months PEG: 0.9 vs. MOM: 0.1; $p<0.01$ for both assessment points), there were no significant differences between the 2 groups at 3 and 6 months. The medication dosage (mean doses and range) for children who were doing well or improved (PEG, g/kg; MOM, ml/kg) was 0.6 ± 0.2 (0.3 to 1.1) for PEG and 1.4 ± 0.6 (0.6 to 2.6) for MOM at 1 month; and 0.6 ± 0.3 (0.3 to 1.4) for PEG and 1.2 ± 0.5 (0.6 to 2.4) for MOM at 3 months. At 12 months the dose for PEG was: 0.4 ± 0.1(0.1 to 0.7). Only two children still required MOM at 12 months. Their dosages were 0.4 and 1.6 ml/kg, both less than the initial treatment dosage. The mean doses for both treatments at 12 months did not differ significantly between children with or without initial palpable abdominal faecal masses. None of the patients required an increased dosage of either medication over time. Five children received a stimulant laxative in addition to PEG 3350 and 1 child received a stimulant laxative in addition to MOM ($p>0.2$). No children reported disliking the taste of PEG 3350 and no parents reported that their child refused to take it in juice or Kool-Aid. At 12 months thirty-three percent of children refused to take MOM and they were rated as not doing well because were taking Miralax® instead. They were exclude form the outcomes reported at previous assessment points

An open label RCT conducted in the USA[70] (2006) [EL=1-] compared the efficacy, safety and patient acceptance of PEG 3350 without added electrolytes vs. magnesium oxide (milk of magnesia, MOM) over 12 months. Seventy-nine children (65 boys, age range: 4 to 16.2 years (median 7.4; mean 8.1 ± 3.0) diagnosed with idiopathic constipation with faecal incontinence were included. Children were randomised to receive PEG 3350 0.7 g/kg body weight daily for 12 months or MOM 2ml/kg body weight daily for 12 months. If necessary, children were disimpacted with 1 or 2 phosphate enemas before starting laxative therapy. There were no significant differences at baseline between the two groups. Both the improvement and the recovery rates at 12 months (%) were not significantly different for children taking PEG 3350 compared to children taking MOM (PEG (n=34): 62; MOM (n=21): 43 and PEG (n=34): 33; MOM (n=21): 23 respectively). At 12 months the frequency of bowel movements and the frequency of episodes of faecal incontinence were not significantly different between children taking PEG and children taking MOM. Two children (5%) continued to refuse PEG vs. 14 children (35%) continued to refuse MOM during the 12 months of the study ($p<0.001$). By 12 months there was a total of 27 children who had left the study or were lost to follow-up (PEG: 7/39 vs. MOM 20/40). In the PEG 3350 group two children were lost to follow-up monitoring, two had refused PEG 3350, one child was allergic to PEG and two children were receiving senna. These seven children were counted as not improved and not recovered. In the MOM group two children were lost to follow-up monitoring, three children had discontinued study participation, 14 children (35%) had refused to take MOM, and 1 child was receiving senna. Treatment doses (mean ± SD) at 1 month were 0.7 ± 0.2 g/kg body weight for PEG and 1.2 ± 0.7 mL/kg body weight. At 3 months doses were 0.6 ± 0.3 g/kg body weight for PEG and 1.2 ± 0.8 for MOM. Mean treatment doses were similar in children who improved and those who did not improve for both treatments.

Osmotic laxatives vs. stimulant laxatives

An open label RCT (crossover) conducted in the UK[71] (1977) [EL=1-] compared effectiveness and side effects between a standardised senna syrup and lactulose in the treatment of childhood idiopathic constipation. Twenty-one children aged <15 years with a history of constipation treated at home for 3 months or more were included. Children were randomised to receive either senna syrup (10 to 20 ml daily) for 2 weeks or lactulose (10 to 15 ml daily) for 2 weeks with 1 intermediate week with no treatment. Each preparation was given throughout the appropriate treatment week in a daily dose varied according to the age of the child. The number of patients passing stools of any kind each day was not significantly different for children taking lactulose as compared to children taking senna. The number of patients passing normal stools each day was significantly larger in patients taking lactulose as compared to patients taking senna (lactulose: 13.4 vs. senna: 8.43; p<0.01). One patient on senna at the beginning of study failed to attend at the end of the 1st week assessment but was included in the analysis.

Osmotic laxatives vs. faecal softeners

An open label RCT conducted in Iran [72] (2007) [EL=1-] compared the clinical efficacy and safety of liquid paraffin and lactulose in the treatment of idiopathic childhood constipation. Two hundred and forty-seven children (127 male) with chronic idiopathic constipation aged 2 to 12 years old (mean 4.1± 2.1 years) were included in the study. All children received 1 or 2 enemas daily for 2 days to clear any rectal impaction (30cc/10 kg of paraffin oil). Children were randomised to received either liquid paraffin orally, 1 to 2 ml/kg, twice daily for 8 weeks or lactulose orally, 1 to 2 ml/kg, twice daily for 8 weeks. For determination of the best dose for each child, parents were asked to increase the volume of each drug by 25% every 3 days as required to yield 1 or 2, firm-loose stools. Outcomes were measured during the first 4 weeks and during the last 4 weeks of treatment. Stool frequency per week (mean ± SD) during the first and last 4 weeks of treatment increased significantly more in children taking liquid paraffin (n=127) as compared to children taking lactulose (n=120): (first 4 weeks 12.1 ± 3.2 vs. 9.2 ± 2.1; p<0.001) (last 4 weeks 13.1 ± 2.3 vs. 8.1 ± 3.1; p<0.001). Encopresis frequency per week (mean ± SD) during the first 4 weeks of treatment decreased significantly more in children taking liquid paraffin compared to children taking lactulose (first 4 weeks: 1 ± 4.3 vs. 2 ± 4.6; p=0.07). During the last 4 weeks no child on liquid paraffin experienced encopresis as compared to a frequency of 3 ± 4.1 in children taking lactulose; p<0.001. Success rate (%) was significantly larger during the first 4 weeks and at the end of 8 weeks of treatment in children taking liquid paraffin compared to children taking lactulose (first 4 weeks: 90 vs. 52; p<0.001), (end of 8 weeks: 85 vs. 29; p<0.001). The final effective dose (mean, ml/kg/day) was significantly larger in children taking lactulose as compared to children taking liquid paraffin (2.08 ± 0.21 vs. 1.72 ± 0.13; p<0.001).

An open label RCT conducted in Turkey [73] (2005) [EL=1-] determined and compared efficacy, safety and optimal dose of liquid paraffin and lactulose in children with chronic idiopathic constipation. Forty children aged 2 to 12 years old (22 male, mean age 3.7 ± 2.7 years) referred for evaluation of constipation with evidence of faecal impaction were included. Children were randomised to receive either liquid paraffin or lactulose for 8 weeks. The medication was administered orally as a suspension at 1 ml/kg, twice daily for each drug. For determination of the best dose for each child, parents were asked to increase or decrease the volume of each drug by 25% every 3 days as required, to yield 2 firm-loose stools per day. The maximum dose used throughout the study was 3ml/kg per day for each drug. Outcomes were measured at 4 and 8 weeks after initiation of treatment. The stool consistency (mean ± SD) during the first 4 weeks of treatment improved significantly more for children taking lactulose (n=20) as compared to children taking liquid paraffin (n=20) (1.71 ± 0.5 vs. 2.17 ± 0.5; p<0.01). There were no significant differences in stool consistency when comparing both groups during the last 4 weeks of treatment. The stool frequency per week (mean ± SD) increased significantly more in children taking liquid paraffin as compared to children taking lactulose, both during the first and the last 4 weeks of treatment (first 4 weeks: 13.3 ± 4.2 vs. 10.2 ± 4.4; p<0.05), (last 4 weeks: 16.1 ± 2.2 vs. 12.3 ± 6.6; p<0.05). The optimal dose of drugs (mean ± SD, ml/kg/day) was not significantly different for children taking liquid paraffin as compared to children taking lactulose (1.88 ± 0.27 vs. 2.08 ± 0.27). (These data were reported in a table, it was assumed that this represented the whole study period.) Data reported in text for the last 4 weeks of treatment established the optimal dose for liquid paraffin was 1.72 ± 0.18 and for lactulose it was 1.82 ± 0.57). Compliance rate during the first 4 weeks of treatment was not significantly different when comparing both groups. At the end of 8 weeks significantly more children complied with taking liquid paraffin than children complied with taking lactulose (n=90% vs. n=60%; p=0.02).

Stimulant laxatives vs. faecal softeners

A single blind RCT conducted in the USA [74] (1982) [EL=1-] compared the efficacy of mineral oil and standardised senna concentrate (Senokot) in the treatment of idiopathic constipation in children. Thirty-seven children aged 3 to 12 years treated for chronic idiopathic constipation in a specialist clinic were included. Children received a 5-day course of oral bisacodyl (most patients) and daily enema for 3-5 days in addition (a minority). Children were randomised into 2 groups. Group 1 (n=19) received mineral oil orally twice daily in doses sufficient to induce loose stools and leakage of oil per rectum. After the first week of treatment, the dose was reduced until the leakage ceased. This dose (range 1.5 to 5.0 ml/kg/day) was maintained for minimum of 3 months. The second group (n=18) received Senokot (tablet or syrup), in dose sufficient to induce at least 1 bowel movement daily during the first 2 weeks of treatment. This dose was maintained for 3 months. Tapering was accomplished by changing from daily to every other day and then every 3rd day of medication. Treatment lasted approximately 6 months. Children in the mineral oil group were followed up for an average of 10.1 months; children in the Senokot group were followed up an average of 10.5 months. At 1 month the percentage of patients experiencing daily bowel movement was not significantly different when comparing the two groups. At 3 months all children on mineral oil were experiencing daily bowel movements as compared to 72% of children on Senokot ($p<0.05$). At the final follow-up significantly more children on mineral oil were experiencing daily bowel movements as compared to children on Senokot® (mineral oil: 89% vs. Senokot 50%; $p<0.05$). At all 3 assessment points daily soiling (% patients) decreased significantly more in children taking mineral oil as compared to children taking Senokot (at 1 month: Mineral oil 11%, Senokot 39%; $p<0.05$; at 3 months: Mineral oil: 11%, Senokot: 50%; $p<0.05$, final follow-up: mineral oil: 6%, Senokot: 44%; $p<0.05$). Sixty-eight per cent of children on mineral oil were reliably compliant with medication during the first 3 months of treatment as compared to 78% of children on Senokot. Fifty-five per cent of children on mineral oil successfully discontinued regular medication at the latest follow-up compared to 22% children on Senokot. An additional 33% of children discontinued Senokot® because of unacceptable symptom control. Forty-five per cent of children in each group remained on regular medication. There were significantly more episodes of symptoms recurrence /treatment/ month in children taking Senokot® as compared to children taking mineral oil (mean ± SD, Senokot: 0.34 ± 0.36, mineral oil: 0.09 ± 0.08; $p<0.01$). There were no significant baseline differences between the two groups regarding mean age, median age at onset of symptoms, percent of patients who had received prior treatment with constipation sex ratio, faecal soiling, overt retentive behaviour, enuresis, "difficult" toilet training and primary failure of toilet training. One patient on mineral oil was lost to follow-up after the 3-month visit and not considered in the results. There was no attrition/loss to follow-up in the Senokot group.

Laxatives vs. placebo:

Osmotic laxatives vs. placebo

A double-blind RCT (cross over, multicentre) conducted in the UK[75] (2008) [EL=1+] assessed the efficacy and safety of PEG 3350+E for the treatment of chronic idiopathic constipation in children. Fifty-one children (29 girls) aged 24 months to

11 years with chronic constipation for at least 3 months were included. Children were randomised to receive PEG 3350+E (6.9g powder/sachet) or placebo (6.9g powder/sachet) for 2 weeks with a 2-week washout period in between. The dosing regime for PEG 3350+E and placebo (number sachets/day) for children aged 2 to 6 years was: days 1-2 (1), days 3-4 (2, taken together), days 5-6: (3: 2 morning, 1 evening) and days 7-8: (4: 2 morning, 2 evening). For children aged 7 to 11 years the dosing regime was: days 1-2 (2, taken together), days 3-4 (2, taken together), days 5-6 (5, 2 in the morning, 3 in the evening) and days 7-8 (6, 3 in the morning, 3 in the evening). For both groups if diarrhoea was present, doses were decreased by 2 sachets or parents were instructed to miss a day of medication. If there were loose stools doses were decreased by 1 sachet. Children on PEG 3350+E experienced significantly more complete defecations per week compared to children on placebo, both for the intention to treat (ITT) population (mean (SD), range) PEG+E (n=47): 3.12 (2.050), 0.00 to 8.87 vs. placebo (n=48): 1.45 (1.202), 0.00 to 3.73, treatment difference: 1.64; $p<0.001$ (95% CI 0.99 to 2.28)) and the per protocol (PP) population (PEG+E (n=36): 3.63 (1.980), 0.00 to 8.87 vs. placebo (n=36): 1.63 (1.229), 0.00 to 3.73, treatment difference: 1.96; $p<0.001$ (1.19 to 2.72)). Data do not include the washout period. Children on PEG 3350+E (ITT population) experienced significantly more defecations in general (mean (SD)) as compared to children on placebo (PEG+E (n=47): 5.68 (2.771) vs. placebo (n=47): 4.10 (2.503), treatment difference: 1.58; $p=0.003$ (95% CI 0.55 to 2.60)). Children on PEG 3350+E (ITT population) experienced significantly less pain on defecation (mean (SD)) as compared to children on placebo (PEG+E (n=47): 0.49 (0.727) vs. placebo (n=47): 0.77 (0.863), treatment difference: -0.28; $p=0.041$ (05% CI -0.52 to -0.01)). Children on PEG 3350+E (ITT population) experienced significantly less straining on defecation (mean (SD)) as compared to children on placebo (PEG+E (n=47): 0.72 (0.789) vs. placebo (n=47): 1.37 (1.041), treatment difference: -0.65; $p=0.001$ (95%CI -0.97 to -0.33)). The stool consistency improved significantly more in children on PEG 3350+E as compared to children on placebo (PEG+E (n=47): 1.73 (0.497) vs. placebo (n=47): 2.21 (0.556), treatment difference: -0.48; $p=0.001$ (95% CI -0.68 to -0.27)). The percentage of hard stools decreased significantly more in children on PEG 3350+E as compared to children on placebo (PEG+E (n=47): 14.64 (26.041) vs. placebo (n = 47): 38.19 (39.508), treatment difference: -23.55; $p<0.001$). There were no significant differences between children on PEG 3350+E and children on placebo regarding abdominal pain on defecation and faecal incontinence. The mean effective dose of PEG 3350+E (g/kg/day) in 2 to 6-year-old children was 0.6 and in 7 to 11-year-old children it was 0.7.

One double-blind RCT (multicentre) conducted in the USA [76] (2008) [EL=1+] established the efficacy and best starting dose of PEG 3350 in the short-term treatment of children with idiopathic constipation. One hundred and three children aged 4 to 16 years (69 boys, mean age: 8.5 ± 3 years) with chronic constipation were included. Patients taking other laxatives were only included if they had <3 bowel movements/week while taking the laxative. All children received behavioural treatment consisting of instructions to sit on the toilet for 10 minutes twice after meals, positive reinforcement using age-appropriate printed calendars and special stickers for days without episodes of faecal incontinence and others with bowel movements. Children were randomly assigned in blinded fashion in a 1:1:1:1 ratio within each participant site into 4 groups: group 1 received PEG 3350 (Miralax®) at 0.2g/kg per day-single dose (maximum: 8.5g per day), group 2 received PEG 3350 at 0.4g/kg per day-single dose (maximum: 17g per day), group 3 received PEG 3350 at 0.8g/kg per day-single dose (maximum: 34g per day) and the last group received a placebo. Treatment lasted 3 weeks. Assessments were conducted at 7 and 14 days after medication started. Response to treatment was defined as ≥3 bowel movements (BM) during the second week of treatment. Patients were considered failures and withdrawn from study if they had no BM for 7 days or developed faecal impaction at any point; however intention to treat analysis was performed. There were no significant differences in baseline characteristics between the 4 groups. The proportion of children who responded to treatment (% children) was significantly higher when comparing all and each treatment groups with placebo (group 1 (n=26): 77, group 2 (n=27): 74, group 3 (n=26): 73, placebo (n=24): 42; $p<0.04$ each group vs. placebo; $p=0.026$ all treatments groups vs. placebo). There were no significant differences between treatment groups regarding this outcome. There were no significant predictors of success by controlling for age, duration of constipation, prior laxative use, presence of stool in rectum, sex and presence of faecal incontinence at baseline. There was a significant increase in the final number of bowel movements in the different treatment groups as compared to placebo (overall difference between treatment groups and placebo $p=0.017$; $p=0.015$ dose-response trend) (note: figures for the after treatment reported in graph from which it is difficult to extract the data). There was no significant difference in weekly number of faecal incontinence episodes amongst the 4 groups. Stool consistency became softer in all treatments groups as compared with placebo, and comparing all treatment groups with each other (changes in stool consistency (mean ± SD): group 1 (n=26): before 2.8±0.8, after 2.1±0.7; group 2 (n=27): before 2.6±0.9, after 1.7±0.6; group 3 (n=26): before 2.9±0.7, after 1.5±0.7; placebo (n=24): before 3.0±0.8 after 2.4±0.9; $p<0.003$ each group vs. placebo, $p<0.003$ test for trend, $p<0.003$ overall difference amongst treatment groups). Straining decreased in all treatments groups as compared with placebo, particularly for those in group 2 and group 3 (straining scores (mean ± SD): group 1 (n=26): before 2.3±1.1, after 1.4±0.9; group 2 (n=27): before 1.9±1.2, after 1.0±1.0; group 3 (n=26): before 2.0±1.0 after 0.9±0.6; placebo (n=24): before 2.7±1.2 after 1.5±1.2; $p<0.003$ each group vs. placebo, $p<0.003$ test for trend, $p<0.003$ overall difference between treatment groups). There were no significant difference amongst groups regarding incidence and severity of adverse effects (group 1: 9/26 (34.6%), group 2: 16/27 (59.3%), group 3: 17/26 (65.4%), placebo: 14/24 (58.3%)). There were no differences in the type of non-gastrointestinal (GI) related events, the most common was headache. There was a higher incidence of GI-related events in patients receiving PEG vs. placebo. As the dose of PEG increased, it also increased incidence of flatulence, abdominal pain, nausea and diarrhoea. There were no electrolyte abnormalities or differences in laboratory values amongst groups. Treatment failure was similar in all treatment groups but lower than the placebo (number of children who failed: group 1: 6/26 (4 BM frequency criteria, 2 with stool impaction), group 2: 7/27 (3 BM frequency criteria, 4 with stool impaction), group 3: 7/26 (6 BM frequency criteria, 1 with stool impaction), placebo (n=24): 14 (all related to BM frequency criteria)). Fourteen patients did not complete the 2-week treatment: 8 because of treatment failure (5 with impaction (2 Group 1, 3 Group 2), and 3 with >7 days without a BM) (2 Group 1, 1 Group 3)), 3 because of adverse events. There was 1 withdrawal (lack of response (placebo)) and 2 non cases of non-compliance (1 Group 2, 1 Group 3). Three serious adverse events occurred requiring hospitalisation (2 cases of impaction and 1 case of exacerbation of bipolar/depression).

Laxatives vs. other interventions:

Laxatives vs. biofeedback

An open label RCT conducted in the USA [77] (1987) [EL=1-] evaluated the efficacy of biofeedback for childhood encopresis. Fifty children (40 boys) aged 6 to 15 years (mean 8.4) with encopresis of at least 6 months of duration were included. Children were randomised to receive either one 25 to 30 minute biofeedback session with reinforcement sessions at 2, 4 and 8 weeks or mineral oil orally in graded amounts (range 1 to 4 tablespoons/day), designed to induce a soft bowel movement daily for 12 weeks. Children were followed up at 3, 6 and 12 months, and outcome measures were frequency of defecation, frequency of gross incontinence, frequency of staining or minor soiling and parental perception of clinical status and overall satisfaction. Based on the previous, children were placed in groups at each assessment: 1-some improvement, 2-some improvement, but major soiling (<1/week), 3-marked improvement (rare major soiling <1/week or minor soiling) and 4-complete remission. There were no significance differences in percentage of children in remission or markedly improved receiving either treatment at 3, 6 or 12 months. At baseline the 2 groups were comparable with respect to age, sex, duration and severity of soiling, anorectal motility parameters and expulsion patterns. There were 2 children who left the study at 3 months (1 from each group) and 3 additional children who left at 6 months (2 on biofeedback). Five children were lost to follow-up at 12 months (3 on biofeedback). All withdrawals were designated as treatment failures for each subsequent assessment point.

Laxatives vs. behavioural intervention

A quasi RCT conducted in the UK [78] (1983) [EL=1-] assessed whether behaviour therapy would suffice on its own in the treatment of severe and persistent faecal soiling or would be improved by employing a laxative as well. Forty-four children (mean age 7.9 years (SD=2.3), gender not reported) who had soiling as a main complaint and uncomplicated idiopathic faecal incontinence after an initial assessment and physical examination were included. All children received behavioural treatment, focusing on use of the toilet and freedom from soiling. Children were quasi randomised into 3 groups to receive either Senokot® placebo tablets in similar dosage to Senokot® or no medication at all. Senokot® and placebo tablets were started at a dose of 1 tablet at night. On the next visit to the clinic, if there were no improvement in the 'use of the toilet' and 'being clean' on the charts the dosage was increased to 2 tablets. The number of tablets was increased to 3 on the following visit if improvement had still not occurred. When the soiling was getting better and the child was using the toilet the dosage was kept the same. Once the child was having regular bowel movements in the toilet and not soiling the tablets were stopped altogether. The duration of treatment was 3 months and after that children were assessed for severity of soiling and number of soiling-free children noted. The severity of soiling and the number of soiling-free children at 3 months were not significantly different between the 3 groups. (Severity of soiling at 3 months: outcomes not reported by group), ((number of soiling-free children): relieved (less than once/week or not at all): Senokot® (n=14): 5 (35%) vs. placebo (n=11): 2 (18%); not relieved: Senokot® (n=14): 9 vs. placebo (n=11): 9.

Laxatives vs. probiotics

A double blind RCT conducted in Taiwan [79] (2007) [EL=1+] investigated the effect of probiotics (Lactobacillus case rhamnosus, Lcr35) alone in the treatment of chronic constipation in children and to compare the effect with magnesium oxide (MgO) and placebo, respectively. Forty-five children (23 male) under 10 years old with chronic idiopathic constipation were included. Children were randomised into 3 groups to receive MgO 50 mg/kg per day, twice a day, Lcr35 8x108 colony forming units/day (Antiobiophilus 250mg, 2 capsules, twice a day) or placebo (starch) during 4 weeks. Lactulose use (1ml/kg/day) was allowed when there was no stool passage noted for 3 days. Glycerine enema was used only when there was no defecation for >5days or when abdominal pain was suffered due to stool impaction. Defecation frequency (times/day) significantly increased in children taking both MgO and probiotic as compared to placebo (MgO (n=18): 0.55 ± 0.13; probiotic (n=18): 0.57 ± 0.17; placebo (n=9): 0.37 ± 0.10; p=0.006 (placebo vs. probiotic); p=0.01 (MgO vs. placebo)) but there were no significant differences between children taking probiotic and children taking MgO regarding this outcome. The percentage of children having hard stools was significantly lower in children taking both MgO and probiotic as compared to placebo (MgO (n=18): 23.5 ± 7.9; probiotic (n=18): 22.4 ± 14.7; placebo (n=9): 75.5 ± 6.1; p=0.02 (placebo vs. probiotic); p=0.03 (MgO vs. placebo)) but there were no significant differences between children taking probiotic and children taking MgO regarding this outcome. Children taking placebo had to make use of glycerine enema significantly more often than children taking either MgO or placebo (number of times, mean, SD, MgO (n=18): 1.3 ± 1.9, probiotic (n=18): 1.6 ± 1.9, placebo (n=9): 4.0 ± 2.1; placebo vs. probiotic p=0.04; MgO vs. placebo; p=0.03) but there were no significant differences between children taking probiotic and children taking MgO regarding this outcome. There were no significant differences regarding use of lactulose and faecal soiling amongst the three groups. Significantly more patients were successfully treated with MgO or probiotic as compared to placebo ((%), MgO (n=18): 72.2, probiotic (n=18): 77.8, placebo (n=9): 11.1, placebo vs. probiotic p=0.01; MgO vs. placebo p=0.01) but there were no significant differences between children taking probiotic and children taking MgO regarding this outcome. No adverse effects were noted in the probiotic and placebo groups and only 1 patient in the MgO group suffered from mild diarrhoea. There were no significant differences at baseline amongst the 3 groups regarding: sex, age of enrolment, age of onset of constipation, duration of constipation, previous treatment, defecation period, stool consistency, abdominal pain, faecal soiling, bleeding during defecation, use of enema and taking fruits or vegetables daily. Four patients discontinued medication during the study period: 2 in the MgO, 1 in the probiotic and 1 in the placebo group. 2 patients suffered form acute gastroenteritis (not clear whether as a consequence of the study medication) and 2 patients were lost to follow-up.

Evidence statement

Laxatives vs. laxatives:

Osmotic laxatives vs. osmotic laxatives: PEG vs. lactulose:

One metanalysis of 4 RCTs (3 [EL=1+], 1 [EL=1-])] comparing polyethylene glycol (PEG) vs. lactulose showed that treatment success was significantly higher for PEG as compared to lactulose.

Evidence statements for individual outcomes:

One double blind RCT [EL=1+] showed that PEG 3350+E was more effective than lactulose at increasing the number of successful defecations/week. One double blind RCT [EL=1+] showed that PEG 3350+E was as effective as lactulose at increasing the number of defecations/week. One open label RCT (crossover) [EL=1-] showed that PEG 3350 without E was as effective as lactulose at increasing the number of defecations/week. One double blind-RCT showed that PEG 3350 without E was as effective as lactulose at increasing the stool frequency for babies (aged 6 months to 12 months) at day 42 of treatment, but PEG 3350 without E was more effective than lactulose at increasing the stool frequency for toddlers (aged 13 months to 3 years) at day 42 of treatment. At day 84 both treatments were equally effective in both babies and toddlers.

Two double blind RCTs [EL=1+] showed that PEG 3350+E was as effective as lactulose at decreasing soiling frequency. Two double blind-RCTs [EL=1+] showed that faecal impaction was diagnosed in significantly more patients taking lactulose as compared to children taking PEG 4000 (in 1 of the studies no children taking PEG+E reimpacted).

One double blind RCT [EL=1+] showed that PEG 3350+E was as effective as lactulose at reducing the pain and straining on passing stools. An open label RCT (crossover) [EL=1-] showed that PEG 3350 without E was as effective as lactulose at improving the easy of stool passage.

One double blind RCT [EL=1+] showed that PEG 3350+E was as effective as lactulose at changing the predominant bowel movement form. One double blind-RCT [EL=1+] showed that PEG 3350 without E was more effective than lactulose at reducing the number of children reporting hard stools. One open label RCT (crossover) [EL=1-] showed that PEG 3350 without E was as effective as lactulose at changing the stool form.

Two double blind RCTs [EL=1+] showed that significantly more sachets a day were taken by children on lactulose as compared to children on PEG 3350+E. One double blind RCT [EL=1+] showed that no children taking PEG 3350+E needed to use senna as rescue medication whereas 8 children taking lactulose did. One double blind-RCT showed that significantly more children taking lactulose reported using enemas as compared to children taking PEG 4000 without E. There were no significant differences in the doses used for both medications in either babies or toddlers.

One double blind RCT [EL=1+] showed that overall assessment of treatment was not significantly different for children taking PEG 3350+E as compared to children taking lactulose. One double blind RCT [EL=1+] showed that success percentages were significantly greater for children taking PEG 3350+E as compared to children taking lactulose. Overall treatment success was independent of age (<6 years and ≥6 years) and use of laxatives for more than 1 year prior to the start of the study. In children previously treated for less than 1 year PEG 3350+E was significantly more successful than lactulose. One open label RCT (crossover) [EL=1-] showed that overall PEG 3350 was significantly more effective than lactulose. One double blind-RCT [EL=1+] of PEG 3350 without E vs. lactulose showed that treatment stopped in one child in the lactulose group because of lack of efficacy, whereas no children on PEG 3350 without E stopped therapy for this reason.

One open label RCT (crossover) [EL=1-] PEG 3350 vs. lactulose showed that 73% of patients said they preferred PEG 3350 as compared to 27% who said they preferred lactulose.

One double blind RCT [EL=1+] of PEG 3350+E vs. lactulose showed that 64% of children on PEG+E (n=27) experienced adverse effects as compared to 83% of children on lactulose. There was a similar incidence of adverse effects in each age group. The most commonly reported events were gastrointestinal and these resolved during the study. One double blind RCT comparing PEG 3350+E vs. lactulose showed that no serious or significant side effects were recorded. Significantly more adverse effects (abdominal pain, pain at defecation and straining at defecation) were seen in patients taking lactulose as compared to PEG. There were no significant differences between the two groups regarding: bloating, diarrhoea, flatulence, nausea, hard stool consistency and vomiting. Significantly more children complained of bad palatability of PEG compared to lactulose and this caused the premature withdrawal of one patient.

PEG (PEG) vs. milk of magnesia (MOM):

One open label RCT [EL=1-] and one prospective cohort [EL=2+] showed that PEG 3350 without E was as effective as MOM at increasing the number of defecations/week.

One open label RCT [EL=1-] showed that PEG 3350 without E was as effective as MOM at decreasing the frequency of episodes of faecal incontinence. One prospective cohort showed that the frequency of soiling decreased significantly more in children taking MOM as compared to children taking PEG 3350 without E at 1 and 12 months, but there were no significant differences between the two treatments at 3 and 6 months.

One open label RCT [EL=1-] showed that mean treatment doses of PEG 3350 without E vs. MOM were similar in children who improved and those who did not improve for both treatments. One prospective cohort [EL=2+] showed that the mean doses for both treatments at 12 months did not differ significantly between children with or without initial palpable abdominal faecal masses. None of the patients required an increased dosage of either medication over time. Five children received a stimulant laxative in addition to PEG and 1 child received a stimulant laxative in addition to MOM, but this was not significant.

One open label RCT [EL=1-] showed that both the improvement and the recovery rates at 12 months were not significantly different for children taking PEG as compared to children taking MOM .

Osmotic laxatives vs. faecal softeners:

Lactulose vs. liquid paraffin

Two open label RCTs [EL=1-] showed that liquid paraffin was more effective than lactulose at increasing the number of defecations/week.

Two open label RCTs [EL=1-] showed that liquid paraffin was more effective than lactulose at decreasing the frequency of soiling per week.

One open label RCT [EL=1-] showed that lactulose was more effective than liquid paraffin at improving the stool consistency during the first 4 weeks of treatment, but both laxatives were equally effective at improving the stool consistency during the last 4 weeks of treatment.

One open label RCT [EL=1-] showed that the optimal dose of drugs was not significantly different for children taking liquid paraffin as compared to children taking lactulose. One open label RCT [EL=1-] showed that the final effective dose was significantly larger in children taking lactulose as compared to children taking liquid paraffin.

One open label RCT [EL=1-] comparing liquid paraffin vs. lactulose showed that's success rate was significantly larger in children taking liquid paraffin as compared to children taking lactulose.

Osmotic laxatives vs. stimulant laxatives:

Lactulose vs. senna

One open label RCT (crossover) [EL=1-] showed that standardised senna syrup was as effective as lactulose at increasing the number of defecations/week. Standardised senna syrup was more effective than lactulose at increasing the number of patients passing normal stools each day.

Stimulant laxatives vs. faecal softeners:

Senna vs. mineral oil

1 single blind RCT [EL1-] showed that mineral oil was more effective than standardised senna (Senokot®) at increasing the percentage of patients experiencing daily bowel movements, and decreasing the number of children experiencing daily soiling. More children on mineral oil successfully discontinued regular medication at the latest follow-up compared to children on Senokot®. Despite better compliance, there were significantly more episodes of symptoms recurrence /treatment/ month in children taking Senokot® compared to children taking mineral oil.

Bulk forming laxatives:

No evidence was found for the clinical effectiveness of bulk forming laxatives for ongoing treatment/maintenance in children with chronic idiopathic constipation.

Laxatives vs. placebo:

PEG (PEG) vs. placebo:

One double-blind RCT (cross over, multicentre) [EL=1+] showed that PEG 3350+E (Movicol) was more effective than placebo at: increasing both the number of defections in general and the number of complete defecations per week, improving faecal incontinence, improving the stool consistency, decreasing the percentage of hard stools and reducing both pain and straining on defecation. Both treatments were equally effective at reducing abdominal pain on defecation.

One double-blind RCT (multicentre) [EL=1+] showed that PEG 3350 without electrolytes (Miralax®) was significantly more effective than placebo at increasing weekly frequency of bowel movements, improving stool consistency and decreasing straining on defection, but there was no significant difference in weekly number of faecal incontinence episodes amongst the treatment groups and placebo.

Laxatives vs. other interventions:

Milk of magnesia vs. probiotic vs. placebo

One double blind RCT [EL=1+] showed that probiotic and milk of magnesia (MgO) were equally effective at increasing daily defecation frequency and decreasing the percentage of children having hard stools, and both were more effective than placebo regarding these outcomes. The three treatments were equally effective at decreasing faecal soiling. Children taking a placebo had to make use of glycerine enema significantly more often than children taking either MgO or probiotic but that there were no significant differences between children taking probiotic and children taking MgO regarding this outcome. There were no significant differences between the three groups regarding the need to use of lactulose. Significantly more patients were successfully treated with MgO or probiotic as compared to placebo but there were no significant differences between children taking probiotic and children taking MgO regarding this outcome. Only one patient in the MgO group suffered from mild diarrhoea.

Mineral oil vs. biofeedback

One open label RCT [EL=1-] comparing mineral oil vs. biofeedback showed that there were no significance differences in percentage of children in remission or markedly improved after receiving either treatment at 3, 6 or 12 months.

Senna vs. placebo vs. behavioural therapy

One quasi RCT [EL=1-] comparing Senokot vs. placebo vs. behavioural therapy showed no significant difference in the severity of soiling and the number of soiling-free children at 3 months between the three groups.

Health economic considerations

An economic model for the maintenance phase of treatment post disimpaction was developed. The model covered maintenance treatment (pharmacological and Antegrade Continent Enema, or ACE procedure) for previously disimpacted children (aged between 2-11 yrs). The ACE strategy was included only as a last resort if other pharmacological strategies failed (see table E.6). Each cycle covered a three month period after initial disimpaction. Results are reported after three months, at the end of year one, (four cycles) and two years (eight cycles). The range of pharmacological treatment strategies described in the disimpaction model were were included, together with two additional treatments which are only offered in the maintenance phase: methylcellulose and liquid paraffin. This gave a total of 15 alternative strategies as first line treatment in the maintenance phase.

Using a modelling approach it was possible to calculate how much more effective a Movicol Paediatric Plain treatment strategy would have to be in the maintenance phase (3 months, one year, two years) in order for it to be cost-effective at the £20,000 per QALY threshold. Since Movicol Paediatric Plain costs more in the maintenance phase, it needs to be more effective for it to be the preferred option. It has been reported earlier (the disimpaction economic model) that higher priced therapeutic strategies with higher levels of effectiveness would become cheaper overall than treatment strategies with lower initial drug costs. It is possible to estimate how much more effective Movicol Paediatric Plain would have to be in order for it to be preferred to all other strategies in the maintenance phase on cost-effectiveness grounds.

The maintenance model showed that, unlike the disimpaction model, the cost of drugs in the pharmacological treatment alternatives had a greater impact on the total of care than hospitalisation, which widened the gap between the cheapest and most expensive treatment options.

The analysis suggested that an increase in effectiveness from 80% to just over 85% effectiveness in the first three months of treatment, (and less in the longer term) would make Movicol Paediatric Plain the more favourable option to the next best in alternative (Senna) in the maintenance phase.

GDG interpretation of the evidence

The GDG notes that the research evidence is limited and evidence is not available for the full range of medications used in clinical practice to treat idiopathic constipation. Many drugs have been used for a long time but have not been tested in clinical trials.

Clinical experience, available evidence and economic modelling support the use of oral PEG as first line treatment for both disimpaction and maintenance: PEG is cost-effective as monotherapy, works quickly and is well tolerated. PEG's full range of doses are licensed only for children >1 year old, but there is evidence from case series and clinical practice which shows that they are also effective in children <1 year. The GDG believes that further research is needed in this particular age group.

The GDG recognises that other medications, used singly or in combination, are available, effective and commonly used. The group's experience is that often children are under-treated because effective doses are outside licensing and therefore not prescribed by health professionals. It is the GDG's view that the optimal dose of any medication is the dose that works for a particular child. Optimal doses of laxatives are also more cost-effective because they prevent unnecessary consultations and treatment failure.

The GDG recognises that the child's/family's preference is an important factor in the success of treatment and must be given due consideration. The GDG believes that families need ongoing support from health care professionals with expertise in constipation

A significant number of children become constipated when there are younger than 1 year. These symptoms often coincide with weaning and changing milk feeds and they might not be recognised and treated. The GDG believes that despite their young age these children need early diagnosis and usually require medication to prevent potential long term problems. There is evidence from case series and clinical practice which shows that PEG is effective in children <1 year and the GDG is aware that it is currently used in practice. Other medications that are licensed for this age group are lactulose and docusate, which need to be given at the optimal dose. It is the GDG's view that the optimal dose of any medication is the dose that works for a particular infant.

5.3 Adverse effects of laxative use

Introduction

There is little published evidence to guide health professionals about the pharmacological management of chronic constipation. It is clear that there is no one treatment regime which will suit all children and there is a variety of approaches taken in different areas as well as large differences in practice regarding management.

In this section, we review the available evidence and make recommendations based on best available evidence both for disimpaction and maintenance regimes.

Clinical Question

What are the adverse effects of the medium- to long-term use of laxatives?

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation
- included adverse effects of the medium (6 months) and long tem (between 6 and 12 months or longer) use of the following laxatives (both oral and rectal medications): stimulant laxatives, osmotic laxatives and bulk forming laxatives
- included outcomes related to palatability*
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

A total of 237 articles were identified from the searches and 45 articles were retrieved for detailed assessment. Of these 14 studies were identified for inclusion in this review plus 1 paper submitted by a GDG expert advisor: 6 RCTs, 1 prospective cohort, 1 retrospective cohort, 4 prospective case series and 3 retrospective case series.

Narrative summary

An RCT (cross over, multicentre) conducted in the UK[75] (2007) [EL=1+] assessed the efficacy and safety of polyethylene glycol 3350 plus electrolytes (PEG+E)

* This outcome was added by the GDG as it was reported by children to be very important even though it cannot technically be considered an adverse effect

(Movicol) for the treatment of chronic constipation in children. Fifty-one children (29 girls) aged 24 months to 11 years with chronic constipation for at least 3 months were included. Children were randomised to receive PEG+E (6.9g powder/sachet) or placebo (6.9g powder/sachet) for 2 weeks with a 2-week washout period in-between. The dosing regime for PEG+E and placebo (number sachets/day) for children aged 2 to 6 years was: days 1-2 (1), days 3-4 (2: taken together), days 5-6: (3, 2 morning, 1 evening) and days 7-8: (4: 2 morning, 2 evening). For children aged 7 to 11 years the dosing regime was: days 1-2 (2, taken together), days 3-4 (2, taken together), days 5-6 (5: 2 in the morning, 3 in the evening) and days 7-8 (6: 3 in the morning, 3 in the evening). For both groups if diarrhoea was present, doses were decreased by 2 sachets or parents were instructed to miss a day of medication. If there were loose stools doses were decreased by 1 sachet. Safety was monitored by adverse events recording, physical examination findings, and weight changes. There were 31 adverse events on children taking PEG+E (63%) and 28 in children taking placebo (57%) during periods I and III. Most adverse effects were judged to be moderate or mild in severity. Twenty children (41%) on PEG+E experienced 41 events and 22 children (45%) on placebo experienced 45 events, judged by the investigator to be at least possibly related to the study treatment. Most of these events were gastro-intestinal disorders (particularly abdominal pain), 39 events (39%) in children on PEG+E and 41 events (45%) in children on placebo. One child in the placebo/PEG+E group withdrew from the study at week 3 because of abdominal pain, assessed by the investigator as being related to study treatment. This child was taking placebo at the time of withdrawal. New clinically significant abnormalities on physical examination (mainly associated with faecal loading) were found in 13 children (8/27 in the PEG+E/placebo group, 5/24 in the placebo/PEG+E group). When analysed for what these children were taking for the 2 weeks before the physical examination, 23 out of the 24 reports (95.8%) occurred when the child was taking placebo. Only one report of an abnormal abdominal examination occurred while the patient was on PEG+E. The mean weight was similar before and after treatment, and no significant difference was found between the two groups for change in weight while on treatment.

An RCT conducted in France[66] (2005) [EL= 1+] assessed the safety of a PEG 4000 laxative without additional salts in paediatric patients. Ninety-six children (51 male) aged 6 months to 3 years with constipation were included. Children were randomised to receive either PEG 4000 (non-branded) (starting dose: 1 sachet (4g) and 1 placebo to be taken at breakfast) or lactulose (starting dose: 1 sachet (3.33g) and 1 placebo to be taken at breakfast) for 3 months. For both drugs, the dose could be doubled if it was ineffective in children aged 13 months to 3 years. If the maximum authorised dose was unsuccessful, one micro-enema of glycerol per day could be prescribed for a maximum of 3 consecutive days. If the child did not produced stools after treatment 2 enemas could be administered at a 48 hour interval. This procedure was only allowed twice during the study. If the child produced liquid stools for more than 1 day or more than 2 or 3 stools/day depending on age, the dose could be decreased by 1 pair of sachets/day to a minimum of 1 pair of sachets every other day and possibly to transitory interruption. Stool frequency, abdominal pain, vomiting, and nausea were recorded by parents on a self-diary evaluation booklet. Six non serious adverse effects occurred during the study period (diarrhoea, 5 episodes in 2 children in both treatment groups and anorexia in 1 child on lactulose). Flatulence (either new onset or worsened) lasted significantly longer in children taking lactulose as compared to children taking PEG 4000 (days, median (interquartile range): PEG 4000: 3 (1 to 4.5) vs. lactulose: 5 (3 to 19.5); $p=0.005$). Vomiting episodes (either new onset or worsened) lasted significantly longer in children taking lactulose as compared to children taking PEG 4000 (days, median (interquartile range): PEG 4000: 1 (1 to 2) vs. Lactulose: 2 (1 to 6); $p<0.05$). Anal irritation was reported in 5% of the children (2/40, both on lactulose). There were no differences between PEG 4000 and lactulose groups with regard to other digestive tolerance outcomes. Body height and body weight were unaffected during the 3-month treatment for both boys and girls. There were no significant differences between treatment groups for the percentage of children with out of normal range values on D84 as compared to baseline status. No treatment-related changes were found in serum iron, electrolytes, total protein, albumin and vitamins A, D and folates. There were no significant differences in the doses used (sachets/day) (median (interquartile range)) for both medications in either babies or toddlers (Babies: 1 (0.9 to 1) PEG vs. 1 (1 to 1.3) lactulose); (Toddlers: 1 (1 to 1.3) PEG vs. 1.1 (0.9 to 1.5) lactulose). Treatment stopped in 1 child in the lactulose group because of lack of efficacy. There were no clinically relevant differences between the 2 treatment groups at baseline for clinical or biological parameters.

A prospective cohort conducted in the USA[69] (2002) [EL= 2+] determined the efficiency, acceptability, and treatment dosage of MiraLax® (polyethylene glycol 3350 without electrolytes) during a 12-month treatment period in children with functional constipation and encopresis. Forty-nine children ≥4 years of age referred for functional constipation and encopresis were included. For 12 months, 28 children (20 boys, mean age ± SD: 8.7 ± 3.6 years, range 4.1 to 17.5 years) received MiraLax® at an initial dose of 0.5 to 1g/kg/daily and 21 children (17 boys, mean ± SD: 7.3 ± 3.0 years, range: 4.0 to 13.9 years) received magnesium oxide (milk of magnesia, MOM) at an initial dose of 1 to 2.5ml/kg. Large laxative dosages could be divided into 2 daily doses. Parents were told to adjust the dose of medication by 30 ml for MiraLax® and by 7.5 ml (one-half tablespoon) for MOM every 3 days to a dosage that resulted in 1 to 2 soft bowel movements/day and prevented soiling and abdominal pain. If the child retained stools despite compliance with the assigned laxative, daily senna could be added to the treatment. Medication dosage, clinically significant side effects and compliance with medication were assessed at 1, 3, 6, and 12 months after initiating treatment. Patients and parents were provided with diary sheets to record each outcome measured. At 1 month the mean doses and range for children who were doing well or improved (PEG, g/kg; MOM, ml/kg) were 0.6 ± 0.2 (0.3 to 1.1) for PEG and 1.4 ± 0.6 (0.6 to 2.6) for MOM. At 3 months these were 0.6 ± 0.3 (0.3 to 1.4) for PEG and 1.2 ± 0.5 (0.6 to 2.4) for MOM. At 12 months the mean dose of PEG was 0.4 ± 0.1(0.1 to 0.7). Only 2 children still required MOM. Their dosages were 0.4 and 1.6 ml/kg, both less than the initial treatment dosage. The mean doses for both treatments at 12 months did not differ significantly between children with or without initial palpable abdominal faecal masses. None of the patients required an increased dosage of either medication over time. Five children received a stimulant laxative in addition to PEG and 1 child received a stimulant laxative in addition to MOM ($p>0.2$). Some children had diarrhoea (number not reported in paper). None of the children in the PEG group became dehydrated. Children receiving PEG and their parents did not report increased flatus, abdominal distension, or new onset of abdominal pain. These outcomes were not reported for MOM. No children reported disliking the taste of PEG and no parents reported that their child refused to take it in juice or Kool-Aid. Thirty-three percent of children refused to take MOM.

A retrospective case series conducted in the USA[80] (2003) [EL=3] reviewed the efficacy of PEG as a single agent for the treatment of constipation in children with dysfunctional elimination and to asses bladder function following treatment. Forty-six children (35 girls, mean age: 7.7 years (range 4.5 to 11.2 years); 11 boys mean age: 7.6 years (range 4.4 to 11.1 years) diagnosed with dysfunctional voiding and constipation who received polyethylene glycol (PEG) 3350 between January 2000 and July 2002 were included. All children received PEG 3350 without electrolytes (MiraLax®) at a starting dose of 8 ounces of mixture each day with instructions to adjust the amount consumed by 1 to 2 ounces every 3 days to achieve the goal of 1 to 2 soft bowel movements per day. The final dose was normalised according to patient weight and the average final dose was 0.63g/kg (as reported in abstract) or 0.59g/kg (as reported in text). The average duration of treatment was 194.3 days

(SD 133.5) and side effects were recorded. It is not clear how side effects were measured. Nine of forty-six children (all female) reported having diarrhoea. Children with diarrhoea were significantly younger at the start of PEG therapy than children without diarrhoea ((age: mean ± SD, years), patients with diarrhoea (n=9): 6.8 ± 1.1 vs. patients without diarrhoea (n=37): 8.2 ± 1.8; p=0.04). The duration of follow-up was significantly longer for children with diarrhoea as compared to children without diarrhoea ((time: mean ± SD, days), patients with diarrhoea (n=9): 336 ± 153 vs. patients without diarrhoea (n=37): 108 ± 11; p=0.0028). One child stopped taking PEG because of side effects.

A retrospective case series conducted in the USA[81] (2004) [EL=3] evaluated the safety and efficacy of PEG 3350 without electrolytes for the treatment of constipation in children <2 years of age. Seventy-five children (mean age 17 months (range 1 to 21 months) with constipation younger than 2 years of age at the start of PEG therapy were included. Children received PEG 3350 without electrolytes (MiraLax®) at a starting average dose of 1g/kg body weight/day. Parents were asked to adjust the dose to yield 1 to 2 soft painless stools per day. Adverse effects were measured at ≤4 months (short term, mean 2 months) and ≥6 months (long term, mean 11 months). The average duration of treatment (months, mean ± SD) at the short-term assessment was 2.3 ± 1.3 (range: 1 to 4) and at the long-term assessment it was 10.6 ± 8.1 (range 6 to 37). It is not completely clear how side effects were measured, but it seems that parents were asked about them at the time of consultation. At ≤4 months 5 children (7%) had experienced “runny stools”. The mean dose of PEG used (g/kg body weight/day) was 1.1 ± 1.2 (median 0.82, range 0.4 to 2.3). At ≥6 months 1 child had experienced watery stools. The diarrhoea disappeared after lowering the dose of PEG. The mean dose of PEG used (g/kg body weight/day) was 0.8 ± 0.4 (median 0.67, range 0.3 to 2.1). Parents did not report increased flatus, abdominal distension, vomiting or new onset abdominal pain. None of the children stopped PEG because of adverse effects. Complete blood counts (in 24 children), electrolytes (in 9 children), renal functions (in 8 children) and liver functions (in 8 children) were occasionally done in children on long-term PEG treatment, and all were within normal limits.

A retrospective case series conducted in the USA [82] (2004) [EL=3] determined safety, efficacy, and optimal dose of PEG powder for treatment of constipation in patients younger than 18 months. Twenty-eight children younger than 18 months treated for constipation with PEG powder were included. Children received PEG 3350* at an initial dose of 0.88 g/kg/day (range, 0.26-2.14 g/kg/day). After initial dose, families were asked to titrate the dose to obtain at least one non-formed bowel movement daily. Change in dose was permitted within 24 hours, if necessary. The mean duration of treatment was 6.2 ± 5 months (range, 3 weeks to 21 months). Children were assessed at an initial visit and subsequent visits every 8 to 12 weeks. The duration of therapy and side effects were retrieved from the patient’s chart and the information not available in the chart was obtained by telephone interview. It is not clear how side effects were measured in the first place. The mean effective maintenance dose was 0.78 g/kg/day (range, 0.26-1.26 g/kg/day). Side effects were recorded in 17.9% of patients. One infant (3.6%) experienced increased passage of gas per rectum, whereas 4 infants (14.3%) experienced transient diarrhoea that resolved after dose adjustment.

A prospective case series conducted in the USA[83] (2003) [EL=3] assessed the biochemical and clinical safety profile of long-term PEG 3350 treatment in a large cohort of children and also its paediatric patients’ acceptance. Eighty-five children older than 2 years (male/female 48/35; mean age 7.4 years (range 2.0-16.9 years) with chronic constipation who were treated daily with PEG for more than 3 months were included. For an average of 8.7 months (range, 3-30 months) all children

* Not reported whether with or without electrolytes, but probably without electrolytes as this is an American study and they generally use Miralax

received PEG 3350 without electrolytes (MiraLax®) orally at an initial dose of 0.8 g/kg per day. Parents were asked to adjust dose of PEG solution as required to yield 2 soft painless stools per day. Over time, parents were instructed to gradually decrease the dose of PEG if the symptoms of constipation and encopresis showed improvement. Adverse effects, both clinical and laboratory variables were assessed. Parents were interviewed using a structured questionnaire and asked about any possible adverse effects of PEG, and particularly about excessively loose or frequent stools, abdominal pain, flatulence, bloating, and nausea. Following interview and physical examination, 4ml of blood was obtained for measurement of different parameters. Clinical adverse effects were minor and over the mean duration of therapy. Eight patients (10%) experienced frequent watery stools some time during therapy, but diarrhoea disappeared with reduction of the dose. Five children (6%) experienced bloating or flatulence and two children (2%) abdominal pain. One patient each (1%) experienced each of the following: thirst, fatigue, and nausea after receiving PEG solution on an empty stomach. General physical examination findings revealed no new significant abnormalities as compared with the pre-treatment. None of the patients stopped treatment due to adverse effects and all were to continue PEG therapy. Laboratory evaluation results: haemoglobin, haematocrit, serum electrolytes, blood urea nitrogen, serum creatinine, serum albumin, and osmolality were normal in all patients (10 patients did not have serum osmolality measured). Ten patients (11%) had slightly elevated ALT level (<1.5 times the upper limit of normal; range, 31 to 45 U/L). Eight of these patients had ALT levels re-measured within 8 weeks, seven of whom were still receiving PEG therapy. Seven of these eight patients had values in the reference range, one had slightly elevated ALT level (<1.2 times normal; 28 U/L). Thre patients (4%) had an elevated aspartate aminotransferase level (<1.5 times normal; range, 42-52 U/L), and all had normal values when re-measured while still receiving PEG therapy. Both the dose and the duration of PEG therapy were not significantly different in patients with abnormal values as compared with those with laboratory values in the reference range.

A prospective case series conducted in Australia[84] (2007) [EL=3] evaluated the safety and efficacy of a PEG 3350-based electrolyte containing preparation in the treatment of chronic constipation in children. Seventy-seven children (44% boys, mean age: 4.9 ± 2.6 years) with chronic constipation for at least 6 months, which was either untreated or inadequately treated by laxatives were included. Children received PEG 3350 plus electrolytes (Movicol) for an average of 75.5 days. Starting dose (number of sachets/day) during the first 5 days was established according to children's age (children aged 2 to 6 years: days 1 & 2: 1, days 3 & 4: 1 twice, day 5: 1 three times and children aged 7 to 11 years: day 1 & 2: 1 twice and day 3, 4 & 5: 2 twice). Thereafter, and until end of the study, the dosage was titrated according to the faecal form. This dose was increased by 1 sachet/day in the event of continued hard stools/no bowel movements, and decreased by 1 to 2 sachets/day in the event of loose stools or diarrhoea. Adverse effects were monitored throughout the study: blood samples for laboratory were taken at baseline, 28 days and 84 days after initiating treatment. Vital signs were measured at baseline and 84 days after initiating treatment. It is not clear how other clinical adverse effects were collected. The mean numbers of sachets/day during the treatment period was 1.3 (6.9 g). Seventy-two children (92%) reported a total of 318 adverse events. Two hundred and forty-one (76%) of those events were assessed as unrelated to the study treatment, 262 (82%) were considered mild and 302 (95%) had resolved by the end of the study. Six serious adverse events occurred in 4 children: 4 affected the gastrointestinal system (the other 2 were not clearly reported). All of them were assessed by the investigator as unrelated or unlikely to be related to the study medication and were resolved at the end of the study. 1 serious adverse event (faecal impaction) led to 1 patient's premature withdrawal from study as the child was admitted to hospital for bowel washout. No clinically significant changes in vital signs as a result of the study medication were observed.

A prospective case series conducted in Sweden[85] (2005) [EL=3] assessed the effectiveness of Movicol (PEG 3350+E), over the course of long term treatment in children with constipation. One hundred and thirty-four children (88 males, age not clearly reported) referred with constipation and/or encopresis were included. All children received PEG 3350+E,13.8g sachets) at a mean starting dose of 0.58 sachets for children aged 2 to 6 years and 0.51 sachets for children aged 7 to 11 years. Doses were adjusted in each patient to achieve symptom relief with the minimally effective dosage. The mean duration of treatment was 50 weeks (SD ±50 weeks; range 1 to 211 weeks). The final treatment dose and side effects were recorded, but it is unclear how this was done. The mean dose at the end of the observational period was 0.42 sachets for children aged 2 to 6 years and 0.49 sachets for children aged 7 to 11 years. The overall mean change was 0.553 to 0.477 sachets per day. Side-effects were reported in 10 (7.5%) patients and these were reported as generally mild and transient.

An RCT conducted in the USA[70] (2006) [EL=1-] compared the efficacy, safety and patient acceptance of PEG 3350 without added electrolytes vs. magnesium oxide (milk of magnesia, MOM) over 12 months. Seventy-nine children (65 boys, age range: 4 to 16.2 years (median 7.4; mean 8.1 ± 3.0) diagnosed with functional constipation with faecal incontinence were included. Children were randomised to receive PEG 3350 without added electrolytes (MiraLax®) 0.7g/kg body weight daily for 12 months or MOM 2ml/kg body weight daily for 12 months. If it was necessary children were disimpacted with 1 or 2 phosphate enemas in the clinic on the day of the visit and then started laxative therapy that evening. Outcomes were patients' acceptance and adherence. Patients and their parents were questioned with respect to side effects during each visit. Several children complained about the taste of both PEG and MOM. Two children (5%) continued to refuse PEG vs. 14 children (35%) continued to refuse MOM during the 12 months of the study ($p<.001$). By 12 months there were a total of 27 children (34%) who had left the study or who were lost to follow-up. In the PEG group, two children were lost to follow-up monitoring, two (5%) had refused PEG, one child was allergic to PEG and two children were receiving senna. These seven children were counted as not improved and not recovered. In the MOM group two children were lost to follow-up, three children had discontinued study participation, 14 children (35%) had refused to take MOM, and one child was receiving senna. Treatment doses (mean ± SD) at 1 month were 0.7 ± 0.2 g/kg body weight for PEG and 1.2 ± 0.7 mL/kg body weight. At 3 months doses were 0.6 ± 0.3 g/kg body weight for PEG and 1.2 ± 0.8 for MOM. Mean treatment doses were similar in children who improved and those who did not improve for both treatments. There were no other significant clinical effects for either medication, apart from transient diarrhoea disappearing with dose reduction.

A retrospective cohort conducted in the USA [86] (2003) [EL=2-] reported efficacy of PEG therapy, effective dose and patient compliance separately for children with constipation and children with constipation and encopresis over the long term. Seventy-four children (40 boys) >2 years of age with chronic constipation treated daily with PEG 3350 without electrolytes (MiraLax®) for >3 months were included. Children received PEG 3350 without electrolytes at a starting dose of 0.8 g/kg/day. Parents were asked to adjust the dose as required to yield two soft painless stools per day. The average duration of the treatment was 8.4 months (range 3 to 30 months) and adverse effects were assessed. Some outcomes variables on effectiveness were gathered by interviewing patients/parents and examining patients, but it is unclear how data on adverse effects were obtained. The average dose of PEG at the time of evaluation was 0.73 g/kg/day (range 0.3 to 1.8) following adjustment of dose by the caretakers. No major clinical adverse effects were observed.

A prospective case series [EL=3] conducted in the USA [87] (1987) prospectively monitored children receiving large doses of mineral oil throughout the early phase of treatment. Twenty-five children (mean age: 7.83 years (range 1.75 to 14.27

years) with constipation, over 1 year old with no previous treatment with mineral oil were included. Following initial disimpaction children received mineral oil, 45ml twice daily between meals for a period of 4 months. The dose was gradually decreased on a monthly basis (usually 30 ml/month) depending on the patient's reported performance and the results of serial rectal examinations (mean dose ± SEM: month 1: 4.0 ± 1.4, month 2: 2.9 ± 1.2, month 3: 2.1 ± 0.5, month 4: 1.4 ± 0.4). Serum beta-carotene levels, retinol levels and alfa tocopherol levels were measured at baseline and at the end of every treatment month. Retinol levels (micromols/l (micrograms/dl), mean ± SEM) at 1 and 2 months were not significantly different from baseline values. After 3 months levels significantly increased as compared to baseline (baseline: 1.48 ± 0.84 (42.3 ± 24.1), treatment: 2.22 ± 0.77 (63.5 ± 22.1); $p<0.01$) but changes were not significant after 4 months. Serum beta-carotene levels (micromols/l (micrograms/dl), mean ± SEM) decreased significantly at 1 month, 2 months and 3 months when compared to baseline, but there were no significant differences after 4 months (month 1 (n=25): baseline: 1.0 ± 0.5, (55.7 ± 26.0) vs. treatment: 0.7± 0.4, (35.9 ± 22.1); $p<0.01$), (month 2 (n=17): baseline: 1.1 ± 0.6, (59.5 ± 30.6) vs. treatment: 0.7 ± 0.5, (38.2 ± 28.4); $p<0.05$), (month 3 (n=10): baseline: 1.1 ± 0.6 (60.4 ± 30.0), treatment: 0.6 ± 0.2, (34.7 ± 12.3); $p<0.05$). Serum alfa tocopherol levels remained relatively unchanged throughout the study. No statistical significant difference was found between baseline levels and those obtained throughout the 4 months of therapy.

An RCT (crossover) conducted in the UK [71] (1977) [EL=1-] compared effectiveness and side effects between a standardised senna syrup and lactulose in the treatment of childhood constipation. Twenty-one children aged <15 years with a history of constipation treated at home for 3 months or more were included. Children were randomised to receive either senna syrup (10 to 20 ml daily) for 2 weeks or lactulose (10 to 15 ml daily) for 2 weeks with 1 intermediate week with not treatment. Each preparation was given throughout the appropriate treatment week in a daily dose varied according to the age of the patient. Outcome measures were stool consistency, number of stools passed each day and adverse effects. These outcomes were recorded by parents in written diaries. There were significantly more adverse effects (number of patients) during the senna week (12: 8 colic, 1 diarrhoea, 2 colic + diarrhoea, 1 colic + distension) as compared to the lactulose week (1 colic) ($p<0.001$). There were no significant differences between the no-treatment week (4: 3 colic, 1 colic + distension) 1 patient on senna at the beginning of study failed to attend at the end of the 1st week assessment but was included in the analysis.

An RCT conducted in Iran [72] (2007) [EL=1-] compared the clinical, efficacy and safety of liquid paraffin and lactulose in the treatment of functional childhood constipation. Two hundred and forty-seven children with chronic functional constipation aged 2 to 12 years old (mean 4.1± 2.1 years) were included in the study. All children received 1 or 2 enemas daily for 2 days to clear any rectal impaction (30cc/10kg of paraffin oil). Children were randomised to received either liquid paraffin orally (n=127) 1 to 2 ml/kg, twice daily for 8 weeks or lactulose orally (n=120), 1 to 2 ml/kg, twice daily for 8 weeks. For determination of the best dose for each child, parents were asked to increase the volume of each drug by 25% every 3 days as required to yield 1 or 2, firm-loose stools. Outcome measures were optimal dose of drug and side effects. Parents received a chart to record side effects. The final effective dose (mean, ml/kg/day) was significantly larger in children taking lactulose as compared to children taking liquid paraffin (2.08 ± 0.21 vs. 1.72 ± 0.13; $p<0.001$). Apart from nausea and hard stool, side effects during weeks 4 to 12 were more frequent* in children taking liquid paraffin as compared to children taking lactulose: abdominal pain (50 vs. 10), bad palatability (40 vs. 15), pain at defecation (50 vs. 10), bloating (20 vs. 10), diarrhoea (30 vs. 10), anal oil

* Not clear whether these are number or percentage of children, but probably percentage. Estimates were taken from a bar chart, as outcomes were not reported in text.

leakage (40 vs. 20), flatulence (20 vs. 10), nausea (5 vs. 10) and hard stool (6 vs. 20). No children in either group experienced vomiting.

An RCT conducted in Turkey [73] (2005) [EL=1-] compared efficacy, safety and optimal dose of liquid paraffin and lactulose in children with chronic functional constipation. Forty children aged 2 to 12 years old (22 male, mean age 3.7 ± 2.7 years) referred for evaluation of constipation with evidence of faecal impaction. Children were randomised to receive either liquid paraffin or lactulose for 8 weeks. The medication was administered orally as a suspension at 1ml/kg, twice daily for each drug. For determination of the best dose for each child, parents were asked to increase or decrease the volume of each drug by 25% every 3 days as required, to yield 2 firm-loose stools per day. The maximum dose used throughout the study was 3ml/kg per day for each drug. Outcomes measured at 4 and 8 weeks after initiation of treatment were: optimal dose of drugs, compliance rate and side effects. Patients were instructed to take both empty and full containers to calculate amount of medication taken. It is unclear how side effects were recorded. The optimal dose of drugs (mean ± SD, ml/kg/day) was not significantly different for children taking liquid paraffin as compared to children taking lactulose (1.88 ± 0.27 vs. 2.08 ± 0.27). These data were reported in a table, it was assumed that figures given were for the whole study period. Data reported in text for the last 4 weeks of treatment stated the optimal dose for liquid paraffin as 1.72 ml/kg/day ± 0.18 and for lactulose as 1.82 ml/kg/day ± 0.57. Adherence rate during the first 4 weeks of treatment was not significantly different when comparing both groups. During the last 4 weeks of therapy significantly more children complied with taking liquid paraffin as did the children taking lactulose (n 90 vs. 60; p=0.02). No patient stopped treatment because of adverse effects (adverse effects not reported). During the first 4 weeks, taste aversion was reported in 1 child on liquid paraffin and abdominal distension in 2 patients on lactulose influenced adherence. During the last 4 weeks, poor symptom control in five patients, side-effects (abdominal distension and cramping) in 3 children on lactulose, and watery stools in two children on liquid paraffin influenced adherence.

Evidence statement

There is evidence showing that adverse effects of using oral preparations of osmotic laxatives, stimulant laxatives and faecal softeners in the medium- to the long-term are generally infrequent and mild.

Adverse effects up to 6 months of treatment:

Stimulant laxatives:

One RCT [EL=1-] showed that senna produced colic, diarrhoea and abdominal distension 52%, 9.5% and 4.8 % of the children respectively.

Osmotic laxatives:

PEG 3350 without electrolytes (MiraLax) was found to produce runny stools in 7% of the children (1 retrospective case series, EL=3). PEG 4000 without electrolytes was found to produce diarrhoea, flatulence and vomiting (1 RCT [EL=1+], figures unclear). PEG 3350 + electrolytes (Movicol) was found to produce gastrointestinal effects (mostly abdominal pain) in 39% of children (1 RCT [EL=1+]).

Lactulose was found to produce most commonly diarrhoea (2 RCTs: 10% and figures unclear, respectively) and flatulence (2 RCTs [EL=1+ and EL=1-]: 10% and figures not reported, respectively). One RCT [EL=1+] reported low incidence of anal irritation (5%) and anorexia (1%). One RCT [EL=1-] reported colic (4.8%). One RCT [EL=1-] reported abdominal pain (10%), bad palatability (15%), pain at defecation

(10%), bloating (10%), anal oil leakage (20%), nausea (10%) and hard stool (20%). Lactulose was not found to produce vomiting (1 RCT [EL=1-]).

One RCT [EL=1+], found that vomiting episodes and flatulence (either new onset or worsened in both cases) lasted significantly longer in children on lactulose as compared to children on PEG 4000 without electrolytes. This study also found that body height and body weight were unaffected in children taking either treatment, for both boys and girls. Mean weight was also unaffected after treatment with PEG 3350 + electrolytes (Movicol) in another RCT [EL=1+].

One RCT [EL=1-] showed that at the end of 8 weeks significantly more children complied with taking liquid paraffin than with taking lactulose. No patient stopped treatment because of adverse effects but during the first 4 weeks abdominal distension in two patients on lactulose influenced adherence. During the last 4 weeks abdominal distension and cramping in three children on lactulose influenced adherence.

Faecal softeners:

One prospective case series [EL=3] showed that therapy with mineral oil did not significantly change the serum levels of alpha tocopherol, retinol and beta-carotene after 4 months.

One RCT [EL=1-] showed that liquid paraffin produced taste aversion (2.5%) and watery stools (0.5%). Another RCT [EL=1-] showed that liquid paraffin produced abdominal pain (50%), bad palatability (40%), pain at defecation (50%), bloating (20%), diarrhoea (30%), anal oil leakage (40%), flatulence (20%), nausea (5%) and hard stool (6%). Liquid paraffin was not found to produce vomiting.

One RCT [EL=1-] showed that at the end of 8 weeks significantly more children complied with taking liquid paraffin than with taking lactulose. No patient stopped treatment because of adverse effects but during the first 4 weeks, taste aversion in 1 child on liquid paraffin influenced adherence. During the last 4 weeks watery stools in 2 children on liquid paraffin influenced adherence.

Adverse effects at between 6 and 12 months of treatment:

Stimulant laxatives:

No evidence was found on the adverse effects of the use of stimulant laxatives for between 6 and 12 months of treatment.

Osmotic laxatives:

PEG 3350 without electrolytes (MiraLax) was found to produced watery stools (1 retrospective case series [EL=3]), diarrhoea in 19.5% (1 retrospective case series [EL=3]), increased passage of gas per rectum (3.6%,1 retrospective case series [EL=3]), and transient diarrhoea that resolved after dose adjustment in 14.3% and 10% of children (1 retrospective case series [EL=3], 1 prospective case series [EL=3], respectively), bloating or flatulence (6%, 1 prospective case series [EL=3]) and abdominal pain (2%, 1 prospective case series [EL=3]). One retrospective case series [EL=3] showed a significant association between diarrhoea while taking MiraLax® and younger age and also with longer follow-up. One child in the series (2.2%) stopped taking MiraLax® because of side effects.

One retrospective case series [EL=3] showed that parents did not report increased flatus, abdominal distension, and vomiting or new onset abdominal pain while children were taking PEG 3350 without electrolytes. None of the children stopped treatment because of adverse effects. One retrospective cohort [EL=2-] found no major clinical adverse effects in children taking PEG 3350 without electrolytes (MiraLax).

A prospective case series [EL=3] showed that general physical examination findings revealed no new significant abnormalities as compared with the pre-treatment in children treated with PEG 3350 without electrolytes (MiraLax®). None of the patients stopped treatment due to adverse effects and all were to continue PEG therapy.

A prospective case series [EL=3] found that 24% adverse events occurred on children taking PEG 3350 with electrolytes but they were considered mild and had resolved by the end of the study. No clinically significant changes in vital signs as a result of the study medication were observed.

Adverse effects at/after 12 months of treatment:

Osmotic laxatives:

PEG 3350 without electrolytes (MiraLax®) was found to produce diarrhoea (1 prospective cohort [EL=2+], figures not reported) and transient diarrhoea disappearing with dose reduction (1 RCT [EL=1-], figures not reported).

One RCT [EL=1-] found that several children complained about the taste of both PEG 3350 without electrolytes (MiraLax®) and magnesium oxide (milk of magnesia, MOM) but significantly more children continued to refuse to refuse MOM as compared to PEG during the 12 months of the study.

One prospective cohort [EL=2+] found that none of the children on PEG 3350 without electrolytes (MiraLax®) became dehydrated. Children receiving PEG 3350 without electrolytes and their parents did not report increased flatus, abdominal distension, or new onset of abdominal pain. No children reported disliking the taste of PEG and no parents reported that their child refused to take it in juice or Kool-Aid whereas 33% of children refused to take MOM.

One prospective case series [EL=3] found that side-effects of Movicol (PEG 3350 with electrolytes) were reported in 10 (7.5%) patients and that these were generally mild and transient.

Stimulant laxatives:

No evidence was found on the adverse effects of the use of stimulant laxatives for between 12 months of treatment or longer.

Bulk forming laxatives:

No evidence was found on the adverse effects of the medium- to long- term use of bulk forming laxatives.

Tables 5.1, 5.2 and 5.3 summarise the results of these studies:

Table 5.1: Adverse effects up to 6 months of treatment

Laxative	Adverse effect/palatability	Study
Up to 6 months of treatment		
Senna	Colic, diarrhoea and abdominal distension 52%, 9.5% and 4.8 % of the children respectively	1 RCT [EL=1-]
PEG 3350 without electrolytes (MiraLax®)	Runny stools in 7% of the children	1 retrospective case series [EL=3]
PEG 4000	Diarrhoea, flatulence and vomiting	1 RCT [EL=1+]

without electrolytes	(figures unclear)	
PEG 3350 + electrolytes (Movicol)	Gastrointestinal effects (mostly abdominal pain) in 39% of children	1 RCT [EL=1+]
	Mean weight unaffected	1 RCT [EL=1+]
Lactulose	Diarrhoea (10% and figures unclear, respectively)	2 RCTs [EL=1+] and [EL=1-]
	Flatulence (10% and figures not reported, respectively)	2 RCTs [EL=1+] and [EL=1-]
	Anal irritation (5%) and anorexia (1%)	1 RCT [EL=1+]
	Colic (4.8%)	1 RCT [EL=1-]
	Abdominal pain (10%), bad palatability (15%), pain at defecation (10%), bloating (10%), anal oil leakage (20%), nausea (10%) and hard stool (20%)	1 RCT [EL=1-]
	Not found to produce vomiting	1 RCT [EL=1-]
Lactulose vs. PEG 4000 without electrolytes	Vomiting episodes and flatulence (either new onset or worsened in both cases) lasted significantly longer in children on lactulose as compared to children on PEG 4000 without electrolytes. Body height and body weight were unaffected in children taking either treatment, for both boys and girls	1 RCT [EL=1+]
Liquid paraffin vs. lactulose	At the end of 8 weeks significantly more children complied with taking liquid paraffin than with taking lactulose. No patient stopped treatment because of adverse effects but during the first 4 weeks abdominal distension in 2 patients on lactulose influenced adherence. During the last 4 weeks abdominal distension and cramping in 3 children on lactulose influenced adherence	1 RCT [EL=1-]
Mineral oil	did not significantly change the serum levels of alpha tocopherol, retinol and beta-carotene after 4 months	1 prospective case series [EL=3]
Liquid paraffin	taste aversion (2.5%) and watery stools (0.5%)	1 RCT [EL=1-]
	abdominal pain (50%), bad palatability (40%), pain at defecation (50%), bloating (20%), diarrhoea (30%), anal oil leakage (40%), flatulence (20%), nausea (5%) and hard stool (6%). Not found to produce vomiting	1 RCT [EL=1-]

Table 5.2: Adverse effects between 6 and 12 months of treatment

Laxative	Adverse effect/palatability	Study
Between 6 and 12 months of treatment		
PEG 3350 without electrolytes	Watery stools	1 retrospective case series [EL=3]
	Diarrhoea (19.5%)	1 retrospective case series [EL=3]
	Increased passage of gas per	1 retrospective case series [EL=3]

(MiraLax®)	rectum (3.6%),1 retrospective case series),	
	Transient diarrhoea that resolved after dose adjustment in 14.3% and 10% of children	1 retrospective case series [EL=3] and 1 prospective case series respectively [EL=3])
	Bloating or flatulence (6%)	1 prospective case series [EL=3])
	Abdominal pain (2%)	1 prospective case series [EL=3])
	Significant association between diarrhoea and younger age and also with longer follow-up. 1 child in the series (2.2%) stopped taking MiraLax® because of side effects	1 retrospective case series [EL=3]
	Parents did not report increased flatus, abdominal distension, and vomiting or new onset abdominal pain. None of the children stopped treatment because of adverse effects.	1 retrospective case series [EL=3]
	No major clinical adverse effects	1 retrospective cohort [EL=2-]
	General physical examination findings revealed no new significant abnormalities as compared with the pre-treatment. None of the patients stopped treatment due to adverse effects and all were to continue PEG therapy	1 prospective case series [EL=3])
PEG 3350 with electrolytes (Movicol)	72 children (92%) reported a total of 318 adverse events. 241 (76%) of those events were assessed as unrelated to the study treatment, 262 (82%) were considered mild and 302 (95%) had resolved by the end of the study. 6 serious adverse events occurred in 4 children: 4 affected the gastrointestinal system (the other 2 were not clearly reported). All of them were assessed by the investigator as unrelated or unlikely to be related to the study medication and were resolved at the end of the study. 1 serious adverse event (faecal impaction) led to 1 patient's premature withdrawal from study as the child was admitted to hospital for bowel washout. No clinically significant changes in vital signs as a result of the study medication were observed	1 prospective case series [EL=3])

Table 5.3: Adverse effects at or after 12 months of treatment

Laxative	Adverse effect/palatability	Study
At / after 12 months of treatment		
PEG 3350 without electrolytes (MiraLax)	diarrhoea (figures not reported)	1 prospective cohort [EL=2+]
	transient diarrhoea disappearing with dose reduction (figures not reported)	1 RCT [EL=1-]
PEG 3350	none of the children became	1 prospective cohort [EL=2+]

without electrolytes (MiraLax)	dehydrated	
	Children and their parents did not report increased flatus, abdominal distension, or new onset of abdominal pain	1 prospective cohort [EL=2+]
	No children reported disliking the taste of PEG and no parents reported that their child refused to take it in juice or Kool-Aid	1 prospective cohort [EL=2+]
Magnesium oxide (milk of magnesia, MOM)	33% of children refused to take it	1 prospective cohort [EL=2+]
PEG 3350 without electrolytes (MiraLax) vs. magnesium oxide (milk of magnesia, MOM)	several children complained about the taste of both PEG 3350 without electrolytes (MiraLax) and magnesium oxide (milk of magnesia, MOM) but significantly more children continued to refuse to refuse MOM as compared to PEG during the 12 months of the study	1 RCT [EL=1-]
PEG 3350 with electrolytes (Movicol)	reported in 10 (7.5%) patients, generally mild and transient	1 prospective case series [EL=3]

GDG interpretation of the evidence

There is no evidence to support the commonly held belief that using laxatives produces a "lazy bowel". Some health care professionals still hold this misconception and communicate it to parents.

Consequences of the medication such as abdominal pain and increased soiling can be clinically similar to the symptoms of constipation and are usually dose related. These symptoms are more likely to occur with higher dosage but this may be mitigated by the effective outcome of the medicine. The GDG believes that parents need information and support in order to know what to expect when using different laxatives to support optimal recommended treatment.

Palatability is an important aspect as children will not take the medication if they do not like it, despite its potential effectiveness. The GDG noted that the consultation with children confirmed that taste and the way that medicines are given is important to them.

Recommendations

Start maintenance therapy as soon as the child's bowel is disimpacted.

Reassess children frequently during maintenance treatment to ensure they do not become reimpacted.

Use the following regimen for ongoing treatment or maintenance therapy:

- Use polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain*) as the first-line treatment

* At the time of publication (October, 2009), Movicol Paediatric Plain did not have UK marketing authorisation for use in faecal impaction in children under 5 years, or for chronic constipation in children under 2

- Adjust the dose of polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain) according to symptoms and response. As a guide for children 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 (Movicol Paediatric Plain) does not work.
- Substitute a stimulant laxative if polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain) is not tolerated by the child. 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. 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.

Research Recommendation

What is the effectiveness of polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain) in treating idiopathic constipation in children younger than 1 year old, and what is the optimum dosage?

Why this is important

There is some evidence that treatment of constipation is less effective if faecal impaction is not dealt with first. Disimpaction with oral macrogols is recommended for children and their use avoids the need for rectal treatments.

Rectal treatments, especially in hospital, are more common than oral treatments at home. Although relatively few infants are admitted to hospital, there would be savings if initially all children were disimpacted at home.

Polyethylene glycol '3350' + electrolytes (Movicol Paediatric Plain), an oral macrogol, is licensed for disimpaction in children older than 5 years. Increasing experience has shown that it is effective in infants younger than 1 year old, but evidence is limited to small case series. If dosage guidelines and evidence on macrogol use in infants were obtained and published, more healthcare professionals might be encouraged to try macrogols in this age group. It would also allow the guideline to be applicable across the whole paediatric age group.

5.4 Diet and lifestyle

Introduction

Acute, simple constipation can usually be treated with a high fibre diet and sufficient fluid intake. In chronic idiopathic constipation, diet and lifestyle interventions remain important, but should be carried out in conjunction with laxative therapy and behavioural modifications.

There seems to be uncertainty amongst health professionals on which aspects of the diet should be modified to help improve constipation. As a result, advice to families varies considerably. There is sometimes the belief that a child's chronic constipation has been caused by a lack of fibre or fluids in the diet, when in fact this is often not the case. It is a common problem that treatment with laxatives is delayed while a number of dietary and lifestyle adjustments are made. This can

years. Informed consent should be obtained and documented. Movicol Paediatric Plain is the only macrogol licensed for children under 12 years which is also unflavoured worsen the constipation and make families reluctant to make any diet and lifestyle changes in the future as initial efforts have failed.

There is guidance from the Department of Health for active living throughout the lifecourse:

"Children and young people should achieve a total of at least 60 minutes of at least moderate intensity physical activity each day. At least twice a week this should include activities to improve bone health (activities that produce high physical stresses on the bones), muscle strength and flexibility." (Summary, page 3) [88]

There is guidance from the Department of Health on goats' milk infant formula:

The Department of Health does not recommend the use of milk based on goats' milk protein for infants (under 1 year of age). The composition of infant formula and follow-on formula is governed by European legislation. The current legislation specifically states the criteria for infant formulas and follow-on formulas to be based on cows' milk protein, hydrolysed protein or soya protein. The Department recommends the use infant formula and follow-on formula based on cows' milk protein or hydrolysed protein or soya protein on the advice of health professionals. In light of the European Food Safety Authority (EFSA) opinion, the Department advises health professionals not to recommend the use of infant milks based on goats' milk protein. Some parents may believe that infant milk based on goats' milk protein is a suitable alternative for babies who they perceive as being intolerant or allergic to cows' milk formula. However, the protein in goats' milk is very similar to that found in cows' milk and most babies who react to cows' milk protein will also react to goats' milk protein. Goats' milk protein can induce allergic reactions and is not a suitable milk source for a cows' milk allergic infant as there is the potential for cross allergenicity. Infants with proven cows' milk protein intolerance can be prescribed an extensively hydrolysed infant formula. Formula derived from goats' milk is also unsuitable for babies who are lactose intolerant as it contains similar levels of lactose to cows' milk based infant formulas.[89]

Clinical Question

What is the clinical effectiveness of the following for ongoing treatment/maintenance in children with chronic idiopathic constipation?

- Increasing physical activity
- Dietary modifications
- Increasing fluid intake
- Excluding cow's and goat's milk protein from diet

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation
- included the following diet and lifestyle modifications: excluding cow's and goat's milk from the diet, increasing fluid intake, increasing physical activity, increasing fibre intake (fibre rich food and fibre supplementing), infant's formulas, prebiotics, omega 3 fish oils, chocolate, low fat / high fat diet, dairy free diet, soy milk and sheep milk

- included the following outcomes: changes in frequency of bowel movements, changes in stools consistency/appearance, changes in pain/difficulty on passing stools, changes in frequency of episodes of soiling, reduction in laxatives use, parent/child views/satisfaction or quality of life
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country

Overview of available evidence

A total of 1022 articles were identified from the searches (154 from a search on excluding cow's and goat's milk from the diet and 868 from a search on the remainder diet and lifestyle modifications). Fifty-nine articles were retrieved for detailed assessment. Of these, 20 studies were identified for inclusion in this review: 1 triple-blind RCT, 6 double-blind RCTs, 3 open-label RCTs, 2 open label non-RCTs and 8 prospective case series (2 with an embedded food tolerance challenge test).

Narrative summary

Infant formulae

One double-blind RCT (cross-over) conducted in The Netherlands[90] (2007) [EL=1+] tested the hypothesis that Nutrilon Omneo (new formula, NF) would have a positive effect on stool characteristics in constipated children. Thirty-eight otherwise healthy, term infants with constipation (19 boys), between 3 to 20 weeks (median age: 1.7 months) of age, who received at least two bottles of milk-based formula per day were included. Infants were randomised to either NF or standard formula (SF) in period 1 and crossed-over after three weeks to treatment period 2. Each treatment period lasted three weeks. Feeding patterns were not described. NF composition (per 100 ml) differed from the SF in that its protein content was higher and 100% of it was based on whey protein hydrolysate (no casein, no intact whey protein), it contained a mixture of prebiotic oligosaccharides (GOS and lcFOS), a higher concentration of sn-2 palmitic acid and a lower lactose content. Defecation frequency, improvement of hard to soft stools and number of children experiencing no painful defecation were not significantly different between the 2 treatment groups after period 1. After the crossover, painful defecation and defecation frequency were not significantly different between the periods on NF and SF. Seventeen percent (n=4) of infants had soft stools when receiving NF but hard stools with SF, compared to no infant with soft stools when receiving SF and no infant with hard stools when receiving NF (p=0.046).Throughout the study there were no serious adverse effects in either group. Both formulae were well tolerated. Only 24 children (63%) completed the cross-over study. In period 1, three patients on SF dropped out: two patients stopped because of severe constipation and one patient switched to hypoallergenic feeding, because of suspected cow's milk protein allergy. Parents of one patient decided that they did not want to cross-over because she was free of symptoms and they started openly with NF instead. Three patients dropped out after switching to NF: two patients stopped after less than one week because of recurrence of constipation symptoms and one patient was lost to follow-up. Seven patients dropped out after switching to SF: six patients stopped after one week because of recurrence of constipation symptoms and one patient was lost to follow-up. Data analysis was based on the group of 35 patients that completed period 1 and the subgroup analysis of 24 patients who completed the cross-over.

There were no significant differences in baseline characteristics between the 2 groups.

One prospective case series conducted in Italy[91] (2003) [EL=3] investigated whether a new infant formula commercially available in Italy was useful as a dietary option in infants with minor feeding problems. Six hundred and four formula-fed healthy term infants up to three months of age seen by paediatrician because of colic and/or constipation and/or regurgitation were included. Two hundred and thirty two children were diagnosed with constipation, defined as a stool frequency of less than one stool a day. (Age at entry (months), total sample: 1.35 ± 0.77, gender not reported). During 14 days all children received a new formula (NF)*. The feeding volume was based on a feeding on demand procedure. The feeding frequency was decided by the parents and not influenced by the study protocol. One hundred and forty seven infants (63.4%) reported an increase in the number of stools per day during the study period as compared to baseline, with a significant average increase of 0.42 (95% CI: 0.55 to 0.27; $p<0.005$). The average increase between day 1 and day 7 was 0.41 (95% CI: 0.51 to 0.23; $p<0.05$) and between day 7 and day 14 it was 0.04 (NS). There was no improvement of symptoms in 85 infants (26.6%). Mean parent evaluation of formula (on a score of 1 to 10) was 7.9 ± 1.8. Five hundred and fifty parents (91%) gave a positive judgement (score 6 to 10). A total study population of 932 infants were enrolled and 604 (65%) completed the study protocol. A total of 358 infants were excluded from the study: 154 completed only the first step and did not return for the visit on day 14, 131 infants were excluded because of incomplete data. Seventy-three infants required medication during the 1st week of study and were therefore excluded. The proportion of these infants who had constipation was not reported in the paper. It should be noted that stool consistency was not assessed in the study.

A prospective case series conducted in Spain[92] (2008) [EL=3] assessed the prevalence of mild gastrointestinal disorders (MGDs) in infants fed with artificial milk formulas in paediatric practice and evaluated the effectiveness and satisfaction with dietetic treatment: specifically elaborated formulas belonging to the Novalac line of products. Three thousand four hundred and eighty seven infants (total population, 52.2% boys, aged 1 to 17 weeks) with MGDs and fed with artificial milk formulae were included. Six hundred and four infants had constipation. For 30 days constipated children received Novalac Anti-Constipation, a formula with an adapted concentration of magnesium and lactose. No other details regarding feeding volume/frequency were provided. In total, 91.6% of cases of constipation resolved within 7 days, but this was not clearly defined in the paper. The number of daily stools increased significantly at the end of the study when compared to baseline ((mean ± SD) baseline: 0.6 ± 0.7 vs. at 30 days: 1.7 ± 0.8). The percentage of children having normal stools increased significantly at the end of the study when compared to baseline (baseline: 33.40 vs. at 30 days: 95.60). The percentage of children presenting with pain or discomfort on defecation was significantly reduced at the end of the study when compared to baseline (baseline: 90.0 vs. at 30 days: 10.4). The percentage of children needing external help at defecation was significantly reduced at the end of the study when compared to baseline (baseline: 76.1 vs. at 30 days: 8.8). Ninety percent of parents reported being satisfied with the treatment. Adverse events (for all formulae, no subgroup analysis) were reported in 3.9% infants of the total population. Effectiveness was evaluated among 1441 infants (total population) who completed follow-up. Premature study termination due to adverse events occurred in 2.7% of cases, parent decision in 6.9%, loss to follow-up in 1.64%, protocol violations in 2.46% and non-specified reasons in 16.62%.

One open label RCT conducted in Taiwan[93] (2007) [EL=1-] evaluated a commercialised formula, Novalac-IT (Intestinal Transit, Paris, France) against a

* It is likely that this formula is also Omneo/Conformil. The authors did not provide any brand name in the paper but the composition of the formula is the same as the one the authors used for their 2005 study

"strengthened regular formula", the traditional approach in infants with digestive problems in Taiwan. Ninety-three children aged 2 to 6 months (47 boys, mean age 3.8 ± 1.7 months) referred to the paediatric gastroenterology clinic at a medical centre with constipation ≥2 weeks and fed exclusively with formula milk were included. Children were randomised to receive either a magnesium-enriched infant formula, Novalac IT or a 20% strengthened infant formula for 2 months. Children were assessed at 2 weeks, 1 month and 2 months. Outcomes measured were remission, improvement or failure according to a severity scoring system based on stool consistency, frequency and volume of stools and difficulties in defecation (1 to 3 mild constipation; 4 to 6 moderate; 7 or 8 severe). Asymptomatic children were considered in remission, a decrease in severity of ≥4 was considered a good response and a decrease in severity of 1 to 3 a fair response. If the score did not change or increased it was considered treatment failure. The severity scoring system comprised the following variables: stool consistency (hard stool: 0, no hard stool: 1, hard and long form: 2), difficulties with defecation (no difficulties: irritability: 1, crying: 2), frequency of defecation (>3 times/week: 0, 1 to 3 times/week: 1, <1 time/week: 2) and stool weight ((g/kg/week): >35: 1, 20 to 35: 2, <20: 3). The number of children who improved was not significantly different in the 2 groups at 2 weeks. At 1 month significantly more children on Novalac-IT had improved as compared to children on the strengthened formula (number and percentage: 39/47 (83) vs. 23/46 (50); p=0.002). At 2 months significantly more children on Novalac-IT had improved as compared to children on the strengthened formula (number and percentage: 42 (89) vs. 25 (54); p<0.001). The number of symptom-free children at 2 weeks was not significantly different between the treatment groups. However, both at 1 month and at 2 months, significantly more children on Novalac-IT were symptom-free as compared to children on the strengthened formula ((number and % of children) 1 month: Novalac-IT: 28/47 (60) vs. strengthened formula: 16/46 (35); p=0.029; 2 months: Novalac-IT: 35/47 (75) vs. strengthened formula:18/46 (39), p<0.001). There were no significant differences in the baseline characteristics (clinical or demographic) between the 2 groups. It should be noted that participation in the trial was proposed before a more complete diagnostic workup for cow's milk protein allergy, Hirschsprung's disease and others was conducted.

One open label RCT conducted in Italy[94] (2005) [EL=1-] evaluated the efficacy on digestive problems of a formula based on palmitic acid predominantly esterified at the β-position, oligosaccharides (GOS and FOS) with a prebiotic activity, partially hydrolysed protein, low lactose content and higher density. Ninety-five formula-fed healthy term infants up to 4 months of age with constipation, defined as a stool frequency of less than 1 stool a day (64.2% with hard stools), were included (50 boys, age at study entry (months) intervention group: 1.55 ± 0.88, control group: 1.28 ± 0.66). Children were randomised to receive either the new formula (NF) (Omneo / Conformil) or a standard formula (SF) for 14 days. The feeding volume was based on a feeding on demand procedure. Feeding frequency was decided by the parents and not influenced by the study protocol. The stool frequency increased significantly more in children receiving NF as compared to children receiving SF, both on day 7 and on day 14 (number/day, mean ± SD) (day 7: NF group (n=55): 1.79 ± 0.96 vs. SF group (40): 1.31 ± 0.89; difference: 0.48 (95% CI: 0.09 to 0.87); p=0.02]); (day 14: NF group (n=55): 2.04 ± 1.04 vs. SF group (40): 1.64 ± 0.99, difference: 0.40 (95% CI: -0.03 to 0.83); p=0.07). The stool frequency (number/day, mean ± SD) also increased significantly more in children receiving NF as compared to children receiving SF, after adjusting for gender, age at entry, maternal instruction, parity, birth weight, number of feedings/day and stool frequency at entry (mean adjusted difference in stool frequency between the 2 groups, days 0 to 7: 0.60 (CI 95%: 0.19; 1.01), p=0.004; days 0 to 14: 0.53 (95% CI: 0.11 to 0.90); p=0.015). Post-treatment outcomes for stool consistency were not reported. There were no significant differences in the baseline characteristics between the two groups. No dropouts/lost to follow-up children were reported.

Increasing fibre

One double-blind RCT conducted in the Netherlands[95] (2008) [EL=1+] assessed the clinical efficacy and safety of a dietary fibre mixture and compared it with lactulose in the treatment of childhood constipation. One hundred and thirty-five children referred to hospital outpatient clinic for idiopathic constipation were included. Children were randomised to receive either a yogurt drink with mixed dietary fibre (10g/125ml; fibre mixture (per 100ml): 3.0g transgalacto-oligosacharides, 3.0g inulin, 1.6 g soy fibre, 0.33g resistant starch) or a yogurt drink containing lactulose (10g/125ml) (Duphalac Lactulose). Forty-two children (20 boys, median age 5.5 years (1 to 12 years)) received yogurt with the fibre mix, whereas 55 children (23 boys, median age 5.0 years (1 to 12 years)) received the yogurt containing lactulose. Both products were taken at breakfast and in case that two or more bottles were needed, they were also taken at lunch. The amount of fibre/fluid intake daily depended on the patient's body weight. If persistent diarrhoea was reported, the original dose was reduced by 50%. If clinical parameters compared to baseline did not improve 3 weeks after the start of intervention period, step-up medication (polyethylene glycol (PEG) 3350) was given per protocol. There was an intervention period lasting 8 weeks and a weaning period lasting 4 weeks when doses where reduced. Defecation frequency/week and number of patients with ≥1 faecal incontinence episodes/week at 8 weeks was not significantly different between the two groups. Stool consistency (mean) was significantly softer in the lactulose group as compared to the fibre group, both at three and at eight weeks (3 weeks: fibre (n=42): 3.5, lactulose (n=55): 4.5, p<0.01); (8 weeks: fibre (n=42): 3.6, lactulose (n=55): 4.0, p=0.01). The number of patients using step-up medication at 3 weeks was significantly smaller in the group taking fibre than in the group taking lactulose (fibre (n=42): 13, lactulose (n=55): 7, p=0.028) but there were not significant differences regarding this outcome at eight and at twelve weeks. No serious or significant side effects were recorded. In the fibre group (n=42) one child experienced dose-related persistent diarrhoea as compared to two children in the lactulose (n=55). No significant differences were found in baseline characteristics between the two groups. Thirty-three patients left the study: 22 in the fibre group after 1 to 56 days (median 7) and 11 in the lactulose group after 1 to 51 days (median 8) (p=0.020). All those patients refused to drink the yogurt. Three patients were lost to follow-up: one on fibre and two on lactulose. Despite the high drop-out rate (24.4%) intention-to-treat analysis was not performed.

One double-blind RCT (cross-over) conducted in the USA and Italy[96] (2004) [EL=1+] evaluated whether fibre supplementation with glucomannan is beneficial in the treatment of children with idiopathic constipation. Thirty-one otherwise healthy children (16 boys) older than 4 years (age: 4.5 to 11.7 years (mean: 7.1 ± 2.0 years)) who had chronic idiopathic constipation for ≥6 months with or without encopresis were included. General disimpaction was carried out with one or two phosphate enemas if rectal impaction felt during rectal examination. Fifty-eight percent of patients continued with their pre-evaluation laxative during the whole study period. Children were randomised to receive Glucomannan B (one capsule containing glucomannan, a polysaccharide of d-glucose and d-mannose, equal to 450 mg of alimentary fibre) or Glucomannan A (one capsule containing maltodextrins as placebo). After 4 weeks children were switched to the other treatment for another 4 weeks, with no washout period in between. Both glucomannan and placebo were given at a dose of 100 mg/kg body weight daily (maximal 5g/day), rounded to the nearest 500 mg, because each capsule contained 500 mg. Each capsule was either: opened and sprinkled on food and given with 50 ml of fluid per capsule; given as a solution, whereby the content of each 500-mg capsule was mixed with 50 ml of fluid of the child's choice; or swallowed as a capsule with 50 ml of fluid for each capsule. In addition, parents were instructed to have the child sit on the toilet four times daily after meals and to keep a stool diary.

No enemas were given during each treatment period, unless rectal disimpaction felt during rectal examination at assessment visits. Successful treatment was rated by physician and defined as ≥3 bowel movements per week and ≤1 soiling episode in the last three weeks with no abdominal pain. Parents' global assessments related to whether they believed that the child was better during the first or second treatment period. Stool consistency and frequency of soiling episodes per week were not significantly different when comparing the fibre treatment period with the placebo period. However, significantly more children on placebo reported having <3 bowel movement week as compared to children on fibre (placebo (n=31): 52% vs. fibre (n= 31): 19%, p<0.05). Significantly more physicians rated the fibre treatment as "successful" when compared to placebo (45% vs. 13%; p<0.05). Significantly more parents in the fibre period rated their children as "improved" when compared to parents in the placebo period (68% vs. 13%; p<0.05). Successful treatment (physician rating) and improvement (parent rating) were independent of low or acceptable fibre intake (p>0.6). More children who had encopresis and were taking laxatives at enrolment (78% vs. 31%; p<0.02), and significantly more children who were taking laxatives at enrolment were treated successfully with fibre than with placebo (p<0.01). Children with constipation only were significantly more likely to be treated successfully with fibre than those with constipation and encopresis (69% vs. 28%; p<0.04). No significant side effects such as new onset of abdominal pain, bloating, abdominal distension, excessive gas, diarrhoea, or anaphylactic symptoms were reported. No significant differences in baseline characteristics between the two groups were observed. Forty-six children were originally recruited. Thirteen children did not attend their appointment: seven children randomized to placebo first and six children randomized to fibre first. Two constipated girls completed the first four weeks of the study only: one received placebo and one received fibre; both recovered from chronic constipation and abdominal pain during the first four weeks of treatment and did not return for the 8-week visit. Data from the 13 children who entered the study and were randomized but did not come for follow-up and the two children who did not complete the study were excluded from the analysis. Initial data from these 15 children were not significantly different from the data of the 31 children who completed the study, except soiling frequency per week was significantly less (4.0 ± 1.4; p<0.001). Data analysis thus includes 31 children with idiopathic constipation with or without encopresis. Despite the high attrition rate (28%) intention-to-treat analysis was not performed.

One double-blind RCT (pilot study) conducted in Spain [97] (2006) [EL=1+] evaluated the effect of a palatable cocoa husk supplement that is rich in fibre on intestinal transit time and other indices of constipation in children with idiopathic chronic constipation. Fifty-six children aged 3 to 10 years (22 boys, mean age 6.3 ± 2.2 years) referred to paediatric gastroenterology outpatients' clinic with chronic idiopathic constipation, defined in accordance with Rome II diagnostic criteria, were included. Children were randomised to receive either a cocoa husk supplement rich in dietary fibre (1 sachet (5.2 g): 4g cocoa husk + 1g betafructosans) or placebo (1 sachet (5.2g): glucose, cocoa flavouring, and excipients) during 4 weeks. The fibre supplement of cocoa husk contained 53.2g of fibre (39.6g of total fibre and 13.6 g of betafructosans) per 100g of product. Insoluble fibre represented 37.2% and soluble fibre represented 2.4% of the total fibre. Cellulose and uronic acids were the main type of insoluble fibre and soluble fibre, respectively. In addition both groups received the same standardized toilet training procedures during the study period. Doses for both products in children aged 3 to 6 years were one sachet before lunch and one sachet before dinner and in children aged 7 to 10 years, two sachets before lunch and dinner. Parents were instructed to dissolve the content of the sachets in 200ml of whole milk before ingestion. The number of bowel movements per week (mean) did not differ significantly between the two treatment groups. The percentage of children reporting hard stool consistency decreased significantly more in children taking the cocoa husk supplement when compared to children taking placebo (cocoa husk group: 41.7 vs. placebo group: 75.0; p=0.017).

Significantly more children on the cocoa husk group reported a subjective improvement in stool consistency as compared to children on placebo (Cocoa husk group (n=24), improvement: 14, no Improvement: 10 vs. placebo group (n=24), improvement: 6, no Improvement: 18; p=0.039). Subjective improvement in pain on defecation was not significantly different between the two groups. No significant adverse effects, such as a new onset of abdominal pain, bloating, abdominal distension, excessive gas, diarrhoea, or anaphylactic symptoms, were reported during the 4-week period with either treatment. There were no significant differences in baseline characteristics between the two groups. Eight children withdrew from the study before its completion (five children discontinued study because of the difficulty of the protocol, and three were excluded because of the presence of positive antigliadin and antiendomysium antibodies). Data refer only to 48 participants who completed the study. Intention to treat analysis was not performed.

One prospective case series conducted in Italy [98] (2000) [EL=3] evaluated the efficacy of glucomannan as a treatment for chronic constipation in children with severe neurological damage. Twenty children (14 boys mean age 5.7 ± 4.2 years) with severe neurological damage and constipation of at least 12 months were included. In most patients evacuation was not possible without enema. Children were fed by mouth with semi-liquid diet including formula and purèed food. All children received treatment for disimpaction with enemas for two or three days (not clear what medication was used). After that children were randomised to receive during 12 weeks either glucomannan at a dose of 100mg/kg two times a day, or placebo at the same dose. Both glucomannan and placebo consisted of a 500mg capsule which was given orally mixed with 100ml of water. An arbitrary scoring system was used for assessment of symptoms: stool consistency: 1, pellets; 2, hard; 3, soft; 4, loose; 5, liquid and presence of painful defecation: 1, often; 2, occasionally; 3, none. None of the outcomes changed significantly at any of the study periods for the placebo group when compared to baseline. The number of stools per week significantly increased in the glucomannan group at all assessment points when compared to baseline (mean ± SD) (at 4 weeks: 4.0 ± 1.3; at 8 weeks: 3.3 ± 1.0; at 12 weeks: 3.8 ± 0.9; p<0.001 for all). Stool consistency significantly improved in the glucomannan group at all assessment points when compared to baseline (score (mean ± SD), at 4 weeks: 2.4 ± 0.5; at 8 weeks: 2.8 ± 0.7; at 12 weeks: 2.7 ± 0.7; p<0.001 for all). Painful defecation improved significantly only at the 12-week assessment for the glucomannan group as compared to baseline (score (mean ± SD), at 12 weeks: 1.9 ± 1.2; p<0.01). Laxative use was significantly reduced in the glucomannan group at the 4- and 12-week assessments (number per week, (mean ± SD), at 4 weeks: 0.3 ± 0.8; at 12 weeks:: 0.3 ± 0.5; p<0.01). There were no significant differences in baseline characteristics between the two groups. One patient receiving glucomannan withdrew from the study after three weeks of treatment because of concomitant increase in seizure frequency associated with blood level of phenobarbital below the therapeutic range.

One prospective case series (pilot study) conducted in Hong Kong[99] (2000) [EL=3] evaluated the fibre intake of severe developmentally disabled children living in a residential institution along with the possibility of reducing the use of laxatives by increasing their fibre intake. Twenty severely developmentally disabled children (age range 3 to 17 years) with idiopathic constipation, able to take oral feeding and medically stable were included. All children received fibre supplementation with wheat bran (All Bran, Kellogg's®) added in breakfast. During stage 1 (20 days), 15g was added to each serving of breakfast (total fibre intake, 17g). Following stage 1 there was a period of 10 days where children received their normal diet without any supplementation. During stage 2 (6 weeks) 19g were added to each serving of breakfast (total fibre intake, 21g). Baseline fibre intake was around 2g/day. The number of laxatives per week decreased significantly at the end of stage 1 when compared to baseline (baseline: 1.22 (SD 0.36) vs. end of stage 1: 0.9 (SD 0.75); p<0.05) and at the end of stage 2 when compared to baseline (baseline: 1.22 (SD

0.36) vs. end of stage 2: 0.7 (SD 0.40); p<0.01) but there were no significant differences when comparing end of stage 1 and end of stage 2. Outcomes for bowel movements were not reported in the paper.

An open label non-RCT conducted in the USA[100] (1955) [EL=1-] evaluated the effectiveness of a palatable mixture containing prune and fig concentrate and non-diastatic malt syrup neutralised with potassium carbonate for the treatment of idiopathic constipation in infants and children. Two hundred infants and children aged 3 months to 8 year with idiopathic constipation were included. One group had Prune-Malt® added to their diet for three weeks and the control group received no intervention. Prune-Malt® was given to infants aged 3 weeks to 1 year as two tablespoonfuls daily added to milk or juice. Children aged 1 to 4 years received three tablespoonfuls daily added to milk or food and children aged 4 to 8 years received four tablespoonfuls daily added to milk or food. No changes were made in their usual diet and no drugs were given. No definitions/scoring system were given for: "improvement", "no improvement", "return to normality", "good" "fair" and "poor". Twenty-eight children who received Prune-Malt® returned to normality as compared to 16 children in the control group. Fifty-one children who received Prune-Malt® improved as compared to 25 children in the control group. Only 21 children who received Prune-Malt® did not improve as compared to 59 children in the control group. One hundred and thirty two parents rated the treatment as good, 47 as acceptable and 21 as poor (p values not reported in the study). No comparison was made between baseline characteristics of the two groups, although the author stated that wherever possible, cases of equal severity and ages were equally divided between the two groups. No attrition/loss to follow-up was reported.

Probiotics

A double blind RCT conducted in Taiwan [79] (2007) [EL=1+] investigated the effect of Probiotics (Lactobacillus case rhamnosus, Lcr35) alone in the treatment of chronic constipation in children and to compare the effect with magnesium oxide (MgO) and placebo, respectively. Forty-five children (23 male) under 10 years old with chronic constipation were included. Children were randomised into three groups to receive MgO 50 mg/kg per day, twice a day, Lcr35 8 X 108 colony forming units per day (Antiobiophilus 250mg, two capsules, twice a day) or placebo (starch in content) during 4 weeks. Lactulose use (1ml/kg/day) was allowed when there was no stool passage noted for three days. Glycerine enema was used only when there was no defecation for >5days or when abdominal pain was suffered due to stool impaction. Defecation frequency (times/day, mean ± SD) significantly increased in children taking MgO and probiotic as compared to placebo (MgO (n=18): 0.55 ± 0.13; probiotic (n=18): 0.57 ± 0.17; placebo (n=9): 0.37 ± 0.10; p=0.006 (placebo vs. probiotic); p=0.01 (MgO vs. placebo)) but there were no significant differences between children taking probiotic and children taking MgO regarding this outcome. The percentage of children having hard stools was significantly lower in children taking MgO and in those taking probiotic as compared to placebo (MgO (n=18): 23.5 ± 7.9; probiotic (n=18): 22.4 ± 14.7; placebo (n=9): 75.5 ± 6.1; p=0.02 (placebo vs. probiotic); p=0.03 (MgO vs. placebo)) but there were no significant differences between children taking probiotic and children taking MgO regarding this outcome. Children taking placebo had to make use of glycerine enemas significantly more often than children taking either MgO or placebo (number of times, (mean, SD), MgO (n=18): 1.3 ± 1.9, probiotic (n=18): 1.6 ± 1.9, placebo (n=9): 4.0 ± 2.1; placebo vs. probiotic p=0.04; MgO vs. placebo; p=0.03) but there were no significant differences between children taking probiotic and children taking MgO regarding this outcome. There were no significant differences regarding use of lactulose and faecal soiling amongst the three groups. Significantly more patients were successfully treated with MgO or probiotic as compared to placebo ((%), MgO (n=18): 72.2, probiotic (n=18): 77.8, placebo (n=9): 11.1, placebo vs.

probiotic p=0.01; MgO vs. placebo p=0.01) but there were no significant differences between children taking probiotic and children taking MgO regarding this outcome. No adverse effects were noted in the probiotic and placebo groups and only one patient in the MgO group suffered from mild diarrhoea. There were no significant differences at baseline amongst the three groups regarding: sex, age of enrolment, age of onset of constipation, duration of constipation, previous treatment, defecation period, stool consistency, abdominal pain, faecal soiling, bleeding during defecation, use of enema and taking fruits or vegetables daily. Four patients discontinued medication during the study period: two in the MgO, one in the probiotic and one in the placebo group. Two patients suffered form acute gastroenteritis (not clear whether as a consequence of the study medication) and two patients were lost to follow-up.

A triple-blind RCT conducted in Poland [101] (2005) [EL=1+] assessed the effectiveness of lactobacillus rhamnosus GG (LGG) as an adjunct to lactulose in the treatment of constipation in children. Eighty-four children aged 2 to 16 years with idiopathic constipation defined as <3 bowel movements per week for at least 12 weeks were included; (age (months): lactulose + LGG group 79 ± 47, lactulose + placebo group 65 ± 36, gender not reported). All children received treatment for disimpaction with phosphate and saline enema before study treatment started. Children were then randomised to receive during 12 weeks either lactulose 70%, 1ml/kg/day (in 2 divided doses) + 109 colony forming units (CFU) of lactobacillus rhamnosus GG (LGG) or lactulose 70%, 1 ml/kg/day (in 2 divided doses) + placebo. From weeks 13 to 24 patients were instructed to continue the use of lactulose or other laxatives as needed. Treatment success was defined as ≥3 spontaneous bowel movements per week with no episodes of faecal soiling. Treatment success at 12 and 24 weeks was not significantly different between the two treatment groups. The average number of spontaneous bowel movements per week, episodes of faecal soiling per week as well as the straining frequency per week were not significantly different when comparing both treatment groups at 4, 8 and 12 weeks. The percentage of patients using laxatives at 24 weeks was not significantly different between the two groups. LGG was well tolerated. The number of patients experiencing side effects was not significantly different between the two groups, and side effects profile of LGG was similar to that of placebo: three patients in the LGG group vs. five patients in the placebo group developed abdominal pain. One patient in the LGG group developed vomiting and one in the placebo group experienced headache. There were no significant differences in baseline characteristics between the two groups. Five children in the LGG group discontinued the intervention (four because of clinical improvement, one developed abdominal pain) vs. three patients in placebo group who discontinued the study without receiving any intervention (two refused to participate and one because of another reason, not provided). Outcomes for stool consistency were not reported in the paper.

One prospective case series (pilot study) conducted in The Netherlands[102] (2007) [EL=3] determined the therapeutic effect of a combination of probiotics strains, containing the bifidobacteria B. bifidus, B. infantis and B. longum and the lactobacilli L. casei, L. plantarum and L. rhamnosus, on childhood constipation. Twenty children (10 boys) between 4 to 16 years of age (median age: 8 years) referred to outpatient clinic with idiopathic constipation, as defined by Rome III criteria were included. All children received treatment for disimpaction: rectal enema (Klyx: sodium-dioctylsulfosuccinate and sorbitol) once daily for three days. For the following 4 weeks children received a daily probiotics mixture of 4x109 colony forming units, containing Bifidobacteria (B.) bifidum, B. infantis, B. longum, Lactobacilli (L.) casei, L. plantarum and L. rhamnosus. During the treatment period children were instructed to start toilet training. Toilet training consisted of sitting on the toilet three times per day for five minutes after each meal with the intention of trying to defecate. Use of laxatives not allowed during treatment period. The frequency of bowel movements (BMs) per week in the total sample did not change significantly at weeks 2 and 4 when compared to baseline. The frequency of BMs per week in 12 children presenting with <3 BMs per week at baseline increased significantly at week 2 and 4 when compared to baseline (baseline (median and range): 1.0 (0.0 to 2.0), week 2: 3.0 (0.0 to 7.0), p =0.01; week 4: 3.0 (0.0 to 10.0), p=0.009). The number of children reporting hard stools did not change significantly at week 2 and week 4 as compared to baseline. At week 4, hard stools appeared in five children who also had had hard stools at baseline. One child with normal stools at baseline reported hard stools only at the end of the study. Two of the seven children who presented with hard stools reported normal stools at the end of the study. The number of faecal incontinence episodes per week decreased significantly at both week 2 and week 4 when compared to baseline (baseline (median and range): 4.0 (0.0 to 35.0), week 2: 1.5 (0.0 to 14.0), week 4: 0.3 (0.0 to 7.0); p=0.007 and p=0.001 respectively). There were no side effects such as vomiting, bloating and increased flatulence during the study period. No attrition/loss to follow-up was reported.

*Excluding cows' and goats' milk**

A double-blind cross over RCT conducted in Italy [103] (1998) [EL=1+] compared the effects of cow's milk and soy milk in children with chronic constipation. Sixty-five consecutive children diagnosed with chronic idiopathic constipation underwent an observation period during weeks 1 and 2 when all medications were stopped. During weeks 3 and 4, one group (n=33) was randomly assigned to receive cow's milk and unrestricted diet and the other (n=32) had cow's milk and its derivatives excluded from their diet and received soy milk instead. During week 5 there was a "washout" period for both groups with unrestricted diet and intake of soy or cow's milk and its derivatives. During weeks 6 and 7 patients were switched to the other type of milk. After the two study periods children with a response to cow's-milk free diet were given the soy-milk diet for another month and then underwent a 2-week double-blind challenge with cow's milk at hospital. Children with eight or more bowel movements during a treatment period were considered to have a response. Children were randomly assigned to receive cow's milk or a placebo containing soy milk. If no clinical reactions were observed within 12 hours, patients were discharged and the challenge continued at home. A qualitative faecal score was defined as 1 (mushy or liquid stool), 2 (soft faeces and no pain in passing stools) and 3 (hard faeces and difficulty and pain on passing stools). Patients were followed up for a mean period of 10 months (range 3 to 20). During the observation period (n=65) the number of bowel movements was a median of 4 (25th to 75th percentile: 3-5) and the qualitative faecal score was 3 for all 65 patients. During the two study periods neither the number of bowel movements, nor the qualitative faecal score changed significantly for the cow's milk group (n=65), as compared to the observation period. For the group who had a response to soy milk diet (n=44) the number of bowel movements increased significantly (Median: 10; 25th to 75th percentile: 4-12) and 44 patients stopped having pain or difficulty passing stools (qualitative faecal score (QFS) QFS 1: 2; QFS 2: 42; QFS 3: 21) (p<0.001 for all variables). During the challenge with cow's milk (n=44) no patients in the placebo group (soy milk) showed any clinical reactions. Patients in the cow's milk group did not have any acute reaction, but in all of them, constipation associated with hard stools and discomfort on defecation reappeared after 5-10 days on the diet. Cow's-milk-free diet was therefore recommenced, with a consequent normalisation of bowel movements in all patients. Neither the number of bowel movements nor the qualitative faecal score were specifically measured during the challenge period. During the follow-up period none of the children with response had constipation. Cow's milk was reintroduced into the diets of 15 children after 8-12 months of cow's milk-free diet and in all cases constipation returned within 5-10 days. Children with no response to soy-milk diet were treated with high doses of

* All 4 studies included in this section are by the same centre and authors

laxatives, with subsequent improvement in stool frequency. In all cases symptoms returned once treatment with laxatives was stopped. There were significant baseline differences in the group of children with and those without a response. Anal fissures with erythema or oedema were more common among those with a response (40 of 44 patients vs. 9 of 21, $p<0.001$). Furthermore, at diagnosis, symptoms of suspected intolerance to cow's milk were more common in children with a response (11 of 44 patients vs. 1 of 21, $p=0.05$): recurrent bronchospasm in four patients, rhinitis in four, and dermatitis in three. Six patients were withdrawn from the study during the cow's-milk study period (on days 9-12) because of the reappearance of constipation and other related disorders. For children withdrawn from study during the cow's-milk study period the number of bowel movements per period was prorated. Intention to treat analysis was used. Patients included in this study were highly selected and this might have led to overestimate the frequency of cow's milk intolerance as a cause of constipation. Paediatricians who referred the patients may have pre-selected them as being likely to have a food intolerance since the study centre specialized in the treatment of food allergies. The inclusion of patients with no response to laxatives may have also contributed to this issue. It should be noted that the two types of milk taste different from one another thus undermining the degree of blinding achievable

A small prospective case series and embedded randomised controlled challenge conducted in Italy[104] (2006) [EL=3] evaluated the histology and manometry characteristics of patients with food intolerance-related constipation. Thirty-six children (age range 9 months to 10 years) with chronic constipation underwent a cow's milk-free diet for 4 weeks, following a 2-week observation period where all medications were stopped. After 12 weeks all patients cured on cow's milk free diet or oligoantigenic diet (n=17) underwent a 2-week double-blind placebo-controlled challenge with cow's milk at the hospital. Patients were randomised to receive either cow's milk or ass's milk as placebo. If no clinical reactions (not specified which ones) occurred after 12 hours, patients were discharged and the challenge continued at home with bottles coded A or B. The challenge was stopped when a clinical reaction occurred. Outcome measures were number of bowel movements/week, appearance of stools and child's degree of difficulty in passing stools. The last two measures were combined in a qualitative faecal score. A score of 1 was given if mushy or liquid stools, 2 if soft faeces and no pain in passing stools and 3 if hard stools and difficulty and pain on passing stools. During the observation period both for patients further diagnosed with food intolerance (n=17; 14 to cow's milk only, 3 multiple food intolerance) and for patients with constipation unrelated to food intolerance (n=19) the number of bowel movements/week (median: 1.5; 25th to 75th percentile: 1-2) and the qualitative faecal score (1: 0; 2: 0; 3: 17) were the same. During the elimination diet period the number of bowel movements/week in patients with food intolerance (n=17) significantly increased (median: 5 ($p<0.01$); 25th to 75th percentile: 3-7) and no children presented with hard stools or difficulty and pain on passing stools (qualitative faecal score (QFS) QFS 1: 1; QFS 2: 16; QFS 3: 0; $p<0.01$ for the three values). For patients with constipation unrelated to food intolerance (n=19) both the number of bowel movements/week and qualitative faecal score remained the same as during the observation period and were significantly different from the results obtained in the group with food allergy ($p<0.01$). During the cow's milk challenge period cow's milk readministration caused the reappearance of constipation in all cases, very often associated with painful defecation, within five days after the commencement of the challenge (median 2 days, range 1-5 days). These symptoms disappeared on returning to the cow's milk free diet or oligoantigenic diet in the three patients with multiple food intolerance. Patients with chronic constipation caused by food intolerance showed at baseline a higher frequency of a personal history of previous food intolerance ($p<0.01$) and concomitant signs of food intolerance (bronchospasm four cases, dermatitis two cases) ($p=0.05$) than patients with constipation unrelated to food intolerance.

A second small prospective case series and embedded randomised controlled challenge conducted in Italy [105] (2005) [EL=3] evaluated the histologic data in patients with food intolerance-related constipation. Fifty-two infants and children with chronic constipation unresponsive to previous treatments underwent a 2-week observation period where all medications were stopped and at the end of the second week they were given a clean-out with a single dose of PEG 4000 (0.75g/kg). For the next 4 weeks cow's milk and all its derivatives were excluded from the diet of all patients. Patients unresponsive to cow's milk-free diet were placed on an oligoantigenic diet for 4 weeks (also excluding cow's milk). After 12 weeks all patients cured on cow's milk free or oligoantigenic diet underwent a two-week double-blind placebo-controlled challenge with cow's milk at hospital. Patients were randomised to receive either cow's milk or ass's milk as placebo. If no clinical reactions (not specified) occurred after 12 hours, patients were discharged and the challenge continued at home with bottles coded A or B. The challenge was stopped when a clinical reaction occurred. Outcome measures were number of bowels movements/week and qualitative faecal score. Both were recorded by parents during the observation period and the elimination diet period. The qualitative faecal score was defined as 1 (mushy or liquid stool), 2 (soft faeces and no pain in passing stools) and 3 (hard faeces and difficulty and pain on passing stools). Children with eight or more bowel movements during a treatment period were considered to have a response. Normalised stools habits were defined as: bowel frequency of at least five evacuations/week with the elimination of soft stools without pain. During the observation period both patients with food intolerance (n=30) and patients with constipation unrelated to food intolerance (n=22) had a median of 1.5 bowel movements/week (25th to 75th percentile: 1-2) and all 52 patients a qualitative faecal score of 3. During the elimination diet period the number of bowel movements/week increased significantly for patients with food intolerance (median: 5, 25th to 75th percentile: 4-7; $p<0.001$) and no children presented with hard stools or difficulty and pain on passing stools (qualitative faecal score (QFS) QFS 1: 2; QFS 2: 28; QFS 3: 0; $p<0.01$ for the three values). For patients with constipation unrelated to food intolerance both bowel movements/week and qualitative faecal score remained the same as during the observation period. For all children cow's milk readministration caused the reappearance of constipation within five days after commencing the challenge (median 2 days, range 1-5 days). Patients with chronic constipation caused by food intolerance showed at baseline a higher frequency of a personal history of previous food intolerance ($p=0.02$) and concomitant signs of food intolerance (bronchospasm five cases, rhinitis four cases, dermatitis two cases) than patients with constipation unrelated to food intolerance ($p=0.03$). No difference was observed between the 24 patients with cow's milk intolerance and the 6 patients with multiple food intolerance for outcome measures considered (number of bowel movements and qualitative faecal score), either at baseline or on elimination diet. However, in comparison with patients intolerant to cow's milk alone, patients suffering from multiple food intolerance were older ($p=0.04$) and had a higher frequency of family history of atopic disease ($p=0.03$). It should be noted that the high frequency of chronic constipation owing to food intolerance found in this study was likely due to a selection bias, as mainly food-intolerant patients are treated at the centre where the study was conducted.

Another small prospective case series conducted in Italy[106] (1995) [EL=3] aimed to investigate the possible relation between constipation and cow's milk protein (CMP) allergy (CMPA). The study sample comprised 27 infants considered to have idiopathic constipation. During the first 7 days all patients were being fed the same diet as at the time of diagnosis: various forms of commercial formula derived from cow's milk or whole cow's milk and its derivatives. For the next month all patients started a cow's milk protein-free diet. Three patients aged younger than 12 months were fed a formula containing soy protein and the others received soy milk or ass's milk (eight cases) and all cow's milk derivatives were excluded. After a month all patients whose symptoms abated underwent a cow's milk challenge. Cow's milk was given for a maximum of 10 days; then these patients started again an exclusion diet for 1 month and then a second cow's milk challenge was performed. Outcome measures were number of stools/day and qualitative faecal score. The qualitative faecal score was defined as in the studies described above. During the first month of the CMP-free diet there was a significant improvement in symptoms in 21 patients: the frequency of stools significantly increased, faeces were soft and none of the infants had any discomfort when passing stools (mean number (±SD) of stools per day (a) unrestricted diet: 0.24± 0.10; (b) 1st CMP-free diet: 1.04±0.120 (Qualitative score: (a) unrestricted diet: 2.85±0.05; (b) 1st CMP-free diet: 1.90±0.08). During the first challenge constipation returned within 48 hours after the reintroduction of cow's milk, passing stools became painful and in seven patients with abdominal pain, ingestion of cow's milk was discontinued on day 4 (mean number (±SD) of stools per day (c) 1st CMP challenge: 031±0.14) (Qualitative score: (c) 1st CMP challenge: 2.75±0.11). During the second period of CMP-free diet the stools became normal again in the 21 patients and the symptoms accompanying constipation disappeared (mean number (±SD) of stools per day (d) 2nd CMP-free diet: 1.05±0.11; Significance: (b) and (d) vs. (a) and (c), $p<0.0005$) (Qualitative score: (d) 2nd CMP-free diet: 1.85±0.10; $p<0.001$). During the second challenge symptoms reappeared within 24 to 48 hours: all 21 patients had painful passage of stools and for this reason the challenge was suspended on the third day. Six patients did not improve on the first CMP-free diet period (mean number (±SD) of stools per day: unrestricted diet: 0.18±0.12; 1st CMP-free diet: 0.20±0.13 and their difficulty in passing stools did not change (Qualitative score: Control: 3; 1st CMP-free diet: 3). These patients were subsequently treated with lactulose, and only a partial regression in symptoms was observed. They were permanently given an unrestricted diet, except for one infant who had episodes of recurrent bronchospasm related to the ingestion of cow's milk. Patients were followed up monthly for a mean period of 18 months (range 10 to 30 months). Reintroduction of cow's milk was cautiously attempted in 16 children 6-9 months after the diagnosis of CMP allergy-dependant constipation. In eight children CMP did not cause the onset of any problems and it was reintroduced on a permanent basis; in eight patients CMP led to the reappearance of constipation within 2 to 3 days after introduction, and these infants were still following CMP-free diet at the time the paper was written. No harmful reactions with either soy milk or ass's milk were reported. It is important to note that significant differences at baseline were found between patients who were cured with the CMP-free diet and those whose condition did not improve with this diet. Patients who were cured with the CMP-free diet were more likely to have a history of CMP allergy or symptoms of CMP allergy (atopic dermatitis or recurrent episodes of bronchospasm) at the time they entered the study than those whose condition did not improve with this diet (15/21 vs. 1/6, chi square= 3.75; $p<0.05$).

Increasing fluid intake

One open label RCT conducted in the USA[107] (1998) [EL=1-] aimed to determine whether or not increasing fluid intake by either excess water intake or excess hyperosmolar liquid intake would significantly alter the course of simple constipation in children. Ninety prepubertal children (31 boys (47.46%) mean age 7.5 years (range 2.5 to 12.5 years)) with moderate to severe idiopathic constipation were included. Children were randomised into two intervention groups or one control group. During 2 weeks one intervention group was instructed to increase water intake by 50% on the basis of the total measured oral liquid intake during the baseline week. The second group received supplemental liquid in the form of hyperosmolar liquids: Kool-Aid, juice, soda pop or other liquids known to contain more than 600 mOsm/l. The control group received no intervention. Neither increasing water intake nor increasing hyperosmolar liquid intake significantly increased stool frequency or improved stool consistency or difficulty with stool passage within groups when comparisons were made with previous weeks, or between the three groups during the same week (analysis of variance). A second round of analysis excluded all subjects who failed to comply with at least 75% of assigned intervention, and this did not change the study outcomes. No comparison was made of baseline characteristics between the three groups. One hundred and eight children were originally included, but only 90 completed the entire study as assigned. Eighteen children failed to comply with 75% of the intervention.

Increasing Physical Activity

One open non-randomised controlled trial conducted in Israel [108] (2009) [EL=1-] assessed the effect that stepping while standing had on constipation in children with severe cerebral palsy (CP). Twenty-two children (aged between 3.5 and 10 years) with a diagnosis of spastic quadriplegic CP with gross motor function classification system (GMFCS) level 4 or 5 were included. All children were unable to stand and walk with a traditional walker/rollator because of insufficient upper extremity control, would attempt to step when supported in a standing position and had flexion contractures of less than 30° in the hips and the knees. Eleven children began a trial of the David Hart Walker (HW) orthosis (6 males, mean age 6.1±2.1 years) in addition to their physical therapy sessions, and 11 children (6 males, mean age 6.7±1.6 years) who were matched for age and sex with the study group underwent a program with a standing frame (SF) as part of their physical therapy session. At entry the proportion of constipation on both groups was equal (6/11, 54.5%). After 6 months the study (HW) group had significantly reduced their level of constipation (1/11 9.1%) and the control (SF) group had no change in constipation (6/11 54.5%) (p=0.02). It should be noted that the sample size was very small and that the Paediatric Evaluation of Disability Inventory (PEDI) was higher at baseline in the study group when compared to the control group (indicating better self care, mobility and social function). There was no attrition/loss to follow up in either group.

Evidence statement

Dietary modifications

There is no evidence for the clinical effectiveness of dried or fresh fruits, fruit juices, vegetables, cereals, fructo-oligosaccarides, omega 3 fish oils or excluding goat's milk from the diet for ongoing treatment/maintenance in children with chronic idiopathic constipation.

Increasing fibre

One double-blind RCT [EL=1+] showed that a yogurt drink with mixed dietary fibre (transgalacto-oligosacharides, inulin, soy fibre and resistant starch) was as effective as a yogurt drink containing lactulose at increasing defecation frequency/week and decreasing the number of patients with ≥1 faecal incontinence episodes/week. The study also showed that the stool consistency was significantly softer in the lactulose group as compared to the fibre group. The number of patients using of step-up medication at 3 weeks was significantly smaller in the group taking fibre than in the group taking lactulose but there were not significant differences regarding this outcome at 8 and at 12 weeks.

One double-blind RCT (pilot study) [EL=1+] showed that a cocoa husk supplement rich in dietary fibre (cocoa husk + betafructosans) was more effective than placebo at decreasing the number of children reporting hard stool consistency and increasing the number of children reporting a subjective improvement in stool consistency. The study also showed that the cocoa husk supplement was as effective that placebo at subjectively improving pain on defecation and increasing the number of bowel movements per week.

One prospective case series [EL=3] showed that fibre supplementation with wheat bran (All Bran, Kellogg's®) was effective at decreasing the number of laxatives used per week

One open label non-RCT [EL=1-] showed that Prune-Malt®, a palatable mixture containing prune and fig concentrate and non-diastatic malt syrup neutralised with potassium carbonate was effective at improving constipation. One hundred and thirty two parents rated the treatment as good, 47 as acceptable and 21 as poor.

Supplements

There is no evidence for the clinical effectiveness of supplements containing partially hydrolysed guar gum, iron or pectin for ongoing treatment/maintenance in children with chronic idiopathic constipation

One double-blind RCT (cross-over) [EL=1+] showed that glucomannan (a polysaccharide of d-glucose and d-mannose, equal to 450mg of alimentary fibre) was more effective than placebo at successfully treating constipation as per physician rating, and improving children's symptoms as per parent rating. Successful treatment (physician rating) and improvement (parent rating) were independent of amount of fibre intake from the treatment. Significantly more children who were also taking laxatives were treated successfully with glucomannan than with placebo. Children with constipation only were significantly more likely to be treated successfully with glucomannan compared with children with constipation and encopresis

One prospective case series [EL=3] showed that glucomannan was effective at significantly increasing the number of stools per week, improving the stool consistency and painful defecation and reducing laxative use.

Probiotics

One double blind RCT [EL=1+] showed that probiotic (Lactobacillus case rhamnosus, Lcr35) and magnesium oxide (MgO) were equally effective at increasing daily defecation frequency and decreasing the percentage of children having hard stools and both were more effective than placebo at increasing daily defecation frequency and decreasing the percentage of children having hard stools. The three treatments were equally effective at decreasing faecal soiling. Children taking placebo had to make use of glycerine enema significantly more often than children taking either MgO or probiotic (Lactobacillus case rhamnosus, Lcr35) but that there were no significant differences between children taking probiotic (Lactobacillus case rhamnosus, Lcr35) and children taking MgO regarding this outcome. There were no significant differences between the 3 groups regarding the need to use lactulose. Significantly more patients were successfully treated with MgO or probiotic (Lactobacillus case rhamnosus, Lcr35) compared to placebo but there were no significant differences between children taking probiotic and children taking MgO regarding this outcome.

One triple blind RCT [EL=1+] showed that probiotic (lactobacillus rhamnosus GG) + lactulose was as effective as placebo plus lactulose at increasing the average number of spontaneous bowel movements per week and decreasing the episodes of faecal soiling per week, the straining frequency per week and the number of patients using laxatives.

One prospective case series [EL=3] showed that a probiotics mixture (bifidobacteria B. bifidus, B. infantis and B. longum + lactobacilli L. casei, L. plantarum and L. rhamnosus) was effective at significantly decreasing the number of faecal incontinence episodes per week only in children presenting with <3 bowel movements per week at baseline. The study also showed that the probiotics mixture was not effective at improving stool consistency.

Infant formulae

One double-blind RCT (cross-over) [EL=1+] showed that Nutrilon Omneo (new formula, NF), a formula with higher protein content, 100% of it based on whey protein hydrolysate (no casein, no intact whey protein), a mixture of prebiotic oligosaccharides (GOS and lcFOS), a higher concentration of sn-2 palmitic acid and a lower lactose content was as effective as a standard formula (SF) at reducing painful defecation and increasing defecation frequency. The study also showed that NF was significantly more effective than SF at improving the stool consistency.

One open label RCT [EL=1-] showed that Novalac-IT, a magnesium-enriched infant formula was significantly more effective than a 20% strengthened regular infant formula at improving stool consistency, increasing stool frequency and reducing difficulties in defecation.

One open label RCT showed that a new formula (NF) (Omneo / Conformil) based on palmitic acid predominantly esterified at the β-position, oligosaccharides (GOS and FOS) with a prebiotic activity, partially hydrolysed protein, low lactose content and higher density was significantly more effective than a standard formula at increasing stool frequency.

One prospective case series showed that a new formula (NF)* was effective at increasing stool frequency.

One prospective case series [EL=3] showed that Novalac Anti-Constipation, a formula with an adapted concentration of magnesium and lactose was effective at significantly increasing the number of daily stools and the number of children having normal stools, as well as at reducing the number of children presenting with pain or discomfort on defecation and the number of children needing external help at defecation.

Soy milk

One double-blind RCT (cross over) [EL=1+] showed that excluding cow's milk and its derivatives from the diet and giving soy milk instead was more effective than giving an unrestricted diet including cow's milk and its derivatives at significantly increasing the number of bowel movements, improving stool consistency and reducing the pain or difficulty on passing stools in children with chronic constipation and suspected food allergies, but was not effective in children in whom food allergies were not suspected at baseline.

Excluding cow's milk protein from the diet

One double-blind RCT (cross over) [EL=1+] showed that excluding cow's milk and its derivatives from the diet was more effective than giving an unrestricted diet including cow's milk and its derivatives at significantly increasing the number of bowel movements, improving stool consistency and reducing the pain or difficulty on passing stools in children with chronic idiopathic constipation and suspected food allergies, but was no effective in children in whom food allergies were not suspected at baseline.

Three small case series and embedded randomised controlled challenges [EL=3] showed that a cow's milk-free diet was effective at increasing the number of bowel movements, improving stool consistency and reducing the pain or difficulty on passing stools in children with chronic constipation and food intolerance, but was not effective in children with constipation unrelated to food intolerance

* It is likely that this formula is also Omneo/Conformil. The authors did not provide any brand name in the paper but the composition of the formula is the same as the one the authors used for their 2005 study

Increasing fluid intake

One open label RCT [EL=1−] showed that increasing liquid intake by either excess water intake or excess hyperosmolar liquid intake did not have significant impact on stool frequency, stool consistency or difficulty with stool passage in constipated children when compared to controls who did not increase their fluid intake.

Increasing physical activity

One open non-randomised controlled trial [EL=1−] showed that a device which allows children with severe cerebral palsy to step while standing was more effective than passive standing in improving symptoms of constipation.

GDG interpretation of the evidence

The opinion of the GDG is that a poor diet alone is rarely the cause of childhood constipation. The GDG consensus is that it is extremely important to emphasise that diet is important but that it is not the first factor to consider in the treatment of constipation. Dietary manipulations should be carried out alongside treatment with laxatives and behavioural therapy.

Increasing physical activity

Despite the fact that there is no good quality evidence for the effectiveness of increasing physical activity to improve constipation, it is the opinion of the GDG that exercise should be encouraged. It has been recommended by The Department of Health[88] that children should do at least 60 minutes of moderate intensity physical activity per day as part of a healthy lifestyle.

Fibre-rich foods

No evidence was found to suggest that increasing fibre-rich foods such as fruits, vegetables and cereals is effective in treating or managing constipation. The GDG felt that encouraging children to eat more fibre, when they are already having a healthy balanced diet with sufficient fibre, could be detrimental. A high fibre intake in this case could exacerbate symptoms and potentially increase soiling. It is the opinion of the GDG that children should be advised to eat a healthy diet, including fibre containing foods, as outlined by the Paediatric Group of the British Dietetic Association in 'Food for the Growing Years' and 'Food for the School Years' etc.[109, 110]

Fibre supplements

The evidence for using fibre supplements such as Prune-Malt, cocoa husks and glucomannan in the treatment of constipation is very limited. It is the view of the GDG that this evidence is not enough to recommend these products in the treatment or ongoing management of idiopathic constipation.

Probiotics

Although there is some evidence from three studies that suggests probiotics may be useful in the treatment of constipation, this was found to be insufficient to recommend probiotics in the treatment of idiopathic constipation in children.

Infant formulas

The GDG examined four studies, each on a different infant formula; none of which are used in the UK. The GDG believes that there is not enough evidence to suggest that any of the formulas are clinically effective in the treatment or ongoing management of constipation.

The GDG believes that the current common practice of switching from one infant formula to another to alleviate constipation may be detrimental. It takes time to trial infants with different feeds, and this often delays treatment with laxatives.

Excluding cow's milk

Although there is some evidence for excluding cow's milk from the diet to improve constipation, the opinion of the GDG is that the studies are of a poor quality and selection of participants biased. In the studies which were reviewed, both soy and ass's milk were used in the placebo group. Recommendations in the UK are that children with suspected cow's milk protein intolerance should be given feeds based on extensively hydrolysed proteins (http://www.dh.gov.uk/en/Healthcare/Children/Maternity/Maternalandinfantnutrition/DH_4099143).[89] Soy and ass's milk are inappropriate alternatives to cow's milk and should be avoided due to a risk of allergenic cross-reactivity.

Replacing goat's milk

No evidence was found on replacing cow's milk with goat's milk in the diet to improve constipation in children. The recommendation from the Department of Health (http://www.dh.gov.uk/en/Healthcare/Children/Maternity/Maternalandinfantnutrition/DH_4099143) is that goat's milk is not suitable to be used as an infant feed because of its high renal solute load, inadequate vitamin and mineral content and doubtful microbiological safety.[89] Infant formulas based on goat's milk are not available in the UK. In addition, goat's milk protein can be as sensitising as cow's milk protein and is therefore not recommended when a cow's milk protein allergy is suspected.

Increasing fluid intake

The GDG found little evidence for the effectiveness of increasing fluid intake in children with chronic constipation. Despite this, it is the GDG's view that increasing fluid intake to recommended levels is essential. Osmotic laxatives are not effective without sufficient fluid intake

Recommendations

Do not use dietary interventions alone as first-line treatment for childhood constipation.

Advise 60 minutes of physical activity per day as part of ongoing treatment or maintenance in children with idiopathic constipation. This activity should be tailored to the child's stage of development and individual ability.

Treat constipation with laxatives and a combination of:

- Negotiated and non-punitive behavioural interventions suited to the child's stage of development. This 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 (described in recommendation 1.5.4 below).

Advise parents and children (where appropriate) that a balanced diet should include:

- Adequate fibre. Recommend including foods with a high fibre content (such as fruit, vegetables, baked beans and wholegrain breakfast cereals). Do not recommend unprocessed bran, which can cause bloating and flatulence and reduce the absorption of micronutrients.
- Adequate fluid intake (see table 5)

Provide children with idiopathic constipation and their families with written information about diet and fluid intake.

In children with idiopathic constipation, start a cow's milk exclusion diet only on the advice of specialist services.

Table 5 UK dietary reference values for fluid requirements by age groups

Age	Fluid requirements (ml per kg per day)
0-3 months	150
4-6 months	130
7-9 months	120
10-12 months	110
1-3 years	95
4-6 years	85
7-10 years	75
11-14 year	55
15-18 years	50

Research Recommendation

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

Why this is important
It has been shown that along with healthy eating, an active lifestyle is essential to improving and maintaining health.[88] Increasing activity levels contributes to the prevention and management of many conditions and diseases. It may be that increasing physical activity levels could be beneficial in the treatment of children with chronic constipation

In infants with chronic idiopathic constipation, does changing from one infant milk formula to another improve symptoms? (E.g. Standard infant formula vs. infant formula with oligosaccharides vs. standard infant formula + laxative)

Why this is important
It is common practice to change from one formula to another to help alleviate constipation. As it takes time to trial infants with different feeds, this can delay much-needed treatment with laxatives. Good quality evidence for the use of a particular infant formula in the treatment of constipation would thus be beneficial.

5.5 Psychological and behavioural interventions

Introduction

Families of children with idiopathic constipation are often given psychological and/ or behavioural advice as well as being referred for more formal psychological therapy. This advice can be given at varying stages of the child's course of constipation often with little appreciation of the child and families ability to carry it out or indeed whether the child is able to achieve what is asked of them as far as bowel movements are concerned. For the majority of children the psychological component of their constipation is likely to be secondary to the physical discomfort of being unable to pass stools easily or to the accidental leakage as a result of faecal loading.

Psychological and behavioural interventions can range from predominantly behavioural toilet training, bowel retraining which may also involve more formal behavioural modification of chaining and shaping programmes to specific psychological models of therapy such as psychodynamic psychotherapy, cognitive-behavioural therapy and systemic family therapy.

From a clinical perspective it is important that any psychological and/or behavioural intervention is implemented alongside effective laxative therapy[111], [112] in order that the child can achieve comfortable passage of stools and parents have realistic expectations of the child. Any interventions need to be developmentally appropriate for the child and delivered in a child friendly manner as well as facilitating parental support and understanding. In order for any psychological intervention to be carried out effectively it is important that a therapeutic relationship be established to facilitate both parents and child's motivation to engage in the intervention and to feel able to maintain this for long enough to see results that they experience as positive. [113], [114] It is how the health professional working with the family mediates a holistic intervention that initiates a successful working relationship with both child and family.

Clinical Question

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

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation
- included the following interventions in addition to laxatives in at least one of the treatment groups : Intense psychotherapy (cognitive behavioural therapy (CBT), systemic/family therapy or psychodynamic psychotherapy) , psychosocial counselling, mediational models in cognitive or behavioural therapy, minimal intervention models using parents in behaviour therapy or behaviour modification, clinical hypnosis , toilet /bowel / habit training and retraining, 'chaining' and 'shaping' programmes, maintaining toilet diaries, rewarding, positive reinforcement, incentive/reward charts, star charts, reward systems, parenting programmes if clearly specify what the program was, psychoeducation (including biofeedback) and Portage as an educational model
- included the following outcomes: changes in frequency of bowel movements, changes in stools consistency/appearance, changes in pain/difficulty on passing stools, changes in frequency of episodes of soiling, reduction in laxatives use, parent/child views/satisfaction or quality of life
- were not case-reports

- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

A total of 1689 articles were identified from the searches and 48 articles were retrieved for detailed assessment. Of these 10 studies were included in this review: 7 parallel-RCTs, 1 retrospective cohort, 1 quasi-randomised RCT and 1 retrospective audit.

Narrative summary

Conventional treatment alone vs. conventional treatment + biofeedback

Meta-analysis of 4 RCTs comparing conventional treatment alone vs. conventional treatment + biofeedback showed that treatment success was not significantly different between the two treatment groups either in the medium term (fig 6.1) or in the long-term (fig 6.2).

Fig 6.1 Conventional treatment alone vs. conventional treatment + biofeedback: treatment success at medium-term (6 months)

	CT+ biofeedback		CT alone			Odds Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Loening-Baucke, 1990	12	22	1	19	28.2%	21.60 [2.44, 191.38]
Nolan 1998	2	14	2	15	28.9%	1.08 [0.13, 8.95]
van der Plas, 1996	44	94	48	93	42.9%	0.82 [0.46, 1.46]
Total (95% CI)		**130**		**127**	**100.0%**	**2.24 [0.33, 15.08]**
Total events	58		51			

Heterogeneity: Tau² = 2.12; Chi² = 8.41, df = 2 (P = 0.01); I² = 76%
Test for overall effect: Z = 0.83 (P = 0.41)

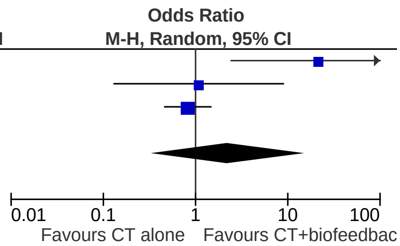
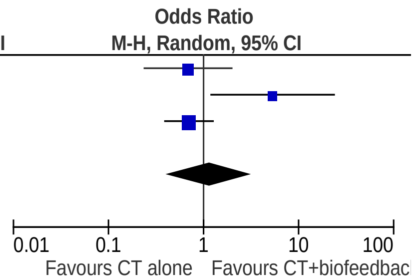


Fig 6.2 Conventional treatment alone vs. conventional treatment + biofeedback: treatment success at long-term (12 months)

	CT+biofeedback		CT alone			Odds Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Borowitz, 2002	11	31	12	27	32.7%	0.69 [0.24, 1.98]
Loening-Baucke, 1990	11	22	3	19	24.5%	5.33 [1.20, 23.66]
van der Plas, 1996	46	92	54	92	42.8%	0.70 [0.39, 1.26]
Total (95% CI)		**145**		**138**	**100.0%**	**1.15 [0.41, 3.23]**
Total events	68		69			

Heterogeneity: Tau² = 0.57; Chi² = 6.42, df = 2 (P = 0.04); I² = 69%
Test for overall effect: Z = 0.26 (P = 0.80)



The following are the narratives summaries for the individual studies included in the metanalysis:

One parallel-RCT conducted in the USA [115] (1990) [EL=1+] determined whether outcome in chronically constipated and encopretic children with abnormal defecation dynamics could be improved with biofeedback training. Forty-three children (33 boys, mean age: 8.9 years (range 5 to 16)) with chronic constipation and encopresis and abnormal defecation dynamics were included. Children were randomised to receive for 6 months conventional treatment alone (CT) (n=19) or conventional treatment + biofeedback (BF) (n=22). CT consisted of use of laxatives, increase of dietary fibre and scheduled toileting. Disimpaction was carried out using enemas (type and dose not reported). For the maintenance phase children received magnesium oxide (milk of magnesia, MOM) at approximately 2ml/kg body weight daily to induce at least 1 bowel movement daily and prevent faecal retention. Doses were decreased gradually to maintain daily bowel movement and prevent faecal retention and soiling. Children in the BF group received the same CT as previous in addition to up to six sessions of biofeedback therapy 5 to 9 days apart. One session included approximately 30 to 35 defection trials and lasted approximately 45 minutes. Patients in both groups were instructed to discontinue laxative therapy at 6 ± 0.5 months after initiation of therapy. Outcome measured was recovery rate at 7 and 12 months after initiation of treatment. Patients were considered to have recovered if they had ≥3 bowel movements/week and soiling ≤2 episodes/month while not receiving laxatives for 4 weeks. At 7 months significantly more children in the BF group recovered as compared to the CT group ((number recovered, %), BF (n=22): 12 (55) vs. CT (n=19): 1(5) p<0.001). Recovery rates did not differ between boys and girls in general and within the biofeedback group in particular. Prior unsuccessful treatment was no related to treatment outcome in either group. Patients with an initial abdominal faecal mass (severe constipation) were significantly more likely to recover with BF training than with CT alone (46% vs. 0%, p<0.02). At 12 months significantly more children in the BF group recovered as compared to the CT group ((number recovered, %), BF (n=22): 11 (50) vs. CT (n=19): 3 (16) p<0.05). A 14-yeor old boy in the BF group had a relapse. He had severe faecal impaction with enormous abdominal distension initially. Faecal impaction recurred 4 months after successful discontinuation of MOM. At the time the study was written he had no soiling but required intermittent treatment for constipation. One boy in the CT was lost to follow-up 1 month after treatment began. At that visit he was taking MOM and his soiling had resolved. One boy was lost to follow-up in the BF group after the first biofeedback session. Baseline characteristics were not significantly different between the two groups apart from gender: there were more girls in the BF group than in the CT group (41% vs. 5%, p<0.02). During initial evaluation severe constipation (an abdominal faecal mass present) was significantly more frequent in girls than in boys: (90% vs. 48%, p<0.03). It was not completely clear who measured outcomes and how and whether questionnaires were piloted. Intention to treat analysis was not performed.

A parallel-RCT conducted in the Netherlands [116] (1996) [EL=1+] evaluated the effect of biofeedback training and conventional treatment on defecation dynamics and outcome in chronically constipated children. One hundred and ninety-two children (126 boys, median age 8 years) with paediatric constipation were included. Patients were randomised to receive conventional laxative treatment alone (CT) (n=94) or conventional laxative treatment and biofeedback (BF) (n= 98). Patients on CT received five outpatient visits lasting approximately 30 minutes during which laxative treatment and information from a diary containing defecation frequency and encopresis and/or soiling episodes were discussed. High-fibre diet was advised but additional fibre supplements were not prescribed. Patients were instructed to try to defecate on the toilet for 5 minutes immediately after each meal. During the first 3 days patients were to use daily enemas (120ml sodiumdioctylsulfosuccinate, 1mg sorbitol, 250mg per ml, Klyx) at home. If on day 3 enemas still resulted in large amounts of stool, they were continued for a maximum of 7 days. After the initial 3-

day enema treatment, patients started oral laxatives with Importal® (lactitol betagalactoside sorbitol, 1 sachet of 5g/10 kg body weight per day divided into two doses). Enemas were given whenever spontaneous defecation was delayed for more than 3 days. Motivation was enhanced by praise and small gifts. Children in the BF group received five outpatient visits, including the same conventional treatment as described above, in combination with five biofeedback training sessions. As far as possible, both groups received equal attention. The treatment period lasted 6 weeks. Treatment was considered successful if the patients achieved ≥3 bowel movements per week and <2 soiling or encopresis episodes per month while not receiving laxatives for 4 weeks. Patients were assessed after the last visit of the intervention period at 6 weeks, then at 6 months, 1 year, and 1½ years. Treatment success was reported as number of children cured, and was not significantly different between the two group at any of the assessment points (at 6 weeks, CT: 31/94 (33%) vs. CT+BF: 31/98 (32%); at 6 months, CT: 48/93 (52%) vs. CT+BF: 44/94 (47%); at 1 year, CT: 54/92 (59%) vs. CT+BF: 46/92 (50%); at 1½ year: CT: 52/92 (57%) vs. CT+BF: 44/92 (48%)). At baseline, patients were comparable for gender, age, frequency of gastrointestinal complaints and urinary problems. During the intervention period, three patients in the CT group refused manometry at the end of the treatment period: one patient was successfully treated and the parents refused permission for manometry; one patient was unsuccessfully treated and refused manometry; and one patient was lost to follow-up after two visits. Two patients of the BF group discontinued treatment: one 5-year-old patient did not cooperate and another patient discontinued treatment because his parents could not afford the cost of transport. At 6 months, five patients were lost (four patients in the CT+BF and one patient in the CT group), and at 1 year eight patients were lost to follow up (another two in the CT+BF and one in the CT group). Patients lost to follow up were withdrawn from further analysis

A parallel RCT conducted in Australia[117] (1998) [EL=1+] determined whether surface electromyographic (EMG) biofeedback training produced sustained faecal continence in medical treatment resistant and/or treatment dependent children with anismus. Twenty-nine children aged ≥4 years (24 boys, age range: 4.8 to 14.9 years) were included. Children were randomised to receive electromyographic biofeedback training and conventional medical treatment (BF) or conventional medical treatment alone (CT). Up to 4 sessions of biofeedback were conducted at weekly intervals for each patient, each session consisting of approximately 30 to 35 defecation attempts. The aim was to achieve 10 relaxations of the external anal sphincter without visual feedback in two successive sessions. If this occurred in fewer than 4 sessions then biofeedback was discontinued. At completion of training, children were followed at monthly intervals by a single paediatrician, who gave verbal reinforcement of the skills learned during training. CT alone comprised laxative therapy, behaviour modification and dietary advice. Laxative therapy occurred in two phases. The initial disimpaction phase: 3-day cycles of 5 mL 'Microlax' enemas (sodium citrate) on day 1, one 5mg bisacodyl tablet after school and 1 in evening of day 2. Up to 4 cycles (12 days) were undertaken. Further cycles were prescribed if there was later evidence of stool re-accumulation. During the maintenance phase different laxatives were administered: liquid paraffin 5 to 30ml once or twice a day, senna granules and or bisacodyl tablets. Medication use was decreased to a level consistent with maintenance of continence as monitored by bowel diary. Standard paediatric behaviour modification consisted of clarification during a joint parent-child interview of the postulates underlying physiological basis for encopresis. The bowel training programme used positive reinforcement for successful defection in the toilet and additional reinforcement for each 24 hours without soiling. Reinforcement consisted of parental praise and use of star-chart diary (fitness training card) to indicate soiling- free days. A regular sitting programme of 5 to 10 minutes toilet-time within 30 minutes of each meal was basis of the programme. Dietary advice, general counselling and support were provided by a paediatrician. Psychiatric assessment or treatment was initiated when indicated clinically. It was unclear how long the CT lasted for. Treatment success was assessed at 6 months after initiation of therapy. Full remission was defined as no medication and no soiling for at least 4 weeks; full remission on medication was defined as on medication and no soiling for at least 4 weeks; partial remission defined as soiling no more than once a week, regardless of medication used. The use of medication was attempted by all those not in full remission, not only those who were worse or not improved. The remainder were those who were soiling more than once a week, regardless of medication use. Improvement was defined as progression by at least one level from baseline status, but without achieving full remission. There were no significant differences between both treatment groups regarding the number of children who achieved full remission (BFT+CT (n=14): 2 (14%) vs. CT (n=15): 2 (13%); 95% CI on difference, −24% to 26%). There were no significant differences between both treatment groups after combining the number of children who achieved full remission and the number of children who improved (BFT+CT (n=14): 2 (14%) vs. CT (n=15): 4 (27%); p = 0.7; 95% CI on difference, −46% to 23%). Three out of 14 patients in the BFT group completed the training in three sessions, and the remainder underwent four sessions. Only one patient was unable to demonstrate relaxation of the external anal sphincter with attempted defecation. Only one patient (same as previous) was unable to defecate the biofeedback balloon by the time of their final session. All patients complied well with the instructions and procedures involved in the training. Two patients complained of transient discomfort when the biofeedback apparatus was inserted. No other adverse effects were seen or reported. At baseline there were slightly more subjects with primary encopresis in the biofeedback group than in the control group. No attrition/loss to follow up was reported. It should be noted that no definition of constipation was given and also the study included a very small sample of children.

Laxatives vs. laxatives + behavioural intervention vs. laxatives + behavioural intervention + biofeedback

A parallel-RCT conducted in the USA [118] (2002) [EL=1+] compared short- and long-term effectiveness of three additive treatment protocols in children experiencing chronic encopresis. Eighty-seven children aged between 5 and 15 years of age (72 boys, mean age at time of enrollment: 8.6 ± 2.0 years (range, 5 to 13 years)) who had experienced encopresis for a minimum of 6 months, defined as at least weekly episodes of faecal soiling for at least 6 months were included. Children were randomised to receive intensive medical therapy (IMT), intensive medical therapy + enhanced toilet training (ETT) or intensive medical therapy + enhanced toilet training + anal sphincter biofeedback (BF). In the IMT group 1 of 2 paediatric gastroenterologists directed the treatment: colonic disimpaction with a series of enemas followed by sufficient laxative therapy to produce at least one soft stool each day without associated pain. Laxatives prescribed were magnesium oxide (milk of magnesia, MOM) and/or senna (Senokot, Ex-Lax, or Fletcher Castoria). Laxative dosages were adjusted regularly to produce 1 to 3 soft bowel movements daily. An enema or suppository was administered if the child had not produced a bowel movement during a 48-hour period. No specific dietary recommendations or manipulations were undertaken. Families received specific instructions and a written brochure detailing the treatment protocol and the need for children to attend the toilet at least twice dally, preferably after breakfast and supper. Children in the ETT group received similar enema and laxative therapy, with one clinical psychologist adjusting the laxative dose. The only difference from the previous therapy was that laxative therapy was decreased gradually when children demonstrated a stable bowel frequency with no soiling episodes. As long as the child had daily bowel movements of normal size for a week, the laxative dose was decreased by one quarter. This process was continued until laxative therapy was discontinued. If the child did not pass daily bowel movements of normal size, the laxative dose was increased. Parents and child were instructed on the psychophysiology of constipation and encopresis, and on how responding to early rectal distension cues along with regular toileting was critical to avoid reimpaction and to establish regular bowel habits. Various incentive programs were established, depending on the developmental age and the motivation of the child. Target behaviours were spontaneous trips to the toilet and clean pants. Toilet training was "enhanced" because instructions were given on the role of paradoxical constriction of the external anal sphincter, and because appropriate defecation straining was modelled. The therapist sat on a portable toilet and demonstrated how to relax the legs and feet, how to take in a deep breathe and hold it while sitting up straight, and how to push down with the held breath and pull in from the lower abdomen to propel out a stool. The child then replicated this while sitting on a portable toilet. The child received "hand feedback" by placing one hand on the abdomen just below the navel to feel the abdomen move out when the breath was pushed down, and placing the second hand just below the first to feel inward movement with contraction of the rectus abdominous. Parents were instructed to prompt these behaviours at home. Additionally, 8 to 12 minutes of "toilet time" was scheduled daily, beginning 15 to 30 minutes after the same two meals. During these times, children were instructed to practice tensing and relaxing the external anal sphincter for the first 4 minutes, with the objective of localizing control of, and fatiguing, the external anal sphincter, and to mechanically stimulate the rectum. To desensitize children to toilet sitting, the second 4 minutes were spent "having fun" while being read to or playing games. During the final 4 minutes, the child was to strain and attempt to have a bowel movement while relaxing his or her legs and feet. This routine toilet sitting was discontinued 2 weeks after the last scheduled treatment session. The third group received the same instructions that previous two groups and simultaneously received surface electromyographic biofeedback training. The same two psychologists who worked with the ETT group also worked with the BF group. It was unclear how long each of the treatments lasted. Data concerning toileting habits were collected for 14 consecutive days, before and after the initial outpatient visit, and again at 3 months, 6 months, and 12 months after initiation of therapy. Treatment was considered successful if the child experienced no episodes of faecal soiling during the 2-week assessment 12 months after initiation of therapy. There were no significant differences between the three groups at any time regarding soiling frequency ((mean, SD) at 3 months: IMT: 0.54 (0.68) vs. ETT: 0.22 (0.21) vs. BF: 0.34 (0.51); at 6 months: IMT: 0.44 (0.52) vs. ETT: 0.38 (0.45) vs. BF: 0.20 (0.26) and at 12 months: IMT: 0.33 (0.48) vs. ETT: 0.36 (0.53) vs. BF: 0.27 (0.37)). At 3 months, 6 months, and 12 months, the number of children who responded in the ETT group was significantly greater than in either the IMT or the BF group ((% children) at 3 months: IMT: 45 vs. ETT: 85 vs. BF: 61; at 6 months: IMT: 41 vs. ETT: 74 vs. BF: 58 and at 12 months: IMT: 41 vs. ETT: 78 vs. BF: 61; p<0.05), and these results were very stable over time (p<0.001). With all three regimens, the response to treatment during the first 2 weeks of therapy strongly correlated with response to treatment at 3, 6, and 12 months (r>0.90, p<0.0001 in all cases). Of those children who had significant improvement after 2 weeks of therapy, 86 continued to improve at 3 months, 83 at 6 months, and 81 at 12 months. There were no significant differences between the three groups in the number of children cured at 12 months (IMT: 10/29 (34.5%) vs. ETT: 12/27 (44.4%) vs. BF: 11/31 (35.5%)). There were no significant differences between the three groups at any time regarding the number of bowel movements passed in the toilet each day ((mean, SD) at 3 months: IMT: 1.44 (0.57) vs. ETT: 1.21 (0.49) vs. BF: 1.25 (0.64); at 6 months: IMT:1.36 (0.61) vs. ETT:1.31 (0.63) vs. BF:1.12 (0.60) and at 12 months: IMT:1.30 (0.61) vs. ETT:1.01 (0.51) vs. BF:1.16 (0.67)). There were no significant differences between the three groups at any time regarding self-initiated toileting each day ((times/day, mean, SD) at 3 months: IMT: 1.53 (0.77) vs. ETT: 1.62 (0.82) vs. BF:1.40 (0.71); at 6 months: IMT:1.49 (0.60) vs. ETT:1.67 (0.95) vs. BF:1.34 (0.72) and at 12 months: IMT:1.40 (0.76) vs. ETT:1.31 (0.83) vs. BF:1.31 (0.69)). There were no significant differences between the three groups regarding laxative use at 12 months IMT: 17/29 (58.6%) vs. ETT: 9/27 (33.3%) vs. BF: 17/31 (54.8%)). There were no significant differences in baseline clinical or demographic characteristics between the three groups. It should be noted that no definition of constipation was given and no sample size calculation was performed.

One parallel-RCT conducted in Croatia[119] (2002) [EL=1+] assessed the success of biofeedback method vs. conventional method in the treatment of chronic idiopathic constipation in childhood over a 12-week period and followed up the effect of biofeedback treatment on defecation dynamics and other anorectal manometric parameters in 49 children aged >5 years (27 male) with chronic idiopathic constipation. Children were randomised to received conventional treatment alone (CT, n=24) or conventional treatment + biofeedback (BF, n=25). Conventional treatment consisted of oral administration of Portalak® (lactulosis, 240mg/day or 10ml syrup) with dose titration for the patient to have at least 3 stools/week. When spontaneous defecation failed to occur for >3 days in spite of appropriate therapy an enema was used. In addition a fibre-rich diet and attempting defecation after meals were advised. Biofeedback was conducted using a pressure technique. The child and the parents were instructed on how to perform Kegel exercises at home. Exercises included alternating 10-second contraction and relaxation of the sphincter and pubo-rectal muscle, performed 5 times a day in 20 cycles. Treatment lasted for 12 weeks. Treatment was considered successful if a frequency of ≥ 3 stools/week and <2 episodes of soiling or encopresis per month were achieved without laxatives. Therapeutic success was evaluated by the use of questionnaires distributed on weekly visits. The number of children cured was significantly higher in the BF group as compared to the CT group (BF: 21/15 (84%) vs. CT: 15/24 (62.5%), $p<0.05$). All children completed treatment. There were no significant differences in baseline characteristics between the two groups. It should be noted that the study included a small sample of children and no sample size calculation was performed. There were insufficient details reported on who measured the outcomes and how they were measured.

One retrospective cohort study conducted in the USA[120] (1995) [EL=2+] evaluated whether patients who received biofeedback treatment (BF) continued with improved outcome compared with patients who received conventional treatment alone (CT). One hundred and twenty-nine children (97 boys) aged 5 to 18 years with chronic constipation and encopresis (≥ 1 soiling episode per week) were included. One group received conventional treatment + biofeedback (BF) and the other group received conventional treatment alone (CT). At least 2 and up to 6 weekly training biofeedback sessions were given. Each session included approximately 30 to 35 defecation trials and lasted approximately 45 to 60 minutes. The number of training sessions given depended on how soon the child learned to relax the external sphincter. Sessions stopped after 10 relaxations of the external sphincter could be accomplished without visual feedback in each of two successive training sessions. CT comprised the use of laxatives, increase of dietary fibre and scheduled toileting (child instructed to defecate for 5 minutes after each meal and after returning from school for the initial months, and try to defecate at least daily once they could recognise the urge to defecate). Disimpaction was carried out with enemas (type and dose not reported). For maintenance magnesium oxide (milk of magnesia, MOM) was administered at approximately 2ml/kg body weight daily to induce at least 1 bowel movement daily and prevent faecal retention. Doses were decreased gradually to maintain daily bowel movement and to prevent faecal retention and soiling. Occasionally mineral oil or senna were used instead of MOM. It was unclear how long the CT lasted for. The follow-up period for the CT group was 4.2 ± 2.5 years and for the BF group it was 4.1 ± 2.4 years. (mean age (years): CT group initial: 9.1 ± 3.3, follow-up: 13.4 ± 3.3; BF group initial:10.4 ± 3.2, follow-up: 14.5 ± 3.3). Patients were considered to have recovered if they had ≥ 3 bowel movements/week and soiling ≤ 2 episodes/month while off laxatives for at least 1 month.

There were no significant differences between groups in any of the outcomes measured (stool frequency/week (mean ± SD): BF (n=63): 5 ± 3 vs. CT (n=66): 6 ± 3; % of children soiling: BF (n=63): 35 vs. CT (n=66): 24; soiling frequency/week (mean ± SD): BF (n=63):1 ± 2 vs. CT (n=66):1 ± 2; recovery rate (number of children, %): BF (n=63): 28 (44) vs. CT (n=66): 41 (62); and laxative use (% children using laxatives): BF (n=63): 25 vs. CT (n=66): 18). Of 64 patients who originally received biofeedback 1 patient did not return after the first unsuccessful biofeedback session and was lost to follow-up. The 63 patients included in the biofeedback group were combined from 2 studies (as clinical characteristics of both groups were similar): 21 patients from one RCT (included already in this review, see Loening-Baucke, 1990) and 42 patients who had not recovered after at least 6 months of conventional treatment. Twenty-three patients had been originally included in the RCT but one boy was lost to follow-up after the first biofeedback session and a second patient received a central nervous system shunt during the follow-up period and was excluded from the analysis. Baseline characteristics were comparable between both groups except for the presence of an abdominal faecal mass (number of children, BF: 60 vs. CT: 41; $p<0.05$). Age and follow-up age were not related to outcome in either group. The length of follow-up was significantly related to recovery for the biofeedback group ($p<0.02$) and for all patients ($p<0.01$) but showed no relationship for the conventionally treated group.

Conventional treatment alone vs. conventional treatment + behavioural intervention

A parallel-RCT conducted in the Netherlands [121] (2008) [EL=1+] evaluated the clinical effectiveness of behavioural therapy with laxatives compared with conventional treatment in treating functional constipation in childhood. One hundred and thirty-four children (76 boys) with functional constipation aged 4 to 18 years referred to a gastrointestinal outpatient clinic were included. Children were randomised to receive conventional treatment alone (CT) (n=67) or laxatives and behavioural therapy (BT) (n=67). All children received treatment for disimpaction with daily Klyx enemas (sodium-dioctylsulfosuccinate and sorbitol; 60 ml/day for children ≤6 years of age; 120 ml/day for children >6 years of age) for 3 consecutive days before starting treatment. During the maintenance phase children received PEG 3350, 1 sachet (10g) per day, and if treatment was considered to have insufficient effect the dose was increased by one sachet. If spontaneous defecation was delayed for >3 days, parents were advised to give an enema or bisacodyl suppository of 5mg. In the BT group it was preferred to give oral bisacodyl tablets of 5mg instead of rectal laxatives. During BT, paediatric psychologists adjusted the laxative dose and consulted the paediatric gastroenterologist when necessary. In both treatment groups, patients kept a bowel diary. The protocolised BT was developed by paediatric psychologists of the authors' hospital. The protocol consisted of two age-related modules: a module for children aged 4 to 8 years and a module for children aged ≥8 years. The learning process for the child and the parents was based on five sequential steps (know, dare, can, will, and do). This approach was derived from a multidisciplinary BT to treat children with defecation disorders. For all involved psychologists, a detailed manual for both age-related modules was available to ensure a standard delivery of therapy. Visits lasted approximately 45 minutes. Conventional treatment was conducted by paediatric gastroenterologists. Visits lasted approximately 20 to 30 minutes when laxative treatment and bowel diary were discussed. Patients and their parents received education to explain that symptoms are not harmful and are common in children with functional constipation and that a positive, non-accusatory approach is essential. Children were instructed not to withhold stool when they feel urge to defecate. Motivation was enhanced by praise and small gifts from the paediatric gastroenterologists. For both the CT and the BT group a total of 12 visits were scheduled during 22 weeks with similar intervals between treatment sessions. Children were assessed at the last visit (post-treatment time point) and 6 months after the 22-week treatment ended (follow-up).

The time between baseline assessment and follow-up was approximately 1 year. Treatment was considered successful if patients achieved a defecation frequency of ≥3 times per week and a faecal incontinence frequency of ≤1 times per 2 weeks, irrespective of laxative use. A secondary outcome measured was stool withholding behaviour. Compared with the BT group, defecation frequency in the CT group was significantly increased (incidence rate ratio (IRR) = 0.75; 95% CI: (0.59 to 0.96); p=0.021). This effect was mainly caused by a difference between interventions at post-treatment ((mean, 95% CI) CT: 7.2 (6.1 to 8.5) BT vs. 5.4 (4.3 to 6.7)) and not at follow-up (6.6 (5.0 to 8.8) BT: 5.3 (4.4 to 6.3). There was no statistically significant difference between both treatment groups regarding faecal incontinence per week (mean) (post-treatment CT: 2.1 (95% CI 0.8 to 5.8) vs. BT: 5.0 (95% CI 2.1 to 12.0); follow-up CT: 6.4 (95% CI 3.5 to 11.7) vs. BT: 8.6 (95% CI 4.0 to 18.3), IRR=2.36 (95% CI 0.77 to 7.31); p=0.135). At post-treatment, success rate was higher in the CT group than in the BT group (%) (CT 62.3 (95% CI 51.1 to 76.1) vs. BT: 51.5 (95% CI 39.7 to 66.9)). However, no statistically significant difference between treatments was found (IRR=0.83 (95% CI 0.60 to 1.14); p=0.249). At follow-up, the number of children successfully treated declined in both groups but again, the difference was not statistically significant (%) CT: 57.3 (95% CI 46.6 to 70.4) vs. BT: 42.3 (95% CI 31.8 to 56.4); IRR=0.74 (95% CI 0.52 to 1.05); p=0.095). There were no significant differences between both treatment groups in the proportion of children who exhibited stool withholding behaviour at follow-up. It should be noted that during treatment 2/64 (3.1%) in the CT group and 9/65 (13.8%) in the BT group discontinued the intervention (p=0.054). At follow-up, four patients dropped out in CT. There was one loss of contact, and three children were referred for BT directly after CT, making them unsuitable for follow-up measurements. Questionnaires were not returned by three patients in both intervention arms at post-treatment and by nine patients (CT: 6; BT: 3) at follow-up. Except for painful defecation (65.0% CT vs. 43.1% BT, p=0 .014), there were no significant differences between the two groups in baseline sociodemographic factors or for clinical characteristics. An intention-to-treat analysis was conducted. Because of withdrawal before treatment start, attrition during the study, failure to fill out questionnaires, or research procedure violations, missing data occurred. Imputation of missing values was used to make intent-to-treat analyses feasible.

Behavioural intervention + laxatives vs. laxatives only

A small parallel-RCT (multicentre) conducted in the USA [122] (2003) [EL=1+] examined the utility and effectiveness of an internet-based version of enhanced toilet training. Twenty-four children aged between 6 and 12 years (19 boys, mean age: 8.46 years (SD 1.81), soiling at least once a week, who had no medical diagnosis other than constipation that could explain their faecal incontinence were included. Children were randomised to receive the web intervention (12 children (10 boys)) or no intervention (12 children (9 boys)). All children were instructed to start with a basic regime of one square of Ex-Lax® (senna), twice a day. The intervention was a web-based program for the treatment of paediatric encopresis (U-CAN-POOP-TOO). This was a child-focused programme, which targets primarily 5 to 10 year old children but was designed to be used by the child and the parent(s) together. The program comprised three core modules which took 60 to 90 minutes to complete, with all users instructed to review them during the first week. The modules were: "The body" (anatomy, physiology and pathophysiology of digestion), "How to poop" (behavioural techniques for treatment of encopresis) and "medication" (clean-out and laxative treatment). New modules were assigned each week based on a follow-up assessment completed by the user about their child's status. Not all modules were necessarily used by all users, only those modules identified as relevant were assigned and reviewed. However, all modules could be viewed by all users. Follow-up comprised 17 to 20 questions, depending on the week. The system contained a total of 22 modules, each taking 5 to 10 minutes to review. Exposure to the program lasted for 3 weeks after which an assessment was conducted. The number of faecal accidents per week decreased significantly more in the web group compared with the no-web group (mean, SD) (0.50 (.85) vs. 8.27 (13.83)). The number of bowel movements passed in the toilet per week increased significantly more in the web group as compared to the no-web group (% change from pre- to post-assessment) (+152% vs. -16%, p=0.001). Using the bathroom without prompts also increased significantly more in the web group as compared to the no-web group (% change from pre- to post-assessment) (+109% vs. -37%, p=0.021). Using the bathroom with prompts was not significantly different between the two groups. There were no significant differences in baseline characteristics between the two groups (age, gender, race, stage of bowel movement training, length of current laxative regime or any of the outcomes measured). No dropouts/lost to follow up were reported. It should be noted that the study included a very small sample of children.

Laxatives + behaviour modification vs. laxatives + behaviour modification + psychotherapy

A quasi-RCT conducted in the UK [113] (1986) [EL=1+] reported the authors' experience with children who presented with faecal soiling, with or without constipation, who were treated by incentive-based behavioural modification, plus or minus psychotherapy, and consider factors that might predict the outcome for a non-intensive approach and in particular, to draw attention to social background as a prognostic indicator. Forty-seven children (26 boys, age not reported) who presented with faecal soiling, with or without constipation were included. For all children in cases where constipation was severe with large faecal masses they were initially admitted to the ward. They were then continued on whatever laxative they had been on before referral. Where no laxative had previously been used the child was offered a twice daily the dose of lactulose. If there was no accumulation of faeces no laxatives were prescribed. No other laxatives were used in this study, and in general their use was minimised, with the parents encouraged to stop the treatment with laxatives as soon as a regular bowel habit was established. In none of the children were suppositories used at any time. All the children were encouraged to take a high residue diet and in particular were asked to take bran with their breakfast cereal. Children were randomised to receive behaviour modification (BM) (n=26) only or behaviour modification + psychotherapy (BM+Psy) (n=21). BM was carried out by a paediatrician. All children were placed on a star chart regimen and offered varying coloured stars for 'sitting on the toilet' and 'remaining unsoiled for a full day'. In some cases stars were awarded to encourage children who were reluctant to take bran in their diet. A contract was negotiated between the child and the parent (usually the father) for an award to be made at the discretion of the paediatrician. The child was to understand that the giving of the award would depend on response to treatment. 'Demystification', alleviation of guilt, and use of explanatory diagrams were used. Children were seen at 6 weekly intervals by the paediatrician for between 3 months and 1 year and were subjected to shows of affection and interest, which included careful and serious inspection of the charts. Failure to keep a star chart on two successive visits resulted in firm statement of displeasure. Two further failures at 6-week intervals led to the stopping of treatment and discharge with the option of psychiatric referral. Discharge of cured patients was at discretion of the parents. Children in the BM+Psy group also received the same BM as previously described. In psychotherapy children were seen by the child psychiatrist at roughly monthly intervals for periods between two and 12 months. At each appointment the mother (and also the father in four cases) was seen for 15 to 30 minutes to explore her feelings in respect of the child's bowel problem and its effect on the family and on her own relationship with the child. Whenever possible the mother's own history was explored and other emotional problems discussed where relevant e.g. expressions of grief, anger, depression, etc. The child was seen for between 15 to 30 minutes for play, including picture drawing, games, and sharing of their own toys and belongings.

Their feelings concerning their problem were also explored. The behavioural star chart was also often brought, and reviewed and the child praised and encouraged according to progress. The mother and child were seen together sometimes early in treatment, sometimes later, depending on their relationship and success with management of the problems to assess to overall progress. One year after initiating treatment success was assessed. Children were considered cured if they had at least 5 normal stools each week without soiling and only occasional use of laxatives (less than once a week). Children were considered improved if they had at least three stools each week and soiling less than once a week. Non-responders were children who had less than three stools each week or soiling more than once a week. These children were considered as failing to improve, despite the fact that in most cases there was less soiling than at the beginning of treatment. Treatment success did not differ between the groups. It is not possible to report the figures here, as they were only analysed by the authors according to compliance with treatment and with the children's social class, but not according to treatment groups. Four children left the study and 13 failed to keep adequate 'star charts'. Two children were subsequently found to be cured. It should be noted that no definition of constipation was given. Additionally the study included a small sample of children and no sample size calculation was performed.

Systemic / Family therapy: externalising vs. behavioural approach

A retrospective audit conducted in the UK [123] (1998) [EL=3] aimed to asses the effectiveness of externalizing treatment (EXT) as compared to other traditional treatments (OTH) in children with soiling problems. One hundred and eight children treated for soiling problems (45 aged 3 to 5 years, 63 aged >6 years) and their families were included. Referrals included 'faecal soiling', 'encopresis', 'psychological soiling', 'failed toileting', 'constipation with overflow' and 'deliberate soiling'. It should be noted that some children were clearly diagnosed in the referral letter as 'constipated' or 'not constipated', but in some referral letters it was not stated whether the referring doctor had checked for constipation. Families who received EXT (n=54) were only included in the study if the treatment approach included: externalizing the poo from the first interview with the child and family; developing a narrative with the child and family where they could see themselves as capable, skilful and determined "to teach the poo a lesson", "outwit the poo" or "defeat the poo"; not using rewards, interpretation, confrontation or paradoxical interventions as therapeutic manoeuvres and finally, attempting to see the whole family at least once. Other treatments (OTH) (n=54) included a mixed group of traditional treatments with predominantly (but not only) a behavioural approach in a family systems context. There were no elements of externalizing in any OTH sessions. The treatment given depended only on the current approach of the therapist who received the referral. Treatment lasted an average of 7.8 months for the EXT group and 6.6 months for the OTH group. At a minimum of 6 months' follow-up (mean 23 months), all parents (including those who left the study) were sent a questionnaire and asked whether there had been any further soiling incidents since they were last seen and the frequency of these incidents in the past month. Where children had returned for paediatric consultation, the frequency of soiling stated in paediatric notes was recorded even if parents did not reply to the audit. GPs were also asked whether they were aware of any further soiling after treatment had ended. Significantly more children who received EXT stopped soiling or improved as compared to children who received OTH, however this outcome was assessed (from notes: EXT 42/47 vs. OTH: 30/40, p=0.02; from GP follow-up: EXT: 29/37 vs. OTH: 24/42, p=0.045; from parent follow-up: EXT: 24/38 vs. OTH: 13/35, p=0.026). Significantly more parents assessed EXT as helpful as compared to OTH (number of parents: 24 vs. 10, p=0.0001). Externalizing proved to be superior for boys, for children aged ≥6 years, for those with frequent soiling at the outset, for those with over 2 years' continuous soiling and those diagnosed as constipated on referral. The average number of appointments was not significantly different between the groups. There were no significant differences between the groups on baseline variables. It was unclear exactly how many children left the study/were lost to follow up.

Evidence statement

One metanalysis of 4 RCTs [EL=1+] showed that conventional treatment plus biofeedback was as effective as conventional treatment alone (including use of laxatives, advice on a high-fibre diet and attempting defecation after meals) at increasing the frequency of bowel movements and decreasing the frequency of soiling in children with chronic constipation both at medium-term (6 months) and long-term (12 months).

One RCT [EL=1+] showed that in the short term (12 weeks) conventional treatment plus biofeedback was more effective than conventional treatment alone (including laxatives, advice on a high-fibre diet and attempting defecation after meals) at increasing the frequency of bowel movements and decreasing the frequency of soiling in children with chronic constipation.

One retrospective cohort study [EL=2+] showed that after 4 years there were no significant differences between children with chronic idiopathic constipation who received conventional treatment plus biofeedback treatment and children who received conventional treatment alone (including use of laxatives, increase of dietary fibre and scheduled toileting) regarding stool frequency, proportion of children soiling, soiling frequency, recovery rate and proportion of children using laxatives.

One RCT [EL=1+] showed that a protocolised behavioural therapy conducted by paediatric psychologists (including teaching parents behavioural procedures) along with use of laxatives was as effective as conventional treatment conducted by paediatric gastroenterologists (including laxatives, discussion of bowel diary, education on symptoms of constipation, instructions to not withhold stools and use of motivation enhancers) regarding frequency of faecal incontinence and proportion of children who exhibited stool withholding behaviour. Conventional treatment was significantly more effective than behavioural therapy at increasing defecation frequency, but overall success rate was not significantly different between the two treatment groups.

One RCT [EL=1+] showed that intensive medical therapy (including laxatives and attempting defecation after meals) was as effective as intensive medical therapy plus enhanced toilet training (including modelling of appropriate defecation straining) or intensive medical therapy plus enhanced toilet training plus anal sphincter biofeedback at decreasing soiling frequency and the proportion of children using laxatives, and at increasing the number of bowel movements passed in the toilet each day and the proportion of children who self-initiated toileting each day. There were no significant differences between the three groups in the overall number of children cured.

One RCT (multicentre) [EL=1+] showed that an internet-based version of an enhanced toilet training programme for the treatment of paediatric encopresis plus laxatives was more effective that laxatives alone at decreasing the number of faecal accidents per week, increasing the number of bowel movements passed in the toilet per week and increasing the use of the bathroom without prompts. Using the bathroom with prompts was not significantly different between the two groups. Most parents found the material understandable, easy to use, believed their child liked the program and found it understandable and easy to use.

One retrospective audit [EL=3] showed that externalizing treatment was more effective than traditional treatments with a predominant behavioural approach in a family systems context at reducing the number of children experiencing soiling.

One quasi-RCT [EL=1+] showed that laxatives plus an incentive-based behavioural modification, was as effective as laxatives plus an incentive-based behavioural modification plus psychotherapy at increasing frequency of bowel movement and decreasing frequency of soiling, in children presenting with faecal soiling, with or without constipation.

- No evidence was found on the following interventions:
- Intense psychotherapy: Cognitive behavioural therapy (CBT) and psychodynamic psychotherapy.
- Psychosocial counselling
- Mediational models in cognitive or behavioural therapy
- Clinical hypnosis
- Toilet /bowel / habit retraining
- 'Chaining' and 'shaping' programmes
- Parenting programmes which clearly specify what the program is
- Portage as an educational model

GDG interpretation of the evidence

The lack of evidence to support the effectiveness of psychological and behavioural interventions may be as a result of the patient selection in the studies included in the review. In these studies the children and families allocated to psychological and behavioural interventions did not appear to meet the usual criteria for psychological referral and in usual clinical situations would have been expected to do as well on laxative medication alone. The evidence therefore suggests that as a matter of routine, children with idiopathic constipation do not do any better when psychological interventions are added to laxative therapy as part of constipation management. The GDG felt that the research settings reported do not reflect clinical reality.

It is the experience of the GDG that many health professionals use behavioural advice as part of their routine practice, especially incorporating star charts to toileting routines. However, this is often initiated when the child is still constipated or not on an effective dose of laxative medication with the result that the child and family are set up to fail. As the child will continue to soil as a result of either overflow or lack of appropriate control this is then seen as a behavioural problem and referred on to psychological services where the involuntary soiling can be misinterpreted as a symptom of psychological distress. It is the view of the GDG that in the majority of children with idiopathic constipation any psychological problems are secondary to the symptoms of the constipation and not the cause.

It is the view of the GDG that psychological and behavioural interventions are effective only when the child is on effective laxative medication and when the outcomes sought are negotiated with both parent and child as being achievable. The advice given needs to be developmentally appropriate and child focussed. Referral on to CAMHS services for psychological issues related to idiopathic constipation in children may be beneficial and cost-effective where there is psychological distress related to the symptoms of constipation, and/or family difficulties that maintain or exacerbate the constipation.

Recommendations

Do not use biofeedback for ongoing treatment in children with idiopathic constipation.

Do not routinely refer children with idiopathic constipation to a psychologist or child and adolescent mental health services unless they have identified psychological needs.

5.6 Complementary therapies

Introduction

Many families consider the use of complementary and/or alternative therapies as a treatment option when conventional treatment 'fails'.

The terms 'alternative' and 'complementary' are usually used to define the use and setting of a therapy in relation to orthodox medicine. 'Alternative' usually refers to treatment modalities that are generally a substitute for orthodox treatment whereas 'complementary' refers to treatments that are used alongside orthodox medical treatments.

There may be very little evidence about the efficacy of many complementary and alternative treatments but their use is widespread and increasing across the developed world. There is a clear need for more effective guidance for the public and health professionals who advise patients as to what does and does not work and what is and is not safe.[124]

Clinical Question

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

- Abdominal massage
- Reflexology
- Hypnotherapy
- Osteopathy
- Cranial osteopathy
- Craniosacral therapy
- Homeopathy

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation being treated with any of the following complementary therapies: abdominal massage, reflexology, hypnotherapy, osteopathy, cranial osteopathy, craniosacral therapy or homeopathy.
- included the following outcomes: changes in frequency of bowel movements, changes in stools consistency/appearance, changes in pain/difficulty on passing stools, changes in frequency of episodes of

soiling, reduction in laxatives use, parent/child views/satisfaction or quality of life

- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

A total of 119 articles were identified from the searches and 14 articles were retrieved for detailed assessment. Of these 1 study was identified for inclusion in this review: a prospective case series [EL=3]

Narrative summary

One prospective case series conducted in the UK [125] (2003) [EL=3] aimed to investigate the efficacy of treating patients with encopresis and chronic idiopathic constipation with reflexology. Fifty children (age range 3 to 14 years, 64% boys) diagnosed with encopresis/chronic idiopathic constipation were included. All children received 6 sessions of reflexology, 30 minutes each at weekly intervals for 6 weeks. Existing medications were unaltered. Frequency of bowel movements (BMs), soiling frequency and parents' attitude towards reflexology were measured before and immediately after treatment was completed. With the help of their parents, children completed questionnaires on bowel motions and soiling patterns before, during and after treatment whereas parents completed questionnaires on their attitude towards reflexology. Frequency of soiling decreased after treatment was completed (children soiling at least daily: 78% vs. 20%, between 1 to 3 times/week: 16% vs. 30% and no soiling at all: 6% vs. 48%; $p<0.05$). Frequency of BMs increased after treatment (children having daily BMs: 18% vs. 24%, between 1 and 4 BMs per week: 46% vs. 72% and no BMs/week: 36% vs. 2%; $p<0.05$). At the beginning of the study 70% of parents were keen to try the treatment and after the treatment was completed 72% were satisfied with the outcome. Baseline outcomes for 2 children who only attended the first session were reported but it is unclear whether they were also included in the final analysis.

Evidence statement

One prospective case series [EL=3] showed that reflexology was effective at decreasing the frequency of soiling and increasing the frequency of bowel movements in children with chronic constipation

No published evidence was found on the effectiveness of the following complementary therapies for ongoing treatment/maintenance in children with chronic idiopathic constipation:

- Abdominal massage
- Hypnotherapy
- Osteopathy
- Cranial osteopathy
- Craniosacral therapy
- Homeopathy

GDG interpretation of the evidence

Due to the lack of evidence of effectiveness or cost-effectiveness, the GDG felt unable to make a recommendation for the use of complementary/alternative therapies for use in the NHS.

The GDG is aware that complementary therapies are frequently used in infants. Sometimes patients use them but feel unable to discuss their usage with health professionals. Certain complementary therapies are available on the NHS only in some areas, whereas in other areas parents pay for them. Current regulations of different complementary therapies (standards and training) are varied.

It is the GDG's view that complementary therapies can encourage positive relationships between parents and children but more research is needed to confirm this and other potential benefits in children with chronic idiopathic constipation.

Research Recommendation

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

Why this is important

Many families consider the use of complementary and or alternative medicine (CAM) as a treatment option when conventional treatment 'fails'. There is very little evidence about the efficacy of many complementary and alternative treatments but the use of CAM is widespread and increasing across the developed world. There is a clear need for more effective guidance for the public and health professionals who advise patients as to what does and does not work and what is and is not safe.[124] There is moderately good evidence for the effectiveness of hypnotherapy in improving global symptoms in adults with irritable bowel syndrome compared with attention control or symptom monitoring or usual management, mainly in patients with refractory IBS, both in primary and secondary care.[126] The use of hypnotherapy may therefore be an effective intervention in children with chronic constipation that has not resolved with usual treatment and may offer an additional approach to treatment which works.

5.7 Antegrade colonic enema procedure

Introduction

Optimal medical management of children with chronic idiopathic constipation will tend to reduce the number requiring surgical intervention. However, for patients with chronic treatment-resistant symptoms, other surgical interventions may be considered.

The Antegrade Colonic Enema (ACE) has now been demonstrated to have a role in the management of patients with constipation.[127] Central to success of the ACE is good case selection coupled with careful post-operative management. Whilst patients should be considered for ACE after a period of optimal medical management, referral of appropriate patients should not be delayed unduly. Management of washouts and of the sequelae of the ACE procedure is vital if symptoms are to remain controlled. As a failure rate exists, there remains a need both for other interventions (including resection and stoma formation) and for ongoing research for this sub-group of patients.

This section discusses the place of the ACE in the management of children with constipation.

Clinical Question

What is the effectiveness of the Antegrade Colonic Enema (ACE) procedure in children with chronic idiopathic constipation?

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation
- included the Antegrade Colonic Enema (ACE) procedure, regardless of what surgical technique was used
- included the following outcomes: changes in frequency of bowel movements, changes in stools consistency/appearance, changes in pain/difficulty on passing stools, changes in frequency of episodes of soiling, reduction in laxatives use, parent/child views/satisfaction or quality of life
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

One single search was performed on pharmacological and surgical interventions for disimpaction and ongoing maintenance in children with chronic idiopathic constipation. A total of 986 articles were identified from this search and 143 articles were retrieved for detailed assessment. In addition, GDG members submitted 11 papers. Of these 6 studies were identified for inclusion in this review (including 1 of the papers submitted by the GDG members): 3 retrospective cohort studies, 1 prospective case series, 1 retrospective case series and 1 retrospective survey.

Narrative summary

A retrospective cohort conducted in Australia[127] (2005) [EL=2+] investigated whether antegrade colonic enemas (ACEs) are effective in idiopathic paediatric slow transit constipation (STC) in children. Fifty-six patients with appendicostomy for idiopathic constipation formed between January 1995 and October 2004, who satisfied Rome II criteria for functional constipation, with/without faecal incontinence and who had undergone a prolonged period of unsuccessful medical management, were included in the study. Data were available for 42 children only (31 boys, mean age at interview: 13.1 years (median 12.4; range 6.9 to 25.0). Median initial regimes used for washouts were varied: polyethylene glycol 3350 and electrolytes (PEG 3350+E) (Golytely®) (79%), liquorice (12%), water (2%) and other (7%). The median regime used at the time of interview was PEG 3350+E 500ml to 750ml administered every second day, infused over 10 to 20 minutes with no need for disimpaction. Defecation occurred 20 to 30 minutes after ACE had finished, with 20 to 30 minutes spent on the toilet. The majority of patients (25/42, 60%) were either using the initial regime or had tried one regimen change at the time the study was conducted. There was no correlation between the number of ACE regimens tried, patient satisfaction or the length of ACE usage. Many families believed that regime changes were a necessary response to increased tolerance to a particular

ACE solution. Patient input into the ACE regimen varied: seven children (all older than 10 years) were completely independent, five children required supervision only, 15 needed help setting up and cleaning up and 15 were completely dependent. Thirty-seven children (88%) were very satisfied or satisfied with the procedure. Forty-one families (98%) said they would recommend the ACE to other children. Thirty-nine families (93%) felt there was a significant improvement in the quality of their child's life. Families felt that the mean optimal age for appendicostomy formation was 4.9 years (median 4, range 2 to 12). 15 children (36%) had ceased ACE at the time of interview (mean period usage: 2.6 years; range 0.7 to 5.8 years): symptoms resolved in seven children, in four a colostomy was formed, in two an ileostomy was formed and two patients returned to conservative management. The mean period of usage for children who had ceased ACE was not significantly different form those who were still using ACE at the time the study was conducted. Regarding the ACE efficacy there were significant improvements as compared to baseline in both continence and quality of life, as well as significant reduction in soiling frequency, abdominal pain frequency and abdominal pain severity (mean, median and range), (continence score: pre-ACE: 2.5 (2; 0 to 8); post-ACE: 5.2 (5; 1 to 12); p<0.0001); (quality of life score: pre-ACE: 1.4 (1.5; 0.5 to 3.0); post-ACE: 2.2 (2.5; 0.5 to 3.0); p<0.0001); (soiling frequency score: pre-ACE: 5.7 (6; 0 to 6); post-ACE: 3.0 (3; 0 to 6); p<0.0001); (abdominal pain severity score: pre-ACE: 7.4 (8; 0 to 10); post-ACE: 3.0 (3; 0 to 8); p<0.0001); (abdominal pain frequency score: pre-ACE: 5 (6; 0-6 to 3-6 d/week); post-ACE: 2.5 (2.5; 0-6 to 1-2 d/month); p<0.0001). Thirty (71%) children experienced symptoms at some stage of the treatment: cramping (18/30), nausea (17/30), vomiting (7/30), sweating (14/30) dizziness (10/30) and pallor (10/30). Three or more of these symptoms were present in 12/30 patients. The three most common long-term complications were granulation tissue in 33 children (79%), anxiety about ACE in 21 children (50%) and stomal infection in 18 (43%). These were unresolved in 15%, 29% and 11% of patients respectively.

A retrospective cohort conducted in the UK[128] (2004) [EL=2+] compared the results, complications and outcomes of the Malone antegrade colonic enema (MACE) with the caecostomy button (CB) in children with intractable constipation. Forty-nine children (15 boys) who underwent MACE or CB between June 1998 and August 2002 for intractable idiopathic constipation and faecal soiling that had failed conventional treatment were included. Thirty-seven children underwent MACE and 12 children underwent CB. Both groups started saline enemas (20ml/kg) on the 4th postoperative day. Children not responding to saline wash-out used Klean-Prep. The frequency and volume of enemas were individualised to each patient to achieve cleanliness and stop soiling. In 39/49 children (79.6%, 30 with MACE, 9 with CB) the soiling stopped completely. Occasional soiling was still present in three children (one with MACE, two with CB). One child with CB resumed regular activity and thus the CB was removed. MACE failed in six children (16.2%): in four patients the colonic washouts were ineffective, in one patient the colonic washouts were associated with abdominal pain during enema and one patient required revision for perforation of appendicostomy and the fibrotic-ischaemic appendix was replaced with a CB. CB failed in one patient (8.3%) and the reason was leaking faecal content around the button which was converted to MACE after 20 months. Surgical complications requiring operative intervention were significantly more frequent in children who underwent MACE as compared to CB (MACE: 9 (24%) vs. CB: 0, p=0.009). Surgical complications not requiring operative intervention were significantly more frequent in children who underwent CB as compared to MACE (MACE: 7 (19%) vs. CB: 11 (92%), p<0.001).

A retrospective cohort [129] (2006) [EL=2+] conducted in the USA reported the authors' 4-year experience with two different techniques of the caecostomy procedure compared the clinical outcome of caecostomy in children with defection disorders secondary to idiopathic constipation, imperforate anus and spinal abnormalities. A total of 31 children (58% boys) who received the procedure due to the previous underlying disorders were included. Nine of the children had idiopathic constipation and a median age at time of caecostomy of 12 years old (range 3 to 16). The bowel movement frequency significantly increased after caecostomy (n=9; pre: <5/week, post: 5/week to 3/day; p<0.01). The soiling frequency, the number of medications used, as well as the number of physician visits related to defecation problems all decreased significantly after caecostomy was performed (soiling, pre: constant, post: none; p=0.0; medications, pre: 4, post: 1; p=0.01 and physician visits, pre: 6, post: 2; p<0.01 respectively). No child was admitted to hospital for disimpaction after the procedure was performed (pre: 4, post: 0; p<0.01). Both the global health score and the global emotional score improved significantly after the procedure (global health, pre: poor, post: good; p=0.01 and global emotional, pre: poor, post: good; p=0.01 respectively) and children also experienced significantly less limitation of activity (pre: moderate, post: mild; p<0.01). No subgroup analysis was performed for the type of antegrade enemas used; therefore these outcomes are not reported here. There were no significant differences in relation to the number of missed school days per month before and after the procedure. There were no major complications such as perforation, stoma stenosis, or stoma prolapse. No difference was found in occurrence of number of complications between different procedures/techniques. Other outcomes are not reported here as no subgroup analysis was performed.

One prospective case series in the UK[130] (2009) [EL=3] analysed the outcomes of ACE procedure in children with idiopathic constipation who had not responded to 3 years of medically supervised conservative management. Eighty children with idiopathic constipation undergoing ACE surgery by one surgeon were included. The lavage regime used a saline solution prepared at a volume of 20ml/kg body weight and was supervised by specialist nurses. Children were followed up in a nurse-led continence clinic over a period of 6 months to 10 years (median 6.2 years). Outcome measures were: ongoing lavage, failure (cease technique because lavage not improve bowel habit or colon not lavagable) and cure (appendicostomy closed/reversed because of child achieving normal bowel habit). Of the 80 children included, 53 had conventional ACE surgery and 27 had laparoscopic surgery. ACE lavage failed in 12 children (Kaplan Meier probability - 0.3 at 8.5 years). ACE lavage provided cure for 12 children (Kaplan Meier probability - 0.2 at 6.2 years), all of whom went on to have their appendicostomy closed. Gender was significantly associated with ACE failure (p=0.04) with a higher failure rate amongst girls (p=0.02). Colonic transit time (CTT), age at surgery and duration of follow-up were not significantly associated with ACE failure. CTT was a significant factor in predicting failure in children accommodating a very large volume of lavage fluid (>10L) in their colon without bowel evacuation. No patients were discharged from the study and none were lost to follow-up.

A small retrospective case series conducted in the USA [131] (2002) [EL=3] assessed the benefit of ACEs through caecostomy catheters in children with severe constipation. Twelve children (nine boys, mean age: 8.7 ± 4.4 years) referred to a tertiary care motility centre for further evaluation of intractable constipation, who had undergone caecostomy placement for administration of antegrade enemas were included. After the procedure children significantly improved in relation to all the outcomes measured: bowel movements/week increased (before: 1.4 ± 0.7, after: 7.1 ± 3.8; p<0.005), soiling episodes/week decreased (before: 4.7 ± 3.2; after: 1.0 ± 1.4; p<0.01), the number of medications used for constipation decreased (before: 4.0 ± 1.0, after: 0.8 ± 0.6; p<0.005) and children suffered less severe abdominal pain (score before: 2.9 ± 1.6, after: 0.9 ± 1.0; p<0.005). Parents also considered that both the emotional and the overall health of their children had improved following the procedure (emotional health score before: 1.9 ± 0.8, after: 3.6 ±1.1; p<0.005); (overall health score before: 1.7 ± 0.9, after: 3.6 ± 0.9; p<0.005; respectively). Children missed fewer school days every month (before: 7.5 ± 6.9, after: 1.5 ± 2.5; p<0.02) and had to attend fewer physician office visits per year (before: 24.0 ± 19.1, after: 9.2 ± 14.2; p<0.05). The choice of irrigation solution used after caecostomy varied based on preference of the treating physician. Most patients began with low volume infusions of solution, which were increased according to therapeutic response. Sixty-seven percent of patients used 200ml to 1,000ml (mean 478 ml ± 262 ml) polyethylene glycol irrigation solution, daily to every other day. Twenty-five percent of patients used a combination of saline and glycerine, mixing 60ml to 75ml of glycerine in 240ml to 300ml of saline. One patient received 90ml phosphate soda solution followed by 300ml of saline. Evacuation occurred within one hour of enema administration in seven children and occurred within three hours in the other five children. No comparisons were made between the different solutions used. There were no acute adverse events and only four children experienced postoperative adverse events: skin breakdown and development of granulation tissue (n=1), leakage of irrigation solution (n=1) and accidental removal of the catheter with subsequent easy catheter replacement by the interventional radiologist (n=2). No adverse event led to discontinuation of the antegrade enema use. No child required admission to hospital because of faecal impaction since starting antegrade enemas. Five patients discontinued antegrade enemas with removal of the caecostomy at a mean of 14.6 ± 9.1 months after beginning treatment. None of these children redeveloped problems with constipation or faecal soiling.

A retrospective survey conducted in the UK[132] (1999) [EL=3] followed up the success of the MACE procedure. Fifty-eight children who underwent a MACE performed by UK members of the British Association of Paediatric Surgeons (or their units) up to the end of 1996 were included. Children who took part in a previous study conducted by the same authors as well as reported figures from one other UK centre were also included making a total population of 273 children. Patients (mean age 12.3 years) were followed up on average 2.4 years (range 0.3 to 6). Success criteria were defined as full success (totally clean or minor rectal leakage on the night of the washout); partial success (clean, but significant stomal or rectal leakage, occasional major leak, still wearing protection but perceived by the child or parent to be an improvement) and failure (regular soiling or constipation persisted, no perceived improvements, procedure abandoned usually to a colostomy). Twenty-three patients had been diagnosed with constipation. In these patients a full success rate was seen in 52%, partial success in 10%, the procedure was considered a failure in 38% and its outcomes were unknown in 1%. Main complications of the procedure were not reported in relation to the clinical diagnosis and therefore are not included here.

Evidence statement

Three retrospective cohorts [EL=2+], one retrospective case series [EL=3] and one retrospective survey [EL=3] showed that the frequency of episodes of soiling significantly decreased after ACE was performed.

Two retrospective cohorts [EL=2+] and one retrospective case series [EL=3] showed that frequency of bowel movements increased significantly after ACE was performed.

Two retrospective cohorts and one retrospective case series [EL=3] showed that children's quality of life significantly improved after ACE was performed.

One retrospective cohort and one retrospective case series [EL=3] showed that there was a significant reduction in the use of laxatives after ACE was performed.

One prospective case series [EL=3] involving children with idiopathic constipation who did not respond to 3 years of medically supervised conservative management and underwent the ACE procedure showed that the probability of an ACE failing was 0.3 at 8.5 years; with an estimated mean failure time of 8.6 years (95% CI 7.9 to 9.2). The probability of an ACE being reversed was 0.2 at 6.2 years, with an estimated mean time to reversal of 9.1 years (95% CI: 8.4 to 9.7). Colonic transit time, age at surgery and duration of follow-up were not significantly associated with ACE failure, but the higher failure rate amongst girls was significant. The colonic transit time was a significant factor in predicting failure in children who accommodated very large volume of lavage fluid (>10l) in their colon without bowel evacuation

GDG interpretation of the evidence

It is the GDG's view that there needs to be a balance between offering ACE procedure early to children who might require it (those who remain symptomatic on optimal specialist management) and making sure that optimal specialist management has actually failed, and therefore children are not referred prematurely since this would not be a cost-effective use of scarce NHS resources.

The procedure needs to be performed in a surgical unit with expertise in assessing for suitability and performing ACE if indicated. The GDG believes that nurse support is essential for effectiveness of ACE procedure. The level of specialist nurses is not equitable across the UK.

The choice of washout solution, its type and volume, is empirical: there is no evidence on what works. There is no evidence on why ACE works in some children and not in others; therefore it is difficult for clinicians to choose the "right" patient.

Recommendations

Refer children with idiopathic constipation who still have symptoms on optimum specialist management to a specialist surgical centre to assess their suitability for an antegrade colonic enema (ACE) procedure.

Ensure that all children who are referred for ACE procedure have access to support, information and follow-up from paediatric health professionals with experience in managing children who have had ACE procedure.

Research Recommendations

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

Why this is important

The ACE has a role in the management of people with treatment-resistant symptoms. Close follow-up is integral to the effectiveness of this technique to allow safe and effective administration of washout solutions.

The choice of washout solutions and frequency of administration varies between centres. Outcomes may be improved by evaluating how experienced centres choose washout solutions and by comparing techniques.

Centres offering ACE as treatment for children with chronic idiopathic constipation should be surveyed for their choice of washout solution. The survey should cover enema, washout fluid, volumes and frequency of administration, and how solutions are varied to determine the perceived strengths and weaknesses of each solution.

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

Why this is important

There is a difference of opinion between healthcare professionals regarding the use of surgery in the management of intractable idiopathic constipation. Whilst some professionals feel that it is unnecessarily invasive others feel strongly that surgery has an important part to play. In addition, many families find the prospect of surgery daunting and there is little evidence to help professionals provide impartial information regarding children's and families' experience of ACE and its subsequent management, leaving them to rely upon their own opinion and experience.

The primary outcome measure of this research should be quality of life recorded using a validated health related quality of life measure.

6 Information and support

Introduction

The level of information and support provided to children and their families is thought to play a significant role in determining the effectiveness and success of the management of constipation in children.

The provision of both written and verbal information regarding the causes of constipation and its treatment, in essence providing guidance for both parents and children about how the bowel works, what can go wrong and how it can be managed, may help towards empowering children and their parents or caregivers and increasing their involvement in all aspects of treatment. As parents have a key role to play in supporting the child's self-management, it is important that they are provided with clear information about the condition. In this 'coaching/training' role the parent has an active part to play, helping the child to sit on the toilet on a regular basis to try to push out a stool, as well as administering laxative therapy when required, assessing response and changing dosage as needed. The aim of providing information is to help the child understand how his/her bowel works, how food is turned into faeces and the importance of passing a stool on a regular basis and trying to do this every day when a toilet is available. It is important to make clear that the health professional alone cannot solve the problem. The child and family have to find a way, on a daily basis, to sustain a curative programme of treatment. Skilled s*upervision* is needed from the health professional to support the parent how to take on the role of trainer. This may help prevent inappropriate blame and problems around adherence to treatment. Relapse is a common problem amongst children with constipation, and often can occur when laxatives are stopped too soon. Treatment may continue for many months and sustaining changes can be challenging so appropriate access to ongoing advice and support around the continuation of treatment is important.

Families often feel very isolated, as conditions such as constipation and any associated soiling are not something openly discussed by parents with other families. Parents often feel that they are the 'only one' with a child with such a problem. There may also be issues with schools in terms of managing the soiling. The availability of local support to address not only these issues but ongoing treatments is therefore vital.

Clinical Question

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?

Studies considered in this section

Studies were considered if they:

- included neonates, infants and children up to their 18th birthday with chronic idiopathic constipation
- included the provision of information and support in the following formats/contexts: nurse led clinics, written information or handout/leaflet, help-line, web based intervention or internet intervention, telephone support, face to face / additional appointments
- included the following outcomes: changes in frequency of bowel movements, changes in stools consistency/appearance, changes in pain/difficulty on passing stools, changes in frequency of episodes of soiling, reduction in laxatives use, parent/child views/satisfaction or quality of life
- were not case-reports
- were published in English

No restrictions were applied on the publication date or country.

Overview of available evidence

A total of 1155 articles were identified from the searches and 26 articles were retrieved for detailed assessment. Of these 8 studies are included in this review: 1 parallel-RCT, 1 survey-RCT, 1 RCT (multicentre), 1 RCT-Survey, 1 single sample cross-over multicentre RCT, 2 prospective case series and 1 online survey.

Narrative summary

Clinic-based interventions

An RCT conducted in the UK[133] (2004) [EL=1+] evaluated the effectiveness of a nurse led clinic (NLC) compared with a consultant led paediatric gastroenterology clinic (PGC) in the management of chronic idiopathic constipation. One hundred and two children aged 1 to 15 years (55 males, median age at study entry: 4.6 (NLC) and 4.8 years (PGC), age range: 13 months to 14.7 years) presenting to the paediatric gastroenterology service at the John Radcliffe Hospital, Oxford, UK with constipation were included. Children were randomised to be followed-up at an NLC or a PGC. The nurse led clinic was designed to be a follow up clinic for children who had undergone a full and detailed medical assessment in the paediatric gastroenterology clinic leading to a diagnosis of "idiopathic functional constipation". Where it was clinically appropriate, an abdominal radiograph was obtained at the time of initial assessment, both as a diagnostic tool and as a semi-quantitative marker of the severity of constipation. A standardised treatment algorithm (constructed for the study, similar to a number of published guidelines) provided the basis for management decisions in all consultations in both clinics. Initial phases involved child and parent education about diet (fibre and fluid), exercise, toilet training, and the actions of the laxatives prescribed. Laxative therapy comprised a combination of stool softeners (for example, lactulose, docusate sodium) and stimulants. Stimulants of different potencies (senna, bisacodyl, sodium picosulphate) were prescribed according to the clinical response as indicated by the children's bowel diaries. If there was an inadequate clinical response to this initial phase, the patient moved on to an advanced treatment regime which might include, enemas, intestinal lavage, manual removal of faeces under general anaesthesia, or psychological referral as was appropriate in each case. Bowel diaries, which report the frequency, size, and consistency of stools, presence or absence of soiling, and a record of daily laxative medication, were used in both clinics to monitor progress and response to treatment. Dedicated case report forms were used for each study participant and, together with detailed clinical history (including a detailed dietetic history) and clinical findings on initial assessment, documented details of bowel habit and drug therapy at all subsequent outpatient visits. Any other contact with the families, e.g. on the telephone or a home visit, was documented using inter-visit contact forms. A child was defined as having been ''cured'' of their constipation when, for a period of at least 1 month, they had been opening their bowels, producing a normal formed stool without difficulty at least 3 times per week and without any laxative therapy. Time to cure relates to all those children confirmed cured either at their last visit, or subsequently, confirmed over the telephone. Children who were close to achieving the definition of ''cured'' at their last visit but who were still being weaned off medication, were not required to attend for a further follow up appointment but received their follow up via the telephone. Time to cure at last visit relates to only those children confirmed cured at their last visit (a subset of the previous outcome). Premature study termination comprised those patients who were either lost to follow up or withdrawn for whatever reason. Fifty-nine children were confirmed to be cured at last visit or later confirmed by telephone; of these, 49 were confirmed to be cured at the last visit. Of those children cured at their last clinic visit or confirmed by subsequent telephone follow up, 34 of 52 (65.4%) were cured in the NLC and 25 of 50 (50.0%) in the PGC. The median time to cure was 18.0 months (95% CI 8.5 to 27.5) in the NLC and 23.2 months (95% CI 17.3 to 29.2) in the PGC. The probability of cure was estimated as 33% higher in the NLC as compared to the PGC (hazard ratio 1.33, one sided 95% CI 0.86 to ∞, p=0.3). Attending the NLC hastened time to cure by a factor of 0.816 (one sided 95% CI 0 to 1.032): compared to the PGC, the NLC reduced time to cure by an estimated 18.4%. Children who attended the NLC were equally as likely to be cured as those attending the PGC, but their cure was more likely to occur earlier. More children were cured in the NLC (27/52 vs. 22/50 in PGC) and median time to cure was reduced (22.1 vs. 25.1 months in PGC). 5 (9.6%) children in the NLC and 14 (28.0%) in the PGC were lost to follow up or withdrawn. The risk of premature study termination was significantly reduced by an estimated 66% in the NLC compared to the PGC (hazard ratio 0.33, one sided 95% CI 0 to 0.79, p=0.036). The median number of visits in each clinic was 6.0. The median number of inter-visit contacts to the NLC was 6.0 (range 2 to 16) as compared to the PGC: 0.0 (range 0.0 to 29). The number of patients requiring additional medication/in-patient procedures during the scheduled treatment period was not significantly different between both groups. Ten children (5 NLC, 5 PGC) completed the study as per the protocol but were not cured (treatment failures): 8/10 children were formally referred for psychological/psychiatric management, 9/10 had documented serious behavioural problems and 3/10 were also referred for surgical assessment and management. A total of 15/102 children were still undergoing follow-up, as they were not cured. In this group, 7/15 children were followed up in the PGC and 8/15 in the NLC. Seven of 15 children had documented psychosocial problems associated with poor compliance in attending clinic appointments. Baseline demographic and clinical presentation characteristics as well as previous laxative usage were well balanced across clinics. Intention to treat analysis was conducted for all outcomes. Survival analysis was conducted for the primary time-to-event outcomes

A survey-RCT conducted in the UK[1] (2006) [EL=1+] assessed parents' satisfaction with a nurse led clinic (NLC) for children with intractable, functional constipation compared with a consultant led paediatric gastroenterology clinic (PGC). This study is a follow-up evaluation of the RCT reported above. One hundred and two children aged 1 to 15 years (55 males, median age at study entry: 4.6 (NLC) and 4.8 years (PGC), age range: 13 months to 14.7 years) presenting to the paediatric gastroenterology service at the John Radcliffe Hospital, Oxford, UK with constipation were included. Parents' satisfaction was measured after 12 months' follow-up or before this if the child has been "cured". Satisfaction with care defined as "the degree to which parents perceive the needs of their children are met". Parent satisfaction was measured using a validated instrument based on the Leeds Satisfaction Questionnaire (LSQ). Five point Likert scales were used for responses ranging from "strongly agree" to "strongly disagree"; stability of the instrument was tested using the test-retest method. An attempt was made to record all "inter-visit" contacts (by telephone or day ward attendances) made by parents outside their schedules outpatients appointment. A total of 90 questionnaires returned from 107 families canvassed (84%); 40/51 (78%) from the PGC and 50/56 (89%) from the NLC. The NLC scored significantly higher in most of the outcomes measured (all values are median): provision of information (NLC: 8.7 vs. PGC: 7.5, $p<0.001$), empathy with patient (NLC: 9.0 vs. PGC: 7.3, $p<0.001$), technical quality and competence scores (NLC: 9.1 vs. PGC: 8.0, $p<0.001$), attitude towards the patient scores (NLC: 8.7 vs. PGC: 7.3, $p<0.001$), access to and continuity with the caregiver scores (NLC: 8.2 vs. PGC: 6.7, $p<0.001$) and overall satisfaction scores (NLC: 8.7 vs. PGC: 7.3, $p<0.001$). There were no significant differences between the NLC and PGC regarding the number of inter-visit contacts. Intention to treat analysis was performed for all outcomes.

A prospective case series conducted in Canada [134] (1997) [EL=3] presented the experience of the first 16 months of a multidisciplinary clinic for the treatment of functional constipation. One hundred and fourteen children up to 19 years old (51.4% boys, mean age: 5.4 ± 3.8 years (range 4 months to 19 years)) referred to the clinic with constipation after a 3-month unsuccessful course of treatment were included. The Bowel Management Clinic (BMC) is staffed by a physician (rotating between two paediatricians, one paediatric gastroenterologist and one paediatric general surgeon), a nurse practitioner, a dietician, an enterostomal therapist/nurse educator and a psychosocial nurse specialist. All new patients are always assessed by clinic nurse and physician assessment to identify potential organic causes of constipation and to establish components of individualised management. Further referral to other BMC staff as needed. Investigations are only performed if there is suspicion of organic cause of constipation or lack of improvement after adequate intervention (abdominal radiograph with lumbosacral spine, barium enema, anorectal manometry and rectal mucosa biopsy). The only compulsory treatment modality was patient education. Enemas were only used in the initial treatment if faecal impaction, to provide social continence for children with persistent encopresis and avoid undue rectal distension until laxatives could start taking effect. Choice of enemas comprised: phosphate and tap water or saline. High colonic saline irrigations were used in severe cases, suppositories were not routinely employed. Choice of laxative was based on compliance and nature of symptoms. Most patients were treated with senna, docusate sodium and mineral oil. Multiple laxatives were avoided. Patients started on recommended dosages, then increased by 50% every 4 to 5 days until symptomatic improvement noted. Individualised dosage then maintained minimum 3 to 6 months, during which dietary and psychosocial issues were dealt with. Patients were then slowly weaned off medications. Follow-up was arranged by each health care professional as needed. Visits were used to monitor progress and continue education process. Patients who showed no progress were reassessed by a physician and could become candidates for diagnostic testing. Patients were discharged when asymptomatic and off medications. Patients were then referred back to the referring physician, with information for maintaining healthy bowel routine. Outcome measures were stool frequency per month, stool consistency, occurrence and frequency of symptoms (soiling, rectal pain, rectal bleeding) and satisfaction with care. Sample size varies in each category of symptoms because of incomplete observations and stool frequencies were only included for non-soiling patients. A Measure of Processes of Care (MOPC) questionnaire was also administered at the 4-month point. MPOC is a self report measure of the parents' perceptions of the extent to which 5 behaviours of health care professionals occur (respectful and supportive care, enabling and partnership, providing general information, providing specific information, coordinated and comprehensive care). The scores from the study group were compared with those from a normative group of 653 patients (no further details provided). The total number of visits was 257 with an average of 6 patients per clinic. 62 patients were seen more than once with a mean of 3.1 visits per patient and a mean time span between the first and the last visit to clinic of 4.5 months. The average stool frequency per month (n=26) increased significantly from the first to the last visit (11.73 vs. 29.77, p=0.00026). Stool frequencies were only included for non-soiling patients. Stool consistency (n=55) (unclear whether the following are number of children or %) improved form the first to the last visit (liquid: 0 vs.1, soft: 4 vs.13, formed: 16 vs.13, and hard: 10 vs. 3, p=0.00004).The proportion of children who experienced soiling (n=42) did not change significantly from the first to the last visit. Significantly fewer children experienced rectal pain and rectal bleeding at the last visit as compared to the first visit (rectal pain (n=51): first visit: 53% vs. last visit: 22%, p=0.0003 and rectal bleeding (n=54): first visit: 26% vs. last visit: 4%, p=0.00035). The frequency of soiling per month (n=26) decreased significantly from the first to the last visit (30.7 vs. 12.8, p=0.015). There were no significant differences regarding the frequency of rectal pain per month and the frequency of rectal bleeding per month from the first to the last visit. Satisfaction with care scores were normal or higher than those in the normative group of children for: respectful and supportive care, enabling and partnership and coordinated and comprehensive care. Scores were lower than the norm for providing general information and providing specific information. Results only reported in a graph from which it is difficult to extract estimates. Thirteen children appeared to be lost to follow-up (no return to clinic in over 6 months) and 11 were discharged. Among the discharges the mean number of clinics visits was 3.5.

Internet-based interventions

A small multicentre RCT conducted in the USA [122] (2003) [EL=1+] aimed to examine the utility and effectiveness of an Internet-based version of enhanced toilet training. Twenty-four children aged between 6 and 12 years (19 boys, mean age: 8.46 years (SD1.81), soiling at least once a week, who had no medical diagnosis other than constipation that could explain their faecal incontinence were included. Children were randomised to receive the web intervention (12 children (10 boys)) or no intervention (12 children (9 boys)). The intervention was a web-based program for the treatment of paediatric encopresis (U-CAN-POOP-TOO). Exposure to the program lasted for 3 weeks after which an assessment was conducted. The number of faecal accidents per week decreased significantly more in the web group as compared to the no-web group (mean, SD) (0.50 (0.85) vs. 8.27 (13.83), p=0.18). The number of bowel movements passed in the toilet per week increased significantly more in the web group as compared to the no-web group (% change from pre- to post-assessment) (+152% vs. -16%, p=0.001). Using the bathroom without prompts also increased significantly more in the web group as compared to the no-web group (% change from pre- to post-assessment) (+109% vs. -37%, p=0.021). Using the bathroom with prompts was not significantly different between the two groups. Amongst the most useful aspects of the programme parents cited: the step by step program to get the child regulated, understanding why his body does what it needs to do everyday-and what happens when he doesn't have a bowel movement and health consequences. Amongst the least useful aspects of the programme parents cited: difficulty with connections, modules regarding fear of toilet and "monsters", art work of the body did not print out, MiraLax® should have been included (as a choice of laxative) and nutrition portion was too limited. Most parents found the material understandable (mean 5.00, SD 0.00, n=20), easy to use (mean 4.62, SD 0.74, n=21), believed their child liked the program (mean 4.05, SD 1.28, n=21), believed their child found it understandable (mean 4.32, SD 0.89, n=19), believed their child found it easy to use (mean 4.47, SD 0.77, n=19). There were no significant differences in baseline characteristics between the two groups (age, gender, race, stage of bowel movement training, length of current laxative regime or any of the outcomes measured). No dropouts/lost to follow up were reported, however it should be noted the numbers involved were small.

An RCT/survey mixed methods study conducted in the USA [135] (2005) [EL=1+] (RCT component); [EL=3] (survey component) determined if families of children suffering from chronic constipation and/or encopresis will visit an educational web site that is specifically prescribed by their physician and whether an e-mail reminder increases the likelihood that they will visit the web site. In addition, barriers to accessing the prescribed web site were identified. Families with a child who was being seen for the first time in the paediatric gastroenterology clinic at the University of Virginia with a chief complaint of chronic constipation and/or encopresis were included. There were 83 families and children (children's mean age: 7 years 10 months (median 94 ± 38 months; range: 25 months to 14.5 years). The web site was an abbreviated version of a larger web-based program for the treatment of paediatric encopresis (U-CAN-POOP-TOO). At the conclusion of the patient's clinic visit, one of the two attending gastroenterologists provided a form with the web-site address and a log-in identification number. The handout, signed by the physician, stated: "It is important to learn as much as you can about bowel problems and how to manage them. As part of your child's care, I want you to go to this website and review the relevant material. This should be beneficial to your child's treatment." Families were assigned randomly into a "prompt" group (n=43) or "no-prompt" group (n= 40). Two business days after the clinic visit, an e-mail containing the web-site address and a reminder to visit the web site was sent to those in the "prompt" group. Approximately 1 week after the clinic visit, the study coordinator attempted to contact the primary caretaker of each patient by telephone or e-mail to ask about their experience accessing the website. Families who did not access the website were encouraged to identify barriers that they may have experienced in accessing the prescribed website. Fifty-four (65%) families visited the prescribed web site within 1 week of their clinic visit. Families who received the e-mail remainder were significantly more likely to visit the website than families who did not receive the email remainder (77% vs. 53%). Eighteen interviewed subjects did not go to the website. The main reasons for not doing so were reported as: just forgot: 61%, didn't have much time 61%, lost flyer 33%. No parent reported that their child did not cooperate, that they did not know how to use internet or that the family thought the program was a bad idea. No significant differences were found in identified obstacles between the families who received the e-mail reminder and those who did not. There were no significant differences between the two groups on type and speed of Internet connection, the number of times they reported checking their e-mail, or frequency of using the internet. There were no significant differences in the ages of the children between the two groups.

A single sample cross-over multicentre RCT conducted in the USA[136] (2006) [EL=1+] determined the usefulness and user preference for audio (use of sound), graphics (use of images) and interactivity (triggering of events by the user causing various actions, i.e. clickable buttons) in a paediatric internet-based health intervention specifically designed for patients with encopresis. Forty-nine children aged 5 to 12 years (32 boys, mean age: 7.98 years (SD=1.88)) who were being seeing for encopresis at two paediatric gastroenterology clinics were included. Two modules of the original U-CAN-POOP-TOO intervention were revised: "Giving and Getting Enemas": reviewed techniques for administering enemas and "How to Strain": reviewed proper defecation, dynamics, including proper positioning, straining, and muscle control/strength-building exercises. All children received one modified module including audio, graphics and interactivity and then the other module without audio, graphics or interactivity. Design was significantly improved with special emphasis given to graphical, animation and interactive elements. For each of the three studies conducted, the two modules were modified to either include the three constructs of interest (audio, graphics and interactivity) or not. For the study examining audio both modules were created with and without sound. For the study examining graphics both modules were created with graphics and completely text based; and for the study examining interactivity both modules were created with interaction (use the mouse to click various aspects of the screen and navigation) and as a movie (where no interaction was necessary and the participant could just watch the module play from beginning to end). Each module with or without each component was presented once. Participants were assessed immediately after each module was presented. Outcomes measured were motivation and readiness to change. Parents were asked to complete the motivation and readiness to change items from their child's perspective. Children's motivation significantly improved when the computer audio was used (pre: 6.00 vs. post: 5.13, $p \leq 0.004$) but not when someone in the room read the content aloud. Parents believed that their children's motivation significantly improved when someone in the room read the content aloud (pre: 8.75 vs. post: 7.13, $p \leq 0.02$) but not when the computer audio was used. Children's motivation was not affected by either the presence or the absence of graphics but parents believed the presence of graphics improved their children's motivation (pre: 7.13 vs. post: 6.06, $p \leq 0.03$). Children's motivation significantly improved both with interactive (pre: 6.00 vs. post: 4.71, $p \leq 0.03$) and non-interactive modules (pre: 5.18 vs. post: 4.41, $p=0.02$) but parents did not believe that was the case for either situation. Readiness to change did not improve for children when the computer audio was used and parents also believed that. Readiness to change did not improve for children when someone in the room read the content aloud but parents believed it did improve (pre: 2.25 vs. post: 2.75, $p \leq 0.04$). Readiness to change did not improve for children when there were no graphics and parents also believed that. Readiness to change did not improve for children when there were graphics but parents believed it did improve (pre: 2.44 vs. post: 2.88, $p=0.01$). Children did not improve their readiness to change with either system (interactive modules or non-interactive modules) and parents also believed that.

A prospective case series conducted in the USA [137] (2008) [EL=3] examined the utility and impact of the same Internet intervention for childhood encopresis as part of standard medical care in a "real world" setting. Twenty-two children (13 males, mean age: 8.10 years (SD 2.3 years) range 5.1 years to 12.11 years) with a documented diagnosis of encopresis (as noted in their medical records) and their families, seen at the Paediatric Gastroenterology Clinic at the University of Virginia Children's Hospital were included. All children had been given access to the paediatric encopresis internet intervention as part of their treatment. During 2 weeks all children received an internet-based intervention for childhood encopresis: U-CAN-POOP-TOO. Children were assessed 2 weeks before they were enrolled in the program and 2 weeks after being exposed to the intervention. The average number of faecal accidents over a 2-week period decreased significantly when compared the initial period with the follow-up period (13.86 (SD 10.40, median 13.00) vs. 2.14 (SD 2.21, median 1.00), $p<0.001$). There were no significant differences between number of bowel movements (BM) passed in the toilet over a 2-week period or average amount of perianal pain experienced during defection over a 2-week period when compared to initial with the follow-up period. Most parents liked program (mean, SD) (4.62, 0.50, n=21), found it understandable (5.00, 0.00, n=20), found it easy to use (4.62, 0.74, n=21), believed their child liked the program (4.05, 1.28, n=21), believed their child found it understandable (4.32, 0.89, n=19) and believed their child found it easy to use it (4.47, 0.77, n=19). The most helpful components of the program cited by the parents were: the tutorials about anatomy and pathophysiology, they liked that the program was geared toward the child, but that it was comprehensive and non-judgemental. No clear themes emerged regarding the least helpful components of the program: On average, 19/25 items (76%) were rated by the parents at least “somewhat helpful,” no item described as “not at all helpful.” On the 1- to 5-point scale, average responses ranged from a low of 2.33 (the program helped reduce the number of times parents had to remind their child to use the bathroom) to a high of 4.2 (the program helped the child feel more comfortable using the toilet at home). Sixteen out of twenty two patients examined stopped using the program for some reason other than that their problem was “resolved.” The most cited obstacles to using the program were "I just forgot [to go to the website]” (mean 2.00, SD 0.89) and “I didn’t have time in my schedule” (mean 2.06, SD 0.85).

An online survey conducted in the USA [138] (2001) [EL=4]described the feedback received regarding a web-based tutorial about chronic childhood constipation and encopresis during 28 months between January 1998 and April 2000. Participants included were 1142 children and parents who accessed a tutorial about childhood constipation and encopresis, developed and installed on the web pages of the Children’s Medical centre at the University of Virginia, who also completed an online feedback form. No internal or external announcement was made to communicate the availability of the tutorial, but access to the website was not limited in any way. The multimedia tutorial was directed primarily at parents and older children. It included information about differential diagnosis, aetiology, treatment and potential side effects, method of follow-up including regular monitoring, natural history and prognosis and a list of references. The one-page feedback form comprised of six multiple-choice questions and one open-ended comment field. Only 887 participants (78%) answered the questions categorising the reader: 789 (89%) were parents and guardians of a child with constipation or encopresis, 44 (5%) were grandparents or other family members, 30 (3%) were teachers, 9 (1%) were physicians and 35 (4%) were other healthcare providers. The tutorial received 157,326 successful page requests from 38,012 distinct hosts. Eight hundred and twelve parents (92%) said the information presented in the tutorial was “very clear” and easy to understand whereas 71 (8%) said it was “pretty clear”. Nobody chose the “not very clear” or “not clear at all” responses. A total of 883 parents answered this question. 174 parents said (25%) the tutorial completely helped them to understand why children develop constipation and/or encopresis. One hundred and seventy four (25%) answered that “somewhat” this had been the case and 13 parents (2%) answered “a little”. No parents chose the “not al all” option. A total of 696 parents answered this question. Four hundred and eight parents (59%) said that after completing the tutorial, they thought they were “much“ better able to take care of a child suffering from constipation and/or encopresis; 226 parents (32%) responded “somewhat”, 42 (6%) “a little” and 20 (3%) “not at all”. A total of 696 parents answered this question. Six hundred and ninety one participants answered the question on whether they thought this type of tutorial was a good way to teach people about health problems; 599 (87%) thought it was very good, 89 (13%) pretty good and 3 (0.4%) thought it was not good at all. No participant thought the tutorial was “not very good”. Eight hundred and forty five parents had questions or comments or suggestions as to how to improve the tutorial. Four hundred and forty three (52%) showed an appreciation for making the information available, 167 (20%) had questions about a particular child’s symptoms or treatment, 96 (11%) had a general question not specific to any particular child, 46 (5%) made a referral request, 34 (4%) made a request for dietary recommendations, 21 (2%) made a request for additional online information, such as online forum or a frequently asked questions (FAQ) site and 38 (4%) made specific recommendations as to how to improve the tutorial.

Evidence statement

Clinic-based interventions

One RCT [EL=1+] showed that a nurse led clinic was more effective as compared with a consultant led paediatric gastroenterology clinic in the management of chronic constipation at reducing the time for children to be cured and reducing the risk of children lost to follow-up. The number of patients requiring additional medication/in-patient procedures during the scheduled treatment period was no significantly different between both clinics.

One survey-RCT [EL=1+] showed that parents' satisfaction with a nurse led clinic for children with intractable, functional constipation was significantly higher as compared with a consultant led paediatric gastroenterology clinic in the following indicators: provision of information, empathy with patient, technical quality and competence, attitude towards the patient, access to and continuity with the caregiver and overall satisfaction. There were no significant differences between both clinics regarding the number of inter-visit contacts.

One prospective case series [EL=3] showed that a multidisciplinary clinic for the treatment of functional constipation was effective at decreasing frequency of soiling per month and improving stool consistency in all children treated and at significantly increasing average stool frequency per month in non-soiling children. The clinic was not effective at decreasing the proportion of children who experienced soiling. Significantly fewer children treated and followed up in this clinic experienced rectal pain and rectal bleeding at the last visit as compared to the first visit although the frequency of rectal pain per month and the frequency of rectal bleeding per month did not change significantly. Parents' satisfaction with the health care professionals of the clinic was equal or higher than for a normative comparison group for: respectful and supportive care, enabling and partnership and coordinated and comprehensive care. Scores were lower than the normative comparison group for providing general information and providing specific information.

Web-based interventions

One online survey [EL=4] showed that a web-based tutorial about chronic childhood constipation and encopresis helped parents to understand why children develop constipation and/or encopresis, made parents better able to take care of their child and was useful as a good way to teach people about health problems. The majority of parents showed an appreciation for making the information available.

One RCT (multicentre) [EL=1+] showed that an internet-based version of an enhanced toilet training programme for the treatment of paediatric encopresis was more effective that no intervention at decreasing the number of faecal accidents per week, increasing the number of bowel movements passed in the toilet per week and increasing the use of the bathroom without prompts. Using the bathroom with prompts was not significantly different between the two groups. Most parents found the material understandable, easy to use, believed their child liked the program and found it understandable and easy to use.

One RCT-Survey [EL=1+] (RCT component); [EL=3] (survey component)] showed that families of children suffering from chronic constipation and/or encopresis who received an email remainder were more likely to visit an educational web site that is specifically prescribed by their physician than families who did not receive the email remainder.

A single sample cross-over multicentre RCT [EL=1+] assessing the usefulness and user preference for audio, graphics and interactivity in a paediatric internet-based health intervention specifically designed for patients with encopresis showed that children's motivation significantly improved when the computer audio was used but not when someone in the room read the content aloud. Children's motivation significantly improved both with interactive and non-interactive modules. Children did not improve their readiness to change with either system (interactive modules or non-interactive modules) and parents also believed that.

A prospective case series [EL=3] showed that internet intervention for childhood encopresis as part of standard medical care in a “real world” setting significantly decreased the average number of faecal accidents over a 2-week period but was not effective at increasing the number of bowel movements passed in the toilet over a 2-week period or reducing the average amount of perianal pain experienced during defection over a 2-week period. Most parents liked the program, found it understandable and easy to use and believed their child also liked the program and found it understandable and easy to use

GDG interpretation of the evidence

The GDG is aware that some patients are prescribed medication and not seen again for 1 month or longer. Also there is a sense that some children are passed from one professional to another because some may feel “it’s not their problem”. There is evidence from other chronic conditions that spending time with the patient is cost-effective in the long term.

In the GDG’s opinion consistency of follow-up (both in terms of message content and of person delivering it) can improve the effectiveness and therefore the cost-effectiveness of treatment.

The GDG is aware that the lack of information for some health professionals is an important issue. As children do not “grow out” of constipation without treatment, it is important for health professionals to understand this, and not to suggest parents that this might be the case. Constipation is a self perpetuating condition, the longer it is left untreated the more difficult to treat it becomes.

Children’s responses from the consultation highlighted the importance of receiving information in a variety of formats including web-based resources and child-friendly leaflets. These responses also highlighted the negative effect that idiopathic constipation can have on children’s social lives.

Recommendations

Provide tailored follow-up to children and their parents or carers according to a child’s response to treatment, measured by frequency, amount and consistency of stools (use the Bristol Stool Form Scale to assess this – Appendix G). This could include:

- telephoning or face-to-face talks
- giving detailed evidence-based information about their condition, for example the ‘Understanding NICE guidance’ leaflet 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.

Offer children with idiopathic constipation and their families a point of contact with specialist health professionals who can give ongoing support.

Refer children with idiopathic constipation who do not respond to initial treatment within 3 months to a practitioner with expertise in the problem.

Research recommendation

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?

Why this is important

When treating idiopathic constipation it is helpful if children understand how the bowel works, what can go wrong and what they can do about it. Younger children (pre toilet training) need to allow stools to come out. Older children have a more active role and need to develop a habit of sitting on the toilet each day, pushing stools out and taking any medication. Volition from the child is vital to establish and sustain a regular toilet habit. Intended learning outcomes are similar for all age groups.

Theory-based research has led to the development of some materials such as 'Sneaky-poo' that are not appropriate for young children. To help clinicians and parents motivate children to fully participate in managing their constipation it is important to discover how best to communicate information to them, what materials are most effective and, specifically, what works at different ages.

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.

Why this is important

Findings from one trial [1] have suggested that children referred to a tertiary gastroenterology service and diagnosed as having idiopathic constipation are managed as effectively by nurse-led follow-up as by a consultant paediatric gastroenterology service. Parent satisfaction was improved by the nurse-led service. However the nurse-led service may require increased resources because many more contacts are made. Several services with a similar model of care have been established but cost effectiveness has not been formally assessed.

By the time children reach tertiary care they have often suffered years of constipation with or without faecal incontinence and have intractable constipation.

For coherent services to develop across the UK, the cost effectiveness of specialist nurse-led services provided as first referral point if primary treatment regimens have not worked needs to be examined.

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?

Why this is important

There has been no research to explore the social impact on children with constipation and their families, and many of the clinical studies have been of mediocre quality. A comprehensive study is needed that investigates the effectiveness of specific models of care, and that takes into consideration both the clinical and social impact of this complex condition.

Appendix A

Scope of the guideline

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Constipation: the diagnosis and management of idiopathic childhood constipation in primary and secondary care

1.1 Short title

Constipation in children

2 Background

a) The National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') has commissioned the National Collaborating Centre for Women's and Children's Health to develop a clinical guideline on the diagnosis and treatment of idiopathic childhood constipation for use in the NHS in England and Wales. This follows referral of the topic by the Department of Health (see appendix). The guideline will provide recommendations for good practice that are based on the best available evidence of clinical and cost effectiveness.

b) The Institute's clinical guidelines support the implementation of National Service Frameworks (NSFs) in those aspects of care for which a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisals published by the Institute after an NSF has been issued have the effect of updating the Framework.

c) NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their individual needs and preferences, and ensuring that patients (and their carers and families, where appropriate) can make informed decisions about their care and treatment.

3 Clinical need for the guideline

a) Idiopathic (functional) constipation is defined as the subjective complaint of passing abnormally delayed or infrequent dry, hardened faeces (stools) often accompanied by straining and/or pain. It may also be associated with soiling, defined as involuntary passage of fluid or semi-solid stool into clothing, usually as a result of overflow from a faecally loaded bowel. Constipation is termed idiopathic if it cannot be explained by a known cause (anatomical, physiological, radiological or histological abnormalities). The exact aetiology is not fully understood, but it is generally accepted that a combination of factors may contribute to the condition.

b) There are several ways of characterising constipation by quantifying the timing and passage of stools and qualifying the type of stool. The 'normal' number and type of bowel movements, or defaecation, is dependant on the age of the child. Normal stool frequency in infants and children in industrialised countries ranges from an average of four per day in the 1st week of life to two per day at 1 year of age. The normal adult range (between three per day and three per week) is usually attained by 4 years of age.

c) Constipation is common in childhood. It is rarely life threatening, and therefore might be expected to have little impact on healthcare provision. The reality is somewhat different, with many children requiring medical and nursing management for a condition that causes great misery and discomfort. In the UK, 5% of children between the ages of 4 and 11 years suffer from constipation lasting more than 6 months. Chronic constipation generally develops between the ages of 1 and 4 years and the pattern of bowel movement tends to be established by the age of 4 years, although childhood constipation may continue beyond puberty in as many as a third of those followed up beyond this age. Children may present with a variety of symptoms that may lead to a diagnosis of idiopathic constipation. As the second most referred condition in paediatric gastroenterology, constipation is estimated to account for at least 25% of visits and often requires prolonged support from a multidisciplinary team.

d) Acute constipation is short lasting and usually clears up easily with treatment, but it is not always easily recognised or treated appropriately. This may lead to the development of chronic (longstanding) and more serious constipation. Parents are frequently worried about the possibility of serious underlying disease, and the impact of the condition on the family may be considerable – causing distress, disruption and frustration. Families may delay seeking help because they feel that the condition will not be taken seriously.

e) The majority of children with constipation are seen by their own doctors in primary care. A health visitor may be the first point of contact for families whose newborn or preschool children have constipation. The emergency department may serve as the first port of call for concerned parents of older children. Constipation can be a complex condition to manage and if children do not respond to initial treatment, or if there are concerns regarding underlying disorders, referral to specialist services may be needed.

f) Currently there is wide variation in practice because:

- there are no national evidence-based guidelines to address the diagnosis and management of childhood constipation in England and Wales
- the condition may be difficult to recognise because of the diversity of presenting symptoms
- the outcomes for children with idiopathic constipation are variable
- there is no single treatment
- many children do not respond to treatment and continue to have chronic problems
- current treatment is often unpleasant, traumatic, invasive and there is believed to be a high level of non-concordance, leading to repeated long-term treatment

children and families are often given conflicting advice.

g) It is vital that early identification of symptoms, diagnosis, effective treatment and consistent advice and support are offered to children who suffer from constipation and their families. It is also important to differentiate between children with functional constipation (the vast majority) and those with organic disease, so that they all receive appropriate diagnosis and management.

4 The guideline

a) The guideline development process is described in detail in two publications that are available from the NICE website (see 'Further information'). 'The guideline development process: an overview for stakeholders, the public and the NHS' describes how organisations can become involved in the development of a guideline. 'The guidelines manual' provides advice on the technical aspects of guideline development.

b) This document is the scope. It defines exactly what this guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health (see appendix).

c) The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

Newborns, infants and children up to their 18th birthday who have idiopathic constipation.

4.1.2 Groups that will not be covered

Newborns, infants and children who have constipation with a known cause.

4.2 Healthcare setting

Diagnosis and management in community and hospital care, and referral to specialist services.

4.3 Clinical management

Areas that will be covered

a) Diagnosis of idiopathic constipation, including:

- patient history
- clinical examination, including the role of digital rectal examination
- diagnostic criteria (for example, Rome III criteria)
- the following investigations to rule out alternative diagnoses such as Hirschprung’s disease or coeliac disease:
  - blood tests
  - radiological investigations
  - gastrointestinal endoscopy
  - manometry
  - rectal biopsy.

b) Management, including:

- dietary manipulation, including role of water and milk intake, fruits, vegetables (fibres and roughage), fruit juices, cereals
- exclusion of cows' milk protein
- physical activity
- pharmacological treatments, specifically bulk-forming laxatives, stimulant laxatives and osmotic laxatives
- psychological and behavioural management including toilet training, behavioural modification, maintaining toilet diaries, rewarding, psychosocial counselling including biofeedback therapy and intense psychotherapy
- complementary and alternative interventions, specifically abdominal massage, reflexology and hypnotherapy

surgical management, including manual evacuation under general anaesthetic and antegrade colonic enema (ACE procedure).

c) Indications for referral to specialist services.

d) Information and support needs for children and families.

e) The Guideline Development Group will take reasonable steps to identify ineffective interventions and approaches to care. If robust and credible recommendations for re-positioning the intervention for optimal use, or changing the approach to care to make more efficient use of resources can be made, they will be clearly stated. If the resources released are substantial, consideration will be given to listing such recommendations in the 'Key priorities for implementation' section of the guideline.

f) Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform their decisions for individual patients.

Areas that will not be covered

g) If during the process of diagnosis for childhood idiopathic constipation another disease is suspected, further diagnosis and treatment of this disease will not be covered.

h) Management and diagnosis of comorbidity.

i) Care received in specialist services after referral.

j) Children with an underlying, congenital, genetic, metabolic, endocrine or neurological disorder may also have constipation. The principles of assessment and management covered in points a–f will apply to them, but the guideline will not address any additional management that these children might require.

4.4 Status

4.4.1 Scope

This is the final scope.

4.4.2 Guideline

The development of the guideline recommendations will begin in May 2008.

4.4.3 Related NICE guidance

- Urinary tract infection in children: diagnosis, management and long-term treatment. NICE clinical guideline 54 (2007).
- Nocturnal enuresis: the management of nocturnal enuresis (bedwetting) in children and young people. NICE clinical guideline. (Publication expected August 2010.)

5 Further information

Information on the guideline development process is provided in:

- 'The guideline development process: an overview for stakeholders, the public and the NHS'
- 'The guidelines manual'.

These booklets are available as PDF files from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the website.

Appendix: Referral from the Department of Health

The Department of Health asked NICE:

'To prepare a clinical guideline on the diagnosis and treatment of idiopathic childhood constipation'.

Appendix B

Declarations of interest

All GDG members' interests were recorded on declaration forms provided by NICE. The form covered consultancies, fee-paid work, shareholdings, fellowships and support from the healthcare industry. GDG members' interests are listed in this section. No material conflicts of interest were identified

This appendix includes all interests declared on or before 1st September

GDG member	Interest
Jenny Gordon	Personal non-pecuniary interest: Research interest in the use of reflexology in the treatment of idiopathic constipation
Kate Blakeley	No interests declared
Janet Blannin	No interest declared
James Cave	Personal pecuniary interest: Director of a dispensing pharmacy and a partner of a dispensing general practice, both of which receive payments for dispensing medication
Sian Hooban	No interests declared
Huw Jenkins	Personal non-pecuniary interests: Co-investigator in a multi-centre trial on Movicol (2004) Attended two European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) working group meetings sponsored by Norgine (2007)
Sarah Mancell	No interests declared
Nick Nelhans	Non-personal pecuniary interests: Received six honoraria of £200 for lectures on behalf of the Impact Bowel Care Pathway Working Group Received honorarium of £300 for a presentation at the ERIC Study Day
Zoe Rawlinson	No interests declared
June Rogers	Non-personal pecuniary interests: Performs a number of talks on and training in paediatric incontinence including constipation. Speaker fees sometimes paid through sponsorship funding from Norgine. This payment is made directly to Disabled Living (employer). Company (PromoCon) received an unrestricted educational grant from Norgine used to pay for printing of a booklet about constipation for children Non-personal non-pecuniary interests: Member of the "Education and Resources for Improving Childhood Continence" (ERIC) clinical advisory board
Jonathan Sutcliffe	Personal non-pecuniary interest: Research interest in idiopathic constipation

David Tappin	*Personal pecuniary interest:* Currently performing research into developing a nurse-led intervention for children with constipation and soiling funded by the Yorkhill children's Foundation and the NHS East Glasgow CHSP
Karen Tucker	No interests declared
Lynne Watson	No interests declared
NCC-WCH staff	**Interest**
Monica Lakhanpaul	*Personal pecuniary interests*: Honorarium for Medicine for Children Research Network Honorarium for articles reviewed for Archives of Disease in Childhood Honorarium to attend a meeting of the advisory board for the Prio-med Child EU work package 4 project Funding to lead the Eranet Priomed child project for the MRC through employment at the University of Leicester *Non-personal pecuniary interests*: University dept funded by: DH to develop internet-based educational tool 'spotting the sick child 2', SDO on a project 'promoting partnerships with children and adolescents in medicine taking', MRC for 'medicines for children' European research network, Leicester PCT for a project on improving health outcomes for children with acute and chronic illness Maximum of one place per year across the department at Leicester funded by Astra Zeneca to attend the ATS conference *Personal non-pecuniary interests*: Member of the NHS Evidence Advisory Board Community lead for non medicine for children Trent research network Lead for LNR non medicines specialty group Community lead on the medicine for children specialty group
Hannah Rose Douglas	No interests declared
Roz Ullman	No interests declared
Lauren Bardisa-Ezcurra	No interests declared
Michela Tinelli	No interests declared
Rosalind Lai	No interests declared
Debbie Pledge	No interests declared
Rupert Franklin	No interests declared
Rosie Crossley	No interests declared
External Advisor	**Interest**

David Candy	*Personal Pecuniary interests:* Received honoraria for two articles written for nutritional companies Received honoraria for attendance at two Norgine Advisory Boards *Non-personal pecuniary interests:* Funding from Yakult Ltd (£20,000 for one year) into a study on prevention of diarrhoea in patients admitted to elderly care rehabilitation wards by Lactobacillus casei Shirota Funding from Norgine (£30,000 for one year) into a single centre study to assess the safety and efficacy of Movicol in the treatment of children with faecal impaction in children followed by a double, randomised phase to compare the safety and efficacy of Movicol and Lactulose Dry for maintenance therapy *Personal non-pecuniary interests:* Principal investigator in an open label study of PEG+E conducted at the Royal West Sussex NHS Trust Involved in a randomised controlled trial comparing PEG+E with lactulose in children with constipation conducted at the Royal West Sussex NHS Trust Principal investigator in a multicentre study comparing the clinical and economic impact of using Macrogol 3350 plus electrolytes with the use of enemas and suppositories and manual evacuation to treat paediatric faecal impaction
Peer Reviewers	**Interest**
Graham Clayden	
Michael Green	*Non-personal pecuniary interest*: Contributed three patients to a phase III study of Movicol in children with chronic constipation sponsored by Norgine Ltd. Individual patient fees paid directly to department

Appendix C

Registered stakeholder organisations

This list is correct as of 1st September 2009. For the most recent list of stakeholders, check the NICE website

Action for Sick Children
Airedale Acute Trust
Airedale and Bradford Teaching PCT
Alder Hey Children's NHS Foundation Trust
Association for Continence Advice
Association of Psychoanalytic Psychotherapy in the NHS
Association of the British Pharmaceuticals Industry (ABPI)
Autism Medical
Barnsley Hospital NHS Foundation Trust
Barnsley PCT
Birmingham City Council
BMJ
Boehringer Ingelheim Ltd
Bolton Council
Bournemouth and Poole PCT
Breastfeeding Network, The
British Association for Community Child Health
British Association of Psychodrama and Sociodrama (BPA)
British Dietetic Association
British Heart Foundation Health Promotion Research Group
British National Formulary (BNF)
British Paediatric Mental Health Group
British Psychodrama Association
British Psychological Society
British Society of Gastrointestinal and Abdominal Radiology (BSGAR)
British Society of Paediatric Gastroenterology, Hepatology & Nutrition (BSPGHAN)
Calderdale PCT
Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)
Care Quality Commission (CQC)

Central Surrey Health NHS Trust
Chartered Physiotherapists Promoting Continence (CPPC)
Chartered Society of Physiotherapy (CSP)
CIS'ters
Coeliac UK
Commission for Social Care Inspection
Connecting for Health
Cornwall & Isles of Scilly PCT
Department for Children, Schools and Families
Department for Communities and Local Government
Department of Health
Department of Health, Social Services & Public Safety, Northern Ireland (DHSSPSNI)
Devon PCT
East Kent Coastal PCT
East Sussex Hospitals Acute Trust
Education and Resources for Improving Childhood Continence
Griffiths and Nielsen
Harrogate and District NHS Foundation Trust
Heart of England NHS Foundation Trust
Institute of Biomedical Science
Leeds PCT
Liverpool PCT
Luton & Dunstable Hospital NHS Foundation Trust
Luton PCT
Medicines and Healthcare Products Regulatory Agency (MHRA)
Medicines for Children Research Network (MCRN)
Milton Keynes PCT
National Patient Safety Agency (NPSA)
National Pharmacy Association
Neonatal & Paediatric Pharmacists Group (NPPG)
NETSCC, Health Technology Assessment
Newham University Hospital NHS Trust
NHS Bedfordshire
NHS Clinical Knowledge Summaries Service (SCHIN)
NHS Direct
NHS Kirklees
NHS Knowsley
NHS Plus
NHS Purchasing & Supply Agency

NHS Quality Improvement Scotland
NHS Sheffield
Norgine Pharmaceuticals Ltd
North East London Mental Health Trust
North East Wales NHS Trust
North Staffordshire PCT
North Tees PCT
North Yorkshire and York PCT
Nottingham University Hospitals NHS Trust
Oldham PCT
Oxfordshire & Buckinghamshire Mental Health Partnership NHS Trust
Oxfordshire PCT
Pembrokeshire and Derwen NHS Trust
PERIGON Healthcare Ltd
Primary Care Society for Gastroenterology (PCSG)
PromoCon
Rainbows Childrens Hospice
Reckitt BenckiserHealthcare (UK) Ltd
Royal College of General Practitioners
Royal College of Midwives
Royal College of Nursing
Royal College of Paediatrics and Child Health
Royal College of Pathologists
Royal College of Physicians London
Royal College of Radiologists
Royal Pharmaceutical Society of Great Britain
Royal Society of Medicine
Royal West Sussex Trust
SACAR
Sandwell PCT
SCHOOL AND PUBLIC HEALTH NURSES ASSOCIATION
Scottish Intercollegiate Guidelines Network (SIGN)
Scottish Nutrition & Diet Resources Initiative
Sedgefield PCT
Sheffield Children's NHS Foundation Trust
Sheffield PCT
Sheffield Teaching Hospitals NHS Foundation Trust
Shrewsbury & Telford Hospital NHS Trust
Social Care Institute for Excellence (SCIE)

Southampton City PCT
Southampton University Hospitals NHS Trust
Stafford General Hospital
Staffordshire County Council
University College London Hospitals (UCLH) Acute Trust
Vygon (UK) Ltd
Weight Concern
Welsh Assembly Government
Welsh Scientific Advisory Committee (WSAC)
West Hertfordshire PCT & East and North Hertfordshire PCT
West Herts Hospitals NHS Trust
West Midlands SHA
Western Cheshire Primary Care Trust
Western Health and Social Care Trust
Winchester and Eastleigh Healthcare Trust
Yeovil District Hospital
York NHS Foundation Trust

Appendix D

Clinical questions

What is the diagnostic value of the history taking and the physical examination in diagnosing chronic idiopathic constipation in newborns, infants and children?

What is the diagnostic value of the digital rectal examination in children with chronic idiopathic constipation?

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

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

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

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

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

What is the diagnostic value of transit studies in children?

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

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

What is the clinical effectiveness of pharmacological interventions for ongoing treatment/maintenance in children with chronic idiopathic constipation?

What are the adverse effects of the medium- to long-term use of laxatives?

What is the effectiveness of the Antegrade Colonic Enema (ACE) procedure in children with chronic idiopathic constipation?

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

- Abdominal massage
- Reflexology
- Hypnotherapy
- Osteopathy
- Cranial osteopathy
- Craniosacral therapy
- Homeopathy

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?

What is the clinical effectiveness of the following for ongoing treatment/maintenance in children with chronic idiopathic constipation?

- Increasing physical activity
- Dietary modifications
- Increasing fluid intake
- Excluding cow's and goat's milk protein from diet

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

Appendix E

Health Economics

E.1 The cost effectiveness of methods of disimpaction and maintenance of idiopathic constipation in children

Introduction

The various combinations of strategies for managing idiopathic constipation in children are numerous, combining pharmacological treatments in various doses, switching treatments where one fails, and titrating doses as treatments succeed or fail. There is a clear obligation on health care providers to provide treatments that are safe, effective and provide the greatest relief from suffering at the lowest possible cost since, where resources are finite, lower costs of care mean that more people can be treated for this condition or for other health problems. However, treatment with the lowest cost drug does not mean the most cost-effective treatment since the cost of failure associated with drugs that are less effective may outweigh the cost of higher priced alternatives. Furthermore high cost drugs may be cost-effective where they provide more health gain at an acceptable additional cost.

Cost-effectiveness analysis can provide insights into which treatment strategies provide the best health outcomes for the available NHS resources. Decisions on whether a more costly treatment is "worth" the additional benefit are decided on the basis of additional cost per additional health gain. In order to be able to make comparisons across different health outcomes and maximise the use of NHS resources, NICE prefers health gain to be measured in terms of the quality adjusted life year (QALY) which is a generic measure of health benefit taking into account both years of life and quality of life. NICE has a guiding principle that an intervention is cost-effective compared to the next best treatment if the additional cost per QALY is less than £20,000.

Health economic modelling can be helpful in developing guideline recommendations by showing the costs and benefits of all the alternative treatments available for a given population of children, including the downstream consequences of therapeutic success and failure. The economic evaluation of alternative treatments for idiopathic constipation requires data on both the costs and the consequences of using each treatment option. Although a wide range of treatments are available for disimpaction and maintenance for children and are prescribed by NHS practitioners, there is sparse clinical evidence of clinical effectiveness or on the downstream costs and consequences when treatments fail.

Review of the published economic evidence

A review of the health economics literature identified three studies by the same team of authors [63], [139], [140] addressing the cost effectiveness of Movicol Paediatric Plain for the treatment of faecal impaction in children. Some of the studies used the specific brand of PEG Movicol in the analysis rather than the generic term macrogol.

The first of these studies[63] aimed to estimate the clinical and economic impact of using Movicol Paediatric Plain in outpatient settings compared to enemas and suppositories and manual evacuation to treat paediatric faecal impaction. This is a UK-based economic analysis of treatment for childhood constipation and the data were based on clinical practice in England and Wales. A retrospective cohort study of two hundred and twenty four children aged 2-11 years with faecal impaction who initially received Movicol Paediatric Plain, enemas and suppositories, or manual evacuation for initial disimpaction was undertaken. The follow-up time was 3 months after disimpaction. The results showed comparable outcomes across groups. QALY values were reported but the quality of life weights were taken from previously published studies on constipation (0.94 for healthy children between the ages of 2-11 and 0.66 QALY for adults with constipation). The authors developed an algorithm to adapt the quality of life values for constipation in adults (0.66) to a value of 0.70 for children with constipation. Details of their methods are not given in the paper. The results of the analysis reported an equal number of QALYs at 3 months irrespective of treatment (0.21 in all groups; 95% CI: 0.18; 0.24), therefore a cost-minimisation analysis was sufficient. It showed that Movicol Paediatric Plain was the preferred option on cost alone (£694 vs. £2759 for enemas and suppositories respectively and £2333 for manual evacuation).

The second study was also a UK [140] based study that estimated the cost-effectiveness of Macrogol versus lactulose for the treatment of chronic functional constipation in adults greater than 18 years old. The study enrolled a total of 977 patients. Authors obtained quality of life weights from 308 members of the general public using appropriate health economic techniques (standard gamble and time trade-off methods). The economic model limited the analysis to three-months cycles for treatment, and patients were categorised as either successfully treated or not during this period. The authors concluded that Macrogol was a cost effective option relative to lactulose, the same conclusion as the first study.

The quality of life weightings reported for this study were 0.74 (95% CI 0.71, 0.75) for adults experiencing symptoms of constipation and 0.90 (95% CI 0.88, 0.93) for people suffering from constipation but being well managed.

The final paper was an Australian study[139] which looked at the costs and consequences of oral Macrogol in the disimpaction of paediatric faecal impaction in children aged between 4 and 11 years old. The model compared oral Macrogol, enemas and suppositories or manual evacuation. Model inputs (clinical outcomes and quality of life weightings) reported in this paper were obtained from the earlier studies. The authors found that oral Macrogol was a cost-effective treatment for faecal impaction when compared to other alternatives.

Health economic analysis undertaken for the guideline

The body of published health economic evidence is sparse and does not address the scope of this guideline therefore additional health economic analysis was required.

The aim of the health economic analysis for this guideline was to develop a model to compare all the pharmacological interventions and combinations of interventions that could be offered to a child with idiopathic constipation. The comparisons of drug therapies in the model are those the GDG considered to be widely used in practice in England and Wales rather than simply mirror the comparative analyses in the published literature which did not reflect usual practice. The intention was to undertake a cost-utility analysis within a decision analytic framework comparing the different modalities of treating children with a history of idiopathic constipation confirmed by a first physical examination in terms of incremental cost per QALY. It became clear early on in the development of the guideline that the data on clinical effectiveness would be sparse. The health economic analysis used estimates made by the GDG since mean dosages and effect sizes for treatment were missing for almost all alternatives. We are aware of the limitations of this approach and discuss its implications for each of our analyses throughout this chapter.

The interpretation by the GDG of the clinical data on effectiveness was that there was no robust evidence of difference between pharmacological preparations used as first line treatment for disimpaction and that one strategy could not be recommended over any other on effectiveness grounds alone. Therefore recommendations for clinical practice should be based on other factors affecting concordance with treatment in children, such as tolerance and palatability, time to disimpaction in the initial phase of treatment and ease of use, as well as cost to the NHS.

The health economic analysis for this guideline was undertaken with the a priori assumption that all first line pharmacological strategies had the same level of effectiveness, although different assumptions provided by the GDG were used for some of the second and third line treatments where first line treatments failed. Failure is defined as on-going constipation requiring further treatment. The GDG were interested in finding out the difference in cost for a range of strategies for disimpaction and maintenance and whether the cost of a high-priced drug would be off-set by the lower cost of failure if that high-priced drug was more effective, leading to overall savings. The economic analysis also compared the total costs per patient (including the cost of failure) of various pharmacological strategies, and considered the effect of different doses of treatment where these clinical data were available.

The economic analysis also calculated thresholds of cost-effectiveness of treatment. Where one treatment or group of treatments was more effective than the alternative, there would need to be some additional therapeutic benefit of the more expensive option in order for it to be the preferred option on cost-effectiveness grounds. This additional therapeutic benefit was converted into quality adjusted life years in order to apply the NICE threshold of £20,000 per QALY to this analysis. Data on QALY weights were obtained from the published literature reviewed above.

The only data identified which estimated the effectiveness of different doses of treatment was one small study based on treatment with Movicol Paediatric Plain. An economic analysis of the cost-effectiveness of treatment by dose was undertaken using this clinical effectiveness data.

Aims

The following health economic analyses were undertaken:

i. a cost analysis for disimpaction assuming high, medium and low levels of effectiveness, to consider whether the cost of higher priced treatments that were more effective would be offset by savings due to lower failure rates than cheaper alternatives (with more children requiring high cost care after initial treatment had failed), and equally whether higher, more effective doses of treatment would also offset such savings. Threshold analysis was undertaken if high cost treatments lead to higher costs overall to assess the cut-off for effectiveness at which a higher cost treatment becomes the cost-effective option;

ii. an analysis of a macrogol (PEG+E, Movicol Paediatric Plain) alone to assess the cost-effectiveness of different doses of treatment;

iii. a decision analytic model of strategies for disimpaction and initial maintenance in the first three months of treatment with all combinations of treatments by pharmacological type, including drug and downstream cost data;

iv. a decision analytic model of strategies for on-going maintenance after disimpaction (including treatment for reimpaction), in the following three months after disimpaction and initial maintenance, one year later and two years later.

Methods

i) Cost analysis of treatments for disimpaction

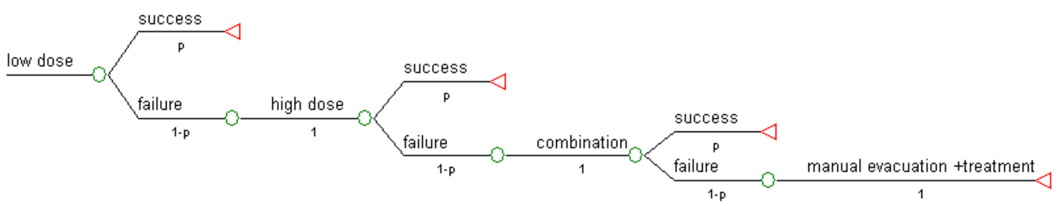
Different treatment pathways were modelled: treatments for disimpaction covered oral pharmacological treatments, in various preparations and dosages as well as other methods of treatment (such as suppositories, enemas and manual evacuation). Treatments for the maintenance phase once disimpaction has been achieved included lower dose pharmacological treatments as first line treatment, with higher doses, combinations of treatments and other more invasive procedures where pharmacological treatments fail.

The cost analysis was based on a hypothetical case of a five-year-old constipated child treated in a primary care setting with no indication of a serious underlying disorder after history and physical examination. The time frame is the first 3 months after first referral (disimpaction followed by maintenance up to 3 months). It was assumed that the maintenance dose was equal to half of the disimpaction dose. Equal numbers of follow-up hospitalisations and outpatient visits were considered across treatments. Four different pharmacological treatment groups were compared (see tables E.1 and E.2)).

For each pharmacological treatment two different starting doses were considered (lowest and highest reported on BNF children website (last accessed December 2008). Combinations of treatments included baseline dosages for the different options (table E.1). The pathways for such doses are summarised in figure E.1.

The exercise was repeated including three different rates of success: low (20% success rate); medium (50% success rate); high (80% success rate). In total, 21 different pathways were modelled.

Figure E.1. Cost analysis of disimpaction treatments: treatment pathways



P = probability of having success
Combination = combination of treatments
Manual evacuation + treatment = combination treatment after successful manual disimpaction

Resources use was calculated for each pathway, including pharmacological treatment costs and hospitalisation costs (related to manual evaluation and enemas only). Data sources for unit costs are summarised in table 1 and unit costs used in the model reported in table 2. Days of hospitalisation for enemas and manual evacuation were assumed to be four days in the first instance, and sensitivity analysis was performed to assess the impact of fewer days of hospitalisation required (day case, two days, three days). In reality, children come into hospital as a day case for manual evacuation and don't come in at all for the enemas. Some patients will present not as chronic idiopathic constipation but as abdominal pain and be admitted for investigation.

'Combination of treatment' costs were calculated as the mean cost of the possible combination treatments available for each group. After successful manual disimpaction, all patients were assumed to be on a combination treatment for the rest of the three month initial treatment phase. Total costs of disimpaction and maintenance in the 3-month time frame were calculated for all possible pathways.

Table E.1: Disimpaction treatments, mean times to disimpaction, mean daily doses

Group1	Mean time to disimpact (days)	Data source	Mean doses for disimpaction	Data source for doses and unit costs
Movicol Paediatric Plain baseline dose	4	GDG members	4 sachets daily	BNFc *
Movicol Paediatric Plain higher dose	4	GDG members	7.5 sachets daily	BNF
Combination:				BNFc
Movicol Paediatric Plain+sodium picosulphate	4	GDG members	See baseline doses	BNFc
Group2				BNFc
picosulphate baseline dose	4	GDG members	2.5mg daily	BNFc
picosulphate higher dose	4	GDG members	5mg daily	BNFc
Combinations:				BNFc
Movicol Paediatric Plain+sodium picosulphate	4	GDG members	See baseline doses	BNFc
picosulphate+Senna	4	GDG members	See baseline doses	BNFc
picosulphate +lactulose	4	GDG members	Sodium picosulphate: see baseline dose Lactulose: 10ml daily	BNFc
Group3				
Senna baseline dose	24	GDG members	2.5ml daily	BNFc
Senna higher dose	24	GDG members	5ml daily	BNFc
Combinations:				BNFc
picosulphate+Senna	4	GDG members		BNFc
lactulose+Senna	24	GDG members	Lactulose: 10ml daily Senna: see baseline dose	BNFc
docusate+Senna	24	GDG members	Docusate: 12.5ml 3 times daily Senna: see baseline dose	BNFc
Group4				
enemas micralax	1	GDG members	5ml daily	BNFc NHS reference costs 2006/7
manual evacuation	1	GDG members	n/a	NHS reference costs 2006/7

* BNFc Last accessed December 2008

Table E.2: Unit costs used in the model, 2008

Group1	Daily disimpaction dose cost (£)	Hospitalisation cost (£)
Movicol Paediatric Plain baseline dose	£1.08	
Movicol Paediatric Plain higher dose	£1.35	
Combination:		
Movicol Paediatric Plain+sodium picosulphate	£1.14	
Group2		
picosulphate baseline dose	6p	
picosulphate higher dose	8p	
Combinations:		No hospitalisation required
Movicol Paediatric Plain+sodium picosulphate	£1.14	
picosulphate+ Senna	8p	
picosulphate + lactulose	68p	
Group3		
Senna baseline dose	1p	
Senna higher dose	2p	
Combinations:		
picosulphate+Senna	7p	
lactulose+Senna	12p	
docusate+Senna	22p	
Group4		
enemas micralax	n/a	£1198 (4 days base case)
manual evacuation	n/a	£904

ii) Cost effectiveness of disimpaction by dose of a specific pharmacological treatment (PEG+E, Movicol Paediatric Plain)

A decision analytic model was undertaken to model alternative Movicol Paediatric Plain doses in the treatment of disimpaction. Clinical outcomes and treatment doses came from a RCT conducted in the USA [61] which aimed to investigate the effectiveness and safety of 4 different doses of Movicol Paediatric Plain (polyethylene glycol (PEG) 3350) in the treatment of childhood faecal disimpaction.

In the clinical trial, children were randomized into 4 groups and each group received a different daily dose (g/kg) of Movicol Paediatric Plain. Table E.3 shows the doses received by group and the proportion of children treated successfully ('success rate').

Table E.3: Doses and success rates, and cost per day

	Dose 1	Dose 2	Dose 3	Dose 4	Source of data
Daily doses g/kg	0.25	0.5	1	1.5	Youssef NN et al 2002[61]
Daily dose for 25 kg child	6.25	12.5	25	37.5	
Number of sachets (6.563g each) per day	1	2	4	6	BNFc**
Costs per sachet	15p	15p	15p	15p	BNFc
5 days treatment cost	77p	£1.54	£3.09	£4.63	
Success rate*	0.55	0.55	0.95	0.95	Youssef NN et al 2002[61]

*Values for each group are estimates taken from a bar chart ($p<0.05$ groups 1 and 2 vs. groups 3 and 4).

** Last accessed Dec 2008

For the economic model, these success rates were converted into quality adjusted life years (QALYs). Estimates of the quality of life weights for constipation-related health states were obtained from economic literature reviewed earlier[140] and are presented in table E.4. QALY values presented in this paper were used as they were elicited especially for the study from members of the general population using appropriate health economic methods (time trade off and standard gamble). The data were also from a large study of an adult population which was conducted in the UK.

Table E.4. Utility values for constipation-related health states[140]

Health state	QALY (95% confidence intervals)	QALY values for 3 months in health state
Experiencing symptoms of constipation	0.74 (0.71;0.75)	0.185
Suffering from constipation but being well managed on medication	0.90 (0.88;0.93)	0.225
Utility for successful treatment – reference case	1.00	0.25

The values used in the model developed for this guideline were 0.125 (three months experiencing symptoms of constipation) and 0.235 (three months well managed on medication). The QALY gain of moving from an unwell to a well-managed health state was 0.04 QALYs (0.225-0.185).

Cost data

To calculate the correct dose of treatment, we assumed a 25kg child and calculated the corresponding number of sachets per day for the four groups. The cost of manual evacuation is reported in table E.2 above. The cost of failure was modelled based on the following simplifying assumptions (see figure E.2):

- Children who were still impacted after five days on dose 1 or 2 moved to dose 3. If this failed, it was assumed that a child underwent a successful manual evacuation;

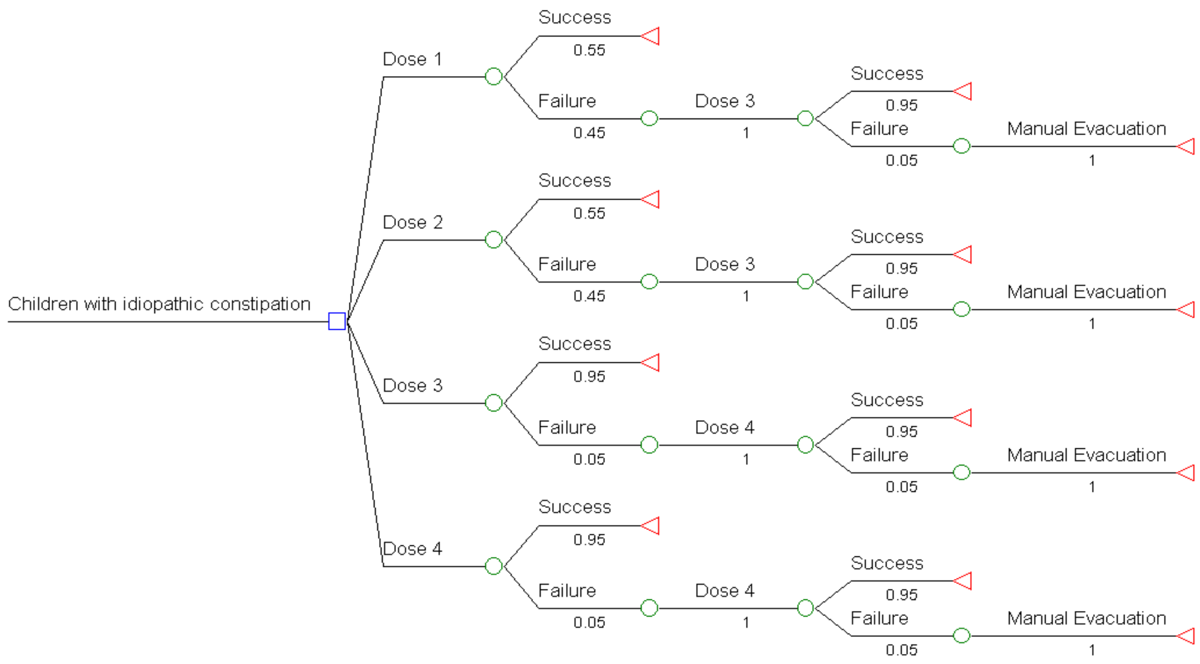
- Children who were still impacted after five days on dose 3 moved to dose 4. If this failed, they underwent a successful manual evacuation

- Children who were still impacted after five days with dose 4 repeated another five days of treatment with the same dose. If this failed, they underwent a successful manual evacuation

Sachet doses and daily treatment costs were derived from BNFc (table E.1). Manual evacuation costs were derived from NHS reference costs 2007 (table E.2).

Cost-effectiveness (incremental cost per disimpacted child and incremental cost per QALY) was undertaken from an NHS perspective. The time frame considered was the 5 days disimpaction period. The model applied is presented in figure E.2.

Figure E.2: Modelling pharmacological treatment for disimpaction: different doses



(iii) Pharmacological treatment for disimpaction: comparing different alternatives

The disimpaction model was developed assuming clinical equivalence of first line treatment for disimpaction to establish which group of pharmacological treatments, including all combinations of treatments and dose of treatments, including manual evacuation as a last resort for disimpaction, provided care at the lowest cost to the NHS over the initial three months of treatment. Using the clinical outcomes and resource used values obtained from GDG consensus, a model was constructed considering the decision to treat in primary care setting constipated children aged between 2-11 yrs (to be consistent with the published economic[63]) with no flag to a serious underlying disorder after history and physical examination.

Different treatments pathways were proposed under four groups of pharmacological treatment strategies: group 1, group 2, group 3 and group 4. For each treatment group, there were alternative decisions available if initial treatment with a baseline dose failed. The GDG specified all the different strategies (change of treatment, change of dose or combinations of treatments). For each group, the mean three-month cost was calculated. This provided the GDG with information on which group of strategies provided the best value for money to the NHS given clinical equivalence.

Group1: The first treatment group started with Movicol Paediatric Plain at a baseline dose. It the treatment was successful, the child stayed on this preparation during the maintenance phase, at half the dose for the maintenance phase. If this baseline treatment failed, patients moved to a higher dose of Movicol Paediatric Plain; if the higher dose failed they then moved to a combination treatment with Movicol Paediatric Plain® and sodium picosulphate. If all strategies from group 1 failed patients then moved to other treatment groups (2, 3 or 4). If all strategies from group 1 and another subsequent group failed the last choice treatment was manual evacuation.

Group 2: the first choice treatment was sodium picosulphate baseline dose; if this failed patients then moved to a higher dose; if the higher dose failed they then moved to one of these three possible combinations: with Movicol Paediatric Plain; with Senna; or with lactulose. If all strategies from group 2 failed the patients moved to other groups of treatment (1, 3 or 4). If all strategies from group 2 and another subsequent group failed the last choice treatment was manual evacuation.

Group 3: the first choice treatment was Senna baseline dose; if this failed patients then moved to a higher dose; if the higher dose failed they then moved to one of these three possible combinations: with picosulphate; with lactulose; or with docusate. If all group 1 strategies failed the patients moved to other groups (1, 2, or 4). If all strategies from group 3 and another subsequent group failed the last choice treatment was manual evacuation.

Group 4: the first choice is enemas Micralax. If it failed patients move to another group (1, 2, or 3). If group 4 and the subsequent group strategies failed last choice treatment was manual evacuation.

In all, 136 possible treatment pathways were identified. A list of all 136 alternative pathways combination is presented at the end of the chapter.

Resource use:

The analysis was undertaken from the NHS perspective and the time frame was the first three months of treatment. All pharmacological treatments were assumed to be administered at home, while a hospitalisation was required for enemas and manual evacuation procedures see above. Hospitalisations and GP/nurse outpatient visits following disimpaction were considered equal across the treatment options. Estimates of pharmacological treatment failure rates were agreed with the GDG members on a consensus base (table E.5). Daily doses and unit costs were derived from BNF children (last visited December 2008). When a range of doses was available, the lowest was considered as baseline dose. A higher dose was calculated applying a 25% increase to the baseline option, as advised by the GDG. Combinations of treatments included baseline doses for both options. Daily doses for the remaining maintenance period were calculated applying a 25% decrease to the disimpaction doses. Details of mean time to disimpaction, dosages, failure rate and hospitalisation unit costs are the same as those reported in table E.5. Total costs (for disimpaction phase, maintenance phase, and overall 3 month time frame) were calculated for all possible pathways and group options.

Resource use data, mean time to disimpact and failure rates for the different treatment options were obtained from discussions with the GDG (table E.5).

Effectiveness:

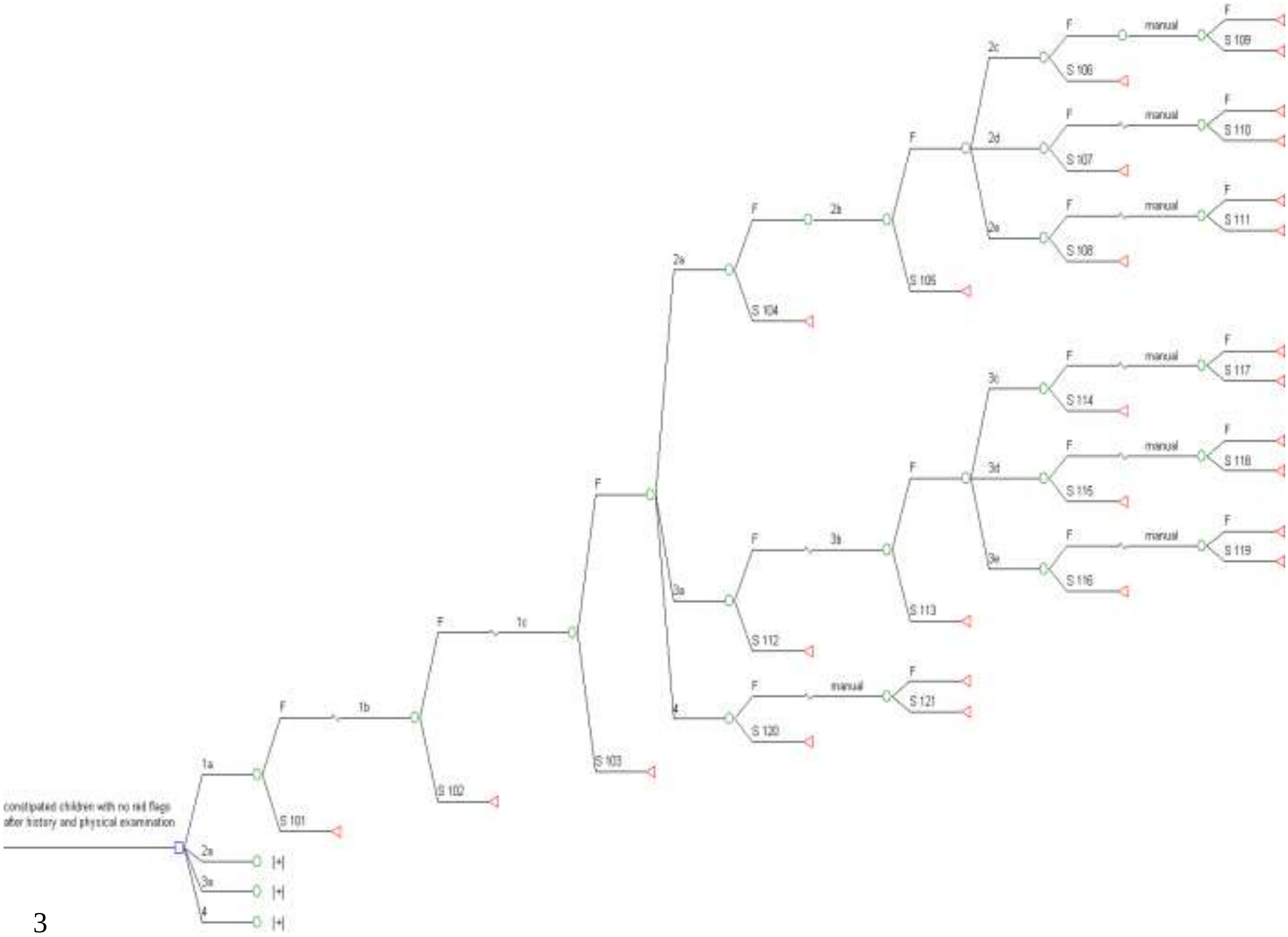
In the first instance, the same level of clinical effectiveness for all first line treatments was assumed. For a specific combination of pharmacological treatments (docusate plus senna) offered when first line treatment had failed, clinical effectiveness was not assumed to be equivalent, but to be worse. Enemas also had a higher failure rate based on GDG consensus.

Table E.5: Mean times to disimpaction, failure rate, mean daily doses and hospitalisation unit costs

Group1	**Failure rate**	**Mean doses for disimpaction**	**Data source**
Movicol Paediatric Plain baseline dose	0.2	4 sachets on first day, increased in steps of 2 sachets daily to max. 12 sachets daily	GDG members
Movicol Paediatric Plain higher dose	0.2	25% increase from baseline	GDG members
Combinations:			
Movicol Paediatric Plain+sodium picosulphate	0.2	See baseline doses	GDG members
Group2			
picosulphate baseline dose	0.2	2.5mg daily	GDG members
picosulphate higher dose	0.2	25% increase from baseline	GDG members
Combinations:			
Movicol Paediatric Plain+sodium picosulphate	0.2	See baseline doses	GDG members
picosulphate+Senna	0.2	See baseline doses	GDG members
picosulphate +lactulose	0.2	Sodium picosulphate: see baseline dose Lactulose: 10ml daily	GDG members
Group3			
Senna baseline dose	0.2	2.5ml daily	GDG members
Senna higher dose	0.2	25% increase from baseline	GDG members
Combinations:			
picosulphate+Senna	0.2		GDG members
lactulose+Senna	0.2	Lactulose: 10ml daily Senna: see baseline dose	GDG members
docusate+Senna	0.5	Docusate: 12.5ml 3 times daily Senna: see baseline dose	GDG members
Group4			
enemas micralax	0.75	5ml daily	GDG members

manual evacuation	0.2	n/a	GDG members

Figure E.3. Tree structure for the disimpaction model



iv) Maintenance phase following disimpaction and initial management

An economic model for the maintenance phase of treatment post disimpaction was developed separately given the very large number of alternative pathways that would arise from combining the disimpaction and maintenance models. The model covered maintenance treatment (pharmacological and Antegrade Continent Enema, or ACE procedure) for disimpacted children (aged between 2-11 yrs). The ACE strategy was included only as a last resort if other pharmacological strategies failed (see table E.6). Each cycle covered a three month period after initial disimpaction. Results are reported after three months, at the end of year one, (four cycles) and two years (eight cycles). A discount rate of 3.5% was applied for the 2-year time frame*. ACE costs depend on what washout solution is used.

The pharmacological treatment strategies described in the disimpaction model were included (groups 1, 2 and 3) together with two additional treatments which are only offered in the

* Discounting is applied to allow for higher time preference for benefits that accrue closer to the present

maintenance phase: methylcellulose and liquid paraffin. This gave a total of 15 alternative strategies as first line treatment in the maintenance phase.

Table E.6: Maintenance model: reimpaction failure rates and costs applied to the maintenance model

	Code	Reimpaction rate	Cost of reimpaction requiring treatment	Maintenance dose	Cost of remaining healthy	Cost of remaining healthy
			3 months cost (£)	Daily cost (£)	3 months cost (£)	last 3 months before stopping (2 years period only; £)
Movicol Paediatric Plain baseline dose	101	0.2	£91	81p	£72.92	£36.46
Movicol Paediatric Plain higher dose	102	0.2	£95.89	£1.01	£91.15	£45.58
Movicol Paediatric Plain baseline dose followed by Movicol Paediatric Plain+sodium picosulphate	103	0.2	£98.45	86p	£77.27	£38.63
Picosulphate baseline dose	201	0.2	£87.93	5p	£4.34	32.17
Picosulphate higher dose	202	0.2	£85.86	6p	£5.43	32.71
Picosulphate baseline dose followed by Movicol Paediatric Plain+sodium picosulphate	203	0.2	£88.42	86p	£77.27	£38.63
Picosulphate baseline dose followed by picosulphate+Senna	204	0.2	£83.79	6p	£7.03	£2.63
Picosulphate baseline dose followed by picosulphate +lactulose	205	0.5	£86.42	9p	37.89	£3.95
Senna baseline dose	301	0.2	£68.69	1p	£2.69	45p
Senna higher dose	302	0.2	£47.38	1p	£2.69	57p
Senna baseline dose followed by picosulphate+Senna	303	0.2	£48.00	6p	£7.03	32.63
Senna baseline dose followed by lactulose+Senna	304	0.2	£28.7	5p	£6.24	£2.23
Senna baseline dose followed by docusate+Senna	305	0.2	£30.96	6p	£7.27	£2.75
Methylcellulose	601	0.2	n/a	10p	£8.65	£15.13
Liquid paraffin light BP	701	0.5	n/a	6p	£5.40	£13.50
ACE`	801	0.2	n/a	1p	£2.69	45p

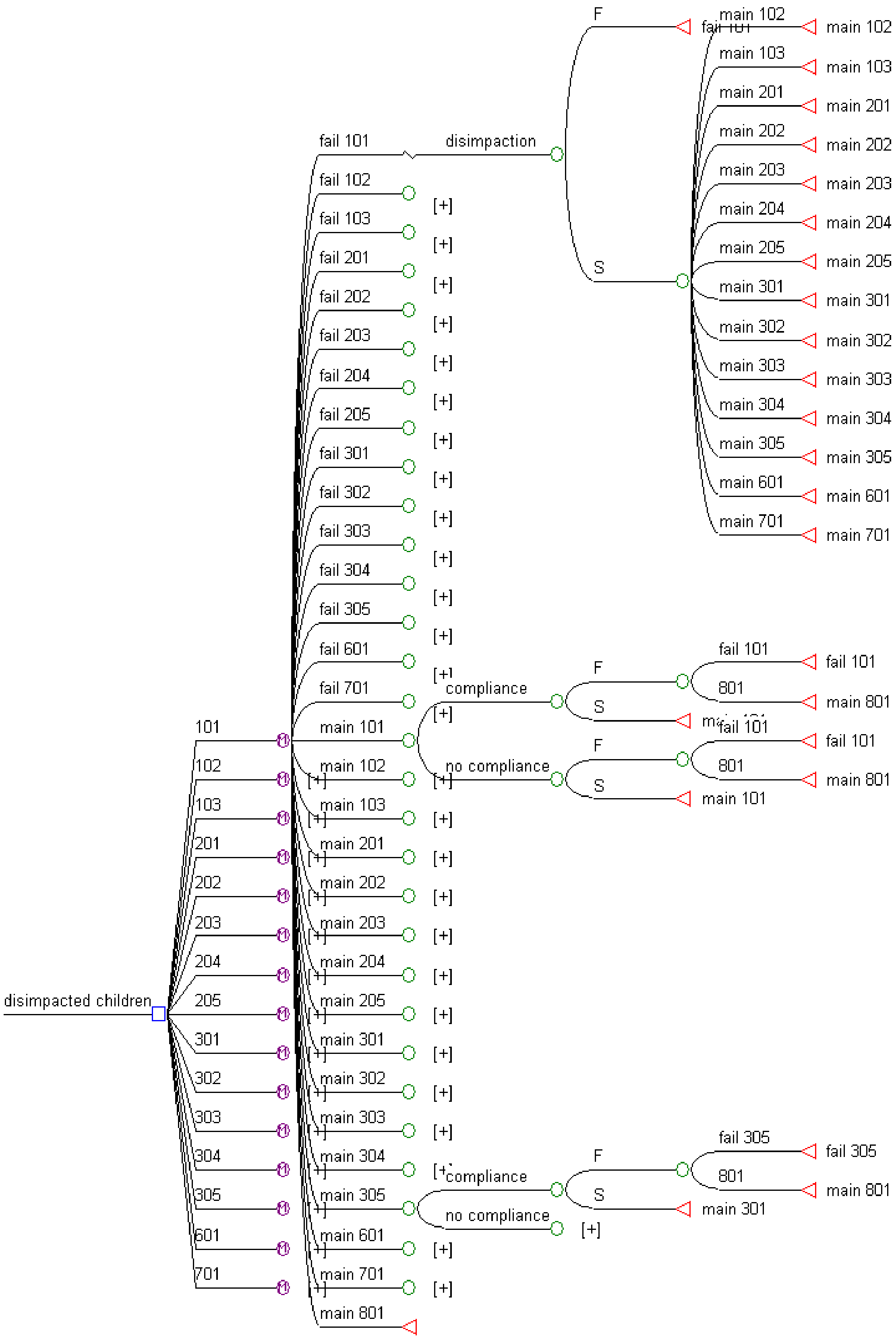
Drug doses were taken from the BNFc (see table E.5). All other health care resources and failure rates were agreed by GDG consensus. A decreased dose of 25% was applied to all successful disimpaction strategies to be continued as maintenance treatment. Three months disimpaction and maintenance costs are presented in table E.6. Compliance to treatment was also included in the model and adjustment to rate of success applied depending on whether the patients complied or not. For the purpose of this preliminary work a 100% compliance rate was considered for all treatments on offer.

Failure of one particular pharmacological strategy led to a switch to another alternative at the beginning of the following cycle. A maximum of 8 different treatments were possible within the maximum length of 2 years. As instructed by the GDG, in the last 3 months of a completely successful maintenance period the doses were gradually decrease each month to 75%, 50% and 25%, respectively, before stopping.

The expected numbers of QALYs for the 3 time frames were estimated applying the same procedure as in the disimpaction model (see above).

The model is summarised in figure E.4.

Figure E.4: Tree structure for the maintenance model



Results

i) Cost analysis by success rate for disimpaction

Table E.7 shows the range of costs associated with four alternative strategies for disimpaction of children with idiopathic constipation. These costs relate to the different starting doses published on the BNFc website (accessed December 2008). The table shows the drug costs and the total cost of care for the first three months of treatment starting with an initial baseline dose, moving to a higher dose if that fails, then a combination of pharmacological treatments, and finally manual evacuation as the last resort if all else fails. Once a treatment has been successful a maintenance dose of treatment is given for the rest of the three-month period.

Table E.7. Results from costing hypothetical scenarios

		Movicol Paediatric Plain	Picosulphate	Senna	Enemas micralax
		Low to high dose cost range			
Daily cost of drugs/ cost of one off procedure to treat impaction		62p –£1.16	10p – 19p	1p – 3p	n/a
3 months costs (disimpaction + maintenance)	low success (20%)	£ 501 – £508	£ 474 – £476	£ 464 – £465	£ 478
	medium success (50%)	£145 – £157	£121 – £123	£114 – £114	£ 127
	high success (80%)	£37– £56	£12 – £16	£8	£ 20

The results show that the treatment options using Senna as the baseline drug resulted in lower overall costs compared with all other options. If all treatment effectiveness was the same for all treatments, this would be the least cost and therefore the most cost-effective option. However, if Senna was not as effective as all the others, then all other treatments would be lower cost at medium or high levels of effectiveness, despite their higher drug prices. At these thresholds for effectiveness, there is no overlap between total costs between 'success rate' rows, indicating that if the GDG believe that one drug is effective at the medium (50%) or high (80%) level, then it will always be cheaper than one of the low-priced drugs at low level of effectiveness (20%). For all treatment options total costs were driven by success rate. High success implied a decrease in cost given the high cost of failure (that is, manual evacuation requiring hospitalisation).

The differences in effectiveness in the analysis were fairly large. The subsequent question therefore is how much more effective a higher cost drug would have to be to lead be a) cost-effectiveness at the £20,000 per QALY threshold for cost-effectiveness or b) cost saving.

a) Baseline scenario: we consider low dosages and low effectiveness rates (20%) for all treatments. Movicol Paediatric Plain® would need to increase the effectiveness by 0.021 to be the more cost-effective than Senna at the £20,000 per QALY threshold.

Table E.8. Cost-effectiveness analysis of pharmacological treatment in the first three months of treatment, given £20,000 per QALY threshold

Treatment for one child	Cost	Additional cost	Effectiveness	Additional effectiveness	Additional QALYs	ICER
senna	£464		0.2			
picosulphate	£474	£10	0.2			
enemas	£478	£14	0.2			
Movicol Paediatric Plain®	£489	£25	0.221	0.021	0.00126	£ 20,032

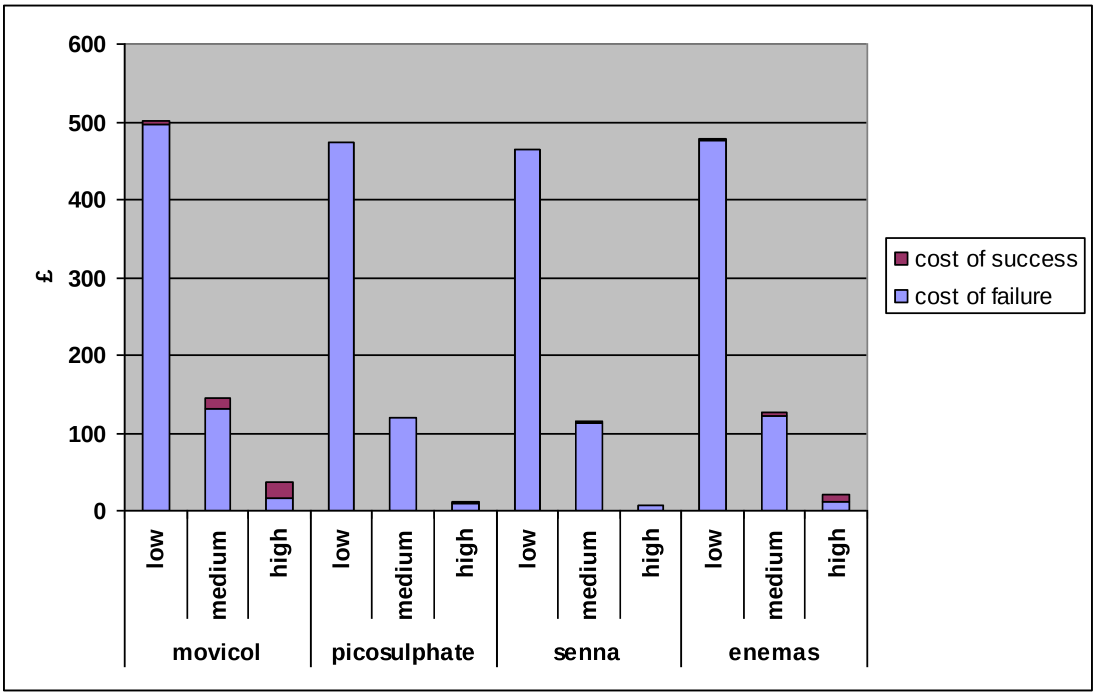
b) Movicol Paediatric Plain base dosage with 0.3 success rate is cheaper than senna base dosage with 0.2 success rate (£444 vs. £501).

Table E.9: Cost saving threshold for pharmacological treatment in the first three months of treatment

Treatment for one child	Cost	Additional cost/saving	Effectiveness	Additional effectiveness
senna	464		0.2	
picosulphate	474	£10	0.2	
enemas	478	£14	0.2	
Movicol Paediatric Plain	444	£-20	0.3	0.1

Table E.9 suggests that the cost of a package of care does not alter greatly depending on the dose of treatment given. Total costs did not vary by more than 2% between the low dose and high dose preparations for any treatment, indicating that dose does not have a big impact on total cost. In fact, the cost of pharmacological treatment to treat impaction is dwarfed by the cost of failure when initial treatment fails. Figure E.5 gives a graphic representation of this, showing that at all levels of success, the cost of success hardly registers on the chart next to the cost of failure. This is a strong indication than effectiveness is the dominant factor in determining the overall cost of treatment for disimpaction. Since success is determined by effectiveness and adherence to treatment, the treatment with the greatest chance of overall success should be the preferred option on cost-effectiveness grounds.

Figure E.5: Cost of success and failure per treatment according to success rate (low dose only)



ii) Cost effectiveness of disimpaction by dose of a specific pharmacological treatment (PEG+E, Movicol Paediatric Plain)

The baseline cost analysis of Movicol Paediatric Plain by dose of treatment showed that Dose 3 (1g/Kg, four sachets per day) was the preferred option. This is obvious since dose 3 costs less than the higher dose alternative (Dose 4) but has the same reported level of effectiveness (see table E.10).

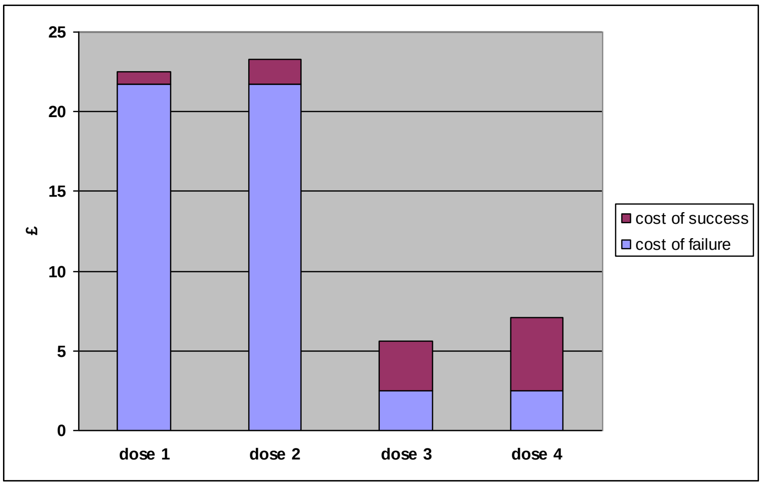
Again, the data suggests a higher dose of treatment with higher success rate and higher short term disimpaction costs (i.e. cost of success, see Dose 3) is more cost-effective than lower doses at lower initial pharmacological costs which are less effective and therefore require costly intervention when they fail.

However, given the NICE threshold for cost-effectiveness of £20,000 per QALY, the effectiveness of Dose 4 has to rise by only 0.21% in order for this to be the preferred option, indicating that these results are highly sensitive to the effectiveness of the treatment (Table E.11). Figure E.6 illustrates that these results are driven by the cost of failure which are far higher proportion of the total costs than the drug costs themselves.

Table E.10: Cost-effectiveness analysis of treatment by dose of Movicol Paediatric Plain in the first three months of treatment, given £20,000 per QALY threshold

Treatment for one child	Cost	Additional cost	Effectiveness	Additional effectiveness	QALYs (3 months)	ICER
Dose 3	£5.40		95%			
Dose 4	£7.10	£1.70	95.21%	0.21%	0.000084	£20,238
Dose 1	£22.50	£15.40	55%			
Dose 2	£23.30	80p	55%			

Figure E.6. Total three-month cost of success and failure, by dose of Movicol Paediatric Plain



(iii) Treatment for disimpaction: comparing different alternatives

Total costs per patient per group are reported in table E.10. Since effectiveness did not differ across pharmacological strategy groups, a cost minimisation exercise was considered. The treatment option with lowest costs was group 3 (Senna; £73), followed by groups 2 (Picosulphate; £95) and 1 (Movicol Paediatric Plain; £97). The most expensive option was enemas (group 4; £1,208).

Table E.11. Decision modelling for disimpaction and initial maintenance: total costs over three months assuming equal effectiveness

Groups	Total costs	QALYs
1 Movicol Paediatric Plain	£97	0.23
2 Picosulphate	£95	
3 Senna	£73	
4 Enemas	£1,208	

The cost results show that, using the treatment pathways suggested by the GDG, the difference in cost over three months between alternatives based on pharmacological treatments is around £20 to £25 per child. In this analysis, enemas are much less successful than pharmacological treatments (failure rates 75% and 20% respectively, see table E.5) leading to higher use of manual evacuation as a last resort. The cost of enemas is high and is driven by the cost of four days hospitalisation which is based on GDG opinion of the likely treatment pathway for a child with idiopathic constipation.

Like the first cost model, Senna is the cheapest treatment alternative based on its lower drug costs and assumed clinical equivalence. However, threshold analysis shows that Movicol Paediatric Plain has to increase by 2.6% for Movicol Paediatric Plain to be the preferred option on cost-effectiveness grounds.

Table E.12: Cost-effectiveness threshold analysis of disimpaction treatment and first maintenance in the first three months of treatment, given £20,000 per QALY threshold

1 child	Cost	Additional cost	Effectiveness	Additional effectiveness	Additional QALYs (3 months)	ICER
Senna	73		80%			
Picosulphate	95	21.33831	80%			
Enemas	1208	1134.509	80%			
Movicol Paediatric Plain	96	22.06581	82.6%	**2.6%**	0.00104	£ 20,708

iv) Decision modelling for strategies for on-going maintenance after disimpaction

Total costs and outcomes per patient per group are shown in table E.13. Since equal effectiveness across groups was assumed in the first instance, the differential costs of care only are reported with equal numbers of QALYs. The total cost for the first three months of maintenance treatment using Movicol Paediatric Plain at baseline dose is much higher than for any other pharmacological treatments at the baseline dose (over £70 where all other treatments are under £10). The only alternative that is equally as costly is a strategy of starting with picosulphate and switching to Movicol Paediatric Plain and sodium picosulphate where that fails.

The cost per child of the treatment option using Senna in the first cycle (3 months) is £2.70, and for Movicol Paediatric Plain it is £73. This is based on the cost of half the dose of treatment used in the first three months of disimpaction and initial maintenance, and is based on a strategy using more pharmacological options if a treatment fails before opting for a manual evacuation (requiring hospitalisation) as a last resort. In this model, fewer children require hospitalisation in the maintenance phase than in the disimpaction phase, reflected in lower costs overall for the same time period. This widened the gap between the cheapest option (Senna and the most expensive) since the cost of hospitalisation was no longer the largest cost driver in the overall cost of treatment.

Table E.13. Maintenance model: total costs and outcomes per patient after first 3 months of disimpaction & initial maintenance

		3 month (1 cycle)		1 year (4 cycles)		2 year (8 cycles)	
	Coding	Cost	QALYs (assuming equal effectiveness)	Cost	QALYs	Cost	QALYs
Movicol Paediatric Plain baseline dose	101	£72.9	0.2	£276	0.9	£467	1.7
Movicol Paediatric Plain higher dose	102	£91.2		£331		£544	
Movicol Paediatric Plain baseline dose, followed by Movicol Paediatric Plain+sodium picosulphate	103	£77.3		£292.4		£492	
Picosulphate baseline dose	201	£4.30		£76		£194	
Picosulphate higher dose	202	£5.40		£78		£197	
Picosulphate baseline dose followed by Movicol Paediatric Plain+sodium picosulphate	203	£77		£287		£482	
Picosulphate baseline dose followed by picosulphate+Senna	204	£7.00		£81		£201	
Picosulphate baseline dose followed by picosulphate +lactulose	205	£7.90		£153		£308	
Senna baseline dose	301	£2.70		£60		£170	
Senna higher dose	302	£2.70		£49		£151	
Senna baseline dose followed by picosulphate+Senna	303	£7.00		£60		£169	
Senna baseline dose followed by lactulose+Senna	304	£6.20		£54		£164	
Senna baseline dose followed by docusate+Senna	305	£7.30		£56		£166	
Methylcellulose	601	£7.30		£42		£141	
Liquid paraffin light BP	701	£7.30		£71		£191	

Using a modelling approach it was possible to calculate how much more effective a Movicol Paediatric Plain strategy would have to be in the maintenance phase (3 months, one year, two years) in order for it to be cost-effective at the £20,000 per QALY threshold, and at what level of effectiveness a more expensive strategy would be cost saving. Since Movicol Paediatric Plain costs more in the maintenance phase, it needs to be more effective for it to be the preferred option. It has been reported earlier that higher priced therapeutic strategies with higher levels of effectiveness would become cheaper overall than strategies with lower initial drug costs. It is possible to estimate how much more effective Movicol Paediatric Plain would have to be in order for it to be preferred to all other strategies on cost-effectiveness grounds.

Table E.14. Cost-effectiveness threshold analysis of maintenance treatment, given £20,000 per QALY threshold after 3 months, 1 year and 2 years of treatment

Treatment option	**No. of cycles**	**Cost per child**	**Cost difference**	**Effectiveness**	**Effectiveness difference**	**QALY* diff**	**ICER**
Senna baseline dose	1 cycle (3 months)	£2.70		0.8			
Macrogol baseline dose		£72.90	£70.20	0.855	0.055	0.0033	£21,273
Senna baseline dose	4 cycles (1 year)	£60		0.80			

Macrogol baseline dose		£276	£216	0.845	0.045	0.0108	£ 20,000
Senna baseline dose	8 cycles (2 years)	£170		0.8			
Macrogol baseline dose		£467	£297	0.86	0.06	£0.01	£22,094

*assuming successful treatment = 0.23 QALYs

The analysis presented in table 14 suggests that an increase in effectiveness from 80% to just over 85% effectiveness in the first three months of treatment, (and less in the longer term) would make Movicol Paediatric Plain the more favourable option.

Conclusion

The effectiveness of pharmacological treatments to treat idiopathic constipation in children is not well established. The cost-effectiveness of alternative pharmacological strategies (initial treatment with a baseline dose and alternative doses or combinations where that fails) can be modelled even where robust data is not available. The NICE threshold for cost effectiveness of £20,000 per QALY provides a decision rule that allows the GDG to consider how much more effective a more costly alternative would have to be in order for it to be preferred on cost-effectiveness grounds.

The results of the economic modelling can be summarised as follows:

i) The 'cost of disimpaction by success rate' model showed that treatments with a high chance (80%) of success cost less than treatment with a low chance of success (20%), regardless of the price of drugs used or the dose provided. Also, the cost of failure (changing doses, combining drugs, and manual evacuation as a last resort) was a far greater determinant of overall cost than the cost of initial treatment.

ii) The analysis by dose of Movicol Paediatric Plain showed that highly effective strategies will lead to cost savings due to the high downstream costs of invasive treatment requiring hospitalisation that are saved. Effectiveness is determined both by the type of drug used and by the dose given. The data we have been able to identify on doses of treatment suggest that higher doses of Movicol Paediatric Plain that lead to effectiveness levels of 95% compared with 55% for lower doses would be cost saving to the NHS.

iii) The disimpaction model based on a consensus of treatment pathways developed by the GDG showed that oral pharmacological alternatives were more than ten times cheaper than enemas which were assumed to be less effective and require hospitalisation. At a 20% failure rate, oral pharmacological treatment provided a mean benefit of 0.23 QALYs per child. The threshold analysis showed that Movicol Paediatric Plain would have to increase its effectiveness by 2.6% in order for it to be the preferred option on cost-effectiveness grounds.

iv) The maintenance model showed that, unlike the disimpaction model, the cost of drugs in the pharmacological treatment alternatives had a greater impact on the total of care than hospitalisation, which widened the gap between the cheapest and most expensive options.

The economic analysis used the clinical effectiveness evidence that was available, along with GDG opinion to model the cost of the pharmacological treatment options available in the NHS to make the GDG's decisions more transparent. It is clear that treatment failure plays a major role in determining the total cost per child of disimpaction and maintenance so that the cheapest priced option is not the most cost-effective overall. Not enough is known about the true difference in effectiveness between options, nor about how children's compliance with treatments that are effective when used properly impacts on the overall effectiveness of a particular treatment strategy. The economic analysis has shown that the treatment with the highest success rate is also likely to be the most cost-effective option, regardless of price.

Appendix F

Involving children in guideline development

Introduction

NICE recognises the importance and benefits of involving patients and carers in guideline development and is committed to this aspect of guideline development. The involvement of children in health care policy and guideline development has been endorsed by the World Health Organisation, UNICEF and the Department of Health (Connexions). This pilot project was undertaken to inform:

1. The guideline recommendations for idiopathic childhood constipation
2. The NCC's understanding of how and when to involve children in paediatric guidelines

Method

Children's involvement in development of the childhood constipation guideline was planned to be carried out in two stages. Stage 1 has been completed and is reported here. Stage 2, consultation on guideline recommendations, is planned for October/November 2009.

Stage 1:
A questionnaire survey was carried out with children who have a diagnosis of idiopathic constipation (n=36). The survey aimed to:

- identify diagnosis and treatment issues that are most important to the children themselves
- identify where children's views differ from those of parents/carers and the health professionals involved in their care
- provide information to support consensus work in areas where there is little clinical evidence.
- inform the reviews and contribute to the decision tree regarding the wording of the final recommendations

Development of the survey questions and analysis of findings was carried out by the project director, senior research fellow and GDG chair supported by GDG members. This work was supported by the Enuresis Resource and Information Centre (ERIC), the NICE editorial team and the NICE Patient and Public Involvement Programme who provided advice on the wording of patient information sheets and questionnaire items.

Questionnaires were distributed to children by clinical members of the GDG. Distribution was done mostly by hand during face to face contact, although a few were posted to recipients. Younger children were helped to read and complete the questionnaire by either their parents or by their health professional.

Stage 2:
A discussion group: will be held during stakeholder consultation (October–November 2009). The aims of this are:

- to explain to the children how their views have been incorporated into the guideline recommendations
- to ask for their views of the guideline draft recommendations
- to inform the GDG interpretation of evidence.
- to ask children for their views on how implementation of the guideline could be encouraged/supported particularly amongst children and carers.

The discussion group will consist of:

- 8–10 of the children who had completed the questionnaire survey,
- Should insufficient numbers be recruited from this source the recruitment would be widened.

This work will be carried out by the senior research fellow and GDG chair, who both have experience of focus group work, working with children and have a valid CRB check completed.

Findings

A narrative summary of the comments made by children in response to the questionnaire are presented below for each of the 6 questionnaire items. Tables detailing each comment in full are also included.

Q.1 What would help you to tell your doctor or nurse about your constipation?

- A number of children indicated that they needed to feel at ease in the clinical setting in order to talk to the doctor or nurse about their constipation. This included approachable, friendly, empathetic staff that could be understood by the patient and parents.
- Several children mentioned that the subject is difficult and embarrassing to speak to doctors about.
- Diagrams and pictures was another popular answer.

Q.2 What is important to you when taking your treatment? (when you take it, how you take it, the taste, what you can do if the treatment does not work, anything else)

Responses to this question tended to follow the examples given in the question, and thus were not as helpful as responses to a more open-ended question would have been.

- The most common answer was the importance of how to take the medication and the taste (some mentioned the need to disguise the horrible taste, others gave examples of how they did this e.g. mixing it with juice).
- A number felt the need to know when to take the medication and what to do if the treatment did not work (a few mentioned the need for some form of back up).
- Several respondents mentioned the importance of further explanation regarding medication.

Q.3 Do you have any other ways of making your constipation better?

- A number of children did not know of any other ways to make their constipation better.
- Several mentioned soothing the tummy either by putting a hot water bottle on it or rubbing it. Several mentioned drinking plenty of fluids or varying their diet.
- The rest of the answers were varied.

Q.4 Have you ever tried to find out more information about your constipation problems? What have you tried? What was useful? If no, would you like more information? What would help you?

- The most frequently mentioned source of information was the internet which was reported as useful.
- Also useful were health care professionals, leaflets, DVDs/CDs and talking to other parents.
- One third of respondents said they would like more information.

Q.5 How would things be different if you did not have the constipation problems?

Children:

- Could have more fun
- Be able to socialise more
- Not be bullied at school
- Could be at school more
- No pain/tummy ache

Parents/carers:

- Life would be easier/less inconvenience
- Less stress/anxiety
- Family life would be better
- Fewer restrictions on trips out.
- Child would be more confident
- Child would not be bullied at school

Q.6 Tell us up to 5 things you would like us to tell doctors and nurses who are looking after children and young people with constipation problems.

- It is embarrassing/difficult for children and parents to talk about
- Need caring, supportive staff. Friendly and approachable, able to communicate well with parents and children.
- Need for information about medications, alternative treatments inc. diet, about constipation itself.
- Need for reassurance

How the findings have informed guideline development

Children's responses were used to inform GDG discussions and, where appropriate, this is recorded in the interpretations of evidence. Where children's comments seemed to contradict the evidence or the GDG's opinion this was noted throughout the guideline and taken into consideration by the GDG when discussing the evidence and deciding on recommendations. Where children's comments supported the evidence and/or GDG opinion this was also recorded in the interpretation of evidence.

Tables of children's/parents responses

Note: All names used in responses have been altered to ensure anonymity.

Q. 1 What would help you to tell your doctor or nurse about your constipation?	
Respondent No.	**Responses**
1	A DVD explaining the problems and treatments.
2	Write them a letter.
3	a) To make it more open e.g. school nurses and teachers talking about the subject. b) No embarrassment around the subject.
4	a) Diagrams b) Books c) Pictures d) CDs
5	Talking and diagrams.
6	My pain passport means I don't have to talk to people.
7	That it is where your bowels tighten up and it is hard to go to the toilet.
8	That it sometimes hurts when I poo and my tummy is bunged up.
9	a) Diagrams b) CDs
10	Is there any other medication that he could take.
11	Pictures to point at instead.
12	12. a) Friendly, relaxed manner. b) Talking in layman's terms and not 'medic' speak. c) Empathy and understanding.
13	Nice easy to talk to doctors and nurses who you can explain things to frankly.
14	Liam has a problem with pooing but he only has sloppy poos and never hard stools.
15	Maybe pictures, drawings etc.
16	16. a) Approachable staff, b) Maybe a questionnaire before seeing the doctor (sent out with appointments, filled in at time by child/parent, may then include things that are embarrassed to say or forget to say.
17	If the subject was easier to talk about or there were drop-in clinics for incontinence matters available to parents or older children.
18	-
19	-
20	-
21	-

22	Only seen by Dr M x2 per year – would like more frequent access to advice from approachable professionals
23	Feel at ease in clinical setting
24	Nothing
25	Picture chart
26	Telling them I squat, telling them who is bullying me
27	It would help if Liam didn't feel uncomfortable talking about it because he gets upset
28	Charts, a constipation diary.
29	A tape recorder at home to make comments on. Likes the poo chart to explain what kind of poo he is doing.
30	To know what they are talking about and if I know more about the bowel problem.
31	It helps to have the Bristol Stool Form Scale. I find this is an easy way to describe the poo problems.
32	If they were kind and they were female.
33	Friendly staff.
34	To see a doctor or nurse at a time when not playing or watching TV. Appointments at weekend or in hospital.
35	May be a leaflet given to parents in the information given by Health Visitor or even in the information given at birth. The leaflet, to describe a few symptoms and to encourage you as a parent to talk about any concerns or views regarding any poo problems. You tend to keep it quiet or think you are failing as a parent with potty training and if it is your first child what is normal?
36	It would help if the doctors were nice and friendly.

Q.2 What is important to you when taking your treatment? (when you take it, how you take it, the taste, what you can do if the treatment does not work, anything else)	
Respondent No.	**Responses**
1	a) when you take it b) how you take it c) the taste d) what you can do if the treatment does not work e) side effects
2	a) when you take it, b) how you take it, c) the taste – would prefer it if it tastes better, d) what you can do if the treatment does not work – would prefer back-up information such as leaflets etc., e) Written format of the scheduling of treatment i.e. how often before medication works etc.
3	a) how you take it, b) the taste, c) what you can do if the treatment does not work.
4	a) when you take it b) how you take it c) the taste d) further explanation on medication.

5	To explain how to take the medication
6	a) It does not taste nice! b) Putting the medicine in other things like ice lollies, c)It doesn't matter what time of day but because it sometimes gives me bellyache I have it in the morning
7	a) I take it before I go to bed or after my dinner b) I take it with orange juice and water c) It tastes like lemon and lime d) Go to the nurse and ask them what else to have e) No
8	a) How you take it.
9	a) The taste.
10	a) How you take it. b) The taste.
11	a) How you take it. b) The taste. c) It is important that it doesn't cause me more pain and that it is easy to take.
12	a) How you take it b) The taste c) Side-effects - does it cause wind/stomach ache d) What it is i.e. is it a natural product or a drug?
13	a) How you take it is important for children b) The taste - they are not going to be so willing if it tastes horrible
14	When you take it
15	a) When you take it b) How you take it c) The taste d) What you can do if your treatment doesn't work e) Important to take regularly and in a way which is easy/pleasant for child to take. No taste/ for easy mixing/dilution works great (or fruit flavours). Also access to info about treatment alternatives.
16	a) How to take it b) What it tastes like c) Being able to contact someone for advice in-between appointments
17	How easy it is to disguise the treatment for the child as a lot of children will not take medicines or powders by choice.
18	When you take it - morning with juice
19	How you take it
20	a) No problems with when to take it, how to take it or the taste b) Have back-ups: Increase medication or ring the doctor's secretary and the secretary leaves him a message.
21	Takes it in her milk
22	How much medication can be taken?
23	a) The taste b) Had enema via 'ACE' - unpleasant but bearable.
24	a) How you take it b) The taste c) If it can taste nicer in the juice
25	The taste, I don't like sleeping at the hospital.
26	When you take it.
27	If it is oral the taste is important but it is also important if it doesn't work to know there are other options.
28	It could taste better.
29	When you take it - like a routine. Very difficult to manage when the medication has to be x minutes before food. How you take it - Jamie is managing well with senna tablets. Taste - The Movicol means he needs a flavoured drink because of the taste. What to do if not working - it is a worry when the stomach pain is very bad. Feel unsure who to see i.e. GP, A&E or wait for next out-patients appointment.
30	How you take it.

31	The taste. When to take it. The knowledge of what to do when the treatment isn't working.
32	The taste, What you can do if the treatment isn't working – Increase it.
33	Takes Movicol in grape or apple juice. It's not unpleasant. Doesn't mind taking it. Whisking makes it easier to mix.
34	How you take it.
35	Treatment to be part of a routine for you as a parent and for the child. Treatment to be given in private (kid's bedroom) and in a relaxed atmosphere- music, TV to distract the child. The Movicol treatment to be given regular times of each day and broken down to what sort of the lifestyle of the child-No red taste as a drop of dilute juice hides any taste present. a) e.g. Movicol by itself-don't feel like you have done something wrong, confirm to your child everyone is different, talk to your consultant, GP and use the support network of the community nurses-ask any questions you may have-doesn't matter how trivial they may seem .b) e.g. suppositories- Don't panic give it time and try not to show any anxiety to the child, give them praise for doing the treatment but monitor it and do continue the treatment given. Don't give up, it's a long road but together you can do it. Basically to sum up the answers to the questions in section 2, just try to fit any treatment given into your family's every day life and don't be ashamed of asking for help. Speak to your child, partner, doctors etc and most of all do not feel guilty, it is nothing either the child or parent could have prevented. Keep confidence and show this to the child and confirm one day it will be alright, it just takes time but with team work you can all get through.
36	That it tastes nice and it works

Q.3 Do you have any other ways of making your constipation better?	
Respondent No.	**Responses**
1	No
2	a) Hot water bottle on abdomen. b) Essential oil on "belly" – cover in cling film and apply heat.
3	No
4	a) Hot water bottle on tummy, b) Homeopathic medication (treatment sympofigs).
5	Hot water bottle on your tummy.
6	Don't know.
7	Go to nurse and ask.
8	Using medicine and moist tissues and try to poo regularly.
9	Rubbing your tummy.
10	Hope for it to go away.
11	a) Sometimes having a bath helps. b) Drinking more water.
12	a) Soft fruit e.g. pear, melon, kiwi help b) Avoiding lots of rice and oats c) Probiotic drink – may be placebo! d) When he was a baby – his condition improved when he started crawling and walking.
13	Not sure!

14	We will try everything we can in every way to help Liam with his pooing problem
15	a) Visit your doctor , b) Drink plenty (apple juice and pineapple juice worked well), c) Being active as much as possible.
16	A reward system (a sticker chart).
17	Making a child feel confident enough and not ashamed or embarrassed to tell anyone if they need the toilet immediately or if they have had an accident.
18	Not answered.
19	No
20	No
21	a) Observe diet. b) Plenty of fluids.
22	None
23	No
24	No
25	Drinking lots of orange juice.
26	Run for it .
27	No
28	Not really.
29	Have a bleeper going off every 5 hours to tell me to try and do a poo.
30	Going on the trampoline.
31	Maybe a change of diet.
32	Drinking more fluids and eating more fruit and veg.
33	Spending time sitting on the toilet with a game or book.
34	Spends 5 minutes a day looking at the internet researching the problem.
35	Keep to a healthy diet and exercise, try not to stress or get uptight about what is happening .
36	Going to hospital and eating enough healthy food.

Have you ever tried to find out more information about your constipation problems? What have you tried? What was useful? If no, would you like more information? What would help you?	
Respondent No.	**Responses**
1	Yes – tried HV and SP. HV was useful. HV gave family information on problems, causes and treatments verbally and with leaflets.
2	Yes – tried the internet. Google and other search engines were useful. Would like more information in the form of pamphlets and CDs.
3	Internet, read leaflets, DVDs and parents' forums.

4	Television programmes and books.
5	Visiting the SP, researching information – magazines etc, CD.
6	Not before but when I met my nurse my book with pictures of poo and my sticker book helped a lot.
7	–
8	Going to the hospital and asking parents.
9	No
10	No, would like more information.
11	a) Sitting on the toilet for a long time. b) Long baths. c) Drinking more.
12	No. Whilst I understand that diet does not cause this condition, I would like info on foods to avoid during an episode to help with tummy ache / pain and foods that may help to prevent an episode arising.
13	Not found out more information.
14	Some information has really helped off the doctor and his advice has really helped us.
15	Tried using the internet – very useful – how we found out about Movicol (which has been brilliant!)
16	Internet was helpful and talking to other mothers whose children have gone through the same thing.
17	Have read books and researched the internet. They have helped but not been entirely accurate to how you have to deal with it day to day. There should be papers available that write about real experiences.
18	No
19	No, I would like more information.
20	Tried the internet, sites and articles were useful.
21	Tried the internet which was useful.
22	Internet / colleagues in NHS.
23	Tried the internet, which was helpful.
24	a) Yes have tried finding out more information, b) No, would not like more information.
25	We saw a “behaviour therapist” who did some “sneaky poo” work – didn’t work. Looked up remedies on the internet.
26	Cartoon DVD.
27	Yes via internet but it has not been explanatory enough. Yes I would like more information.
28	Yes. Internet sites and books.
29	Would you like more information – no. What would help you – my consultant.
30	Knowing what’s best for me and if it will go if I carry on taking [my medication?] and a little booklet about bowel problems.

31	Just read leaflets that have been given out. Would be helpful to know any specific websites that could provide information.
32	We looked on the internet. The information.
33	Have you ever tried to find out more information about your pooing problems? No.
34	Looked on the internet, can't remember which sites.
35	We have looked in and read up a little information in books but the most useful thing was speaking to the community nurse and realising, you are not alone. We think more information on this type of problem needs to be out there so that parents are aware it exist and then are able to seek medical help sooner before it stresses the whole family totally out.
36	Mummy has looked on computer and it tells you the same as the doctor.

Q.5 How would things be different if you did not have the constipation problems?	
Respondent No.	**Responses**
1	a) Parents would feel more relaxed with him b) Parents would not worry so much about him.
2	a) You would not be stressed. b) No pain on defecation / sore abdomen.
3	At school more – patient has been off school due to sickness caused by constipation.
4	a) Play more b) Not have sore tummy!
5	Play outside when it is sunny.
6	a) Would be better because I could be at school more. b) I would not have to have enemas.
7	Won't have to go to toilet as much and won't be as hard.
8	I would be more confident getting changed in public and friends smelling it.
9	a) Play more b) Tummy not so sore.
10	A lot different, I wouldn't get picked on at school.
11	a) No Pain. b) Feel better. c) Feel happy. d) Not miss as much school.
12	No difference currently – not severe enough to cause any real problems.
13	Things would be lovely as it's quite inconvenient at times with a child, you have to try and second guess when they want to go to the toilet.
14	It would make life a lot easier if it's really hard work when a child has this problem.
15	There is no problem at the moment (because of Movicol) but it used to be very different (cancelled outings, carrying spare clothing etc.).

16	Just a little less hassle getting repeat prescriptions (being able to call and pick up medicine when you've run out would be so much easier).
17	Outside school – social life, would be able to go out without taking nappies and pull ups, would be more confident wouldn't be picked on in school.
18	–
19	He would be out of nappies by now.
20	a) Childs confidence would go up socially and school toilets dislikes access, b) Goes to bed later trying to poo, c) Family life affected.
21	Things have improved – ok re family life.
22	Improve child's social, family and school life (bullied in latter).
23	a) No social problems. b) Confidence was affected during initial problem – improved when treatment succeeded.
24	Nice having fun instead of having a wash.
25	Would have to go to hospital. Wouldn't get tummy ache. Wouldn't poo in knickers.
26	I would be able to go to the toilet. Be a normal kid. Would not poo in my pants at school..
27	I would be able to take Liam to school and he wouldn't have any other problems with children taking the mickey.
28	I would feel better in myself.
29	People wouldn't be mean to me when I have [an] accident. I wouldn't get tummy ache.
30	I would be able to go round people's houses and not worry that I could have an accident. I would be able to wear boxer shorts.
31	Would be toilet trained and not be restricted to where and how long to go out for.
32	They wouldn't.
33	Not a problem now. Doesn't stop anything. No sleepovers yet though.
34	It would be better. Less people making fun of me or even none. Wouldn't need to go to the toilet at certain times.
35	Life would be easier and calmer and a lot happier for my son. It has been a long road for someone so young to have to take and he would be able to go to friends' houses more and even have sleepovers. Not having to worry about the delay treatment and generally just easier all around. We are also half way through this but achievement so far has been great and one day we will be able to look back and say–we did this together and son you got through it.
36	I would be happy. I would not have to wear a nappy in bed.

Tell us up to 5 things you would like us to tell doctors and nurses who are looking after children and young people with constipation problems	
Respondent No.	**Responses**

1	a) Health professionals need to be more updated. b) Waited previously in another health board for a year before your appointment (standardised care). c) Parents feel that they need more information on the subject.
2	a) What the nurse/doctor can do to help you. b) Which medicines are best. c) Alternative treatments.
3	a) The service has improved in the last 5 years. b) There is less embarrassment due to it being more in the open now.
4	Wish it wasn't so embarrassing.
5	a) CD given to parents with information on it b) Getting phone numbers and contact numbers for other treatments.
6	a) Medicine makes it taste better especially in lollies. b) Stickers and books help going to the toilet because you can have a sticker when you do a poo because it makes it fun. c) People should listen to me. d) Explain things in an easy way and make me important when you talk to me.
7	No
8	Thank you for helping me and others.
9	-
10	a) Why does this problem start? b) How can it be resolved? c) Will it ever get better? d) Is there any other way to fix i?, e) Will it ever stop?
11	It is good that my mum can phone a nurse for help when I am in pain with my problem.
12	a) It can effect all aspects of a child's life (disrupts sleep, puts them off food, confidence using toilet outside of home). b) Parents feel responsible for the problem yet helpless to do anything about it. c) Tummy ache can be distressing / stressful for the child and parent. d) It is not something that parents like to talk about. e) Info on 'type' of poos was useful when first diagnosed.
13	Try and make going to the toilet fun! Otherwise it becomes very hard work when they don't want to go.
14	a) Having a pooing problem does not mean your child is lazy, dirty. b) It's not their fault just try to help your child in every way you can c) Don't call names or shout at them because it only makes things worse, d) If you keep on saying you are going to sit on the toilet until you do it it won't work either it will only make your child's brain shut off from your voice e) Please help your son and keeps praying him when he does try and use the toilet cause he will every time I go on the toilet mum/dad will say I'm a good girl/boy it does help!
15	a) Advice on diet and drinks, b) Activity c) All our visits have been informative, friendly, helpful. Help given by lovely doctor, nurses and staff.
16	a) Patience b) Friendly and approachable staff always make things easier.

17	17. a) The parents could be very embarrassed about it and be finding the whole thing very stressful so be supportive b) The child is getting bullied so will be taking the subject very seriously and may not want to talk about it.
18	–
19	–
20	a) Talk to other parents with children similar problems. b) Nurses very supportive.
21	Cannot think of anything.
22	a) It is <u>not</u> just behaviour problems b) Child has confidence to say if has pain c) Parental support d) Parental groups e) Made to feel guilty by pharmacist re cost of medication methylcellulose (liquid).
23	Had idiopathic constipation – had to constantly tell problems to doctors and try different medications before diagnosis and appropriate treatment.
24	Nothing. Talking to children. Picture.
25	To play whilst looking at me.
26	Nothing. Doctors don't talk to me much.
27	Do what you can to sort out the problems because it's upsetting because it would give him better quality of life without [the] problems he is currently facing.
28	To make it more easiest to talk about. To explain the treatments better. To be understanding and gentle.
29	Child: I don't want to do a poo in my pants. How do I stop it happening? How many senna tablets should I have? How can I make my poo soft? Can you ask the sticker company to carry on making the stickers (for the sticker reward chart) Parents: Reassurance it will stop. Advice as to emergency care. I have taken him to A&E when rolling around on the floor in pain and felt they didn't understand.
30	It's embarrassing changing my pants. That people can smell the poo. Not being able to wear boxer shorts. Being able to understand words about my problem. Why does it take so long to get to normal and wishing that I could be like a normal boy not pooing in my pants.
31	–
32	–
33	Following "the plan". Give it a go. "Poo" models.
34	Not to interrupt TV programmes, See children at weekends. Simple wording. Make it as interesting as possible.

35	35. a) Depending on the age of the child, stress can play a big part in this type of problem. Speak to them as a child basis and in a friendly manner. b) Generally inform parents support is there if they should choose it or not, but do confirm that other parents and children have found this most useful in the process of achieving results. c) Keep the confidence and rapport going with the child with praise and it they are doing well tell them it makes happier and they are in control feeling. A real benefit to the child is getting better. d) Do make it clear, as it has been to ourselves and our son, it is long process and not a quick fix there just isn't one. One in a daily routine how normal life can resume and it doesn't feel such a big thing and this is in itself a great benefit and helps the child and so has an impact on their happiness and that of the whole family. e) They (doctors, nurses) do a great job not just medically but emotionally to all the children and families with this type of problem and what a difference you all make–Thank you.
36	36. 1) be friendly, 2) Understanding, 3) Help them with going to the toilet, 4) Tell them it wont last forever, 5) Don't worry accidents happen

Appendix G

Bristol Stool Form Scale

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Appendix H

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Appendix I

Search strategies

Please see separate document

Appendix J

Evidence tables

Please see separate document

Appendix K

Excluded studies

Please see separate document