Supplementary Material 16 – Complementarity between evidence syntheses and guideline recommendations

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Table 1: Complementarity with guidelines - What is the effectiveness of different models of service delivery?**Evidence synthesis conclusion**	**Guideline**	**Guideline recommendation**	**Complementarity**
What is the effect of nurse led models of care as compared to alternative models of care?			
Nurse-led clinics are feasible and could result in equivalent (or possibly better) outcomes than traditional physician -led clinics.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	No Guideline recommendations. However, NICE 2010 makes a research recommendation about nurse-led clinics ("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.")	***Silence*** – no recommendations relating to nurse-led clinics
What are the effects of, primary care (level 1) services and models of care?			
While multifaceted models of care within primary care may be beneficial, there is currently insufficient evidence to support this. Further research is required.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	No Guideline recommendation.	***Silence*** – no recommendations relating to Level 1 models of care
What is the effect of a constipation care pathway / algorithm used in primary care / community settings			
An algorithm, or care pathway, used in primary care settings to	Tabbers 2014	No Guideline recommendation within NICE 2010 or updates. Tabbers 2014 provides algorithms "for the evaluation and	Partial agreement

guide the management and referral of children with constipation (including children with ASD) may be beneficial.		treatment", which does include referral to specialist services.	
	NICE 2010, 2012, 2017, 2018, 2019	No Guideline recommendation.	***Silence*** – no recommendations relating to algorithms for use in primary care / community settings
What are the effects of a constipation care pathway / algorithm used for children presenting in emergency departments?			
There were some inconsistencies and lack of reporting of relevant outcomes in studies investigating the effects of a constipation care pathway/algorithm used for children presenting in emergency departments, meaning that there is insufficient evidence on which to reach conclusions.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	No Guideline recommendation.	***Silence*** – no recommendations relating to algorithms for use in emergency departments
What are the effects of, specialist (level 2) services and models of care?			
Consistent findings from studies with some limitations provides low quality evidence that specialist services may have a beneficial impact on outcomes of	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	No Guideline recommendation (referral to specialist services is mentioned, but no specific guideline).	***Silence***

children with chronic constipation, but further research is required.			
What is the effect of different follow-up regimes following appointments with specialists?			
Access to web-based information may benefit recovery from constipation.	NICE 2010	Information and support, recommendation states that support could include: "giving verbal information supported by (but not replaced by) written or website information in several formats…"	***Partial agreement***
What are the effects of highly specialist (level 3) services and models of care?			
A recovery protocol may benefit outcomes following colorectal surgery. This evidence does not relate specifically to the population of children with functional constipation.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	No Guideline recommendation.	***Silence***

Table 2: Complementarity with guidelines - What is the effectiveness of interventions delivered by families / carers, prior to health professional involvement (Everyday life / Level 0 interventions)?

Evidence synthesis conclusion	*Guideline*	*Guideline recommendation*	*Complementarity*
What are the effects of probiotics?			
Probiotics are not more beneficial than control at improving outcomes in children with constipation, but there is no suggestion that probiotics are not safe.	Tabbers 2014	Evidence does not support the use of pre or probiotics Recommend do not use routinely	***Agreement*** – probiotics are not supported by evidence
	NICE 2017	Regarding the use of prebiotics and probiotics, the impact of the new evidence is limited by conflicting reports from small trials with short follow-up periods. Furthermore, during guideline development the topic experts felt it was not possible to recommend specific probiotics due to a lack of consistent evidence. Further research is needed before considering prebiotics and probiotics for inclusion in the guideline	***Partial agreement*** – probiotics are not recommended based on our evidence synthesis; wording of NICE 2017 implies that some specific probiotics may be supported by evidence.
What are the effects of additional dietary fibre			
Additional dietary fibre is not more beneficial than control or laxatives.	NICE 2010	Adequate fibre. Recommend including foods with a high fibre content (such as fruit, vegetables, high-fibre bread, baked beans and wholegrain breakfast cereals) (not applicable to exclusively breastfed infants). Do not recommend unprocessed bran, which can cause bloating and flatulence and reduce the absorption of micronutrients.	***Partial agreement*** (states "adequate", but does not clarify what this is)

	NICE 2017	Limited recent evidence for dietary interventions suggests that fibre can improve constipation	***Dissonance*** (implies additional fibre)
	NICE 2019	Recommend a balanced diet with sufficient fibre (in all children that have been weaned). • Foods with a high fibre content include fruit, vegetables, high-fibre bread, baked beans, and wholegrain breakfast cereals. ◦ Do not recommend unprocessed bran (which may cause bloating and flatulence and reduces the absorption of micronutrients) or fibre supplements.	***Agreement***
	Tabbers 2014	In conclusion, evidence does not support the use of fiber supplements in the treatment of functional constipation.	***Agreement***
What are the effects of different milk formula in infants?			
There is insufficient evidence on which to reach generalised conclusions about the relative effect of different milk formula. Individual studies do demonstrate some benefits, supporting the need for high quality randomised studies.	-	-	***Silence*** – guidelines do not make any recommendations relating to milk formula for infants.
What is the effect of a cow's milk-free diet?			
There is low certainty	NICE 2010	1.5.5 children with idiopathic constipation, start a	***Partial agreement*** – specialist

that a trial of cow's milk free diet may be beneficial to outcomes, in children for whom laxatives have been unsuccessful. Note: Evidence from studies which included participants who had a diagnosis of cows milk allergy were excluded from this review; this evidence will be important to decisions relating to exclusion of cows milk from diet.		cows' milk exclusion diet only on the advice of the relevant specialist services	services should be consulted in order to ensure evidence relating to cows milk allergy informs decisions.
	NICE 2012, 2017, 2018, 2019	-	***Silence***
	Tabbers 2014	Routine allergy testing is not recommended to diagnose cow's-milk allergy in children with functional constipation	***Silence*** (no recommendations relating to trials of cow's milk free diet)
What is the effectiveness of sugars (brown sugar, figs syrup, black sugar molasses)?			
There is insufficient evidence on which to reach generalised conclusions about the relative effect of sugars. Individual studies do demonstrate some benefits, supporting the need for high quality randomised studies.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence*** – no recommendations relating to sugars.

What are the effects of selenium supplements			
There is very low certainty that selenium supplements may improve outcomes of defecation frequency, stool consistency and abdominal pain.	NICE 2010, 2012, 2017, 2018, Clinical Knowledge summary, Tabbers 2014	-	***Silence***- – no recommendations relating to the use of selenium
What is the effectiveness of other / alternative dietary intake?			
There are 3 RCTs, one which is reported only as an abstract, which have investigated a range of alternative dietary intakes, including oral magnesium sulfate, magnesium-containing mineral water and paraffin oil. There is insufficient evidence relating to either of these interventions to support generalised conclusions.	NICE 2010, 2012, 2017, 2018, Clinical Knowledge summary, Tabbers 2014	-	***Silence*** – no recommendations relating to other / alternative dietary intake.
What is the effect of fluid intake on constipation?			
There is insufficient evidence to support any routine change in fluid intake for children with constipation.	NICE 2010	1.5.3 Advise parents and children and young people (if appropriate) that a balanced diet should include adequate fluid intake (see table 5	***Agreement*** – both support "adequate" fluid, and there is no recommendation for an increased fluid intake.
	NICE 2017	There was no new evidence to suggest that increasing fluid intake is an effective treatment	***Agreement*** – both support "adequate" fluid, and there is no

		for childhood constipation. The guideline currently makes recommendations on adequate fluid intake….	recommendation for an increased fluid intake.
	NICE 2019	Encourage children with a poor fluid intake to increase fluids to a recommended level.	***Agreement*** – both support “adequate” fluid, and there is no recommendation for an increased fluid intake.
	Tabbers 2014	Evidence does not support the use of extra fluid intake in the treatment of functional constipation. Normal fluids recommended	***Agreement*** – both support adequate fluids
What are the effects of educational interventions (delivered in addition to routine care)?			
There is some limited evidence that educational interventions – particularly web-based interventions focused on education around toilet training – may have a beneficial effect on bowel movements (including frequency, consistency and incontinence).	NICE 2010	1.5.4 Provide children and young people with idiopathic constipation and their families with written information about diet and fluid intake 1.8 Information and support. Including: • detailed evidence-based information about their condition and its management • giving verbal information supported by (but not replaced by) written or website information in several formats about how the bowels work, symptoms that might indicate a serious underlying problem, how to take their medication, what to expect when taking laxatives, how to poo, origins of constipation, criteria to recognise risk situations for relapse (such as worsening of any symptoms, soiling etc.) and the importance of continuing treatment until advised otherwise by the healthcare professional	***Partial agreement*** – educational interventions are recommended, but details differ.

	NICE 2019	**Give information and advice** to the child and/or their parents/carers: ○ Reassure that underlying causes of constipation have been excluded by the history and physical examination. ○ Advise that idiopathic constipation is treatable with laxatives, although they may need to be taken for several months. ○ Offer sources of information and support — the national charity ERIC, The Children's Bowel & Bladder Charity (ERIC; www.eric.org.uk) has a range of leaflets on constipation and soiling, such as the Constipation toilet tool, and runs a helpline (telephone 0845 370 8008).	***Partial agreement*** – the evidence synthesis conclusions are focussed on the educational element, while the NICE 2019 recommendation is focussed on the giving of information and advice.
	Tabbers 2014	Based on expert opinion, we recommend demystification, explanation, and guidance for toilet training (in children with a developmental age of at least 4 years) in the treatment of childhood constipation	***Agreement*** – both recommend education around toilet training
Physical activity			
(no primary studies were identified relating to physical activity)	NICE 2010	1.5.6 Advise daily physical activity that is tailored to the child or young person's stage of development and individual ability as part of ongoing maintenance in children and young people with idiopathic constipation	***Silence*** – no primary studies were identified which relating to daily physical activity for children with constipation
What is the effect of combined dietary and behavioural interventions?			
There is insufficient evidence to support generalised conclusions relating to	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence*** – no recommendations relating to combined interventions

combined dietary and behavioural interventions.			

Table 3: Complementarity with guidelines - What is the effectiveness of assessment and intervention by primary care services (wider children's workforce / Level 1 interventions)?

Evidence synthesis conclusion	*Guideline*	*Guideline recommendation*	*Complementarity*
*What are the effect of laxatives?**			
Updating the review of	Nice 2010	After disimpaction offer the following regimen for ongoing	***Agreement***

laxatives with new evidence from new RCTs does not change conclusions which can be drawn about laxatives. Our updated analysis re-states the benefit of PEG compared with placebo and with lactulose. However, it should be noted that this finding is limited by the lack of new head-to-head evidence across multiple treatments. Exploration of head-to-head comparisons indicates: PEG appears superior to lactulose and milk of magnesia, milk of magnesia superior to lactulose, and lactulose equivalent to Senna. Quality of evidence is low to very low for all findings.		treatment or maintenance therapy: Polyethylene glycol 3350 + electrolytes as the first-line treatment. Adjust the dose of polyethylene glycol 3350 + electrolytes according to symptoms and response. As a guide for children and young people who have had disimpaction the starting maintenance dose might be half the disimpaction dose (see table 4). Add a stimulant laxative (see table 4) if polyethylene glycol 3350 + electrolytes does not work. Substitute a stimulant laxative if polyethylene glycol 3350 + electrolytes is not tolerated by the child or young person. Add another laxative such as lactulose or docusate (see table 4) if stools are hard. Continue medication at maintenance dose for several weeks after regular bowel habit is established – this may take several months. Children who are toilet training should remain on laxatives until toilet training is well established. Do not stop medication abruptly: gradually reduce the dose over a period of months in response to stool consistency and frequency. Some children may require laxative therapy for several years. A minority may require ongoing laxative therapy.	
	NICE 2017	Evidence update reinforces current recommendations in NICE 2010 for maintenance therapy with PEG. The success with PEG in a young age group suggests the value of early intervention, but the short follow-up may give a misleading indication that medication can be stopped early in these patients.	***Agreement***
	Tabbers 2014	In conclusion, evidence shows that PEG and enemas are equally effective for fecal disimpaction. Comment: High-dose PEG given orally is associated with a higher frequency of fecal incontinence during treatment of the fecal impaction compared with enema use; however, based on the argument that PEG can be administered orally, the working group decided to prefer PEG. In conclusion, evidence shows that PEG is more effective compared with lactulose, milk of magnesia,	***Agreement***

		mineral oil, or placebo. More studies have been performed evaluating the effectiveness of lactulose than studies evaluating the effect of milk of magnesia and mineral oil in children with constipation. More important, lactulose is considered to be safe for all ages. For these reasons, lactulose is recommended in case PEG is not available. Furthermore, evidence does not support the addition of enemas to the chronic use of PEG in children with constipation.	
What are the effects of laxatives plus motilium?			
There is some limited evidence that the combination of PEG plus motilium may be more beneficial than PEG only in children with cerebral palsy. There is no presented data on side effects, but concerns have been reported for this drug in other populations. Note: MHRA advise against use of motilium in children under 16 years, due to serious side effects.	MHRA	Advise against use of motilum in children under 16 years due to serious side effects.	***Dissonance*** – there is a mismatch between the aim of the identified study and the guidance relating to safety. The advice is that motilium should not be used.
What is the effect of physical exercise (focused on pelvic floor muscles)?			
There is low certainty that physical exercise (focussed on pelvic floor muscles) may improve overall symptoms, defecation frequency and stool consistency. Further research to investigate the effect of physical exercise is	NICE 2010	1.5.6 Advise daily physical activity that is tailored to the child or young person's stage of development and individual ability as part of ongoing maintenance in children and young people with idiopathic constipation	***Partial agreement*** – evidence does not address routine daily physical activity, but instead demonstrates that additional exercise focussed on pelvic floor muscles, may be

warranted.			beneficial.
	Tabbers 2014	No RCTs. Recommend normal physical activity levels.	***Partial agreement*** – agreement that there are no RCTs; but evidence from non-randomised studies supports physical exercise, focussed on pelvic floor muscles, in additional to normal physical activity.
What is the effect of a combined pharmacological and behavioural program			
There is some very limited data which suggests that a combined pharmacological, dietary and behavioural program may have some benefits. We have very low certainty in this finding due to the quantity and quality of available studies.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence*** – no recommendations relating to combined interventions

* a limitation of our evidence synthesis was that we did not systematically differentiate between use of laxatives for disimpaction or maintenance.

Table 4: Complementarity with guidelines - What is the effectiveness of interventions delivered by secondary specialist care (continence teams / Level 2 interventions)?

Evidence synthesis conclusion	*Guideline*	*Guideline recommendation*	*Complementarity*
What is the effect of rectal enemas in children with severe constipation?			
There is very low certainty that the addition of regular rectal enemas may increase defecation frequency, but not have any effect on overall treatment success or other outcomes, and may cause some discomfort or distress.	NICE 2010	Do not use rectal medications for disimpaction unless all oral medications have failed and only if the child or young person and their family consent.	***Partial agreement***
	NICE 2012	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/healthcare centre/clinic, and only if all oral medications and sodium citrate enemas have failed.	***Partial agreement***
	NICE 2019	Evidence suggests similar efficacy with polyethylene glycol (PEG) 3350 plus electrolytes2 versus rectal enemas in faecal disimpaction. Evidence suggests similar efficacy with PEG (unspecified) versus rectal enemas in maintenance therapy for constipation, although enemas were negatively perceived by some children.	***Partial agreement***
	NICE 2017	Use of suppositories or enemas in primary care The recommendation on the use of suppositories or enemas in primary care is based on the expert opinion of the NICE GDG, which states that although enemas are effective for rectal disimpaction, the administration route is uncomfortable for children. They should only be used when all oral treatments have failed. If needed, sodium citrate enemas are preferred as phosphate enemas have more adverse effects	***Partial agreement***

		and should only be used under specialist supervision.	
	Tabbers 2014	Evidence shows that PEG and enemas are equally effective for fecal disimpaction. The addition of enemas to the chronic use of PEG is not recommended in children with constipation. Based on expert opinion, we recommend antegrade enemas in the treatment of selected children with intractable constipation.	***Partial agreement***
What is the difference in effectiveness of microenemas and oral laxatives for functional constipation in infants?			
there is low certainty from one RCT that Promelaxin microenemas and oral laxatives are equally effective in the treatment of functional constipation in infants (6-48 months).	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence*** – no recommendations relating to microenemas
What is the effect of combined enemas and oral laxatives for disimpaction in hospitalised patients?			
In summary, there is very low certainty that combined oral and enema therapy may be beneficial for hospitalised patients with fecal impaction, but insufficient evidence to reach conclusions about the relative effectiveness of specific regimens.	NICE 2010, 2012, 2017, 2018, 2019	-	***Silence*** – no recommendations relating to combined interventions
	Tabbers 2014	Evidence does not support the addition of enemas to the chronic use of PEG in children with constipation	***Dissonance*** (although populations referred to differ)
What is the difference in effectiveness of enemas and oral laxatives for disimpaction?			
There is low certainty from	NICE 2017	suggests that macrogols have similar efficacy compared to rectal	***Agreement***

<table>
<tr><td rowspan="2">one RCT that enemas and high dose laxatives are equally effective at reducing rectal faecal impaction in children with CFC.</td><td></td><td>enemas in the treatment of faecal disimpaction</td><td rowspan="2"></td></tr>
<tr><td>Tabbers 2014</td><td>Evidence shows that PEG and enemas are equally effective for faecal disimpaction</td></tr>
<tr><td colspan="4">What is the difference in effectiveness of an enema and a soft suppository for disimpaction</td></tr>
<tr><td rowspan="2">There is low certainty from one RCT that enemas and high dose suppositories may be equally effective at promoting bowel emptying and the suppository may be less invasive</td><td>NICE 2010</td><td>Do not use rectal medications for disimpaction unless all oral medications have failed and only if the child or young person and their family consent.</td><td>Dissonance</td></tr>
<tr><td>Tabbers 2014</td><td></td><td>Silence – no recommendations relating to suppositories</td></tr>
<tr><td colspan="4">What is the effectiveness of transcutaneous electrical stimulation?</td></tr>
<tr><td rowspan="2">There is very low certainty that TES may reduce the number of soiling episodes and improve self-reported quality of life, as compared to sham TES.</td><td>NICE 2010, 2012, 2017, 2018, 2019</td><td>-</td><td>Silence – no recommendations relating to electrical stimulation</td></tr>
<tr><td>Tabbers 2014</td><td>Evidence does not support the use of TNS in children with intractable constipation</td><td>Partial agreement</td></tr>
<tr><td colspan="4">What is the effect of transanal irrigation?</td></tr>
<tr><td>There is very limited evidence about the effectiveness of transanal irrigation. There is some very low certainty evidence</td><td>NICE 2018</td><td>undertaken following the publication of the NICE medical technology guidance published in Feb 2018 which recommends the use of Peristeen in children with bowel dysfunction. After taking into account the views of topic experts, we acknowledge that this is an area of research showing promising results for the treatment of constipation</td><td>Partial agreement</td></tr>
</table>

that transanal irrigation may be safe, feasible and effective for children with intractable symptoms which have not resolved with long term conventional laxatives and management.		in this population. However, the findings from this exceptional review have demonstrated that the evidence on TAI has not substantially progressed since we last checked in 2017 and there is still uncertainty around the safety and efficacy of TAI in this population. For this reason, we will not update the guideline at this time.	
	Tabbers 2014	-	***Silence*** – no recommendations relating to irrigation
What is the effect of biofeedback?			
There is some limited evidence about the effectiveness of biofeedback, suggesting that there may be no additional benefit of supplementing conventional treatment with biofeedback therapy in children with normal defecation dynamics, but potentially some benefit for the subgroup of children with abnormal defecation dynamics. We have very low confidence in this finding.	NICE 2010	Do not use biofeedback for ongoing treatment in children and young people with idiopathic constipation.	***Partial agreement***
	Tabers 2014	Evidence does not support the use of biofeedback	***Partial agreement***
What is the effect of physiotherapy, in combination with conventional treatment?			
Evidence relating to the effectiveness of physiotherapy is	NICE 2010, 2012, 2017, 2018, 2019	-	***Silence*** – no recommendations relating to

inconsistent. Evidence does not support the routine referral to physiotherapy for all children with constipation seen within primary care. There is some limited evidence that physiotherapy may be beneficial for a subgroup of children, but further research is required to confirm (or refute) this. We have very low confidence			physiotherapy
	Tabbers 2014	Based on expert opinion we do not recommend the routine use of multidisciplinary treatment in childhood constipation	***Agreement***
What is the effectiveness of physical therapy for children with cerebral palsy?			
There is some very low quality evidence to suggest that constipation in children with cerebral palsy may be improved with physical therapy. However, evidence is insufficient to support generalised conclusions.	NICE 2010	Advise daily physical activity that is tailored to the child or young person's stage of development and individual ability as part of ongoing maintenance in children and young people with idiopathic CC	***Partial agreement***
	NICE 2017	No studies were found that examined the effect of physical movement, multidisciplinary treatment or alternative medicine.	***Partial agreement***
	Tabbers 2014	Recommends a normal physical activity in children with constipation	***Partial agreement***
What is the effect of dietary exclusion of fructose and lactose?			
There is limited, very low	NICE 2010, 2012,	-	***Silence*** – no

certainty evidence that exclusion of fructose and lactose, with expert health professional advice, could reduce severity of constipation. However, implementation of this diet was challenging. Further research is required.	2017, 2018, 2019, Tabbers 2014		recommendations relating to dietary exclusion of fructose or lactose
What is effect of a combined therapeutic programme?			
There is insufficient evidence to support specific conclusions relating to the effect of a combined treatment programme, but some very low certainty evidence that combined programmes may be beneficial for some children	NICE 2010, 2012, 2017, 2018, 2019	-	***Silence*** – no recommendations relating to combined programmes
	Tabbers 2014	Based on expert opinion we do not recommend the routine use of multidisciplinary treatment in childhood constipation	***Partial agreement***

Table 5: Complementarity with guidelines - What is the effectiveness of interventions delivered by consultant-led teams (Level 3 / highly specialist tertiary care services)?

Evidence synthesis conclusion	*Guideline*	*Guideline recommendation*	*Complementarity*
What is the effect of botulinum toxin?			
There is very low certainty that botulinum toxin may improve outcomes.	NICE 2017	The guideline does not currently include any recommendations on botulinum toxin for treatment/maintenance in children with chronic idiopathic constipation. Further data on longterm outcomes are needed before considering botulinum toxin treatment for inclusion in the guideline.	***Silence*** – no recommendation relating to botulinum toxin
	Tabbers 2014	-	***Silence*** – no recommendation relating to botulinum toxin
What is the effect of antegrade continence enema (ACE)/ Malone antegrade continence enema (MACE?			
There is very low certainty that the use of ACE/MACE may be effective against the symptoms of CFC. Further research is required.	NICE 2010	Refer children and young people with idiopathic constipation who still have unresolved symptoms on optimum management to a paediatric surgical centre to assess their suitability for an antegrade colonic enema (ACE) procedure. Ensure that all children and young people who are referred for an ACE procedure have access to support, information and follow-up from paediatric healthcare professionals with experience in managing children and young people who have had an ACE procedure.	***Partial agreement***
	NICE 2017	children and young people with idiopathic constipation who still have unresolved symptoms on optimum management should be referred to a paediatric surgical centre to assess their suitability for an ACE procedure.	***Partial agreement***
	Tabbers 2014	Six open retrospective studies are available in children	***Agreement***

		suggesting that ACE may be an option in children with intractable constipation. Potential complications (development of granulation tissue, leakage around the tube, tube dislodgment, skin infection, and stoma stenosis) should be thoroughly considered and discussed with parents and children. No data comparing different types of surgical procedures for the administration of antegrade enemas have been published.	
What is the effect of MACE compared to caecostomy button?			
Very limited evidence that use of a caecostomy button has less complications than MACE, but this is insufficient to support generalizable conclusions.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence***
What is the effect of ACE compared to sacral nerve stimulation?			
Very low evidence that sacral nerve stimulation may have less complications than ACE, but inconclusive evidence relating to the effect on other outcomes.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence***
What is the effect of colonic resection?			
There is insufficient evidence to suggest the use of colonic resection is safe and	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence***

effective for the treatment of CFC.			
What is the effect of colonic resection combined with malone appendicostomy?			
Insufficient evidence to support conclusions about effectiveness of colonic resection combined with malone appendicostomy	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence***
What is the effect of anorectal myectomy?			
Insufficient evidence to support conclusions about effectiveness of anorectal myectomy.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence***
What is the effect of surgical intervention (ileostopy, colostomy or (sub)total colectomy)?			
Insufficient evidence to support conclusions about that the effect of ileostopy, colostomy or (sub)total colectomy for treating CFC.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence***
What is the effect of sacral nerve stimulation?			
Very low evidence that SNM may be effective in treating CFC.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence***
What is the effect of manometry as a treatment?			
Very low quality evidence that use of manometry may be useful as a treatment for CFC, but	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence***

insufficient evidence to support manometry as a treatment method.			

Table 6: Complementarity with guidelines - What is the effectiveness of complementary therapy interventions?

Evidence synthesis conclusion	***Guideline***	***Guideline recommendation***	***Complementarity***
What is the effect of abdominal massage (in children with or without disabilities)?			
Abdominal massage	NICE 2010	It is the GDG's view that complementary therapies, such as	***Partial agreement***

for children with CFC may result in equivalent or better outcomes than standard care, but there is insufficient evidence to support generalised conclusions		massage, can encourage positive relationships between parents and children by promoting positive time spent together between them, but more research is needed to confirm this and other potential benefits in children with chronic idiopathic constipation.	
	Tabbers 2014	-	***Silence*** – no recommendations relating to complementary therapies
What is the effect of connective tissue manipulation and kinesio taping in children with cerebral palsy?			
There is low certainty from one RCT that physiotherapy techniques of connective tissue manipulation and kinesiotaping may be beneficial components of a programme for children with cerebral palsy who have constipation and are receiving physiotherapy.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence***
What is the effect of chiropractic or ostepathic manipulation?			
There is insufficient evidence to support conclusions about the effectiveness of chiropractic or osteopathic manipulation.	NICE 2010, 2012, 2017, 2018, 2019,	-	***Silence***
	Tabbers 2014	Based on expert opinion, we do not recommend the use of alternative treatments (including musculoskeletal manipulations such as osteopathic and chiropractic) in childhood constipation.	***Partial agreement***

What is the effect of dry cupping therapy compared to laxatives?			
There is very low certainty that dry cupping therapy of the abdominal wall may be as effective as laxatives. Further research is required to explore this finding.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence***
What is the effect of reflexology?			
There is insufficient evidence to support conclusions relating to the effect of reflexology.	NICE 2010	Due to the lack of evidence of effectiveness or cost effectiveness, the GDG felt unable to make a recommendation for the use of complementary and alternative therapies (including reflexology) for use in the NHS.	***Agreement***
	Tabbers 2014	-	***Silence*** – no recommendations relating to complementary therapies
What is the effect of acupuncture?			
There is insufficient evidence to support conclusions relating to the effect of acupuncture.	NICE 2010, 2012, 2017, 2018, 2019	-	***Silence***
	Tabbers 2014	Based on expert opinion, we do not recommend the use of alternative treatments (including acupuncture) in childhood constipation.	***Partial agreement***
What is the effectiveness of cassia fistula?			
There is some very limited evidence that suggests cassia fistula may have some	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence***

beneficial effects, but this is insufficient to support any generalised conclusions. We have very low confidence in this finding.			
What is the effect of other herbal and/or traditional medicines?			
There is low certainty that herbal/traditional medicine for children with CFC may result in equivalent or improved outcomes. However, studies have investigated different interventions, making it difficult to support clinical decisions.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence***

Table 7: Complementarity with guidelines - What is the effectiveness of psychosocial interventions?

Evidence synthesis conclusion	***Guideline***	***Guideline recommendation***	***Complementarity***
What is the effect of behavioural therapy techniques delivered by specialist practitioners?			
Behavioural therapy techniques delivered by specialist practitioners may be beneficial.	NICE 2010	Treat constipation with laxatives and a combination of: Negotiated and non-punitive behavioural interventions suited to the child's stage of development. These could include scheduled toileting and support to establish a regular bowel habit, maintenance and discussion of a bowel diary Do not routinely refer children and young people with	***Partial agreement***

		idiopathic constipation to a psychologist or child and adolescent mental health services unless the child or young person has been identified as likely to benefit from receiving a psychological intervention.	
	Tabbers 2014	Evidence does not support the use of behavioral therapy in the treatment of childhood constipation. The routine use of an intensive behavioral protocolized therapy program in addition to conventional treatment is not recommended in childhood constipation	***Dissonance***
What is the effect of externalizing treatment, compared to other behavioural interventions?			
There is insufficient evidence to support conclusions about the benefits of externalising treatment, compared to other behavioural interventions.	NICE 2010, 2012, 2017, 2018, 2019, Tabbers 2014	-	***Silence*** – no recommendations specific to externalizing treatment
What is the effect of psychotherapy, given in addition to other behavioural therapy?			
There is insufficient evidence to support conclusions about the benefits of providing psychotherapy in addition to other behavioural therapy.	NICE 2010	Do not routinely refer children and young people with idiopathic constipation to a psychologist or child and adolescent mental health services unless the child or young person has been identified as likely to benefit from receiving a psychological intervention.	***Agreement***

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