Supplementary Material 8

Evidence of effectiveness - Level 3 synthesis – Additional tables

Table 1: Characteristics of Excluded Studies

Study (n=40)	Aim	Reason for exclusion
Alqarni 2017 [1]	To assess long-term efficacy and durability of combined intradetrusor botulinum-A toxin (BTX-A), endoscopic treatment of vesicouerteral reflux and anal irrigation for stool incontinence (SI)	Study population is myelomeningocele children which does not meet the eligibility criteria.
Baeten 2011 [2]	To review the status of sacral neuromodulation for refractory constipation	Narrative review
Bigelli 2005 [3]	To compare the manometric parameters evaluated before and after treatment in children in order to determine possible changes induced by standard treatment	Diagnostic test
Canadian Agency for Drugs and Technologies in Health 2015 [4]	To review clinical benefits/harms and review clinical guidelines for colonoscopy in patients under 50 years of age for investigating constipation.	Narrative review
Chang 2013 [5]	To estimate the prevalence of chronic constipation at paediatric gastroenterology clinics, to investigate clinical characteristics associated with constipation, and to collect data on the treatment practices from paediatric gastroenterologists.	This survey study only reports frequency of treatments and does not investigate the effect of treatments.
Chaney 2017 [6]	To illustrate the importance of nursing input in the performance and interpretation of manometry testing for children with suspected gastrointestinal motility disorders.	This abstract reports on nurse observation at manometry testing, not effectiveness of a treatment.
Clarke 2012 [7]	To determine whether transcutaneous electrical stimulation using interferential current (IFC) applied to the abdomen increased colonic PS in STC children.	Moved to 'Level 2' synthesis
Clayden 2005 [8] ISRCTN24521269	To investigate the role of needle-free injection of botulinum toxin into external anal sphincter versus injection of the toxin into internal anal sphincter using	Study was abandoned due to eligibility

	ordinary needle versus control	
Costigan 2019 [9]	To evaluate the contributory factors for a successful Bowel management programme, including use of trans-anal irrigation devices	Moved to 'Level 2' synthesis
Firestone Baum (2013) [10]	To assess whether there is a sensory abnormality in patients with functional constipation who deny sensation to defecate and/or have an inability to feel incontinence	Study is not focused on effect of an intervention.
Freeman 2014 [11]	To determine the best age to offer a family an appendicostomy or cecostomy.	This survey study includes children with organic causes of constipation but does not split the results between idiopathic and organic.
Iacono 2006 [12]	To evaluate the histology and manometry pattern in patients with food intolerance-related constipation	Investigates pathogenesis of cow's milk intolerance causing constipation therefore not relevant to this review.
Iancona 2019 [13]	To review the literature on the application of the neuromodulation techniques in the management of chronic constipation and fecal incontinence in children.	Risk of bias assessed and judged to be high risk of bias.
Jaffray 2009 [14]	To assess outcomes of ACE in children with CFC who were unresponsive to conservative treatments	No prioritised outcomes reported.
Keohane 2019 [15]	This is a scenario question and answer.	Not about effectiveness of a treatment.
Koppen 2016 [16]	To assess the diagnostic and surgical approach of pediatric surgeons and pediatric gastroenterologists towards children with intractable functional constipation.	The aim of the study was to explore the approaches used, rather than explore the effectiveness.
Kilpatrick 2020 [17]	To examine the long-term outcomes of the bowel management program used in our colorectal specialty clinic.	Moved to 'Care provision' synthesis.
Kuizenga-Wessel 2016a [18]	To provide an overview of the existing literature regarding the outcomes of the antegrade continence enema (ACE) procedure and to assess the present practices of physicians worldwide regarding the use of the ACE.	Narrative review
Levitt 2011 [19]	To review the surgical approach to constipation and its	Narrative review

	role as a contributor to fecal incontinence.	
Li 2018 [20]	To review the evidence for Malone appendicostomy versus cecostomy tube insertion for children with constipation refractory to maximal medical management.	Meta analysis but only refers to one study of FC
Lu 2016 [21]	To review use of neurostimulation of the gastrointestinal tract in children	Narrative review
National Institute For, Health; Clinical, Excellence 2006 [22]	To provide guidance on percutaneous endoscopic colostomy	This is NICE guidance and not a study
Ok 2011 [23]	To determine and measure QOL changes after MACE surgery.	Study population is children with Spina Bifida which does not meet the eligibility criteria.
Pal 2016 [24]	to evaluate and quantify current use of surgical clinic time for CIC (Childhood idiopathic constipation) patients	This is a poster abstract about the use of resource time, not effectiveness of a treatment.
Quitadamo 2016 [25]	To evaluate the effect of preliminary bowel preparation on CTT measured by ROM test (Radio-opaque markers)	Diagnostic test
Rodriguez 2013 [26]	To evaluate changes in colonic motility after ACE in children with constipation refractory to maximal medical therapy.	No prioritised outcomes reported
Rybak 2016 [27]	To assess whether colonic manometry parameters could predict outcome of surgical ostomy formation.	This abstract reports on predictive outcomes, not effectiveness of a treatment.
Saikaly 2016 [28]	To identify risk factors for surgical complications in children who undergo the MACE procedure.	Does not state whether children with functional constipation was included in this study. Does not meet our eligibility criteria.
Siminias 2015 [29]	A systematic review to critically evaluate outcomes of surgery for IC.	Risk of bias assessed and judged to be high risk of bias.
Southwell 2011 [30]	To review treatment of Slow Transit Constipation in Children	Narrative review
Yuan 2016 [31]	To appraise the clinical efficacy and safety of Fecal microbiota transplantation (FMT) for the treatment of	This is a protocol for a SR. An update for this study was found but does not mention CFC (Tan 2020,

	intestinal diseases (such as inflammatory bowel disease, Clostridium difficile colitis and so on).	Fecal Microbiota Transplantation for the Treatment of Inflammatory Bowel Disease: An Update. Excluded as does not meet eligibility criteria.
Tran 2016 [32]	to examine the long-term clinical outcomes of children with severe constipation, as defined by need for rectal biopsy (RB),	This study reports outcomes of rectal biopsy, a prognostic tool, not effectiveness of a treatment.
Traslaviña 2015 [33]	To present the case of a six-year old child with acute urinary retention and constipation.	Single case study
Wester 2013 [34]	To review surgical approaches for functional constipation	Narrative review
van den Berg 2005 [35]	To determine the long term outcome of children with severe functional constipation	Not a study of the effectiveness of interventions
Wheeler 2019 [36]	To describe the application of bedside anorectal manometry including diagnostics and outcomes.	The abstract reports how manometry can be used at bedside for prognosis, not effectiveness of a treatment.
Wood 2016 [37]	To review surgical approaches to children with severe constipation, including assessing the quality and levels of evidence and the use of objective measures to determine outcomes.	Narrative review
Wright 2017 [38]	To review use of electroneurostimulation for the management of bladder bowel dysfunction in childhood	Narrative review
Yik 2012 [39]	To determine if TES use affected appendicostomy-formation rates and to monitor changes in practice	Moved to ‘Level 2’ synthesis
Zhong 2015 [40]	To investigate whether integrative medicine (IM), mainly including Chinese medicine and conventional medicine has better effectiveness and safety than conventional medicine or Chinese medicine alone for constipation patients.	This is a protocol for a SR. Anticipated completion date is stated as 2015. Included in the Complementary synthesis.

Table 2: Characteristics of ongoing studies

Study (n=7)	Aim	Study design	Anticipated completion date
Adams 2019 NCT04182633 [41]	To investigate Microbiota Transfer Therapy (MTT) for treating children with Autism Spectrum Disorder (ASD) and gastrointestinal problems (primarily constipation and/or diarrhoea).	RCT	2023
Harofeh 2020 NCT04246398 [42]	To investigate faecal microbiota transplant (FMT) for treating children with Autism Spectrum Disorder (ASD) and gastrointestinal problems	RCT	2022
Heemskerk 2018 NCT02961582 [43]	To assess the effectiveness of SNM compared to personalized conservative treatment (PCT), in patients with idiopathic slow-transit constipation who are refractory to conservative treatment	RCT	December 2021
NCT02255747 2014 [44]	Anal Dilatation for Infants and Children With Constipation	RCT	Recruitment status – unknown
Chen 2020 (NCT03819062) [45]	To study if low level laser therapy will do more good than harm for patients with severe chronic refractory constipation. It is a proof of concept study without a placebo arm.	RCT	February 2027
Briatico 2018 NCT03593252[46]	To check the feasibility of conducting a randomized controlled trial to assess the efficacy of oral nonabsorbable antibiotics, with or without the use of mechanical bowel preparation, in reducing the rate of post-operative infectious complications occurring within 30 days post-operatively in children and adolescents (aged 6 months to 18 years) undergoing elective intestinal surgery.	RCT	January 2024
NCT02361749 2015 [47]	Botulinum Toxin Injection Versus Anal Myectomy in Management of Idiopathic Constipation	RCT	Active – not recruiting (last updated on clinical trials website on 30/1/2018)

Table 3: Risk of bias judgements of cross sectional studies, using JBI Critical Appraisal Checklist for Analytical Cross Sectional Studies tool

Study	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?
Church 2017 [48]	Yes	Yes	Unclear	Unclear	No	No	No	Yes
Har 2013 [49]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
King 2005 [50]	Yes	Yes	Unclear	Yes	No	No	No	Yes

Table 4: Risk of bias judgements for cohort studies, using CASP tool for cohort Studies

Study	Did the study address a clearly focused issue?	Was the cohort recruited in an acceptable way?	Was the exposure accurately measured to minimise bias?	Was the outcome accurately measured to minimise bias?	Have the authors identified all important confounding factors?	Have they taken account of the confounding factors in the design and/or analysis?	Was the follow up of subjects complete enough?	Was the follow up of subjects long enough?	Do you believe the results?	Can the results be applied to the population of interest?	OVERALL ASSESSMENT
Ahmadi 2013 [51]	yes	Can't tell	yes	no	no	no	yes	yes	yes	yes	Moderate concerns
Basson 2014 [52]	Yes	Yes	No	No	Yes	Yes	Yes	No	Can't tell	Can't tell	Serious concerns
Basson 2014a [53]	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	No	Can't tell	Can't tell	Moderate concerns
Bellomo-Branda 2018 [54]	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	Minor concerns
Bonilla 2013 [55]	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Can't tell	Yes	Moderate concerns
Cascio 2004 [56]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No or very minor concerns
Chong 2016 [57]	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	No or very minor concerns
Dolejs 2017 [58]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No or very minor concerns
Gasior 2018 [59]	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Moderate concerns
Gomez-Suarez	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Can't tell	Minor concerns

2016 [60]											
Hallagan 2019 [61]	Yes	Yes	Can't tell	Can't tell	Yes	No	Can't tell	Can't tell	Can't tell	Can't tell	Serious concerns
Hameed 2018 [62]	yes	Can't tell	yes	no	no	no	yes	yes	yes	yes	Moderate concerns
Hoekstra 2011 [63]	Yes	Yes	No	Can't tell	Yes	No	Can't tell	Can't tell	Can't tell	Can't tell	Serious concerns
Husberg 2011 [64]	yes	yes	Can't tell	Can't tell	no	no	no	yes	yes	no	Moderate concerns
Janssen 2018 [65]	yes	yes	yes	Can't tell	yes	yes	yes	yes	yes	yes	Minor concerns
Kuizenga -Wessel 2017 [66]	yes	yes	Can't tell	Can't tell	yes	yes	Can't tell	yes	yes	yes	Minor concerns
Khoo 2017 [67]	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	No or very minor concerns
Lu 2017 [68]	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	Minor concerns
Lu 2016 [69]	yes	yes	yes	yes	Can't tell	Can't tell	yes	yes	yes	yes	Minor concerns
Mousa 2006 [70]	Yes	Yes	Yes	No	Can't tell	No	Yes	No	Can't tell	yes	Serious concerns
Mousavi 2014 [71]	Yes	Yes	Yes	Can't tell	yes	No	yes	Yes	Can't tell	No	Serious concerns
Mugie 2012 [72]	Can't tell	Yes	No	Can't tell	No	No	Yes	Can't tell	Can't tell	No	Serious concerns
Peeters 2011 [73]	yes	yes	yes	yes	no	no	yes	no	Can't tell	yes	Moderate concerns
Peeraully 2014 [89]	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	No or very minor concerns
Peyvasteh 2015 [74]	Yes	Yes	yes	No	Yes	No	Yes	Yes	Can't tell	No	Serious concerns
Randall	Can't	yes	no	Can't tell	Can't tell	no	yes	yes	Can't	no	Serious

2014 [75]	tell								tell		concerns
Redkar 2012 [76]	Yes	Yes	Yes	Can’t tell	No	No	Yes	Yes	Can’t tell	Can’t tell	Serious concerns
Redkar 2018 [77]	Yes	Can’t tell	Yes	Can’t tell	Yes	Yes	Can’t tell	Yes	Can’t tell	Yes	Moderate concerns
Siddiqui 2011 [78]	Can’t tell	Yes	Can’t tell	Yes	Yes	Yes	Yes	Yes	Yes	Can’t tell	Minor concerns
Sulkowski 2015 [79]	yes	yes	yes	yes	yes	yes	yes	Can’t tell	yes	yes	Minor concerns
Tamura 2020 [80]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No or very minor concerns
Van der wilt 2014 [81]	yes	Can't tell	Can't tell	Can't tell	Can’t tell	Can’t tell	Can’t tell	yes	Can’t tell	yes	Serious concerns
Van der Wilt 2016 [82]	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	No or very minor concerns
Van der Wilt 2017 [83]	Yes	Yes	Yes	Can’t tell	Yes	Yes	Can’t tell	No	Yes	Yes	Moderate concerns
Van Wunnik 2012 [84]	yes	yes	yes	Can't tell	yes	yes	yes	yes	yes	yes	Minor concerns
Vriesman 2020 [85]	Yes	Yes	Yes	Can’t tell	Yes	Yes	Yes	Yes	Yes	Yes	No or very minor concerns
Wang 2019 [86]	Yes	Yes	Can’t tell	Can’t tell	Yes	Yes	Can’t tell	Yes	Can’t tell	Yes	Moderate concerns
Youssef 2002b [87]	Yes	Yes	Yes	Can’t tell	Yes	Can’t tell	Yes	Yes	Can’t tell	Yes	Minor concerns
Zar-Kessler 2018 [88]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can’t tell	No or very minor concerns

Table 5: Reported Outcomes of Included Studies

Study	Outcomes Addressed								
	Painful Defecation	QOL	Stool Frequency	Stool Consistency	Side Effects	Faecal Incontinence	Abdominal Pain	School Attendance	Other
Ahmadi 2013 [51]	x		x	x		x			
Basson 2014 [52]					x				Overall success rate.
Basson 2014a [53]					x				Overall success rate.
Bellomo-Branda 2018 [54]					x	x			Successfully stopped using enemas at the end of follow-up
Bonilla 2013 [55]					x				Overall success rate.
Cascio 2004 [56]					x	x			Failure rate.
Chong 2016 [57]			x			x			Continued use of ACE. Failure rate. Redo surgery conducted.
Church 2017 [48]		x			x	x		x	Stooling score
Dolejs 2017 [58]			x		x	x			Dependence from ACE.
Gasior 2018 [59]						x			
Gomez-Suarez 2016 [60]					x		x		Good vs poor outcome. Risk factors for poor outcome.
Hallagan 2019 [61]			x		x	x	x		Positive clinical response
Hameed 2018 [62]	x		x	x	x	x			
Har 2013 [49]		x							
Hoekstra 2011 [63]		x	x		x	x	x		

Husberg 2011 [64]						x			Satisfaction
Janssen 2018 [65]		x	x				x		Use of laxatives and enemas.
Khoo 2017 [67]					x	x			Age at closure, Duration of ACE, Factors predicting closure
King 2005 [50]		x			x	x	x		Length of hospital admission. Postoperative complications. Satisfaction. Perceived optimal age for ACE. Overall success.
Kuizenga-Wessel 2017 [66]			x		x	x	x	x	Satisfaction. Success rate
Lu 2016 [2]		x	x		x	x			Gastrointestinal Symptom Scale
Lu 2017 [68]		x	x		x				Gastrointestinal Symptom Scale
Mousa 2006 [70]		x	x			x		x	Number of medications. Number of physician visits.
Mousavi 2014 [71]			x		x	x*			Ganglion Cells
Mugie 2012 [72]					x				Overall success based on the number of weekly bowel movements, number of weekly faecal incontinence episodes, number of hospital visits for disimpaction, number of oral medications, and complications.
Peeraully 2014 [89]						x			Granulation, leak, stoma prolapse, infection, pain with enema, acute admission, stoma stenosis, stoma closure.
Peeters 2011 [73]			x				x		Lead revision and pacemaker relocations required.
Peyvasteh 2015 [74]			x	x					Faecal diameter.
Randall 2014 [75]						x			Continued use of ACE. Reversed, Not used. Failed,
Redkar 2012 [76]					x				Patient satisfaction regarding symptomatic relief and regular bowel habits
Redkar 2018 [77]			x						
Siddiqui 2011 [78]					x				Bowel management success
Sulkowski 2015 [79]		x				x	x		Dysfunctional voiding. Use of cecostomy. Use of anticholinergic medications for bladder overactivity.

Tamura 2020 [80]					x				Bowel function: 1) Good: defecating through anus with no soiling. 2) Intermediate: defecating through anus with occasional soiling or requiring ACE. 3) Poor: permanent stoma.
Van der wilt 2014 [81]			x						Additional laxatives or bowel irrigation
Van der Wilt 2016 [82]	x	x	x			x	x		Revisions performed and rationale.
Van der wilt 2017 [83]					x				
Van Wunnik 2012 [84]			x		x		x	x	Use of laxatives and enemas.
Vriesman 2020 [85]			x		x	x	x		Laxative use. Patient benefit and satisfaction.
Wang 2019 [86]			x	x	x	x	x		Laxative use. Patient benefit and satisfaction.
Youssef 2002b [87]		x		x	x	x	x	x	Overall Health score. Medications used. Physician visits per year.
Zar-Kessler 2018 [88]	x		x		x				Laxative use. Response (defined as a decrease in defecatory pain or an increase in frequency of stool passage). Anal sphincter dynamics.
Total studies	4	11	21	5	27	23	13	5	

Table 6: Studies addressing questions relating to Level 3 of the pyramid

Question	*What is the effect of*	*What is the effect of sacral nerve*	*What is the effect of anorectal*	*What is the effect of ACE/MACE*	*What is the effect of MACE*	*What is the effect of ACE*	*What is the effect of colonic*	*What is the effect of colonic resection*	*What is the effect of surgical*

	botulinum toxin?	*stimulation?*	*myectomy?*		*compared to caecostomy button?*	*compared to sacral nerve stimulation?*	*resection?*	*combined with malone appendicostomy?*	*intervention (**ileostopy, colostomy or (sub)total colectomy**)*
Cohort study (retrospective)	Basson 2014 [52] Hallagan 2019 [61] Zar-Kessler 2018 [88]	Van Wunnik 2012 [84] Janssen 2018 [65] Sulkowski 2015 [79] Peeters 2011 [73]	Redkar 2012 [76]	Basson 2014a [53] Chong 2016 [57] Dolejs 2017 [58] Gomez-Suarez 2016 [60] Hoekstra 2011 [63] Khoo 2017 [67] Mugie 2012 [72] Siddiqui 2011 [78] Youssef 2002b [87] Husberg 2011 [64] Bellomo-Branda 2018 [54] Peeraully 2014 [89]	Cascio 2004 [56]	Vriesman 2020 [85]	Bonilla 2013 [55]	Gasior 2018 [59]	
Cohort study		Van der wilt	Peyvasteh	Mousa 2006		Wang 2019	Tamura		Kuizenga-

(prospective)		2014 Van der wilt 2017 Lu 2017 Lu 2016 Van der Wilt 2016	2015 [74] Mousavi 2014 [71] Redkar 2018 [77]	[70] Randall 2014		[86]	2020 [80]		Wessel 2017 [66]
Non-comparative study									
Survey study				Har 2013 [49] King 2005 [50] Church 2017 [48]					
Controlled before after study	Ahmadi 2013 [51] Hameed 2018 [62]								
Other									

* - published abstract only. Red = high ROB, Amber = Moderate ROB, Green = Low ROB, RCT=Randomized controlled trial

Table 7: Judgement of certainty in evidence and summary of findings relating to each research question

Question	Studies	Limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Judgement of certainty in evidence	**Summary of findings**
What is the effect of botulinum toxin?	Controlled Before/After Study: Ahmadi 2013 [51] Hameed 2018 [62] Retrospective cohort study:	Downgrade once – concerns about ROB of majority of evidence	No downgrade – consistent findings	No downgrade	Downgrade once - unable to determine which patients have CFC in some studies	No downgrade	VERY LOW	There is very low certainty that botulinum toxin may improve outcomes.
What is the effect of ACE/MACE	Retrospective cohort: Basson 2014a [53] Chong 2016 [57] Dolejs 2017 [58] Gomez-Suarez 2016 [60] Hoekstra 2011 [63] Khoo 2017 [67] Mugie 2012 [72] Siddiqui 2011 [78] Youssef 2002b [87] Husberg 2011 [64] Bellomo-Branda 2018 [54] Peeraully 2014 [89] Prospective cohort Mousa 2006 [71]	Downgrade once – small study sizes	No downgrade – consistent findings	No downgrade	Downgrade once - unable to determine which patients have CFC in some studies	No downgrade	VERY LOW	There is very low certainty that the use of ACE/MACE may be effective against the symptoms of CFC. Further research is required.

	Randall 2014 [75] Survey: Har 2013 [49] King 2005 [50] Church 2017 [48]							
What is the effect of MACE compared to caecostomy button?	Cascio 2004 [56], Wang 2019 [86]	Downgrade – small studies Downgrade – only 2 studies (conducted by same research team)	No downgrade	No downgrade	No downgrade	No downgrade	Insufficient evidence	Very limited evidence that use of a caecostomy button has less complications than MACE, but this is insufficient to support generalizable conclusions.
What is the effect of ACE compared to sacral nerve stimulation?	Vriesmen 2020 [85]	Downgrade once – small studies only Downgrade once only 1 study	No downgrade	No downgrade	No downgrade	No downgrade	VERY LOW	Very low evidence that sacral nerve stimulation may have less complications than ACE, but inconclusive evidence relating to

								the effect on other outcomes.
What is the effect of colonic resection?	Tamura 2020 [80] Bonilla 2013 [55]	Downgrade – small studies Downgrade – only 2 studies	No downgrade	No downgrade	No downgrade	Downgrade - No outcomes of interest (other than side effects) reported in studies	Insufficient evidence	There is insufficient evidence to suggest the use of colonic resection is safe and effective for the treatment of CFC.
What is the effect of colonic resection combined with malone appendicostomy?	Gasior 2018 [59]	Downgrade once – small studies only Downgrade once only 1 study	No downgrade	No downgrade	No downgrade	No downgrade	Insufficient evidence	Insufficient evidence to support conclusions about effectiveness of colonic resection combined with malone appendicostomy
What is the effect of anorectal myectomy?	Redkar 2018 [77] Peyvasteh 2015 [74] Redkar 2012 [76]	Donwgrade once – moderate/low risk of bias studies Downgrade once – only 3 studies	No downgrade	No downgrade	No downgrade	No downgrade	Insufficient evidence	Insufficient evidence to support conclusions about effectiveness of anorectal myectomy.
What is the effect of surgical intervention ***(ileostopy, colostomy or (sub)total colectomy)***	Kuizenga-Wessel 2017 [66]	Downgrade once – only 1 study	No downgrade	No downgrade	Dowgrade once – there is a lack of data pre-surgical intervention limits understanding of effectiveness of the interventions	No downgrade	Insufficient evidence	Insufficient evidence to support conclusions about that the effect of ileostopy, colostomy or (sub)total colectomy for treating CFC.
What is the effect	Retrospective	Downgrade	No downgrade –	No downgrade	No downgrade	No	VERY LOW	Very low evidence

of sacral nerve stimulation?	cohort: Van Wunnik 2012 [84] Janssen 2018 [65] Sulkowski 2015 [79] Peeters 2011 [73] Prospective cohort: Van der wilt 2014 [81] Van der wilt 2017 [83] Lu 2017 [68] Lu 2016 [69] Van der Wilt 2016 [82]	once – small studies only Downgrade once- medium ROB	consistent findings	– consistent findings	– consistent findings	downgrade – consistent findings		that SNM may be effective in treating CFC.

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