Supplementary Material 3 – scoping review results

Table 1. Service delivery - strategies to organise care provision within or across the different 'levels'

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
Athanasakos (2020)(Athanasakos, Dalton et al. 2020)	To assess the impact of an innovative Children's Anorectal Physiology Service (CAPS) focusing on improving outcomes in children with CC/FI	Other primary study (non-comparative study)	112 children; 89 (79%) had functional CC and/or FU	NR	United Kingdom	Hospital	Specialist (Level 2) services / models of care Specialist physiology service *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Bowel and quality of life questionnaires, /risk of distress questionnaires.
Auth (2012)(Auth 2012)	To provide a summary of the current evidence and aims to provide practical advice in primary care - for constipation	Narrative review	Children with constipation. Used the PACCT definition for CFC.	NR	More than one	More than one	More than one intervention: Education of children and parents or guardians, Medical treatment, Disimpaction, Maintenance, Diet and lifestyle interventions, Management plan: when and where to refer	NA
Banoub (2019)(Banoub 2019)	An audit of clinical practice to identify areas of clinical improvement.	Other primary study (retrospective cohort)	40 children with complex neurodisability, feeding and Gastrointestinal issues	Yes	United Kingdom	Hospital	Specialist (Level 2) services / models of care Multidisciplinary model for children with AN *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Parent's Satisfaction
Bellesheim (2018)(Bellesheim, Cole et al. 2018)	Our primary aim is to present lessons learned by the Learning Collaborative and any process improvements made to insomnia and constipation practice pathways	Other primary study (non-comparative)	82 Children with ASD and constipation and 101 children with ASD and insomnia	Yes	United States	Other	Constipation care pathway / algorithm Practice pathway comprising framework of flowcharts for children with ASD *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Families identified up to 4 intervention goals from a predefined list of constipation goals (e.g., more frequent stooling, decreased pain with stooling, presence of soft stools, and decreased encopresis) and insomnia goals (e.g., decreased time to sleep onset, decreased night-time awakening,
Burnett (2004)(Burnett, Juszczak et al. 2004)	To evaluate the effectiveness of a nurse led clinic compared with a consultant led paediatric gastroenterology clinic in the management of CFC.	RCT	102 children presenting with constipation.	No	United Kingdom	Hospital	Nurse-led vs physician-led clinic *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Primary outcome: time to cure at last visit or later confirmed by telephone. Secondary outcomes: number of clinic visits, and number requiring additional medication/in-patient procedures during the scheduled treatment period.
Costigan (2019)(Costigan, Orr et al. 2019)	To describe an individualised bowel management programme and evaluate contributory factors for successful bowel management in children.	Other primary study (Retrospective cohort)	15/192 children attending the bowel management clinic with on-going issues of FI or refractory constipation	NR	Ireland	Hospital	TAI *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	Programme success: defined as the child being clean with no episodes of soiling during the day or night.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
Faramarzian (2018)(Faramarzian, Kargar et al. 2017)	To investigate the impact of nurse-based approaches paediatric CFC	RCT	120 children aged 3 – 14 years diagnosed with CFC	U	Iran, Islamic Rep.	Hospital	Additional nurse-led input vs usual care *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Daily notebooks
Feng (2013)(Feng, Li et al. 2013)	A systematic review protocol which aims to answer whether specialist nursing interventions improve the care and management of patients with CFC	SR protocol (Still on-going)	Children and adults with any diagnosis of CFC. Plan to include constipation caused by underlying disease will also be included. Diagnosis of CFC will be based on Rome II or III criteria	NR	More than one	More than one category	Nurse-led model of care Plan to include specialist nursing interventions	Primary outcome: proportion of patients entering remission and the proportion in whom remission is maintained. Secondary outcomes: compliance or adherence, clinical improvement; duration of remission, utilisation of nurse-led services - number of appointments/contacts with nurses versus access to medical services/physicians; patient satisfaction; hospital admission; outpatient attendance; progression to surgery; length of hospital stay; and cost effectiveness.
Furuta (2012) (Furuta 2012)	To develop a practical, readily applied algorithm for primary health care providers to identify, evaluate, and manage constipation in children with autism spectrum disorders	Narrative review	Children with ASD who also have autism spectrum disorders	Yes	United States	Hospital	Constipation care pathway / algorithm	Algorithm development and testing
Gabr (2020)(Gabr, Gad et al. 2020)	To evaluate the impact of implementing a Bowel Management Program on the quality of life	Other primary study (non-comparative study)	111 Children with pseudo-incontinence	NR	Egypt, Arab Rep.	Hospital	Highly specialist (Level 3) services / models of care Bowel management programme / management pathway *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	QOL and severity of FI
Garman (2012) (Garman 2012)	To discuss diagnosis and treatment, and describe the vital role of the school nurse in assisting children and families with managing this medical	NR	Children with encopresis	Mixed	United States	Education (School / University)	Primary care (Level 1) services / models of care	Diagnosis of encopresis as well as the principles of management

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
	condition							
Gonring (2019)(Gonring, Dolan et al. 2019)	To describe an interdisciplinary group-based treatment for FI in school-aged children.	Other primary study (retrospective cohort)	26 children with FI and CFC who met diagnostic criteria	No	United States	Hospital	Specialist (Level 2) services / models of care Interdisciplinary, "carer-assisted medical-behavioural, group-based intervention". *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Stooling frequency, soiling frequency, and medication adherence
Gordon (2014) (Gordon 2014)	Describe the PEBBLES programme which aims to broadly promote continence for children and young people with disabilities living in the community.	Other primary	Children aged 0–16 years with disabilities or those who meet the eligibility conditions of the Incontinent Pad Scheme, a Western Australian continence product subsidy scheme.	Yes	Australia	Primary care / Community / Patient's home	Primary care (Level 1) services / models of care	Family satisfaction with the service, economic evaluation and client out
Gulati (2017) (Gulati 2017)	Describe a model of collaboration between the Gastroenterology and Paediatrics to increase awareness about importance of early detection of constipation in children using systematic screening in primary care and develop a comprehensive constipation tool-kit to facilitate high quality, evidence-based care.	Other primary study	Children with constipation	U	United States	Hospital	Primary care (Level 1) services / models of care	NR
Huang (2018) (Huang, Jiang et al. 2018)	To evaluate whether nurse-led interventions with or without other treatments are effective in the management of CFC	SR Protocol	Children and adolescents with functional constipation definitely diagnosed by Rome criteria.	NR	China	U	Nurse-led model of care	Primary outcomes: children's symptoms: cure rate, recurrence rate, stool consistency and frequency, adverse event, self-reported quality of life, constipation self-efficacy, adherence to laxatives or other therapy. parent's satisfaction. Secondary outcome: self-report anxiety, self-report defecation pain.
Ismail (2011)	To assess the impact of	Other primary	Children referred	NR	United	Primary	Nurse-led model of care	Bowel frequency, pain on defaecation,

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
(Ismail, Ratchford et al. 2011)	involving experienced children's outpatient nurses in the management of children with CFC who were not making satisfactory progress	study (non-comparative study)	to the nurse-led clinic had been constipated for a minimum of six months and had attended at least three appointments at a general paediatric clinic.		Kingdom	care / Community / Patient's home	*This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	soiling, reluctance to use a toilet, current treatment for constipation and parental understanding of constipation and its management.
Karagiozoglou-Lampoudi (2012) (Karagiozoglou-Lampoudi, Daskalou et al. 2012)	To evaluate adherence of paediatric patients with refractory functional constipation to a high-water, high-fiber diet following the physician's dietary instructions based on official treatment guidelines or personalized dietetic management according to patient's needs, based on the same official treatment guidelines	RCT	86 children with functional constipation. constipation was refractory to treatment by paediatrician for several months and/or presented with complications.	NR		U	Specialist (Level 2) services / models of care Model with personalised dietary advice from a registered dietician *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Water and fiber consumption before and after intervention were used as compliance criteria
Khan (2018) (Khan 2018)	To clarify the diagnostic process and provide a clear treatment path to be used for CFC in primary care.	Narrative review	Children with constipation	NR	More than one	More than one	More than one intervention (dependent on age): Infants: Dietary measures, education for parents, rectal stimulation using a lubricated rectal thermometer, osmotic laxatives or glycerin suppositories. Toddlers and Children: stepwise approach to treatment. The first step is disimpaction (laxatives or physical disimpaction, enema, a lubricated rectal thermometer can also be used). Once disimpaction has been accomplished, the next step is prolonged laxative treatment (osmotic laxative, polyethylene glycol (PEG).3 Although other osmotic laxatives such as sorbitol and lactulose are valuable) and behaviour therapy (toileting, reward, monitoring). This is called maintenance therapy and should continue for at least 2 months, education for parents. The third step is focused on dietary changes (fibre and fluid, limiting cow's milk) and step four involves the gradual tapering and withdrawal of laxatives.	NA

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
Kilpatrick (2020)(Kilpatrick, Zobell et al. 2020)	We sought to examine the long-term outcomes of the bowel management program used in our colorectal specialty clinic.	Other primary study (retrospective cohort)	112 children < 18 years of age who were prescribed a bowel management week	NR	United States	Hospital	Specialist (Level 2) services / models of care "Bowel management week" with structured regime *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Treatment success was defined as no soiling accidents. Fewer than two "smears" on undergarments per week was considered success. For children who were not toilet trained or had a stoma present, success was defined as a regular stooling pattern. Other measures included: adherence, follow-up visits, phone communications with our clinic, emergency department visits, and surgical interventions related to bowel management were reviewed.
Lawton (2017) (Lawton 2017)	To provide an overview of management of constipation in children	Narrative review	Children with constipation. Rome IV Criteria was used.	NR	More than one	More than one	More than one intervention: Laxatives: Macrogol 3350/ Polyethylene Glycol (PEG), Movicol and GoLYTELY - PEG with electrolytes, Osmalolax (PEG). Maintenance - stool softeners, toileting - footstool, reward.	NA
Malamisura (2018) (Malamisura 2018)	This retrospective study documented the incidence as well as the clinical features of children presenting to emergency department for CFC.	Other primary study (retrospective cohort)	380 children with CFC	NR	Italy	Hospital	Constipation care pathway / algorithm Care pathway in ED *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Demographics and disease characteristics
Mallon (2015) (Mallon, Vernacchio et al. 2015)	We investigated whether Shared Care (a collaborative quality improvement initiative) reduces referrals and improves adherence to established clinical guidelines	Other primary study (retrospective cohort)	61 CFC	NR	United States	Primary care / Community / Patient's home	Constipation care pathway / algorithm Management algorithm aimed at adherence to guidelines *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Referral rates and improved adherence to established clinical guidelines and rate of faecal impaction.
Modin (2016) (Modin, Walsted et al. 2016)	To evaluate whether follow-up by phone or self-management through Web-based information improves treatment outcomes.	RCT	235 children, aged 2 to 16 years, referred from general practitioners to the paediatric outpatient clinic. To be included, children had to fulfil 2 Rome III criteria for FC for	U	Denmark	Hospital	Follow-up regimes. Website + phone follow-up *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Primary outcome: number of successfully treated children. Being successfully treated was defined as the presence of <2 Rome III criteria with or without the use of laxatives. Rectal impaction at 3, 6, and 12 months was evaluated by transabdominal ultrasound. Secondary outcomes: extra contacts, relapse, faecal incontinence, and use of laxatives.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
			2 months.					
Mosca (2013) (Mosca and Schatz 2013)	This article will assist the school nurse in understanding typical causes for functional encopresis, knowing how to help a student who soils, and developing an individualized healthcare plan that assists a student to become continent of stool again. Encopresis is not just an accident.	NR	School-aged children with encopresis	U	United States	Education (School / University)	Nurse-led model of care	NR
Moser (2014) (Moser, Plante et al. 2014)	Our aim in this article is to stimulate the development of integrated behavioral health services that reflect biopsychosocial models of health using a pediatric gastroenterology (GI) service as a model. We provide a rationale for integrating care in the pediatric GI setting by briefly reviewing the literature on the psychological correlates of common pediatric GI disorders. Then we describe a model of integration implemented in a hospital-based outpatient clinic, including data about utilization trends and logistical, administrative, and financial considerations. Finally, we share more informal	Other primary study (retrospective cohort)	111 Children with gastrointesinal conditions (encopresis, abdominal pain, and irritable bowel syndrome) We selected for patients who were seen in the general GI clinic for at least one general psychology visit between the dates of October 24, 2006, and May 31, 2009. This population did not include patients who were seen by psychologists within the multidisciplinary feeding and food allergy teams	U	United States	Hospital	Specialist (Level 2) services / models of care Paediatric psychology service *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	NOT REPORTED

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
	observations regarding the impact of the program on overall clinical and academic goals.							
NCT02354820 (NCT02354820 2015)	Child Health Improvement Through Computer Automation of Constipation Management in Primary Care	RCT	Patients presenting to one of 5 primary care clinics in the Eskenazi Health system in Indianapolis, IN. Constipation or encopresis	NR	United States	Hospital	Primary care (Level 1) services / models of care	Primary = Number of patients with persistent constipation within 6 months, Secondary = Number of patients who receive a screening workup - Celiac panel and/or T4/TSH within 6 months, Number of patients who receive a sub-specialty referral within 6 months
Norbedo (2017) (Norbedo, Bassanese et al. 2017)	to investigate the incidence and the clinically relevant features of functional constipation in patients evaluated for acute abdominal pain in a tertiary care pediatric emergency department	Other primary study (retrospective cohort)	1020 patients admitted for acute abdominal pain to the ED, with CFC	No	Italy	Hospital	Constipation care pathway / algorithm Practice within ED *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Discharge treatments were recorded, as well as readmissions of patients who had received a previous evaluation
Peck (2017) (Peck 2017)	to create an expert care team consisting of a pediatric nurse practitioner, a pediatric psychologist and an attending gastroenterologist who would see families frequently and provide consistent medical management, emotional support and behavioral therapy to promote adherence.	Other primary study (retrospective cohort)	Patients with functional constipation diagnosed by a pediatric gastroenterologist are referred to the DDC. - Defecation Disorders Center	U	United States	Hospital	Specialist (Level 2) services / models of care Multidisciplinary 'expert care team' *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	adherence
Perez (2014) (Perez 2014)	Not stated	Narrative review	continence	U	United Kingdom	Primary care / Community / Patient's home	Primary care (Level 1) services / models of care	"maintain healthy childhood bladders and bowels"
Poenaru (1997)	The multifactorial nature	Other primary	114 children	No	Canada	Hospital	Specialist (Level 2) services / models of care	tlies themselves and (2) the clinic staff.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
(Poenaru, Roblin et al. 1997)	of functional constipation in children suggests that a multidisciplinary management approach may be effective. The authors tested this hypothesis in a newly created paediatric Bowel Management Clinic	study (non-comparative study)	There is no lower age limit for referral, and the upper limit is the 19th birthday. Children with obvious associated anomalies causing constipation or encopresis were treated separately and not included in the study.				Multidisciplinary bowel management clinic *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Before the initial clinic visit, families filled out several matled questionnatres covering medical, psychological, and social issues surrounding the child's problem. These include a medical information questionnaire, a family information questionnaire. the Family Assessment Device (FAD); the Chronic Illness Psychosocial Inventory (CI-PSI), and a knowledge quiz. Parents were also requested to complete a "constipation/soiling diary" for one week, detailing the child's stools and symptoms, At the first clinic visit a structured history/physical examination form was completed by the physician, At each follow-up clinic the famihes completed a short progress questionnaire, and they were asked to contmue the diaries throughout. The FAD, CI-PSI questionnaires and knowledge quiz were repeated 3 and 4 months after the imtial clinic visit. A Measure of Processes of Care (MPOC) questionnaire8 was also administered at the 4.month point. The MPOC is a self-report measure of the parents'

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
								perceptrons of the extent to which five behaviors of health care professionals occur (enabling and partnership, providmg general mformation. providing specific information, coordinated and comprehensive care, and respectful and supportive care). The scores from our group were then compared with those from a normative group of 653 patients. Data Analysis All chmc data were ent
Poo Passport (2016) (Our Lady's Hospital for Sick Children 2016)	During a review of services by the Stoma / Colorectal service Clinical Nurse specialists in 2014 it was determined that the numbers of children with idiopathic constipation who attended the service for assessment and management was increasing exponentially. It was identified that no tool was used to assess this patient group in the community leading to many referrals of children to the surgical service in OLCHC for assessment and management when this could be very appropriately manged in the community with the appropriate tools.	Other primary study (intervention development)	45 children with idiopathic constipation	U	Ireland	Primary care / Community / Patient's home	Constipation care pathway / algorithm Standard assessment tool and treatment plan *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Number of referrals

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
Protheroe (2004) (ISRCTN07833068 2004)	To assess the effect of the introduction of a primary care-based intervention for children with constipation compared to conventional hospital-based management.	ONGOING TRIAL / PROTOCOL FOR TRIAL	Children with chronic constipation	NR	United Kingdom	More than one category	More than one service delivery level involved Note on clinical trial website: 29/04/2016: No publications found, verifying study status with principal investigator	Primary: 1. Clinical outcomes: remission and relapse of symptoms 2. Quality of life/patient and parental satisfaction 3. Cost benefits: on-going treatment, nurse contacts, out-patient visits and hospital admission
Prynn (2011) (Prynn 2011)	In this article: causes of idiopathic constipation, diagnosing the condition, different therapies to manage idiopathic constipation, the importance of follow-up	Other (PLEASE SPECIFY)	idiopathic constipation	NR	United Kingdom	U	More than one service delivery level involved	NA
Puoti (2019) (Puoti 2019)	we reported the preliminary result of a multidisciplinary approach of CRC tested in a new Lower Gastrointestinal Dysmotility Clinic. We aimed at identifying psychosocial factors, establishing the need for further interventions and defining individualised managements.	Other primary study (retrospective cohort)	16 children with chronic refractory constipation	NR	United Kingdom	Hospital	Specialist (Level 2) services / models of care Specialist multidisciplinary clinic, including psychology *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Three outcome points at the end of clinic were set: 1) further follow-up; 2) discharge to the local team; 3) surgery assessment
Raghu (2019) (Raghu, Gaughan et al. 2019)	to collect baseline data on the management of constipation at our hospital, use these data to develop a clinical pathway for constipation management, and assess the pathway's effect on utilization of hospital services, readmission rate, and length of stay.	Other primary study (non-comparative)	CFC	NR		Hospital	Constipation care pathway / algorithm Practice within ED *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	improved process control, length of stay or return rate
Rogers (2012)	discusses new care	OTHER	idiopathic	NR	United	Primary	Primary care (Level 1) services / models of care	objective of new care model was to redce

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
(Rogers 2012)	model for managing idiopathic peadiatric continence problems	(PLEASE SPECIFY)	peadiatric continence problems		Kingdom	care / Community / Patient's home	Bowel management programme with dedicated nurse *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	long waiting lists and high "did not attend" rates
Russell (2015) (Russell, Barnhart et al. 2015)	to assess the effectiveness of a structured bowel management program in these children. - -CFC	Other primary study (retrospective cohort)	44 children with CFC, failing dietary and medical management.	Mixed	United States	More than one category	Specialist (Level 2) services / models of care *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	The goal of treatment is for patients to empty their colon daily and to be free of soiling
Sanders (2014) (Sanders 2014)	To explore and understand the information, education and support needs of parents and professionals using transanal irrigation with children. A second aim was to apply this knowledge in the design, development and evaluation of a shared health transanal irrigation resource for parents and professionals to use with children.	QUALITATIVE	No children involved. Professionals and parents only	NR	United Kingdom	Hospital	Specialist (Level 2) services / models of care	To inform choice and decision-making between parents and professionals. Study outcome culminated in the development of an shared health resource (SHR) to provide clinical guidance, education and information for both parents and professionals and as such aimed to address the concern that professionals may fail to engage in using an SHR.
Sandweiss (2018) (Sandweiss, Allen et al. 2018)	The objective was to develop a standardized approach, emphasizing clinical history, physical examination, less reliance on AR and home management.	Other primary study (non-comparative)	3240 Patients presenting to a paediatric ED with symptoms consistent with constipation	U	United States	Hospital	Constipation care pathway / algorithm Standardised triage and management algorithm *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	The primary outcome measures were 1) the percentage of discharged patients assigned an ED disposition diagnosis of constipation treated with the ED pathway, defined as receiving standardized educational materials and a gift basket; 2) the percentage of patients with constipation who had AR performed; and 3) the admission rate for constipation. The first primary outcome measure was calculated by tracking how frequently ED providers used the home medication checklist, where a completed checklist was considered adherence to the pathway. Secondary outcome measures included 1) average per-

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
								patient ED cost for patients with constipation pre- versus postintervention and 2) average per-patient ED LOS for constipation patients pre- versus postintervention. As a balance measure, we compared ED revisit rates within 7 days for patients discharged from the ED with a diagnosis of constipation and performed chart reviews of all revisits to check for concerning missed diagnoses or significant illness, defined as patients requiring pediatric intensive care unit admission to the or surgical intervention.
Schuster-Bruce (2016) (Schuster Bruce 2016)	Aims to improve understanding of this condition and incorporates the guideline recommendations and identify the role of the nurse	Narrative review	Children with constipation	NR	More than one	More than one	More than one intervention	NA
Shabde (2016) (Shabde and Harrison 2016)	Describes the Cumbrian experience of the development of a child centred constipation pathway, based on NICE guidance	Other primary study (intervention development)	Children with constipation	NR	United Kingdom	Primary care / Community / Patient's home	Constipation care pathway / algorithm Pathway based on NICE guidance *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	NR
Short (2018) (Short, Heiss et al. 2018)	To compare outcomes before and after implementation of an ERP in children undergoing colorectal surgery.	Other primary study (retrospective cohort study)	3 children and young people aged 5 to 20 years who underwent elective major colon and rectal operation	U	United States	Hospital	Highly specialist (Level 3) services / models of care. Recovery protocol after colorectal surgery *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Primary outcome: LOS or time to discharge. Secondary outcomes: number of ERP elements received by each patient, volume of intraoperative fluids received, volume of narcotics received, time to regular diet, complication rate and 30-day readmission rate.
Singh (2018) (Singh 2018)	To review the assessment and management of children with constipation to empower GPs to initiate treatment and know when to refer to a paediatrician	Narrative review	Children with constipation	NR	More than one	More than one	More than one intervention	NA
Stienen (2011)	Reports on the	Other primary	Children aged	NR	Netherlands	More than	More than one intervention: mentions laxatives	NA

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
(Stienen 2011)	development of quality indicators for care delivered to children with functional constipation, based on the Dutch evidence-based multidisciplinary guideline	study (development of quality indicators using modified Delphi)	between 0 and 18 years with CFC. CFC defined using Rome III criteria.			one	and professional contact	
Tappin (2013) (Tappin, Nawaz et al. 2013)	To describe an audit and service development was to assess routine consultant paediatrician-led care against minimum standards and if appropriate to develop a nurse-led intervention.	Mixed methods	Children aged 0 - 13 years with a main complaint of constipation who were referred by their GPs. Other conditions that made a simple nurse-led intervention inappropriate had to be absent e.g. Autistic Spectrum Disorder. Allocation to either the new nurse-led intervention or the comparison group depended on postcode of residence.	U	United Kingdom	Hospital	Nurse-led clinic vs physician-led clinic *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Appointments, modalities of care, modified parent satisfaction questionnaire for children with constipation. Parents were also asked 3 open ended questions: What did you like most about your care? What did you like least about your care? Do you have any suggestions for improvements? This questionnaire was sent out to the 17 parents who attended their first appointment. The primary outcome for the service evaluation was a measure of constipation less than 3 stools per week for all children, and soiling in the last week for children aged 4+ years. Secondary outcomes: parent satisfaction with the service; still taking medication at follow-up; overall better than prior to first clinic visit; pain passing stools in the last week; with-holding behaviour during the last week; stool that blocked the toilet in the last week.
Trajanovska (2020) (Trajanovska 2020)	To explore referral and triage pathways for paediatric patients referred to an Australian hospital with bowel dysfunction (isolated or mixed bowel and bladder)	Other primary study (audit of referral and triage pathways)	Children with encopresis. CFC defined using Rome IV criteria.	Mixed population	Australia	Hospital	More than one intervention: education, disimpaction, toileting programme, laxatives	NR
Waterham (2017) (Waterham 2017)	This article aims to provide a structure for evaluating, diagnosing and managing childhood functional constipation in	Narrative review	Children with constipation. Rome IV Criteria was used.	U	More than one	More than one	More than one intervention: Toileting behaviours and education. Disimpaction - polyethylene glycol (PEG) with or without electrolytes. Maintenance Treatment - laxatives. Diet and food intolerance - fibre.	NA

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
	general practice.							
Webster (2018) (Webster 2018)	To describe a quality improvement project which aims to decrease referrals from the CHOP primary care network to CHOP paediatric gastroenterology for functional constipation by 25 percent	Other primary study (survey)	Children with constipation	NR	United States	Primary care / Community / Patient's home	Primary care (Level 1) services / models of care Constipation action plan and education program for paediatricians *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	Number of referrals
Wolfe (2019) (Wolfe, Lemer et al. 2019)	The Children and Young People's Health Partnership (CYPHP) is a health system strengthening initiative implementing and evaluating a new model of care	Other (PLEASE SPECIFY)	Children and young people	U	United Kingdom	More than one category	Primary care (Level 1) services / models of care *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 18*	CYP health and wellbeing, healthcare quality, patterns of healthcare use, and cost effectiveness

Table 2. Level 0 – Everyday life: interventions delivered by families / carers, prior to healthcare professional involvement.

Abbreviations: AP: abdominal pain; BM: bowel movements, CFC: chronic functional constipation; FI: faecal incontinence; IBS-C: irritable bowel syndrome with constipation; N: no; NR: not reported; RCT: randomised controlled trial; SR: systematic review; Y: yes

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
Abediny (2016) (Abediny 2016) IRCT20130415 13021N1	Evaluated effect of probiotics on CFC in children	RCT	90 children aged 4-12 years ROME III	No.	Iran, Islamic Rep.	Home	Diet. Probiotics plus standard care (i.e., laxative (Pidrolax)	BM frequency, stool consistency, number of FI per week, and AP and painful defecation
Aulia (2016)(Aulia, Supriatmo et al. 2016)	To determine the role of glucomannan for the treatment of CFC	RCT (cross-over)	36 children aged 7-12 years with CFC	NR	Indonesia	Primary care / Community / Patient's home	Lifestyle: additional dietary fibre (Glucomannan vs placebo: maltodextrin; 4 weeks of treatment *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Stool frequency and consistency
Axelrod (2018)(Axelrod 2018)	To synthesise the available evidence on the role of fiber, in the treatment of CFC and IBS-C	SR	Children aged 0-21 years were included in the syntheses; 13 studies (723 participants) CFC definition was NR	NR	More than one	Unclear	More than one intervention delivered; Included all studies comparing fiber with lactulose, PEG, or placebo	NR
Bae (2014)(Bae 2014)		Narrative review			More than one	Home	Lifestyle: Diet - other	
Banaszkiewicz (2005) (Banaszkiewicz and Szajewska 2005)	To evaluate the efficacy, safety, and tolerability of Lactobacillus in treatment of CFC	RCT	84 children aged 2- 16 years; children had CFC between 4 weeks and 3 months. CFC was defined as <3 spontaneous BMs per week for at least 12 weeks. Children were all disimpacted prior to starting the study.	NR	Poland	Hospital but intervention delivered at home	Probiotics as an adjunct to laxatives (Children received either 1 mL/kg/day of 70% lactulose (in two divided doses) plus either 109 colony-forming units (CFU) of LGG or a comparable placebo, twice daily orally for 12 weeks)	Primary outcome: treatment success, defined as ≥3 spontaneous BMs per week with no episodes of faecal soiling. Secondary outcomes: number of BMs per week, number of episodes of faecal soiling per week, stool consistency, and straining frequency per week
Basturk (2017) (Basturk, Artan et al. 2017)	To evaluate the efficacy of synbiotic (Lactobacillus casei, L. rhamnosus, L. plantarum, and Bifidobacterium lactis and prebiotics	RCT	146 children aged between 4 and 18 years diagnosed with CFC using ROME III criteria.	NR	Turkey	Home	More than one intervention: fibre (Synbiotics and prebiotics mixture vs placebo) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Primary outcomes: resolution of all complaints of the patient with the 4-week synbiotic treatment. Secondary outcomes: weekly number of BM, stool consistency, number of FI incidence, presence of AP, painful BM, rectal bleeding, avoidance behaviour, side effects.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
Bekkali (2007) (Bekkali, Bongers et al. 2007)	To determine the effect of a mixture of probiotics containing bifidobacteria and lactobacilli in the treatment of CFC	Other primary study	20 children diagnosed with at least 2 out of 6 of ROME III symptoms. All children received a rectal enema before starting intervention.	No	Netherlands	Home	Probiotics. (Daily probiotics mixture of 4 × 109 colony forming units (CFU), containing Bifidobacteria (B.) bifidum, B. infantis, B. longum, Lactobacilli (L.) casei, L. plantarum and L. rhamnosus for 4 weeks. Plus toilet training i.e. sitting on the toilet 3 times/ day for 5 minutes after each meal with the intention of trying to defecate	Primary outcome: frequency of BM and stool consistency. Secondary outcomes: number of faecal incontinence episodes per week, presence of AP and adverse effects
Beleli (2015) (Beleli, Antonio et al. 2015) NCT02183766	To determine the effects of galactooligosaccharide in CFC	Other primary study (Non-randomised crossover study)	23 children diagnosed using ROME III criteria	NR	Brazil	Attended to at a primary healthcare unit Primary care / Community / Patient's home	Diet - prebiotic Group 1: ingested galactooligosaccharide (1.7 g) for 30 days, followed by a 15-day washout period, and a 30-day period of placebo (maltodextrin). Group 2: maltodextrin for 30 days, followed by 15-day washout period, and galactooligosaccharide (1.7 g) for 30 days. *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Primary outcomes: BM per week, faecal consistency and straining/ pain
CTRI/2019/04/ 018561 (CTRI/2019/04/ 018561 2019)	To examine the acceptability of the product Vitazyme Drops to manage AP	Other primary study	200 children aged 1 month – 2 years, with symptoms of indigestion, flatulence, CFC, persistent loose stools or poor appetite in general (as perceived by the parent) with or without colicky AP	NR	India	NR	Vitazyme Drops	Improved digestion & flatulence, a reduction in mean daily crying time. Safety also profiled.
Boilesen (2017) (Boilesen, Tahan et al. 2017)	To study the evidence on the role of water and fluid intake in the prevention and treatment of CFC	SR	Children and Adolescents 11 studies (participant number range: 84-1426) included. CFC not defined	U	More than one	NR	Lifestyle	Not explicit but fluid Intake (the role of water and/or fluid intake in the treatment and prevention of intestinal constipation in children and adolescents)

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
Bongers (2007) (Bongers, de Lorijn et al. 2007)	To test if a new milk formula will have positive effect in constipated infants	RCT (cross-over)	38 healthy, term infants with constipation aged between 3 – 20 weeks of age, who received at least 2 bottles of milk-based formula per day.	NR	Netherlands	Conducted in Academic and non-academic hospital. Intervention delivered at home	Diet. Different milk formula (Infant formula (NF; Nutrilon Omneo) vs whey-based control formula; cross-over 3 weeks) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Primary outcomes: defecation frequency, stool consistency; no more painful defecation; absence of abdominal or rectal palpable mass at physical examination. Secondary outcomes: formula tolerance and weight gain.
Mohammadi Bourkheili 2021 (Mohammadi Bourkheili, Mehrabani et al. 2021) IRCT20190306042946N1		RCT	70			Home	Cow's milk free and dairy free diet *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	
Bu (2007) (Bu, Chang et al. 2007)	To investigate the effect of probiotics alone compared with magnesium oxide (MgO) and placebo	RCT	45 children aged < 10 years diagnosed with CFC; length of time with CFC was > 2 months	No	Taiwan, China	Home	Diet. Three groups: A (n = 18) with MgO (50 mg/kg per day, b.i.d.), group B (n = 18) with Lcr35, 8 × 10 8 c.f.u./day (Antibiophilus 250 mg, two capsules, b.i.d., Laboratoires Lyocentre, Aurillac , France) and group C (n = 9) with placebo (starch in content).	Treatment success: defined as 3 spontaneous BM/week with no episodes of faecal soiling in the fourth week. Other outcomes: frequency of defecation, stool consistency, episodes of soiling or AP and the use of lactulose or enema.
Capra (2003) (Capra 2003)	To identify the available evidence on dietetic treatment and management of CFC in adults and children	SR protocol	Participants will include children or adults, who are defined as constipated	NR	Australia	NR	More than one intervention	Frequency and/or consistency of BMs per week, symptom improvement (including anal blockage), reduction in AP, need for breakthrough laxatives and cost.
Carroccio (2005) (Carroccio, Scalici et al. 2005)	To determine whether or not a food intolerance-dependent rectal mucosa inflammation is present in CFC.	Other primary study	included all the consecutive infants and children with chronic constipation unresponsive to previous treatments. Inclusion criteria were: a) a history of chronic constipation lasting at least 6 months; b) lack of response	UNCLEAR	Italy	Home	More than one intervention	compare the number of bowel movements per day and the qualitative fecal scores during the baseline period and during the elimination diet period. compare the histologic data recorded in the patients with a final diagnosis of food intolerance, at baseline and after 12 weeks of elimination diet. compare the

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
			to a previous increase in dietary fiber intake and/or to laxative treatment (milk of magnesia 1 /2 ml per kilogram bodyweight, polyethylene glycol 4000 mean dose 0.75 g per kilogram daily) attempted for at least one month; c) regular dietary intake of cow's milk and derivatives. Exclusion criteria were: a) prior anal surgery; b) use of medications that can cause constipation; c) referral for reasons other than chronic constipation. All patients included were being fed a normal diet, without any restrictions. On the basis of the above criteria 75 patients were initially recruited, but preliminary investigations showed that 5 of them had anatomical/neurological causes of constipation (Hirschsprung's disease 2 cases, spinal disease 1 case, psychomotor retardation 2 cases) and 4 cases of constipation owing to another disease (celiac disease 3 cases, hypothyroidism 1 case).					histologic findings in patients with constipation due to food intolerance and in those with constipation unrelated to food intolerance. correlations between the histologic data.
Cassettari (2019)(Cassettari, Machado et al. 2019)	To explore the effect of combining green banana biomass and laxatives on CFC	RCT	80 children aged 5 – 15 years with CFC diagnosed according to Rome IV criteria	No	Brazil	Referred to an outpatient clinic of the Botucatu Medical School. Intervention used at home and follow-up assessment a	More than one intervention Green banana biomass vs different combinations of laxatives Five groups: (1) green banana biomass alone; (2) green banana biomass plus PEG 3350 with electrolytes; (3) green banana biomass plus sodium	Primary outcome: reduction of the proportion of patients with Bristol Stool Form Scale ratings 1 or 2. Secondary outcomes: increase of the proportion of >3 BM/week and reduction of the proportion of FI, straining on defecation, painful defecation, blood in stool, AP, and decreased laxative doses

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
						week later at the clinic	picosulfate; (4) PEG 3350 with electrolytes alone; and (5) sodium picosulfate alone *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	
Castillejo (2006) (Castillejo, Bullo et al. 2006)	Our aim with this pilot study was to evaluate if fiber supplementation is beneficial for the treatment of children with idiopathic chronic constipation.	RCT	Children who were between 3 and 10 years of age and were referred to the pediatric gastroenterology outpatients clinic between january 2004 and april 2005 with chronic constipation were asked to participate in a double-blind, randomized parallel group study to compare the effects of a cocoa husk supplement rich in fiber with the ffects of a placebo. Exclusion criteria for the study were 1) the presence of fecal impaction that required enema in the 7 days before the start of the study; 2) treatment with dietary fibre, bulk-forming agents or laxatives in the 2 weeks before the start of the study; 3) constipation attributable to organic or anatomic causes (hirschsprung disease, hyopthyroidism, mental deficiency, psychiatric illness, chronic debiliitating disease, neurologic abnormalities or previous surgery of the colon or anus); 4) renal insufficiency, hypocalcemia, hyperkalemia or any other metabolic	UNCLEAR	Spain	Home	More than one level 0 intervention delivered by carers prior to HCP involvement	At baseline and after 4 weeks of treatment we (1) performed antropometry, conducted a physical examination and took routine laboratory measurements; (2) determined total and segemental colonic transit time (CTT); (3) evaluated bowel movement habits and stool consistency using a diary that was completed by the patient's parents and (4) received a subjective evaluation from the parents regarding the efficacy of treatment. Three days before the start of the intervention and 3 days before the end of the intervention, patinets feces were collected to evaluate their weight and level of hydration. Energy, fat, carbohydrate, protein and fibre intake were measured using a 3-day dietary record before and at the end of the study. The dietitian completed food records on the chuldren from information that was provided by the children and their parents or guardians. We chose CTT as the primary outcome measurement to verify the efficacy of the treatment. CTT was measured after the intake of 10 radio-opaque markers.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
			diseases at the start of the study; 5) long-term use of drugs that affect gastro-motility (e.g. imipramine, iron or calcium supplements, anti-convulsants; and 6) inability to adhere to the studys medications or procedures.					
Ceresola (2018) (Ceresola, Ferrarese et al. 2018)	In this review, we evaluate recent attempts that used prebiotics, natural fibers or probiotics to treat FC, with a deep microbiome-based focus.	Narrative review	Children with functional constipation	UNCLEAR	Italy	Home	Lifestyle: Diet - Prebiotics /probiotics	NOT REPORTED
Chao (2007) (Chao and Vandenplas 2007)	Evaluated the therapeutic and nutritional effects of a magnesium-enriched infant formula on constipation.	RCT	93 healthy infants 2 to 6 months of age with constipation for 2 weeks.	No	Taiwan, China	Infants were initially seen at the paediatric gastroenterology clinic; assume the intervention was delivered 'as required'	Diet – different milk formula (Magnesium-enriched infant formula vs 20% strengthened formula) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Outcomes: remission if infants were asymptomatic; a decrease in severity of 4 was considered a "good response" and a decrease of 1 to 3 was considered a "fair response." If the score did not change or increased, the intervention was considered a failure.
Chao (2017)(Chao 2016) (NCT03054805)	To compare the differences of faecal microflora between constipated and non-constipated healthy children, and evaluate the efficacy of probiotics in reducing symptoms of constipation and the influence of intestinal microflora in children with CFC	RCT	109 children aged from 6 months – 18 years diagnosed with CFC according to the Rome III criteria	NR	Taiwan	Home	Lifestyle: Diet - Prebiotics /probiotics Magnesium oxide and probiotics (MIYAIRI-BM) vs Magnesium oxide. 12 weeks of intervention. *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Primary outcome: change in Clostridium butyricum Miyairi expression Other outcomes: adverse events
Chmielewska (2011) (Chmielewska, Horvath et al. 2011)	To investigate the effectiveness of Glucomannan in the treatment of CFC in children	RCT	72 children aged 3 to16 years with CFC diagnosed according to the Rome III Criteria. Length of time with CFC was reported as >2months	No	Poland	Home	Disimpaction (using phosphate enema if required). Children received either GNN (at a dosage of 2.52 g/day, i.e., one sachet of 1.26 g two times a day, or a comparable placebo (maltodextrine) at the same dosage. Consumed twice	Primary outcome: treatment success, defined as 3 or more bowel movements with no episodes of soiling during the last week of product consumption. Secondary outcomes: stool consistency, stool frequency per week, and the

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
							daily for 4 weeks. Toilet training was recommended. Children were instructed to attempt defecation 3 times a day, preferably after meals	number of episodes of faecal soiling, pain during defecation, flatulence, and AP per week. All adverse events were recorded.
Closa-Monasterolo (2017)(Closa-Monasterolo, Ferre et al. 2017) (NCT02863848)	To investigate possible benefits of supplementing the daily diet with inulin-type fructans in children with CFC	RCT	17 children aged 2-5 years who were potty trained but who had CFC based on Rome III criteria.	NR	Spain	Primary care / Community / Patient's home Monitoring was carried out in the hospital	Lifestyle: Diet – Sugars (Daily supplementation of inulin-type fructans or the same amount of placebo (maltodextrin) over 6 weeks) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Primary outcome: stool consistency. Secondary outcomes: stool frequency and gastrointestinal symptoms.
Coccorullo (2010) (Coccorullo, Strisciuglio et al. 2010)	The aim of our study was to evaluate the beneficial effects of Lactobacillus reuteri (DSM 17938), one of the few endogenous Lactobacillus species in the human gastrointestinal tract, in infants with functional chronic constipation	RCT	formula-fed infants >6 months of age referred for functional chronic constipation. Infants with organic causes of constipation such as Hirschsprung's disease, spinal bifida (occulta), hypothyroidism or other metabolic or renal abnormalities, and mental retardation, infants taking oral laxatives or antibiotics, and infants who were fed breast milk and formula with the addition of probiotics, prebiotics, or both were excluded. Probiotic or prebiotic food supplements were not allowed through the study period	TYPICAL DEVELOPMENT	Italy	Home	Lifestyle: Diet - Prebiotics /probiotics	Primary outcome measures were frequency of bowel movements per week, stool consistency, and presence of inconsolable crying episodes. Secondary outcome was comparison of the frequency of defecation, stool consistency, and presence of inconsolable crying episodes in the two groups.
Coehlo 2011 (Coehlo 2011)		Other primary study	Single case study			Home	Multi-faceted *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
Cohn (2011) (Cohn 2011)	This article aims to explain some of the physiological and behavioural concepts behind stool withholding, its links with constipation, and appropriate management options.	Other primary study (case studies with CPD learnig outcomes)	Children with constipation	Mixed population	United Kingdom	Unclear	More than one intervention: fibre, fluid and laxatives. Suppositries and enemas. Psychology	NR
Cruchet (2015) (Cruchet, Furnes et al. 2015)	The purpose of this review was to update scientific evidence and grade of recommendation to develop future guidance in the medical use of probiotics in pediatric patients. Three main objectives were established by the working group: 1. To develop evidence-based guidelines for probiotic use in pediatric patients through a critical and comprehensive literature review. 2. To provide a useful tool for probiotic use aimed at general practitioners, pediatricians, and pediatric gastroenterologists. 3. To contribute to the rational clinical use of probiotics in pediatric diseases, supported by scientific evidence.	Narrative review	Children with childhood diseases including: acute infectious diarrhea (AID), antibiotic-associated diarrhea (AAD), traveler's diarrhea, Helicobacter pylori infection, infantile colic, necrotizing enterocolitis (NEC), inflammatory bowel disease (IBD), and functional gastrointestinal disorders; e.g., irritable bowel syndrome (IBS), constipation, and allergy.	UNCLEAR	More than one	Home	Lifestyle: Diet - Prebiotics /probiotics	benefits, tolerability, and safety
CTRI/2017/11/010706 (2017) (CTRI/2017/11/010706 2017)		ON-GOING (RCT)	Plan to enrol children aged between 5 -12 years	Not reported	India	Home	Lifestyle: Diet - Prebiotics /probiotics	
Day (1995) (Day and Monsma 1995)	To gain evaluatory data about the use of Fruitlax as a treatment for constipation in children with disabilities	Other primary study	9 children; aged 3-9 years with a disability: eg. Down's Syndrome, CP. With chronic constipation	ATYPICAL DEVELOPMENT	United States	Primary care / Community / Patient's home	Lifestyle: Diet - Sugars	Stool consistency and colour, average No of stools per day, frequency, No of pharmaceutical used, difficulty to defecate
Dehghani (2012)(Dehgha	To investigate the role of cow's milk allergy as a	RCT	70 children aged between 1-13 years with CFC diagnosed	No	Iran, Islamic Rep.	Seen at the paediatric GI	Diet – cow's milk free diet.	Response was defined as decrease in signs and symptoms using Rome III

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
ni, Ahmadpour et al. 2012)	cause of chronic constipation and effect of cow's milk free diet		using Rome III criteria Children had all previously been given laxatives as frontline treatment with no success.			clinic at the Hospital; intervention delivered at home	(4 weeks cow's milk free diet or no intervention i.e. cow's milk diet alone) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	criteria
Dehghani (2019)(Dehghani, Bahroloolomifard et al. 2019)	To evaluate efficacy and safety of oral intake of black strap molasses syrup (BSM) on FC in children.	RCT	47 aged 4-12 years diagnosed with FC		Iran, Islamic Rep.	Home	Lifestyle: Diet – Sugars Black sugar molasses syrup vs PEG *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Primary outcome = Frequency of bowel habit per week. Secondary outcome = Frequency of painful bowel habit per week. Possible serological side effects
Di Mauro (2013) (Di Mauro 2013)	To investigate if oral supplementation with L.reuteri DSM 17938 during the first three months of life can reduce the onset of colic, GER and constipation in term newborns and thereby reduce the socio-economic impact of these conditions	RCT	Newborn aged 1 week	UNCLEAR	Italy	Home	Lifestyle: Diet - Prebiotics /probiotics	Main outcomes and measures reduction of incidence of colic regurgitation and constipation during the first three month of life, cost benefit of probiotic supplementation.
Elia (2008) (Elia, Engfer et al. 2008)	to evaluate the effect of fibre-supplemented enteral feeds on objective and subjective measures of gastrointestinal function in both healthy volunteers and patient populations.	SR	Subjects eligible for inclusion were healthy volunteers or patients >1 year of age of any nutritional status	UNCLEAR	Netherlands	Home	Other / alternative dietary intake	Both subjective (incidence of diarrhoea/constipation, stool consistency and gastrointestinal symptoms) and objective (transit time, stool weight and bowel frequency) outcome measures were considered.
Fernandes (2018) (Fernandes, Fonseca et al. 2018)	Is Lactobacillus reuteri DSM 17938 effective and safe in childhood pathologies?	ON-GOING (SR PROTOCOL)	All childhood pathologies treatable with Lactobacillus reuteri DSM 17938, such as: asthma, functional constipation, regurgitation, functional abdominal pain, diarrhea, colic and	NOT REPORTED	More than one	Home	Lifestyle: Diet - Prebiotics /probiotics	The results should assess and guarantee efficacy and safety in different pathologies in children

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
			enterocolitis.					
Francavilla (2016) (Francavilla 2016)	In this review, we evaluate the evidence behind the most recent indications/recommendations by Societies and Institutions for the use of probiotics and prebiotics in functional intestinal disorders focusing specifically on those for which a position is available: infant colic, irritable bowel syndrome and constipations.	Narrative review	Children with functional intestinal disorders: infant colic, irritable bowel syndrome and constipations.	UNCLEAR	Italy	Home	Lifestyle: Diet - Prebiotics /probiotics	NOT REPORTED
Franulovic (2013) (Franulovic 2013)	The aim of this study is to investigate whether Lactobacillus reuteri could have a beneficial role in treatment of children and adolescents with Anorexia nervosa who develop motility disorder due to the malnutrition regarding the normalization of the motility, as well as the possible role of probiotics on nutritional recovery, especially on bone health.	RCT	Children and adolescents with Anorexia nervosa and constipation	UNCLEAR	Croatia	Hospital	Lifestyle: Diet - Prebiotics /probiotics	Primary Outcome Measures : Drop out from Rome III criteria for constipation [Time Frame: 3 month] Secondary Outcome Measures : normalization of body weight [Time Frame: 6 month]
Gafencu (2018) (Gafencu 2018)	to evaluate the efficacy and safety of the food supplement Physiomanna Baby® in pediatric patients with a history of functional constipation defined by Rome III criteria; secondary objective was to evaluate the adherence to the tested product in the enrolled children.	Other primary study	infants aged less than 8 years addressed for functional constipation in one community hospital and two private medical practice. To be included in the study, each subject had two or fewer SBM during the previous week and was otherwise in good health as judged by a physical examination at the baseline visit. Cerebral palsy was part of exclusion	NOT REPORTED	Romania	Primary care / Community / Patient's home	Other / alternative dietary intake	Assessment of efficacy consisted of the number of Spontaneous Bowel Movements (SBM) recorded per day and per week; SBM. Safety = the occurrence of any adverse event during the study. Adherence =

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
			criteria. offices located in Timisoara, Romania					
Gomes (2019) (Gomes 2019)	systematic review of literature data on gut microbiota and the efficacy of using probiotics for the treatment of constipation in children and adolescents was performed.	SR	constipation	NOT REPORTED	Brazil	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	changes in fecal microbiota. therapeutic success = Higher bowel movement frequency, improved stool consistency, reduced abdominal pain, reduced pain during bowel movements and flatulence reduction
Guerra (2011) (Guerra 2011)	To evaluate the treatment of pediatric functional chronic intestinal constipation (FCIC) with a probiotic goat yogurt.	RCT	Children aged 5-15 years and with FCIC. Exclusion criteria were the use of any oral laxative < 4 wk before intake, metabolic disease, a history of gastrointestinal surgery and fecal incontinence.	NOT REPORTED	Brazil	EDUCATION (SCHOOL / UNI)	Lifestyle: Diet - Prebiotics /probiotics	Defecation frequency, stool consistency and abdominal and defecation pain were assessed.
Harris (2019)(Harris, Neale et al. 2019)	To critically review and update the evidence on the efficacy of probiotics in the treatment of CFC	SR	1408 (17 RCTs) Included children with CFC	NR	More than one	More than one but most likely home	Lifestyle: Diet - Prebiotics /probiotics Probiotics vs placebo or treatment as usual *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Primary outcomes: differences between probiotic and control groups in defecation frequency and treatment success rates (defined by the authors, acknowledging the current absence of a standardized measure of treatment success in the context of functional constipation. Differences between groups in rates and types of adverse events during treatments were also investigated as a secondary outcome.
Hassanein (2021) (Hassanein, Deifallah et al. 2021)	The therapeutic effect of oral Magnesium sulfate on spasticity and constipation will be studied	RCT	100 children with Cerebal Palsy - Presence of spasticity without joint contracture Spasticity is defined as velocity dependent, increased resistance to passive muscle stretch. Constipation	Yes	Egypt, Arab Rep.	Primary care / Community / Patient's home	Oral magnesium sulfate vs placebo *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	primary = Decrease in muscle tone evaluated by Modified Ashworth Index and constipation ROM-lll criteria. Secondary = Improvement in H/M ratio in H-reflex by electrophysiologic assessmen
Horvath (2013c) (Horvath 2013)	The goal of our study was to assess the efficacy of glucomannan (GNN) as the sole treatment for FGIDs in children.	RCT	The RCT included children aged 7-17 years with abdominal painrelated FGIDs classified according to the Rome IIIdiagnostic criteria (Table 1)[5]. Patients with	NOT REPORTED	Poland	Home	More than one intervention	The primary outcome measures included the proportion of patients with self-reported no pain and that of patients with treatment success, which was defined as no pain or a decrease of ≥ 2/6 points on

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
			organic gastrointestinal diseases (as established by the medical history, complete blood count, urinalysis, stool examination for occult blood, ova and parasites, blood chemistries, abdominal ultrasound, breath hydrogen testing, and endoscopy, if needed), other chronic disease, or growth failure were excluded from the study.					the FACES Pain Scale Revised[15]. The subjective assessment of pain frequency, abdominal cramps, abdominal bloating/gassiness, the number of episodes of nausea or vomiting; changes in stool consistency (loose or constipated stools) during the study were the secondary outcome measures. Furthermore, the frequencies of school absenteeism and changes in daily activities were assessed, as was the percentage of children requiring rescue therapy. Finally, all adverse effects were recorded, and their possible relation to the study product consumption was evaluated. Compliance was assessed by direct questioning of the subjects or their caregivers during clinic visits.
Horvath (2013) (Horvath 2013)	This paper summarises the clinical evidence from randomised controlled trials (RCTs) and their meta-analyses of the effectiveness of probiotics, prebiotics and dietary fibre in the treatment of FGDs (functional gastrointestinal disorders) in the pediatric population.	Narrative review	Paediatric population	NOT REPORTED	More than one	Home	Lifestyle: Diet - Prebiotics /probiotics	Probiotics - In summary, limited available evidence suggests that L. reuteri DSM17938 may help infants with constipation but more studies are needed. Other probiotics studies thus far do not have any effect on functional constipation in children. Dietary fibre - In summary limted evldence suggests that administration of a fibre supplement is more effective than placebo for the treatment of childhood constipation, However GNN adminsitered in sole treatment was not effective.
Horvath (2012) (Horvath 2012)	To systematically evaluate the effect of dietary fibres for treating abdominal pain-related FGIDs in children. Check this reference – should be **Func constip in**	SR	Pain related FGID	NOT REPORTED	More than one	Home	Lifestyle: additional dietary fibre	The primary outcome measure was the rate of responders to the treatment (defined as a clinically meaningful improvement in gastrointestinal symptoms, such as no pain or a decrease in pain intensity/frequency). The secondary outcome

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
	children- 2013							measures were the frequency and intensity/severity of abdominal pain reported by patients or their caregivers and adverse events.
Huang (2018) (Huang 2018)	To conduct a review on microbial treatment in chronic constipation.	Narrative review	CFC	NOT REPORTED	More than one	Home	Lifestyle: Diet - Prebiotics /probiotics	NOT REPORTED
Huang (2017) (Huang 2017)	This study reviewed the existing literatures of 6 Randomized Control Trials (RCTs) to ascertain some baseline understanding and available information for the effects of probiotics on stool frequency and consistency in children with constipation	SR	Evaluated children aged ≤ 18 years with constipation	Unclear	More than one	Home	Lifestyle: Diet - Prebiotics /probiotics	Reviewers only extracted data for stool frequency and stool consistency
Iacono 1995 (Iacono, Carroccio et al. 1995)	to ascertain whether there is a relation between chronic constipation and CMPA. Cow milf protein allergy	Other primary study (Cohort)	The study group included all the patients with chronic constipation, aged <3 years, referred to our pediatric gastroenterology clinic during the preceding 12 months. Two patients with mental retardation and one with Hirschsprung disease were excluded.	TYPICAL DEVELOPMENT	Italy	Home	Other / alternative dietary intake *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	cure or improvement of CFC
Iacono 1998 (Iacono, Cavataio et al. 1998)	comparing the effects of cow's milk and soy milk in children with chronic constipation. We hypothesized that intolerance of cow's milk can cause severe perianal lesions with pain on defecation and consequent constipation and that, in such cases, a diet free of cow's milk can rapidly resolve both the constipation and related	RCT (Cross-over)	patients under six years of age with chronic constipation. The exclusion criteria were anatomical causes of constipation (Hirschsprung's disease, 1 case; spinal disease, 2 cases), constipation due to another disorder (hypothyroidism, 2 cases; psychomotor retardation, 4 cases), prior anal surgery (2 cases), use of medications that can cause	TYPICAL DEVELOPMENT	Italy	Home	Other / alternative dietary intake (Cow's milk vs soy milk) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	response to intervention

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
	disorders		constipation (chlorpromazine, 1 case), and referral for reasons other than chronic constipation (41 cases). They were all being fed full-fat cow's milk, dairy products, or commercial formulas derived from cow's milk. Previous treatment with laxatives (mainly lactulose and mineral oil) had been unsuccessful in all 65 patients.					
Infante (2011)(Infante, Segarra et al. 2011)	To analyse stool composition and parental assessment of constipation symptoms in infants who received an adapted anti-constipation formula designed to reduce hard stools.	Other primary study	30 constipated formula-fed infants aged 4-10 weeks. All infants were full-term and had a normal birth weight (> 3.100 kg)	No	Spain	Primary care / Community / Patient's home Study was co-ordinated and conducted by Gastroenterology unit at Children's Hospital	Diet – different milk formula. (Novalac AE (IT) (United Pharmaceuticals SA, France) for 2 weeks) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Assessed stools for faecal fat, water, carbohydrates, and protein. Other outcomes included: crying during defecation, stool consistency and need for help with defecation was assessed.
Infante Pina (2008) (Infante Pina, Badia Llach et al. 2008)	To assess the prevalence of mild gastrointestinal disorders (MGD) in milk-fed infants in paediatric practice, and to evaluate the effectiveness and satisfaction with dietetic treatment.	Other primary study	3487 infants < four months of age seen in the clinic for any reason, during a period of one week. The infants of the cross-sectional study presenting MGDs with artificial milk formulas, and who according to medical criterion could be fed with the Novalac range of formulas were enrolled	NR	Spain	Multi-centre study involving 285 paediatricians throughout Spain (except Ceuta and Melilla) participated in the study, under real-world conditions of clinical practice	Diet – different milk formula. (Novalac milk formula) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Effectiveness of the various Novalac formulas, as well as the satisfaction of the parents/tutors and paediatricians with the dietetic treatment was assessed at the final visit (week 4). Specific constipation outcomes included: number of stools/days, consistency, irritability, need for external help to defecate.
Inoue (2019) (Inoue, Sakaue et al. 2019)	to evaluate the effect of prebiotic PHGG (Partially hydrolyzed guar gum) supplementation with no		children with autism spectrum disorders who presented constipation symptoms. - outpatient children	ATYPICAL DEVELOPMENT	Japan	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	defecation frequency, behavioral symptoms, concentrations in serum of cytokines IFN-a, IL-1b, IL-6, IL-10, IL-12p70 and TNF-a and chemokines IP-10,

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
	food intervention on constipation and gut dysbiosis symptoms and behavioral irritability in ASD children.		with ASD living in similar geographic regions in Japan					I-TAC and MIG were simultaneously measured
IRCT13881222 2434N (2015) (IRCT1388122 22434N3 2015)	The comparison between effect polyethylene glycol (PEG) Along with Bacillus coagulans (probiotic) with effect polyethylene glycol (PEG) in treatment of functional constipation in Childrens referred to pediatric gastroenterology clinic of Shiraz University of Medical Sciences	ON-GOING (RCT)	Inclusion criteria:All pediatric patient with constipation that fulfilled Rome III criteria for functional constipation without any treatment;All pediatric patient with constipation that fulfilled Rome III criteria for functional constipation without clinical response to polyethylene glycol (PEG) Exclusion criteria:patients received other drugs for constipation except polyethylene glycol (PEG); The presence of organic cause;	NOT REPORTED	Iran, Islamic Rep.	Home	Lifestyle: Diet - Prebiotics /probiotics	primary outcome - Abdominal pain. Pain on defecation. Stool consistency. Stool frequency. Stool incontinence. Secondary outcomes = Drug adverse effects and clinical response. Evaluation of clinical response of pain during defecation. . Evaluation of Clinical response on Fecal incontinence. Evaluation of Clinical response on abdominal pain. Evaluation of Clinical response on stool Consistency. Evaluation of Clinical response on stool frequency.
IRCT20101227 5479N1 (2011) (IRCT2010122 75479N1 2011)	Determination of the effects of toilet training in the treatment of functional constipation in children	ON-GOING (RCT)	children between 3- 12. Children younger than 3 or older than 12 years, any causes of disability, physical or mental, any systemic diseases will be excluded	No additional support needs	Iran, Islamic Rep.	Home	Education and information provision	Questionnaire: toilet use (daily); Rate of painful defecation; soiling of underwear, laxative use, suppository use.
IRCT20130211 12437N (2017) (IRCT2013021 112437N1 2017)	Comparison the effects of Psyllium seed husk powder Vs. Polyethylene glycol with and without probiotics in functional constipation of 2- to 10-year-old children	ON-GOING (RCT)	children who refer to children's clinic of Shahid Beheshti hospital with functional constipation, diagnosed based on the ROME III criteria. Exclusion criteria: Children beyond 2 and over 10 years old; use of other drugs that can cause constipation or diarrhea; or history of using pidrolax and probiotic in the last year.	NOT REPORTED	Iran, Islamic Rep.	Home	Lifestyle: Diet - Prebiotics /probiotics	primary outcomes = Adverse effects of drugs. Defecation frequency. Defecation incontinency. Defecation without pain. Drug admission. Secondary outcome = Early constipation relapse discontinue medication
IRCT20131006	Comparison the effects of	ON-	Inclusion criteria: functional	UNCLEAR	Iran, Islamic	Home	Lifestyle: Diet - Sugars	Primary outcome = Visual Analogue

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
014915N3 (2018) (IRCT2013100 6014915N3 2018)	syrup of Zyzyphus jujube and Pidrolax Glycol in treatment of 2-10 years Children with Functional Constipation referred to 17-Shahrivar Hospital	GOING (RCT)	constipation age between 2-10 years		Rep.			Scale. Secondary outcome = Pediatric functional constipation scale
IRCT20131204 15530N3 (2015) (IRCT2013120 415530N3 2015)	Comparison of two treatment regimens of powders and syrup of polyethylene glycol 40% in the treatment of chronic functional constipation in children under 15 years [MOVE TO LEVEL 1]	ON-GOING (RCT)	Inclusion criteria: history of large-diameter stools; Record keeping stools Exclusion criteria: children with organic constipation; Obstructive abnormality or anorectal anorectal surgery; ROME III criteria identify children who have irritable bowel syndrome; Children over 2 weeks before entering the study received treatment for constipation; Children with mental retardation or metabolic diseases such as hypothyroidism; Children with Hirschsprung's disease or spinal cord anomalies or pathology anorectal	UNCLEAR	Iran, Islamic Rep.	Home	More than one level 0 intervention delivered by carers prior to HCP involvement	Defication.
IRCT20140901 5330N7 (2014) (IRCT2014090 15330N7 2014)	Effect of probiotics in children constipation	ON-GOING (RCT)	History of childhood constipation ; Ranged in age from 2 to 16 years Exclusion criteria include: There is an organic cause for constipation; A drug that affects the bowel movements; Obstruction or stenosis of the gastrointestinal tract	NOT REPORTED	Iran, Islamic Rep.	Home	More than one level 0 intervention delivered by carers prior to HCP involvement	primary outcome = Defecation frequency more than 3 times in a week and stool consistency. Secondary outcome = Faecal incontinence episodes less than one time in a week
IRCT20150617 22794N1 (2015) (IRCT2015061 722794N1 2015)	To compare efficacy of brown sugar syrup and poly ethylene glycol (PEG) for treatment of constipation in children	ON-GOING (RCT)						
IRCT20171213 037866N	Comparison of that effects of Zizyphus Jujuba Fruit's	ON-GOING	Inclusion criteria: Age between 2–12 years old and	NOT REPORTED	Iran, Islamic Rep.	Home	Lifestyle: Diet - Sugars	Primary outcomes = Frequency of defecation per week. Frequency of drug

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
(2018) (IRCT2017121 3037866N1 2018)	product and Pidrolax in the Childhood Functional Constipation which referred to Rasoul Akram Clinic	(RCT)	presence of Functional Constipation based on ROME IV Exclusion criteria: Any symptom of organic constipation in the history, physical examination or para clinics (such as hypothyroidism, Hirschsprung disease, chronic intestinal pseudo-obstruction) and the presence of other chronic diseases that lead to long-term use of drugs and long-term consumption of any drug that can cause constipation.					adoption by the child per week. Frequency of fecal incontinence per week. The frequency of hard stool in a week. The frequency of painful defecation in the week. The frequency of side effects in weeks.
IRCT20180910 040992N1 (2018) (IRCT2013120 415530N3 2015)	Rosa damascena							
IRCT20190122 042459N3 (IRCT2019012 2042459N3 2019) (2019)	The effect of whey in the treatment of functional constipation in children aged 1 to 16 years old	ON-GOING (RCT)	Inclusion criteria: Age 1 to 16 years chronic functional constipation for at least two months Based on Rome IV Criterion. Exclusion criteria: Patients who have been diagnosed with a history of organic constipation Patients with neurological disorder History of Anorectal Surgery Patients who have taken medication more than six months before the study Patients who use a drug other than pidrolax	UNCLEAR	Iran, Islamic Rep.	Home	Other / alternative dietary intake	Primary outcomes = Stool consistency. Times of defication.
Jadresin (2018)(Jadresin 2018)	To investigate the role of Lactobacillus reuteri DSM 17983 in the treatment of	RCT	33 children aged 2-13 years referred to a paediatric gastroenterologist for CFC	NR	Croatia	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics *This study is included in the*	Primary outcomes: frequency of BM, change of the frequency of BM, and presence of

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
	CFC						*effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	symptoms at the end of the study. Secondary outcomes: need for lactulose at the end of the treatment, dose of the lactulose used, number of days with soiling, and stool consistency
Jin (2018) (Jin 2018)	To evaluate the effect of probiotic supplementation on functional constipation in children.	SR	CFC	NOT REPORTED	China	Home	Lifestyle: Diet - Prebiotics /probiotics	primary outcome was treatment success, which was defined as ≥3 spontaneous bowel movements (sBMs) per week with no fecal soiling, and the secondary outcomes were sBMs per week, fecal soiling episodes per week, straining and pain during defecation, use of lactulose, glycerin enema, and laxatives, abdominal pain, fecal incontinence, flatulence, and adverse events.
JPRN-UMIN000034508 (2018) (JPRN-UMIN000034508 2018)	Examination of the diet cure for the pediatric constipation - assessment of the dietary fiber intake and the cow's milk allergy -	RCT	CFC. Exclusion criteria: 1) Gastroenterological surgical disease before radical operation 2) Food allergy 3) Neurological impaired patients 4) Epilepsy 5) Users of Histamine H1 receptor antagonist 6) Gastroenteritis	UNCLEAR	Japan	Home	Other / alternative dietary intake	Primary outcomes = Defecation frequency without enema. Secondary outcomes = Bristol stool scale Madication. Enema use frequency. Dietary intake state. Fecal microbiotia Completed (11 participants recruited). Results posted online May 2022 (in Japanese: https://www.pref.gunma.jp/contents/100201634.pd)
JPRN-UMIN000034818 (2018) (JPRN-UMIN000034818 2018)	Analysis of the efficacy of brown rice-specific gamma-oryzanol for children with constipation	RCT	Inclusion criteria: Patients who meet the criteria for chronic functional constipation disease Exclusion criteria: Decision of ineligibility by a physician	NOT REPORTED	Japan	OTHER (STATE)	Other / alternative dietary intake	Primary outcomes = Intestinal microbiota at 1 month. Secondary outcomes = Short chain fatty acids (Acetic acid, butyric acid, propionic acid, valeric acid) in serum. Symptoms of constipation
Khatibshahidi (2013) (Khatibshahidi 2013)	Comparison of Brown Sugar and PEG in the treatment of functional constipation in children admitted to Children`s Medical Center of Imam Khomeini Hospital	Other primary study	Children with functional constipation. Careful medical examination of the patient before treatment was applied and other types of constipation pediatric gastroenterologist diagnoses were excluded.	UNCLEAR	Iran, Islamic Rep.	Home	Lifestyle: Diet - Sugars	After completion of medication period, medical condition of patients has been examined in order to compare with patient's medical conditions before the treatment.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
Koppen (2016) (Koppen 2016)	To investigate the efficacy and safety of pre-, pro- and synbiotics in the treatment of pediatric functional constipation (FC).	SR	Children with functional constipation	NOT REPORTED	Netherlands	Home	Lifestyle: Diet - Prebiotics /probiotics	defecation frequency, fecal incontinence, painful defecation, difficulty with defecation, abdominal pain, quality of life or possible harm from treatment (tolerance, adverse effects).
Korterink (2014) (Korterink 2014)	A systematic review and meta-analysis were performed to investigate the quantity and quality of the current evidence regarding the effect of different probiotic strains in the treatment of functional gastrointestinal disorders (FGID) in children and adolescents.	SR	Chidlren and adolescents with functional gastrointestinal disorders (FGID)	UNCLEAR	Netherlands	Home	Lifestyle: Diet - Prebiotics /probiotics	Primary outcome was treatment success, defined as the absence of, or a reduction of, abdominal pain (decrease in intensity or frequency of pain) or an improvement in stool pattern (defecation at least three times per week and no faecal incontinence or episodes of faecal incontinence less than one time in 2 weeks). Secondary outcome measures were abdominal pain (frequency/intensity), stool pattern (defecation frequency/stool consistency), bloating/flatulence and adverse events.
Kranz (2012) (Kranz 2012)	This paper summarizes the currently existing evidence on the implications of dietary fiber intake on constipation, obesity, and diabetes in children.	OTHER (PLEASE SPECIFY)	Children with constipation, obesity, or diabetes	NOT REPORTED	United States	Home	More than one level 0 intervention delivered by carers prior to HCP involvement	NOT REPORTED
Kubota (2020) (Kubota, Ito et al. 2020)	To evaluate the efficacy of the probiotic Lactobacillus (L.) reuteriDSM17938 and magnesium oxide (MgO) for relieving CFC	RCT	60 children with CFC aged > six months old or <six years of age, with a diagnosis of CFC according to the Rome IV criteria.	NR	Japan	Paediatric outpatient clinics / Home	Lifestyle: Diet - Prebiotics /probiotics (L. rueteri DSM 17938 and lactose hydrate vs L. rueteri DSM 17938 and MgO and lactose hydrate vs placebo) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Primary outcome: change in defecation frequency. Secondary outcomes: change in the stool consistency score, changes in the gut microbiome profiles.
Maffei (2011) (Maffei 2011)	The aim of the study was to evaluate, over 24months,theintake of dietary fiber (DF) and the bowel habit (BH) of constipated children	Other primary study	Children with functional constipation	NOT REPORTED	Brazil	Home	Lifestyle: additional dietary fibre	At each visit the BH was rated BAD (worse/unaltered; improved but still complications) or RECOVERY (REC) (improved, no complications; asymptomatic), and a food intake questionnaire was applied. DF intake

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
	advised a DF-rich diet containing wheat bran							was calculated according to age(year)þ5to 10g/dayandbranintakeaccordingto international tables.
Mahdavi (2017)(Mahdavi, Esmaeili-Dooki et al. 2017) IRCT2015072723363N1	This study aimed to determine effects of synbiotics on treatment of CFC	RCT	79 children aged between 2- and 10-year-old diagnosed with CFC according to the Rome III criteria.	NR	Iran, Islamic Rep.	Referred to the hospital for assessment but the intervention is likely to be delivered at home	More than one level intervention delivered: Fibre *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19* Synbiotic + PEG 0.6 gr/kg daily for 4 weeks followed by only PEG for the following four weeks vs PEG alone for 8 weeks	Primary outcome: BM / week, incontinency per week, withholding per week, stool consistency, pain during defecation, acceptance of the drug, and the side effects Secondary outcomes: frequency of defecation, stool consistency and the need for the continued use of anti-constipation drugs
Mazzoni (2017) (Mazzoni, Navarra et al. 2017)	To determinate the role of not-pharmacological therapy (dietary rules and behavioural rules) in treatment of childhood functional constipation.	Other primary study	52 children with CFC	NOT REPORTED	Italy	Home	More than one level 0 intervention delivered by carers prior to HCP involvement (Dietary and behavioural rules) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	The consistency of stools has been evaluated after 8–12 weeks through the Bristol stool chart.
McCartney (2011) (McCartney 2011) ISRCTN04516575	To examine whether feeding a probiotic called Lactobacillus plantarum WCFS1 can change the gut bacteria in ASD children (to be more like that on non-ASD children) and/or reduce gut symptoms	RCT On-going	1. Children / adolescents with clinical diagnosis of ASD 2. Children with gut problems (minimum of 3 episodes in the last 6 months)	ATYPICAL DEVELOPMENT	United States	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	Primary - 1. To use multiple molecular techniques to investigate whether probiotic (Lactobacillus plantarum WCFS1) supplementation can modulate the gut microbiota associated with ASD 2. Particular interest will focus on quantification, and changes in the diversity and dynamics of lactic acid bacteria and clostridia. Secondary - 1. Can probiotic (Lactobacillus plantarum WCFS1) supplementation alleviate the gastrointestinal symptoms commonly suffered by ASD children? 2. Does probiotic (Lactobacillus plantarum WCFS1) supplementation

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
								affect the behaviour of ASD child? 08/04/2019: The trial was stopped due to recruitment delays, funding restrictions and remaining time frame of research staff positions. 14/02/2018: No publications found in PubMed, verifying study status with principal investigator. 18/12/2015: No publications found in PubMed
Modaresi Saryazdi 2013 (Modaresi Saryazdi 2013)		RCT	58		Iran	Home	PEG and senagol syrup, plus paraffin oil, daily (plus high fibre diet) vs PEG and senagol syrup daily (plus high fibre diet *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	
Mosca (2018) (Mosca 2018)	To describe the dietary management of constipated children between the age of one and two and to assess the impact of fiber enriched formula (FEF) on constipation at the age of two in real life settings	Other primary study	constipated children between the age of one and two	NOT REPORTED	France	Home	Lifestyle: additional dietary fibre	NOT REPORTED
Mozaffarpur (2012) (Mozaffarpur 2012)		RCT			Iran	Home	Lifestyle: Diet - Sugars	
Nanji (2012) (Nanji, Ahmed et al. 2012)	The primary objective is to evaluate the efficacy and safety of fiber and bulking agents for the treatment of chronic constipation	ON-GOING (SR PROTOCOL)	Subjects of any age with symptoms of chronic constipation as defined by the included studies will be considered for inclusion	NOT REPORTED	Pakistan	Unclear	More than one level 0 intervention delivered by carers prior to HCP involvement	Primary outcomes The primary outcomes will include: • The proportion of patients with improvement in stool frequency as defined by the included studies; and • The proportion of patients with global improvement in symptoms. Secondary outcomes Secondary outcomes will include: • The proportion of patients experiencing three or more spontaneous bowel movements per week; • Proportion of patients achieving bowel evacuation at defecation; •

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
								Proportion of patients with bowel movements of normal consistency; • Proportion of patients with relief of abdominal pain; • Quality of life; and • Adverse events including: the proportion of patients who experienced any adverse event, serious adverse events, and withdrawal due to adverse events.
Navarro (2016) (Navarro 2016)	to synthetize current data on the association between microbiota dysbiosis and autism, and to assess if its modification could have a beneficial effect in children with autism.	Narrative review	Children with ASD and gastrointestinal symptoms	ATYPICAL DEVELOPMENT	United States	Primary care / Community / Patient's home	More than one level 0 intervention delivered by carers prior to HCP involvement	symptoms and behavior
NCT01333787 (2011) (NCT01333787 2011)	To evaluate the therapeutic effect of a fibers mixture in the treatment of chronic constipation and on the colonic transit time in children	ON-GOING (RCT)	The children having attended the Pediatric Gastroenterology Ambulatory of the Federal University of Sao Paulo and the Santa Casa de Misericórdia hospital in Sao Paulo city. All of the children were undergoing constipation maintenance treatment with the use of a laxative in a dosage less than 1.0 ml/Kg for milk of magnesia, mineral oil or lactulose or less than 0.5 g/Kg for polyethylene glycol 3350	NOT REPORTED	Brazil	Home	More than one level 0 intervention delivered by carers prior to HCP involvement	The primary outcome result measurement was the therapeutic success. This therapeutic success was considered when the patient demonstrated daily evacuations or had interposing days of pasty consistency, without pain or difficulty and the absence of fecal incontinence during the 4 weeks of intervention, without the need of using a laxative or rectal enema. Secondary outcomes = Frequent daily evacuations, format and consistency of the feces, total and segmental transit time
NCT01388712 (2011) (NCT01388712 2011)	primary aim of the study is the assessment of Lactobacillus reuteri DSM 17938 efficacy, provided with macrogol (Forlax), as treatment of constipation in 3-7 years old children. econdary aim of the study is the assessment of	ON-GOING (RCT)	Inclusion Criteria: Children 3-7 years old. Occurrence less than three bowel movement per week. Medical history from at least two months] Ineffective laxative treatment at least two months. Exclusion Criteria: Well-known,	NOT REPORTED	Poland	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	primary outcome = Number of bowel movement per week, without fecal incontinence. Secondary outcome = The number of bowel movements per week [Time Frame: 12 weeks] Other secondary items are: the number of pain episodes during defecation per week, the number of hard stools, the number of fecal incontinence per week,

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
	frequency the additional symptoms connected with defecation disorders: such as: number of pain episodes during defecation, the intensity of pain, number of hard stools, number of fecal incontinence per week, number of macrogol (Forlax) pockets used		organic cause of constipation (i.e. hypothyroidism, Hirschprung disease, cystis fibrosis) . Anatomic defects of the alimentary canal. The surgery of the alimentary canal in the past Treatment of antibiotics/probiotics during last two weeks before start of the study					the number of patients who have to change amount of drug or use of enema.
NCT01629147 (2012) (NCT01629147 2012)	Tto evaluate Lactobacillus reuteri (Biogaia) for treatment of chronic constipation in children 4-10 years of age, and to examine the influence of Lactobacillus reuteri (Biogaia) on constipation in different age groups of school aged children between 4-10 yrs of age.	ON-GOING (PRIMARY)	CFC, Normal Thyroid function test and negative celiac serology (IgA or IgG in patients with IgA deficiency), and no evidence of elevated RAST test for milk.	NOT REPORTED		Home	Lifestyle: Diet - Prebiotics /probiotics	primary = Increase in stool number/week to at least 4 bowel movements. Secondary = Improved stool consistency, Improved defecation pain
NCT01901445 (2013) (NCT01901445 2013)	Quality of Life in Children and Adolescents With Chronic Functional Constipation: Educational Action Effects	ON-GOING (RCT)	CFC	NOT REPORTED	Brazil	Home	Information	Primary - The improvement in the quality of life on participants after the intervention [Time Frame: 3 months]. Secondary - The improvement in clinical parameters of chronic functional constipation [Time Frame: 3 months]
NCT01913665 (2013) (NCT01913665 2013)	to asses the effect of Bifidobacterium lactis and Inulin on functional constipation in children	ON-GOING (RCT)	CFC	NOT REPORTED	Turkey	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	to compare defecation frequency between baseline and 4 th week of treatment
NCT01985867 (2013) (NCT01985867 2013)	Effectiveness of Lactobacillus Casei Rhamnosus Lcr35 in the Management of Children With Functional Constipation:	ON-GOING (RCT)	Functional constipation according to Rome III criteria	NOT REPORTED	Poland	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	Primary = treatment success (≥3 spontaneous defecations per week with no fecal soiling), Secondary = stool consistency (with the use of the Bristol Stool Scale Form), stool frequency, fecal soiling episodes, pain during defecation, abdominal pain and/or flatulence, use of laxatives, adverse effects, fecal microbiological sampling (global evolution of Lactobacillus and Bifidobacterium)
NCT02193997	To examine the effects of	ON-						

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
(2014) (NCT02193997 2014)	dietary fiber in treating functional childhood constipation	GOING (RCT)						
NCT02383758 (2015) (NCT02383758 2015)	The purpose of this study is to try to treat bowel movement (BM) accidents differently with children with autism spectrum disorder (ASD). The study will use over-the-counter (OTC) medications to evoke predictable bowel movements.	ON-GOING (RCT)	Confirmed diagnosis of autistic spectrum disorder using the Social Communication Questionnaire (SCQ) and the Childhood Autism Rating Scale II (CARSII) Clearance from gastroenterologist for use of glycerin suppository, bisacodyl suppository and senna	ATYPICAL DEVELOPMENT	United States	Home	More than one level 0 intervention delivered by carers prior to HCP involvement	Primary = Percent Continent (The percentage of participant's with continent bowel movements (control of passage of stool from the bowel). Secondary = Percent independence is the percentage of independent bowel movements recorded by a caregiver. Mean Clinical Global Impression for Severity (CGI-S) Score, Mean Clinical Global Impression for Improvement (CGI-I) Score
NCT03030664 (2017) (NCT03030664 2017)	Testing the Effect of L. Reuteri on Bowel Movements in Children Aged 6 Months to 4 Years	ON-GOING (RCT)	functional constipation, as defined by modified Rome III criteria for children	NOT REPORTED	France	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	Primary = Change in number of spontaneous bowel movements. Secondary = Total number of rescue medication during the intervention period, number of subjects with 3 or more than 3 stools per week and without fecal retention at the last week of the intervention period, weekly number of spontaneous bowel movements Score of quality of life, Score of pain during defecation
NCT03117322 (2017) (NCT03117322 2017)	Efficacy of the Supplementation With a Symbiotic, a Prebiotic and a Probiotic to Produce a Beneficial Effect on the Intestinal Microbiota and on the Characteristics of Feces in Children With Cerebral Palsy (CP) and Chronic Constipation	ON-GOING (RCT)	Participants attending the outpatient of nutrition and/or pediatric neurology with cerebral palsy diagnosed and confirmed by a pediatric neurologist, and that belong to levels IV or V of the Gross Motor Function Classification System (GMFCS). Participants with constipation according to the Rome IV criteria.	ATYPICAL DEVELOPMENT	Mexico	Home	Lifestyle: Diet - Prebiotics /probiotics	cerebral palsy specific
NCT03333070 (2017) (NCT03333070	The Use of Lactobacillus Reuteri in Functional Constipation in Children:	ON-GOING (RCT)	Diagnosis of functional constipation according to Rome IV criteria	NOT REPORTED	Israel	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	primary = The prevalence of constipation recurrence. failure of maintaining normal bowel movements

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
2017)								without PEG and the need to resume PEG treatment. Secondary = The number of bowel movements per week, The number of episodes of fecal incontinence per week, The stool consistency in patients without PEG treatment.
NCT03639142 (2018) (NCT03639142 2018)	Dried Plums (Prunes) vs. Polyethylene Glycol 4000 for Treatment of Functional Constipation in Children	ON-GOING (RCT)	children with constipation diagnosed with ROME IV criteria	NOT REPORTED	Poland	Primary care / Community / Patient's home	Lifestyle: Diet - Sugars	Primary = treatment success (≥3 spontaneous stools per week, without episodes of fecal soiling (in toilet-trained children). Secondary = stool consistency, frequency of defecation per week . frequency of fecal soiling per week , frequency of pain during defecation per week, frequency of abdominal pain or flatulence per week, need for intake of additional laxative treatment during whole study period, adverse events
NCT03821532 (2019) (NCT03821532 2019)	to assess compliance in pediatric patients with functional constipation that have been provided a constipation action plan plus educational information. The secondary objectives are to assess improvement of constipation symptoms in pediatric patients with functional constipation that have been provided a constipation action plan and educational information and to assess the perceived effectiveness of the constipation action plan from the viewpoint of the family	ON-GOING (RCT)	Inclusion Criteria: Healthy, History of functional constipation, English as primary language Exclusion Criteria: History of medical conditions pre-disposing to constipation, English as a second language, Chronic gastrointestinal disease	TYPICAL DEVELOPMENT	United States	MORE THAN ONE CATEGORY	Education and information provision	Primary = Compliance Questionnaire (Evaluate compliance using the constipation/adherence questionnaire. The questionnaire has 3 questions addressing the total number of days missed per week taking the prescribed medications, toilet sit times and dietary intake) at screening, 1 onth and 3 months. Compliance Reward Chart - at 3 months. Secondary = positive constipation symptoms at 3 time points, Perceived effectiveness at 2 time points, Caregiver Literacy at 0 months
NCT03941925 (2019) (NCT03941925 2019)	to confirm the effectiveness of chicory-derived prebiotic inulin-type fructans on bowel function in young	ON-GOING (RCT)	Diagnosis of functional constipation following ROME4 criteria. Subject is otherwise healthy	UNCLEAR	China	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	Primary = Stool consistency. Secondary = Stool frequency, Stool amount and stool colour. Treatment success, Faecal microbiota, Faecal Short Chain Fatty

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
	children.		at the time of pre-examination.					Acids concentration, Faecal pH
NCT04028258 (2019) (NCT04028258 2019)	Effect of a Mixture of Plant-based Fibers and Carbohydrates on Intestinal Transit in Children Aged 3 to 12 Diagnosed With Functional Constipation	ON-GOING (RCT)	Diagnosis of functional constipation according to Rome IV criteria	NOT REPORTED	Spain	MORE THAN ONE CATEGORY	Lifestyle: additional dietary fibre	Primary = Percentage of clinical change obtained from the difference between the initial value and the final value for a combined score of the frequency of passage of faeces, pain to defecation, consistency of stool. Secondary = Consistency of stool, Valuation of stool characteristics (Bristol scale), Frequency of stool, Change in stool weight, Gastrointestinal symptoms related to the constipation, Record in the patient's dairy all the gastrointestinal symptoms during the study, Adherence record to the complement intake, Patient anthropometric measures: weight, size, waist perimeter
NCT04282551 (NCT04282551 2020)	To study the effects of oligosaccharides vs a placebo on the change in stool consistency and stool frequency in children with functional constipation	ON-GOING (RCT)						
NCT04262648 (2020) (NCT04262648 2020)	To assess clinical effects of probiotics Lactobacillus Reuteri NCIMB 30351 drops on the symptoms of infantile colic, constipation, diarrhea, gastroesophageal reflux, atopic dermatitis/eczema in full-term newborns during the first months of life, laboratory parameters of microbiome will also be assessed.	ON-GOING (RCT)	Parents / guardians speak Russian, Vaginal delivery. Full-term newborn. Breast- and formula-fed infants. Colic , constipation , diarrhea, regurgitation (single symptom or combination of several symptoms).	UNCLEAR	TBC	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	Primary = Change in the number of infantile colics. Secondary = Change in the number of constipations, Change in the number of diarrhea cases, Change in the number of gastroesophageal reflux (posseting) cases, Presence of skin symptoms of food allergy, Change in 16S RNA sequencing, Change in concentrations of stool carbohydrates, Change in concentrations in stool filtrate of volatile fatty acids,
Nouraei (2012) (Nouraei 2012)	not stated	Narrative review	neonates with watery acute diarrhoea, antibiotic-induced diarrhea, atopic dermatitis, functional chronic abdominal pain, constipation	UNCLEAR	Iran, Islamic Rep.	Home	Lifestyle: Diet - Prebiotics /probiotics	UNCLEAR

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
			and necrotizing enterocolitis					
Orel (2013) (Orel 2013)	reviews clinical studies on the effectiveness of Lactobacillus reuteri in the therapy of FGIDs in infants, children and adolescents.	Narrative review	FGID	UNCLEAR	Slovenia	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	Primary outcome measures were the frequency of bowel movements per week, stool consistency, and presence of inconsolable crying episodes, recorded by parents.
Orel (2016) (Orel 2016)	current literature pertaining to the clinical effects of the use of prebiotics for the treatment and prevention of some common pediatric pathology such as infantile colic, constipation, absorption of minerals, weight gain, diarrhea, respiratory infections, and eczema is reviewed.	Narrative review	constipation	NOT REPORTED	Slovenia	Home	Lifestyle: Diet - Prebiotics /probiotics	stool consistency and stool frequency
Paruzynski (2019) (Paruzynski 2019)		Other primary study				Home	Lifestyle: additional dietary fibre	
Parzecka (2012) (Parzecka 2012)	To assess the efficacy of different strains of probiotic bacteria used in the treatment of functional constipation along with dietary and/ or pharmacological interventions.	Other primary study	221 patients ages from 6 weeks to 18 years, who were hospitalised in the clinic of pedicatrics, allergology and gastroenterology and remained under the care of the outpatients' gastroenterological clinic in the years 2008-2009 due to functional constipation.	UNCLEAR	Poland	Home	Lifestyle: Diet - Prebiotics /probiotics	More frequenct defecation, improved stool consistency, less episodes of undergarments soiling, and less painful defecation during the first 3 months of treatment were considered as the indicators of improvement.
Paul, Siba Prosad, Dewdney, Cathy and Lam, Candy (2012) (Paul 2012)	This article focuses on the medical management of functional constipation and outlines some of the non-medical strategies which may help in the overall improvement of the condition. These include dietary modifications and	Narrative review	CFC	NOT REPORTED	United Kingdom	NR but likely to be home	More than one level 0 intervention delivered by carers prior to HCP involvement	strategies which may help in the overall improvement of the condition.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
	instigating a 'table-to-toilet' routine.							
Persels (2016) (Persels and Goldman-Luthy 2016)	An overview of management and prevention of constipation in children with tips for families	Narrative review	Children with constipation	U	More than one	More than one	More than one intervention: clean out and maintenance therapy	NA
Piccoli De Mello (2018)(Piccoli de Mello, Eifer et al. 2018)	To examine the current evidence on the use of fibers in the treatment of CFC	SR	9 RCTs (680 children aged between 1- 18 years with CFC)	NR	Brazil	Primary care / Community / Patient's home	More than one level 0 intervention and intervention at level 1 Compared fibre vs placebo vs laxative *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Outcomes were not explicitly stated. But the review reported results from the following outcomes: bowel movement frequency, stool consistency, therapeutic success, FI, and AP.
Quitadamo (2012) (Quitadamo 2012)	s To compare the effectiveness of a mixture of acacia fiber, psyllium fiber, and fructose (AFPFF) with polyethylene glycol 3350 combined with electrolytes (PEG+E) in the treatment of children with chronic functional constipation (CFC); and to evaluate the safety and effectiveness of AFPFF in the treatment of children with CFC.	RCT	All children aged between 4 and 10 years who were referred to the Pediatric Clinics of the participant centers for CFC from January 2010-June 2010 were eligible for the study. The diagnosis of CFC, as defined by the Rome III Criteria, was considered as having at least 2 out of the following symptoms: 2 or fewer defecations per week, at least 1 episode per week of fecal incontinence after the acquisition of toileting skills, history of excessive stool retention, painful or hard bowel	TYPICAL DEVELOPMENT	Italy	Home	Lifestyle: additional dietary fibre	Outcomes The primary outcome measure was the improvement of constipation, defined as: $3 bowel movements per week, $2 stool consistency grade on BSFS, absence of fecal incontinence, abdominal pain, pain on defecation, and fecal bleeding. Secondary outcome measures were: improvement of other associated gastrointestinal symptoms, such as nausea, vomiting, and flatulence, safety profile, and patient’s acceptance and compliance. Adverse Effects During each visit, patients and their parents were questioned

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
			movements, presence of a large fecal mass in the rectum, and history of large-diameter stools.30 Children with organic causes of defecation disorders, including Hirschsprung disease, spinal bifida (occulta), hypothyroidism or other metabolic or renal abnormalities, mental retardation, and children using lactulose or other laxatives, prebiotics or probiotics, in the previous 4 weeks before the first visit were considered not eligible.					with respect to diarrhea, ease of passage of stool, cramps, flatus, or any other possible adverse effects.
RBR-2x8wqc (2015) (RBR-2x8wqc 2015)	Randomized clinical trial double-blind efficacy of Prebiotics in Chronic Constipation Functional in infants	ON-GOING (RCT)				Home	More than one level 0 intervention delivered by carers prior to HCP involvement	
Ribiero (2014) (Ribiero 2014)	to assess the effect of a follow-up formula with prebiotics on the occurrence of acute respiratory infections and diarrheal disease in children from two daycare centers in Brazil.	RCT	constipation	NOT REPORTED	Brazil	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	NOT REPORTED
Ritterband	This multicentered study	RCT (pilot)	Through posting of fliers and	TYPICAL	United States	Home / remote	Education and information provision	Parents of encopretic children interested

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
(2003) (Ritterband, Cox et al. 2003)	(University of Virginia and Vanderbilt University) examined the utility and effectiveness of an Internet-based version of ETT. All children in the study were encouraged to continue working with their treating physician. It was hypothesized that the children who received the Internet intervention would have greater success in reducing fecal accidents and normalizing bowel function than those who did not receive the intervention.		direct physician referral, 24 encopretic children were recruited from central Virginia (n 12) and middle Tennessee (n 12). There were 19 boys and 5 girls, with a mean age of 8.46 (SD 1.81) years (see Table 1). To be eligible for the study, children had to be between the ages of 6 and 12 years, soiling at least once a week, and have no medical diagnosis, other than constipation, that could explain their fecal incontinence. The participants were assessed at baseline to determine how many accidents they were having prior to the intervention, the child's stage of toilet training, what treatment regimen they were currently following, and how long they had been on that regimen. On average, the children were having approximately one accident each day (M 7.08, SD 6.76, accidents per week), and most parents indicated that their child had completed toilet training. Sixteen of the 24 children were taking some type of laxative, including Ex-Lax (Novartis), Milk of Magnesia (Phillips), Senokot (Purdue Frederick	DEVELOPMENT			(UCanPoopTo internet intervention vs usual care) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	in participating in the study called the Center for Behavioral Medicine Research at the University of Virginia Health System. A brief screening questionnaire of general bowel habits was taken over the telephone. If the inclusion criteria were satisfied, the child's physician was contacted to verify that the physician approved the program content and would follow the child for routine care. Twentytwo different physicians provided approval to participate for the 24 participants in the study. All children in the study were encouraged to continue meeting with their physician. From a retrospective review of symptoms, participants were matched on the basis of fecal accident frequency, and then randomly assigned to either the Internet intervention (Web) or no Internet intervention (No-Web) group. A research assistant then went to the participant's home, obtained approved written informed consent, and administered a questionnaire protocol to the parents, including the Virginia Encopresis/Constipation Apperception Test (VECAT; Cox et al., in press), to assess toileting habits, and the pretreatment Child Information Form. The children received the Encopresis Knowledge Questionnaire (EKQ; a measure developed for this study). If the family was assigned to the Web group, a computer and printer were installed in the home and connected to the Internet, and the researcher introduced the parent and child to the Internet site and answered any questions about its use. The research

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
			Company), or some other laxative, which had been administered for an average of 19.18 months. There were no significant differences on any of the dependent measures between groups at baseline (see Table 1).					assistant telephoned 2 days later, as well as several additional times throughout the family's involvement in the study (typically at 8 days and 15 days from initiation), to answer any questions concerning use of the Internet site. The No-Web families were also called at the same time intervals. A posttreatment home visit was scheduled for all participants approximately 3 weeks following the initial home visit. At this time, the parents were administered the VECAT and the posttreatment Child Information Form concerning the child's bowel habits, and the child was again administered the EKQ. Participants received a $25 gift certificate to a local toy store for completing the pretreatment assessment and another $25 gift certificate for completing the posttreatment assessment. All procedures received prior approval from the Human Investigation Committee. Demographics and bowel habits. Information regarding family demographics and the child's bowel habits was assessed by parent report on the Child Information Form. In addition, questions regarding the child's bowel habits were included, such as number of bowel movements (BMs) in the toilet and use of toilet with and without parental prompts. This form was administered both pre- and postintervention. Questions regarding use of the Internet program were also included on this posttreatment form for the

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
								Web group. EKQ. A questionnaire assessing children's knowledge regarding encopresis was developed for the purposes of this study. It consists of 26 questions, covering three main areas: anatomy (6 items), pathophysiology (6 items), and treatment (14 items). The questions were presented in matching, multiple choice, and true/false formats. Total scores are obtained by summing the number of correct responses, with a range from 0 to 26. VECAT. The VECAT assesses bowel-specific problems related to the process of encopresis, such as avoidance of the toilet, nonresponsiveness to rectal distention cues, and fear of defecation pain. A generic subscale, included as a comparison measure, addresses problem behaviors not related to bowel issues. For example, compliance with parental instructions to sit on the toilet is a bowel-specific issue, whereas the parallel generic item is compliance to parental instructions to make the bed. The VECAT consists of 18 pairs of drawings (9 pairs of bowel-specific and 9 parallel generic events), and the child selects the picture in each pair that best describes him or herself. The VECAT has good internal consistency and test–retest reliability. It has been found to best differentiate encopretic children with bowel-specific and not generic problems (Cox et al., in press). An online version of this measure can be found on the U-CAN-POOP-TOO Internet site (www.ucanpooptoo.com) Internet

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
Ritterband (2005) (Ritterband, Borowitz et al. 2005)	The main objective of this study was to quantify the percentage of families who visit a Web site that was specifically prescribed by their physician. In addition, the use of an e-mail reminder was used to determine if it increases the likelihood that families will visit the prescribed Web site. Finally, barriers to accessing the prescribed Web site were identified.	Other primary study (non-comparative study)	Families were approached for participation in the study if they had a child who was being seen for the first time in the pediatric gastroenterology clinic at the University of Virginia with a chief complaint of chronic constipation and/or encopresis. To be eligible, families had to have access to the Internet in their home and have an active e-mail account.	NOT REPORTED	United States	OTHER (STATE)	Education and information provision (Website training) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	visited the prescribed Web site within 1 week of their clinic visit; barriers to accessibility
Ritterband (2013) (Ritterband, Thorndike et al. 2013)	evaluate hypotheses: children with encopresis receiving the Internet intervention in addition to treatment-as-usual would have significantly fewer accidents at post intervention (Weeks 4-6) and one year post compared to those receiving routine care only. Secondary hypotheses 1) children and parents receiving the Internet intervention in addition to treatment-as-usual would increase their encopresis-specific knowledge (including information about treatment strategies) and 2) would show greater reductions in bowel-specific problems related to encopresis and constipation (e.g., avoidance of the toilet) more than families who	RCT	91 encopresis	TYPICAL DEVELOPMENT	United States	Primary care / Community / Patient's home	Education and information provision UCanPoopToo internet intervention vs usual care *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	child's encopretic symptoms (bowel/accident patterns) and associated problems, caregiver information, computer/Internet usage, previous treatment history, demographics, parental knowledge of encopresis, cost items, and program evaluation.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
	only received routine care.							
Rogers (2014) (Rogers 2014)	outlines the responsibilities of schools to understand continence problems, implement effective policies and procedures to meet children's needs, and recognise those children's rights to be supported in achieving continence and independence. It also describes the development of a toolkit called The Right to Go	Other primary study (intervention development)	Continence problems	UNCLEAR	United Kingdom	EDUCATION (SCHOOL / UNI)	Education and information provision (Right-to-go toolkit) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	NOT REPORTED
Russo (2017) (Russo 2017)	to evaluate the efficacy of a probiotic mixture (PM), including Bifidobacteria breve, infantis, and longum added to oral PEG compared to the traditional therapy with PEG alone on childhood FC. Secondary aims were to assess safety and tolerability of the study products for short-term treatment.	RCT	with CFC	UNCLEAR	Italy	Home	Lifestyle: Diet - Prebiotics /probiotics	Primary = frequency of bowel movements per week, stool consistency, presence of abdominal pain, faecal incontinence, painful defecation, and rectal bleeding. Secondary = safety and tolerability of the study products evaluated through the incidence of adverse effects such as vomiting, nausea or meteorism, flatulence, and diarrhea.
Salvatore (2018) (Salvatore 2018)	Our aim was to carry out a concise review of the literature, evaluate the impact of these common FGIDs on infants and their families, and provide an overview of national and international guidelines and peer-reviewed expert recommendations on their management.	Narrative review	Infants with functional gastrointestinal disorder (FGID) (regurgitation, infantile colic, functional constipation).	UNCLEAR	Italy	Home	More than one level 0 intervention delivered by carers prior to HCP involvement	NOT REPORTED
Sanctuary (2019) (Sanctuary,	To assess tolerability of a probiotic combined with a bovine colostrum product	RCT (Pilot	11 children with a previous diagnosis of ASD, ages 2–11 with a history of frequent	Yes	United States	Unclear	Other / alternative dietary intake (Probiotic Bifidobacterium infantis in	Primary outcome: changes to the intestinal microbiota as well as supplement tolerability. GI symptoms

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
Kain et al. 2019)	as a source of prebiotic oligosaccharides in children with ASD and GI co-morbidities.	cross-over RCT)	gastrointestinal symptoms including chronic constipation, diarrhoea, and/or IBS				combination with a bovine colostrum product (BCP). 12-week study included 5 weeks of probiotic-prebiotic supplementation, followed by a two-week washout period, and 5 weeks of prebiotic only supplementation) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	and any behavioural changes were monitored throughout the study as measures of tolerability. Secondary outcomes: changes to the intestinal microbiota, changes in peripheral blood mononuclear cell and metabolomic analysis of plasma, urine and stool.
Saneian (2013) (Saneian 2013) IRCT20120731 1579N	We evaluated effects of adding a probiotic to mineral oil in the treatment of functional constipation in children	Other primary study	Children with functional constipation. Children 2 to 14 years of age diagnosed to have functional constipation based on the Rome III criteria were included consecutively.[9] Those with immunocompromised condition or other severe diseases, and those receiving antibiotic in the previous four weeks were not included.[10] Exclusion criteria included experiencing severe side-effects, gastroenteritis, or receiving antibiotic for any reason during the study period.	UNCLEAR	Iran, Islamic Rep.	Home	Lifestyle: Diet - Prebiotics /probiotics	A trained general physician interviewed with each subject, and a questionnaire including demographic data and symptoms of constipation, based on the Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III Version, was completed.[12] Major symptoms included defecation frequency (1 = two times a week or less to 5 = more than three times a day), stool consistency (1 = very hard to 5 = watery), stool retention (yes/no), and painful defecation (yes/no). Other symptoms included urgency, straining, passing mucus, and feeling of incomplete evacuation which were scored from 0 (never) to 4 (always) and soiling which was scored from 0 (never) to 5 (every day). Subjects were interviewed at the end of the intervention (8th week) with the same questionnaire including compliance and side-effects as well, and a subjective global improvement (SGI) scale which was scored from 0 (significantly worsen) to 7 (completely improved)
Santocchi (2016) (Santocchi 2016)	The main aim of this study is to determine the effects of supplementation with a probiotic mixture (Vivomixx®) in ASD	ON-GOING (RCT)	100 preschoolers with ASD (with idiopathic or functional GSD disorders?). Inclusion criteria	ATYPICAL DEVELOPMENT	Italy	Home	Lifestyle: Diet - Prebiotics /probiotics	The primary outcome is the improvement of severity level of ASD symptomatology, measured with ADOS-2 Secondary outcomes - clinical outcomes

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
	children with or without GI symptom.		a. age-range: 18–72 months. The interest in assessing the effects of probiotic supplementation in preschoolers with ASD relies on the strong recommendation to lead early treatments in ASD, given the demonstrated positive impact of early interventions on the core symptoms of the disorder [59]. b. ASD diagnosis according to DSM-5 (Diagnostic and Statistical Manual of Mental Disorders-5th Edition) criteria [1]: Participants must have a diagnosis of an ASD as assessed by a senior child psychiatrist with a specific expertise in clinical evaluation of ASD according to DSM-5 criteria before their recruitment in the study. Exclusion criteria a. brain anomalies detected by Magnetic Resonance Imaging; b. neurological syndromes or focal neurological signs; c. anamnesis of birth asphyxia, severe premature birth (≤28 gestational weeks) or perinatal injuries; d. epilepsy; e. significant sensory impairment (e.g., blindness, deafness); f. diagnosis of organic GI Disorder (i.e. gastroesophageal reflux, food allergies, IBD); g. diagnosis of Coeliac Disease; h. special diet (i.e. gluten-free diet, casein-free diet, high-protein					measured by GI severity index, The Childhood Autism Rating Scale, The Social Communication Questionnaire (SCQ), The Child Behavior Checklist 1.5-5 (CBCL 1.5-5), The sensory profile, The Repetitive Behavior Scale-Revised (RBS-R), The parenting stress index, The Vineland Adaptive Behavior Scale II (VABS-II), Developmental level will be assessed trough the Griffiths Mental Development Scales-Extended Revised (GMDS-ER) [78], from which a Developmental Quotient will be obtained. The MacArthur-Bates Communicative Development Inventories (CDIs) Electrophysioloical measures - The modification of the electrophysiological pattern at rest will be evaluated by the comparison of the QEEG features measured at T0 and T2 i.e. power, asymmetry and coherence (a measure of connectivity) computed within each characteristic frequency band of the brain. Biochemical measures - In order to value the effects of probiotics compared with placebo on the intestinal and systemic inflammation, LPS, leptin, resistin, TNF-α, IL- 6, PAI–1, phtalates and calprotectin will be measured before and after the treatment

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
			diet, ketogenic diet). Children already enrolled in dietetic treatment studies will not be included (criteria h.) given the possible interferences of such diets on GI system during the probiotic/placebo supplementation					
Savage (2012) (Savage 2012)	The aim of this study was primarily to determine whether whey-based (vs casein-based) enteral formulas reduce GOR and accelerate GE in enterally fed children with severe CP. Second, we aimed to examine the effect of these formulas on symptoms of poor feed tolerance such as gagging, regurgitation, irritability, pain, and constipation.	RCT	Children with severe cerebral palsy (CP). All patients complied with the following inclusion criteria: (1) CP with severe neurological impairment graded by the Cerebral Palsy Gross Motor Function Classification Scale (levels 4–5), (2) history of GOR, (3) 100% dependent on enteral nutrition (to prevent oral consumption of food proteins that may potentially confound results), (4) well matched for height/weight (to avoid any confounding affect of improved nutrition on GI function),17 (5) no concurrent use of antibiotics (due to their potential affect on GE), and (6) no GI surgery in past 3 months (as delayed GE may occur after surgical placement of a PEG tube).	ATYPICAL DEVELOPMENT	Australia	Home	Other / alternative dietary intake	Symptoms were reported by parents throughout the study using 3 methods: 1. Parent recording sheet (completed at home for the 2-week duration of the study) 2. Visual analog scale (VAS) questionnaire for 5 symptoms (gagging, regurgitation, irritability, pain, and constipation). Scoring for each symptom involved placing a mark along a 10-cm line (far left indicating no symptom and far right indicating severe symptom). 3. A Non-Communicative Children's Pain Checklist (NCCPC)21
Savino (2003) (Savino, Cresi et al. 2003)	To investigate whether a new commercially available infant formula, is useful as a dietary option in infants with minor feeding problems.	Other primary study	932 formula-fed healthy term infants, up to 3 months of age, who were seen by a paediatrician because of colic and/ or constipation and/or regurgitation were enrolled	No	Italy	Conducted in hospital but intervention delivered as required	Diet – different milk formula (Formula based on a partially hydrolysed bovine protein) *This study is included in the*	Detailed history of GI problems, plus feeding practice and stool characteristics Number of stools, episodes of colic and regurgitations were recorded daily by the parents. Parents and paediatricians

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
							effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19	gave a judgement (score of 1–10) to evaluate the compliance and acceptability of the dietary treatment.
Savino (2005) (Savino, Maccario et al. 2005)	A study was carried out on 168 full-term infants with digestive problems such as regurgitation and/or constipation to evaluate the efficacy of new infant formulas containing partially hydrolysed whey protein, modified vegetable oil with a high b-palmitic acid content, prebiotic oligosaccharides and starch.	RCT	The study included 298 formula-fed healthy term infants up to 4 mo of age with digestive problems such as regurgitation and/or constipation, seen by 78 family paediatricians throughout Italy. The inclusion criteria were: gestational age between 37 and 42 wk, normal birthweight (42500 g), normal weight gain (P150 g/ wk) and normal physical examination. Infants with neonatal problems and/or assumption of any kind of medication during the week before the beginning of the study and during the study period were excluded	No	Italy	Home	Other / alternative dietary intake	The day on which the paediatrician saw the infant was defined as day 1. On this occasion, a detailed history of digestive problems as well as feeding practice and stool consistency (watery, runny, formed or hard) were recorded. A structured questionnaire was given to the parents who agreed to participate in the trial, in order to monitor the frequency of the symptoms, feeding volume and side effects. On days 1, 7 and 14, stool characteristics (frequency and consistency) and number of regurgitations were evaluated. Feeding volume was based on a feeding ad libitum procedure. Feeding frequency was decided by the parents and was not influenced by the study protocol. At the end of the study, the parents and the paediatricians gave a judgement (score of 1–10) to evaluate the compliance and the acceptability of the diet. The consulting family physician, who had exclusive responsibility for providing the opportunity and making the decision to use the commercially available study formula, informed the parents and sought their consent to use some of the relevant clinical data for this study with the assurance of anonymity
Shin (2019)	In this review, we focus on	Narrative	Children and adults with	NR	United States	Home	Lifestyle: Diet - Prebiotics /probiotics	NOT REPORTED

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
(Shin 2019)	the current state of knowledge and future directions in microbiome research as it pertains to FGIDs.	review	Functional Gastrointestinal Disorders (FGIDs)					
Staiano (2000) (Staiano, Simeone et al. 2000)	The aim of our study was to evaluate the efficacy of glucomannan as a treatment for CFC in children with severe neurologic damage.	RCT	20 children (mean age ± SD: 5.7 ± 4.2 years) with severe/profound complex needs (severe/profound). All children were fed by mouth with a semi-liquid diet including formula and pureed food.	Yes	Italy	Reports the involvement of caretakers but unclear where the intervention was delivered.	Lifestyle: additional dietary fibre Randomised to receive either glucomannan (Dicoplus; Dicofarm, Rome, Italy) 100 mg/kg two times a day or matching placebo. Intervention lasted 12 weeks	Stool habits, total and segmental gastrointestinal transit times, and anorectal motility were evaluated in all children before and after the treatment period.
Stepurina (2018) (Stepurina 2018)	To substantiate use of magnesium-containing mineral water for optimization of prevention and treatment of CFC	RCT	95 children who had the 'functional constipation' diagnosis according to Rome IV criteria	NR	Russian Federation	U	Magnesium-containing mineral waters. Standard care was (the sparing/training regime, nutritional therapy, exercise therapy, and revitalizing massage) vs Magnesium-containing mineral waters plus standard care *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	NR
Stewart (2013) (Stewart and Schroeder 2013)	To summarize the current literature on the use of dietary fiber and whole grains as treatments for childhood constipation	Narrative review	Childhood constipation. Age groups not clearly reported.	NR	More than one – international evidence	Home	Lifestyle: additional dietary fibre	NR
Sullivan (2012) (Sullivan 2012)	To demonstrate that dietary fibre intakes of children with constipation can be increased using behaviour modification techniques	RCT	43 children aged 2–14 years with functional constipation (defined as less than three bowel movements per week with hard stools and difficulty or delay in defecation), and/or a dietary fibre intake of less age in years + 5 g, and ± taking laxatives were identified and	No	United Kingdom	Recruited from a paediatric gastroenterology clinic and via referrals from community health visitors. Intervention will have been delivered at home and possibly	Behavioural intervention - (Randomised to one of two treatment groups: controls received general advice on increasing dietary fibre intake, or intervention received a specially designed behaviour modification technique with a self-monitoring and reward system)	Parents and carers of children in both groups completed 7-day food diaries and noted laxative use and stool frequency at baseline then again at 3 and 6 months postintervention.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
						outpatient clinic (states that "seen by an attending pediatric research dietitian" No indication if this is in primary or secondary care.) Follow-up for both groups was either at routine clinic appointments, home visits and/or via the telephone.		
Szajewska (2011)(Szajewska 2011)	Brief summary of clinical evidence from RCTs (or their meta-analyses) of the effectiveness of probiotics in the treatment of FGD	Narrative review	Children with functional gastrointestinal disorders (FGD). Rome III criteria.	NR	More than one – international evidence	Home	Lifestyle: Diet - Prebiotics /probiotics	NR
Tabbers (2015)(Tabbers 2015)	Review the evidence of fibre and probiotics as treatments for childhood CFC	SR	Children with CFC 12 studies that met inclusion criteria	NR	More than one – international evidence	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	Treatment success, Quality of life, and adverse effects
Tabbers (2011)(Tabbers 2011)	Assess the effects of the probiotic product B lactis DN-173 010 in children with CFC	RCT	159 children with aged 3- 16 years with CFC (> 2months) diagnosed using Rome III criteria	U	Netherlands	Primary care / Community / Patient's home	Lifestyle: Diet – Probiotics (Randomised to receive fermented milk Activia (125-g pot containing 5 g of lactose) manufactured with lactic cultures including B lactis DN-173 010 or a control product twice a day for 3 weeks)	Primary outcome: change in defecation frequency. Secondary outcomes: stool consistency, frequency of episodes of FI, pain during defecation, frequency of AP, frequency of adverse effects and frequency of intake of bisacodyl.
Tabbers (2011)(Tabbers 2011)	To evaluate the effectiveness of Bifidobacterium breve in the treatment of CFC	Other primary study	20 children aged 3- 16 years with CFC diagnosed using Rome III criteria	U	Netherlands	Primary care / Community / Patient's home	Lifestyle: Diet - Prebiotics /probiotics	Primary outcome: change in defecation frequency. Secondary outcomes: stool consistency, frequency of episodes of FI, pain during defecation, frequency of AP, frequency of adverse effects and frequency of intake of bisacodyl.
Tajik	To investigate the effect of	RCT	60 children aged 2- 10 years	NR	Iran, Islamic	Primary care /	Diet – Sugars	Stool frequency and consistency, pain

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
(2018)(Tajik, Goudarzian et al. 2018)	red sugar on CFC compared to figs syrup		with constipation. Constipation was not defined.		Rep.	Community / Patient's home	30 children with constipation were treated with the usual drug, fig syrup, and 30 other children received red (brown) sugar for 4 weeks *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	during BM, appetite status
Tanjung (2016)(Tanjung, Supriatmo et al. 2016)	To determine the effect of selenium on CFC	RCT	120 children aged 12 to 17 years with functional constipation, diagnosed according to the Rome III criteria	NR	Indonesia	Al-Kautsar Al-Akbar Islamic Boarding School in Medan	Selenium Selenium vs placebo. 2 weeks of treatment *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Frequency of defecation, AP severity, and stool consistency
Tatsuki (2011)(Tatsuki 2011)	To determine whether hypermagnesemia develops in children with CFC taking daily magnesium oxide.	Other primary study	120 children aged 1-14 years diagnosed with CFC using the Rome III criteria	NR	Japan	Home	Daily magnesium oxide for at least 1 month	Hypermagnesemia (Serum magnesium concentration)
Tayag-Lacsina (2019)(Tayag-Lacsina 2019)	To determine the effectiveness of 'Constipation Pamphlet' in improving outcomes.	RCT	90 children aged 2 -18 years fulfilling the ROME IV Criteria for functional constipation, or with Blethyn grade 2 or 3 on abdominal radiograph	NR	Philippines	Intervention was delivered in the participants home	Education and information provision (Information leaflet + usual care vs usual care. The "Constipation Pamphlet" plus usual care involved recording the following daily in a stool calendar: consumption of fruits, vegetables, and water; bowel movement, stool consistency; and laxative intake Usual care was based on the recommendations of the ESPGHAN/ NASPGHAN guidelines. Treatment duration was 8 weeks. *This study is included in the effectiveness review. Further details*	Consumption of fruits, vegetables, and water; number of BMs, stool consistency and laxative intake.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
							about the intervention are profiled in Appendix 5, Table 19	
Thompson (2021)(Thompson, Wine et al. 2021)	To review parents' experiences of caring for a child with CFC and to identify what information parents need to understand CFC, make child-health decisions, and to improve their support when caring for a child with CFC	SR	Children (and parents) who live with CFC, encopresis and FI Identified 13 (n = 10 quantitative, n = 3 qualitative) as suitable for inclusion in the review	NR	More than one – international evidence	Home	Education and information provision	Information needs, experiences, beliefs, knowledge or practices of parents related to CFC
Trajanovska (2018) (Trajanovska 2018)	NR	Narrative review	Children with constipation and encopresis	NR	More than one	More than one	More than one intervention: diet, regular toileting, praise, laxatives, prune juice	NA
Tse (2000)(Tse, Leung et al. 2000)	To evaluate fibre intake of severe DD children living in a residential institution, and the possibility of reducing the use of laxatives by increasing their fibre intake	Other primary study	20 children aged between 3 and 17 years	Yes	Hong Kong	Residential unit	Lifestyle: additional dietary fibre (laxatives were routinely prescribed if there was no spontaneous bowel motion for two consecutive days. Fibre intake was increased in stages by adding All-Bran® (Kellogg Company, Battle Creek, MI, USA) and desserts.) Assessed over a 4-month period	Mean number of laxative usage per week per child
Van Tilburg (2012)(Van Tilburg 2012)	Assessed parental knowledge about FI and determine how this relates to the care and treatment of FI	Other primary study	Children ages 4 to 18 years with constipation FI defined as at least 2 of the following had to be present in addition to FI: <=2 bowel movements in the toilet per week in the last 2 months, history of painful or hard BM, a history of large-diameter stools, which may obstruct the toilet.	No	United States	Primary care / Community / Patient's home	Education and information provision 30 parents completed the questionnaire before and after consultation with a paediatric gastroenterologist and after 2 months of treatment	Questionnaire was developed from qualitative interviews and clinician input. Two subscales were identified with good psychometric properties: "Blame and Punish" and "Worry and Help."
Vandenplas (2013)(Vandenplas 2013)	Review of the relationship between this change in flora composition and health benefits in children.	Narrative review	Infants and children. Not specific to CFC but do present brief overview of the current evidence within this paper.	NR	More than one – international evidence	NR	Lifestyle: Diet - Prebiotics /probiotics	NR
Waingankar	To audit the effect of	Other	29 children with rapid-transit	U	Australia	Bowel clinic,	Diet restriction.	Questionnaire rating severity of

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
(2018)(Waingankar, Lai et al. 2018)	specific fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) elimination diets	primary study (retrospective audit)	constipation aged between 5-15 years. None of these cases had resolved with years of treatment			Hospital	(Exclusion of fermentable oligosaccharides, disaccharides, monosaccharides, and polyols from the diet)	constipation, AP, and pain on defecation
Weber (2014)(Weber 2014)	To test the clinical efficacy and effect on colonic transit time of a dietary fiber mixture in children with CFC after the withdrawal of stool softeners and enemas.	RCT	54 children between the ages of 4 and 12 years diagnosed based on Rome III criteria. All children had controlled CFC and had received maintenance therapy with low doses of stool softeners or lactulose or PEG.	U	Brazil	Recruitment occurred in the hospital, but the intervention was delivered at home	Lifestyle: additional dietary fibre Fiber mixture (several of the components (10.5% fructooligosaccharides, 12.5% inulin, 24% gum arabic, 9% resistant starch, 33% soy polysaccharide, and 12% cellulose) are considered prebiotics) or the maltodextrin placebo. All participants were asked to maintain daily toilet training and regular water ingestion. Duration of intervention was 4 weeks	Daily diet sheet, two questionnaires: daily defecation frequency and type of faeces and a questionnaire addressing symptoms related to constipation and the use of the supplement provided. Primary outcome: therapeutic failure defined as experienced hardened stools, defecation with pain or difficulty, a greater interval between evacuations compared with the previous day, the appearance of faecal incontinence and faecal impaction, or when the patient required a stool softener during the study period.
Wegh (2018)(Wegh 2018)	To investigate the effect of probiotics on children with CFC or functional AP disorders	SR	Children aged 4 to 18 years with functional AP or children aged 0 to 18 years with CFC Identified 17 RCTs; of which 6 were focused on CFC	NR	More than one – international evidence	Home	Lifestyle: Diet - Prebiotics /probiotics	NR
Wojtyniak (2017)(Wojtyniak 2017)	Updated SR which evaluated the efficacy of probiotics in the treatment of CFC	SR	Patients aged 0–18 years with CFC diagnosed (authors' definition or Rome II, III, or IV criteria Identified 7 relevant studies (515 participants)	NR	More than one – international evidence	Home	Lifestyle: Diet - Prebiotics /probiotics	Primary outcome: treatment success (defined by the authors of included studies)
Wojtyniak (2017)(Wojtyniak 2017)	Evaluate the effectiveness of Lactobacillus casei rhamnosus Lcr35 (Lcr35) in CFC	RCT	94 children aged <5 years with constipation according to the Rome III Criteria.	No	Poland	Home	Lifestyle: Diet - Probiotics (Randomised to receive Lcr35 (8x108 colony-forming units or placebo twice daily, for 4 weeks)	Primary outcome: treatment success, defined as ≥3 spontaneous stools per week, without episodes of faecal soiling Secondary outcome measures: stool consistency, frequency of defecation, frequency of faecal soiling, frequency of pain during defecation, frequency of AP or flatulence, need for intake of

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention (Other details)	Main outcomes
								additional laxative treatment, and adverse events
Xinias (2018) (Xinias, Analitis et al. 2018)	To evaluate the efficacy of synbiotic formula with partial whey hydrolysate and high magnesium content	Other primary study (non-randomised)	65 starter formula fed term born infants with an age range between 3 and 13 weeks suffering from constipation for at least one week	NR	Greece	Conducted at a Paediatric Department but intervention delivered 'as required'	Diet – different milk formula Intervention formula was partial whey hydrolysate, synbiotics (*Bifidobacterium lactis* and galacto-oligosaccharides (GOS) supplemented with magnesium. Infants were also given parental reassurance. The control group received parental reassurance alone *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Primary outcomes: Quality of Life, change in stool consistency
Yang (2012) (Yang, Wang et al. 2012)	Meta-analysis of RCTs which investigate the effect of dietary fiber intake on CFC	SR (SR and MA)	Constipation using the Rome criteria or a clinical diagnosis Identified five potentially relevant studies; 4 of which involved children	NR	More than one – international evidence	Primary care / Community / Patient's home	Lifestyle: dietary fibre	Included RCTs which reported at least one of the following outcomes: frequency, stool consistency, treatment success, laxative use, gastrointestinal symptoms.
Yang (2019)(Yang 2019)	Protocol to evaluate the effectiveness and safety of lactobacilli in children with CFC	SR protocol (on-going)	Planned to include studies with children aged between 6 months and 18 years diagnosed using Rome criteria	NR	More than one – international evidence	More than one category	Lifestyle: Diet - Prebiotics /probiotics	Primary outcome: defecation frequency, treatment success (bowl movement >3 times per week. Secondary outcomes: stool consistency, incidence of AP, patients using laxatives, and adverse events.
Young (1998) (Young, Beerman et al. 1998)	To identify whether a concerted effort to increase liquid intake would improve CFC	RCT	108 children between 2 and 12 years of age	No	United States	Home	Lifestyle: fluid intake Three groups: control, increased water intake group, and increased hyperosmolar liquid group *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 19*	Total amount and type of liquid intake, stool characteristics (frequency, consistency, and difficulty with passage)

Table 3. Level 1 – Wider children's workforce: assessment and intervention by primary care services

Abbreviations: ASD: autistic spectrum disorder, ASN: additional support needs; CFC: chronic functional constipation; C-IBS ; PEG: Polyethylene glycol, PEG-E Polyethylene glycol plus electrolytes; RCT: randomised controlled trial; SR: systematic review

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Aboumarzouk (2011) (Aboumarzouk, Agarwal et al. 2011)	To assess Cisapride's role, effectiveness and safety in treating CFC and C-IBS	SR	Children and adult's CFC or C-IBS – no age limitation. Rome III criteria used. Length of time with CFC: >3-6 months. Identified 8 relevant studies (424 participants, of which 157 were children)	NR	More than one – international evidence	More than one category	Cisapride	Primary outcome: global improvement of symptoms and improvement of overall CFC complaints. Secondary outcomes: AP, distension, stool frequency, and bowel transit time.
Acharyya (2018)(Acharyya 2018)	To compare the efficacy of PEG+E alone or as an adjunct	Other primary study (prospective)	101 children aged 2- 14 years diagnosed with CFC as per Rome III criteria	NR	India	Hospital (Tertiary centre)	PEG+E with stimulant laxative (Sodium Picosulfate) or PEG +E solution alone for disimpaction regimen.	Achieving faecal disimpaction
ACTRN12616000561482 (2016) (Actrn 2016)	The efficacy of different sets of instructions for Polyethylene glycol (PEG) and electrolytes (PEG- E) administration for the treatment of constipation in children presenting to the emergency department	RCT (on-going)	Targeting children aged 4-18 years who meet ROME III criteria				Laxatives: PEG (with and without electrolyte)	
Ahmed (2012)(Ahmed 2012)	To review the literature which evaluate the efficacy and safety of PEG	SR	Infants and children younger than age 3 years. Definition of CFC was not reported. Identified 5 relevant studies (participant numbers not reported)	NR	More than one – international evidence	More than one category	Laxatives: PEG (with and without electrolyte)	Not explicit. Focus was on efficacy and safety.
Ala (2015)(Ala 2015)	To explore the response and recurrence rate after treatment with PEG alone versus PEG plus lactulose in children with CFC	RCT	200 children aged 1 - 12 years diagnosed with CFC. Rome III criteria used.	No	Iran, Islamic Rep.	Paediatric outpatient department and home.	Group I (n: 100) was treated with PEG without electrolyte at maximum dose (0.7 g/kg /day, 13.8 - 40 g/day), twice daily and group II (n: 100) received PEG without electrolyte at maximum dose (0.7 g/kg /day, 13.8 - 40 g/day), twice daily and lactulose, maximum dose twice daily (3 cc/kg/day). No more treatment for	Stool diary: recording each bowel movement's amount and consistency, episodes of FI, AP, flatulence, painful defecation, diarrhoea, feeling of bloating, and medication use.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							constipation was allowed during the study. Children with faecal impaction were disimpacted with suppository bisacodyl (2.5 mg/daily/ < 5 years of age and 5 mg/daily > 5 years) for 3 - 5 days (12) and then started laxative therapy. Dietary advice given and toilet training discussed face to face and in pamphlets. Parents were provided with written instructions regarding how to adjust the dosage of medication No other treatment for constipation was allowed during the study	
Alper (2013)(Alper and Pashankar 2013)	To review the biochemistry, efficacy, safety and pharmacoeconomics of PEG as reported in recent paediatric studies	Narrative review	Limited details provided.	NR	More than one – international evidence	More than one category	PEG – limited details	Adverse effects, acceptance, safety
Axelrod (2016)(Axelrod, Tornehl et al. 2016)	To investigate the use of behavioural intervention plus laxative therapy for two children with ASN and CFC	Other primary study (case study)	Two male adolescents with Autism Spectrum Disorder, Intellectual Disability and chronic histories of constipation and frequent faecal accidents. Previously treated with laxatives, enemas, and a toilet training protocol that included self-initiated toileting attempts and rewards for successful BM in the toilet with no effect.	Yes	United Kingdom	More than one category: behavioural intervention was implemented at home by each participant's parents and at school by educational staff	Laxative and behaviour therapy. Behavioural intervention included regularly scheduled toilet sits, an incentive system for BM in the toilet, and a clean-up procedure for faecal accidents, plus a laxative. Both cases achieved full faecal continence after 9-10 weeks *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	Frequency of soiling accidents, frequency of successful bowel movements in the toilet, and percentage of successful self-initiated bowel movements in the toilet. A successful bowel movement in the toilet was recorded when faecal matter was eliminated into the toilet.
Bae (2010) (Bae 2010)	To evaluate the long-term safety of PEG 4000 in children with CFC	Other primary study (cohort)	100 children aged 2 to 17 years who had been taking PEG 4000 for more than 6 months, diagnosed using the ROME III criteria	NR	Korea, Rep.	Hospital	PEG 4000 Duration of therapy; 16.93±7.02 months, dose of PEG 4000; 0.72±0.21 g/kg/day.	Compliance and effect of medication. Clinical and biochemical monitoring. Adverse events.
Bekkali (2018) (Bekkali, Hoekman et al. 2018)	To investigate non-inferiority of PEG3350 with electrolytes compared to PEG4000	RCT (multicentre)	97 children aged 6 months to 16 years, with <3 spontaneous BM per week.	No	Netherlands	Hospital (1 academic hospital and 3 teaching hospitals in the Netherlands).	PEG 3350 with electrolytes vs to PEG 4000 without electrolytes. First 3 days of treatment, all subjects received a rectal enema. Dose was age	Defecation frequency, stool consistency, FI, and adverse events. Daily diary used to record symptoms.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
(NCT01810653)	without electrolytes					Intervention delivered at home.	dependent and could be adjusted based on individual at the follow-up visits, with a maximum of 4 sachets per day. When defecation did not occur within 3 consecutive days, rescue medication was allowed. 8 follow-up visits were scheduled (weeks 0, 1, 2, 4, 8, 12, 26, and 52 after enrolment) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	
Benninga (2022) (Benninga, Hussain et al. 2022) (NCT02042183 and NCT02138136)	To assess the efficacy, safety, and pharmacokinetics of different doses of oral Lubiprostone.	RCT	606 children aged 6 to 17 years with medically confirmed diagnosis of CFC using Rome III criteria	NR	United States	Intervention delivered at home.	Oral lubiprostone 12 or 24 mcg capsules dosed twice daily (BID) (based on subject body weight at baseline) as compared to matching placebo BID, when administered orally for 12 weeks *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	Primary outcome: spontaneous bowel movement. Secondary outcome: change in SBM frequency across the 12-weeks of treatment. Other outcomes: stool type and consistency and stool frequency.
Boles (2015) (Boles, Gaines et al. 2015)	To evaluate the efficacy of PEG-ES compared to PEG-3350 and evaluate the side effects	Other primary study (retrospective cohort)	51 children aged 1 month to 15 years admitted to the hospital with a diagnosis of faecal impaction or CFC.	NR	United States	Hospital. Laxatives delivered at home.	Treated with either PEG-electrolyte solution or PEG-3350	Outpatient and inpatient bowel regimens, inpatient complications (manual or surgical disimpaction, perforation), time to resolution of faecal impaction, and discharge bowel regimen
Bonilla (2018) (Bonilla 2018)	Retrospective study of children with CFC refractory to conventional therapy (regular use of stool softeners and intermittent use of stimulant laxatives only as a rescue therapy)	Other primary study (retrospective)	190 children (median age was 9.45 years (range 0.9 - 21 years) with a frequency of BM of <3 week and were treated with Bisacodyl on a daily basis for longer than 4 weeks in addition to stool softeners.	NR	United States	Hospital (tertiary clinic). Intervention delivered at home	Bisacodyl on a daily basis for longer than 4 weeks in addition to stool softeners	Treatment duration, number of BM per week before and after treatment, side effects and overall response to treatment
Burgers (2012) (Burgers 2012)	To investigate the approach to childhood	Other primary study (survey)	Children suspected to have CFC. Involved 413 primary	NR	More than one	More than one setting.	Combination of treatment approaches were reported. Study focused on the	NR

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	constipation by primary care in three Western countries.		care physicians (PCP); 383 responses were analysable				approach to childhood constipation by PCP. "63% of PCP were convinced that hard stool can be softened by drinking more water. PEG was the most common prescribed drug (85%). Significant differences were found among countries in the use of senna and bisacodyl suppositories"	
CADTH (2014) (Canadian Agency for Drugs and Technologies in Health (CADTH) 2014)	To review the available evidence for the safety and efficacy of stool softeners, laxatives, bulking agents and 5-HT4 agonists for the management of constipation in adults and children.	Narrative review (rapid response)	CFC – all age groups. Identified 12 relevant publications: 3 included children with CFC	NR	More than one – international evidence	More than one category	Stool softeners, stimulant laxatives, osmotic laxatives, 5-HT4 agonists, bulking agents	Clinical effectiveness, safety
CADTH (2015) (Canadian Agency for Drugs and Technologies in Health (CADTH) 2015)	To review PEG for the treatment of constipation in patients in acute and long-term care: Cost-Effectiveness and Guidelines	Narrative review (rapid response)	Children in acute care or long-term care, with constipation that requires treatment. Identified 2 relevant publications.	U	More than one – international evidence	More than one category	PEG (with and without electrolyte)	Cost-effectiveness, guidelines and recommendations
CADTH (2017) (Canadian Agency for Drugs and Technologies in Health (CADTH) 2017)	To explore the clinical effectiveness of Prucalopride for the treatment of gastrointestinal motility disorders	Narrative review (rapid response)	Adults and children who require treatment for gastrointestinal motility disorders (i.e., chronic constipation, ileus, refractory gastroparesis, intestinal pseudo-obstruction). Identified 2 relevant publications	NR	More than one – international evidence	More than one category	Prucalopride (Resotran)	Clinical effectiveness, clinical benefit, safety
Candy (2006) (Candy, Edwards et al. 2006)	To assess the efficacy of PEG 3350 plus electrolytes (PEG + E) as oral monotherapy in the treatment of faecal impaction in children, and to compare PEG + E with lactulose as maintenance therapy	RCT	Children aged 2 -11 years with a clinical diagnosis of faecal impaction who had failed to respond to conventional treatment. Planned to recruit 60 children from the local community to obtain approximately 45 children continuing to the end of phase 2 of the study	NR	United Kingdom	Intervention delivered at home	Phase 1, PEG + E was administered orally according to an escalating daily dose regimen until disimpaction was achieved. A higher dose was given to children in the 5 to 11 years age group than to the 2- to 4-year-olds. .	Successful disimpaction
Candy (2009)	To identify current	SR	Children (under age 18 years)	NR	More than	More than one	7 RCTs: PEG versus placebo; PEG	Quantitative effect on constipation

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
(Candy and Belsey 2009)	literature about osmotic laxatives and to assess the evidence for their use in the treatment of CFC.		with a diagnosis of constipation of 3 months' duration due to non-organic reasons. Identified 7 relevant studies.		one – international evidence	category	versus lactulose; PEG versus milk of magnesia	
Cao (2018) (Cao and Liu 2018)	This study aimed to investigate the efficacy and safety of lactulose for the treatment of Chinese children with CFC.	RCT	100 children aged 2 and 6 years diagnosed with CFC using the ROME II criteria. Experienced CFC for at least 3 months.	No	China	Hospital. Intervention probably delivered at home.	Treatment group received lactulose, while the subjects in the placebo group received placebo intervention. Both groups were treated for a total of 6 weeks *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	Primary outcome: daily stool frequency. Secondary outcome: stool consistency, AP, and any adverse events
Carlin (2011) (Carlin 2011)	Literature review of two commonly used osmotic laxatives: lactulose and PEG.	Narrative review	Adults and children with CFC. Identified 8 relevant studies; of which one included children only (100 participants; aged 6-15 years)	U	More than one – international evidence	More than one category	Osmotic laxatives: lactulose and PEG	NR
Chanpong (2018) (Chanpong 2018)	To evaluate and compare clinical features as well as the clinical course of CFC in children treated with different medications	Other primary study (medical records review)	104 children aged ≤15 years diagnosed with CFC according to the Rome IV criteria. Median age at diagnosis: 2.8 years. Number of follow-up visits per patient ranged from 1 to 35. The median duration of follow-up was 18.0 months (range 6.0-84.2 months)	U	Thailand	Hospital	PEG without electrolyte (PEG4000) was given to 21% of patients; only 7 patients were prescribed PEG at the first visit, while the others were switched from another medication during their follow up visits. Other osmotic laxatives also mentioned: Lactulose and milk of magnesia	Clinical improvement: presence of bowel movement ≥3 times per week together with an absence of hard stool and diagnosed symptoms, which included soiling, painful defecation, and withholding symptoms.
Chen (2014) (Chen 2014)	Meta-analysis of the use of PEG for the treatment of CFC in children	SR (and MA)	Children with constipation. Identified 27 studies for inclusion and 10 relevant studies for the MA. Age of participants not reported.	NR	More than one – international evidence	More than one category	PEG-based laxatives compared with lactulose, milk of magnesia (magnesium hydroxide), oral liquid paraffin (mineral oil), or acacia fiber, psyllium fiber, and fructose in children	Number of stool passage/week and the percentage of patients who reported satisfactory stool consistency.
Choi (2017) (Choi 2017)	Evaluate the incidence and grade of faecal retention in children with overactive bladder (OAB) and to determine the effectiveness of laxative treatment for	Other primary study (cohort study). Limited details reported	88 children aged 5 to 15 years with OAB, defecation symptoms, including pain on defecation and FI. Children had all experienced symptoms for > 2 months. Rome III criteria was used.	NR	Korea, Rep.	Primary care / Community / Patient's home	Laxative treatment, oral PEG 3350/4000 (1–1.5 mg/kg/day) or lactulose (1–2 ml/kg/day) was Prescribed for two weeks	Changes in voiding symptoms within 48 hr of completing the treatment.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	faecal retention in the management of OAB in children.							
De Giorgio (2011) (De Giorgio 2011)	A review that focuses on osmotic laxatives, and particularly PEG	Narrative review	People with chronic constipation. Participant details not clearly reported	NR	More than one – international evidence	More than one category	Osmotic laxatives, specifically focusing on PEG/macrogol 4000 in chronic constipation and as a key agent for bowel cleansing prior to colonoscopy	NR
Dehghani (2014) (Dehghani, Askarian et al. 2014)	To investigate the effect of oral domperidone in the treatment of CFC	RCT	105 children aged less than 12 years with CFC who fulfilled the Rome III criteria	U	India	Hospital and home	Randomly divided into two groups: PEG solution 0.6 g/kg/day two times a day for 6 months plus domperidone syrup 0.15 mL/kg three times a day for 3 months (case group) compared with PEG with the same dose for 6 months and placebo for 3 months with the same dose (control group).	Primary outcome: response to treatment (i.e.) a decrease in signs and symptoms that did not fulfil Rome III criteria. Secondary outcomes: side effects
Dupont (2005) (Dupont, Leluyer et al. 2005)	This clinical trial was performed to evaluate the safety of 3-months treatment with PEG 4000 in children.	RCT (multicentre)	96 ambulatory children aged 6 months to 3 years with CFC. Constipation was defined as less than 1 stool per day for more than 1 month in children 6 to 12 months old and less than 3 stools per week for more than 3 months in children aged 13 months to 3 years.	No	France	Hospital	Randomised to receive either PEG (treated daily with 4–8 g PEG) or Lactulose (daily 3.33 g–6.66 g lactulose) for a 3-month period.	Tolerance and efficacy
Dziechciarz (2015) (Dziechciarz, Horvath et al. 2015) (NCT01875744)	Clinical evaluation of the effectiveness of two different PEG doses for the maintenance treatment of functional constipation in children.	RCT	92 children with CFC according to the Rome III criteria. Mean age of 3.7+/-2.1 years.	NR	Poland	Primary care / Community / Patient's home	Randomised to receive either PEG 4000 at a dose of either 0.7 g/kg (high-dose group; n=45) or 0.3 g/kg (low-dose group; n=47) for 6 weeks	Primary outcome: therapeutic success (passing ≥ 3 stools per week, with no loosening of stool). Secondary outcome: number of stools, number of incontinence episodes, number of painful defecations, number of episodes of AP, the number of patients needed laxatives during treatment, side effects.
El-Shabrawi (2018) (El-Shabrawi, Hanafi et al. 2018)	To evaluate the manometric parameters in children with functional constipation and to assess any possible changes in these parameters after treatment at a single centre.	Other primary study ("prospective descriptive study")	50	No	Egypt, Arab Rep.		High-resolution anorectal manometry plus additional treatment was initiated according the clinical guidelines published for management of functional constipation: education, disimpaction (Laxatives) and maintenance (Behavioural modifications, diet modifications, laxatives)	Anorectal manometry was performed to all children at the initial presentation, and a follow-up manometry procedure was performed again after 6 months of treatment. Changes in manometric parameters were reported using the same protocol used in the initial anorectal manometry

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20	
Eltorki (2019) (Eltorki 2019)	To determine if treatment failure varies based on ROME III classification and adherence to guideline recommended therapy.	Other primary study (retrospective)	712 children aged 1 months to 18.0 years of age with CFC, diagnosed using ROME III criteria	No	Canada	Hospital (children diagnosed in the ED)	Children with CFC were discharged from the ED and prescribed one of the following treatments: oral laxative (i.e., PEG-3350, lactulose, mineral oil, senna, milk of magnesia, bisacodyl), enema, or suppository (i.e., glycerin).	Primary outcome: treatment failure defined as ≥ 2 of the following: 1) presenting symptom persistence; 2) < 1 bowel movement every other day; 3) pain/ difficulty passing stools; and 4) AP between bowel movements. Secondary outcomes: treatment failure based: on 1) age; < 4 years versus ≥ 4 years 2) provision of guideline congruent therapy (yes/no). Other outcomes included 3) individual treatment failure features; 4) days to symptom improvement; and 5) future health care utilization and daycare / school absenteeism
Erickson (2003) (Erickson, Austin et al. 2003)	We reviewed the efficacy of PEG as a single agent for the treatment of constipation in children with dysfunctional elimination	Other primary study (retrospective review)	46 children diagnosed with dysfunctional voiding and constipation who received PEG 3350. The diagnosis of constipation was based on a history of infrequent bowel movements (less than every other day) and/or hard, large or painful BM.	No	United States	Hospital	Each child was initially prescribed PEG 3350. The starting dose was 8 ounces of the 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. 25 children also underwent biofeedback for treatment of detrusor sphincter dyssynergia detected by non-invasive urodynamic studies. Biofeedback consisted of interactive computerized video games controlled by external sphincter activity.	BM frequency, daytime incontinence, side effects
Esmaeilidooki (2016) (Esmaeilidooki, Mozaffarpur et al. 2016)	Comparing the effectiveness of Cassia fistula's emulsion with PEG 4000 in CFC.	RCT	109 children aged between 2 and 15 years diagnosed with CFC according to the Rome III criteria. Mean age +/- SD: 59.7 +/- 28.8 months	U	Iran, Islamic Rep.	Hospital	Randomised to receive Cassia fistula's emulsion or PEG4000 for 4 weeks *This study is included in the effectiveness review. Further details about the intervention are profiled in*	Primary outcome: quantitative and qualitative therapeutic effects. Secondary outcome: safety and compliance.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							Appendix 5, Table 20	
Fantoni Torres (2011) (Fantoni Torres 2011)	To prospectively study outcomes of constipated Brazilian children after therapeutic and behavioural interventions	Other primary study			Brazil	Hospital		NR
Farahmand (2015)(Farahmand, Abedi et al. 2015)	Evaluate the effectiveness of a physical exercise program for the pelvic floor in constipated children refractory to standard medical treatment	Other primary study (prospective cohort)	44 children aged 4 to 18 years, with constipation refractory to standard medical treatment. Constipation was confirmed using the ROME III criteria.	U	Iran, Islamic Rep.	Hospital	Walking in squatting exercise *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	Primary outcome: change in defaecation frequency. Secondary outcomes: subjective and included overall improvement of constipation, stool withholding, painful defecation and stool consistency
Fujii (2019)(Fujii and Morimoto 2019)	Describes the first paediatric experience of Lubiprostone in Japan.	Other primary study (single centre, retrospective study)	6 children with intractable functional constipation	NR	Japan	NR	Lubiprostone 24-micro g capsules, 0.38 to 1.06 micro g/kg/time	Not explicit. Improvement of defecation, faecal frequency stool consistency, adverse events, complete remission, laxative-free status for more than four weeks.
Gartlehner (2007) (Gartlehner 2007)	To make available information regarding the comparative effectiveness and safety profiles of different drugs within pharmaceutical classes for constipation	SR	Children and adults with constipation and IBS-C. Identified 34 relevant studies. Rome III criteria used	NR	Austria	NR	Constipation drugs: docusate calcium, docusate sodium, lactulose, lubiprostone, PEG, psyllium, tegaserod	General Efficacy/Effectiveness, Treatment Duration, Safety and Tolerability
Gomes (2011) (Gomes 2011)	To compare the effectiveness of two drugs, PEG 4000 without electrolytes and magnesium hydroxide	RCT	38 children aged 1-15 years with a history of CFC according to Rome III criteria	NR	Brazil	Outpatient follow-up and home	PEG 4000 without electrolytes vs magnesium hydroxide	Stool consistency, frequency of BM, FI, AP, straining and acceptance of the drugs.
Gordon (2016) (Gordon, MacDonald et al. 2016)	To evaluate the efficacy and safety of osmotic and stimulant laxatives used to treat CFC	SR (Cochrane review)	Children aged 0 to 18 years with a diagnosis of CFC (with or without incontinence) were Diagnosis of constipation was patient self-reported, physician diagnosed, or by consensus criteria (e.g. Rome III). Identified 25 RCTs (2310	NR	More than one – international evidence	More than one category	Studies comparing osmotic or stimulant laxatives with another intervention or placebo were considered for inclusion. All preparations and dosing regimes were considered. Studies using multiple osmotic or stimulant laxative combinations or combinations of both	Primary outcome: frequency of defecation. Secondary outcomes: FI, disimpaction, need for additional therapies and adverse events

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
			participants) as relevant for inclusion				as their intervention were also considered for inclusion *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	
Guest (2006) (Guest and Clegg 2006)	To compare the costs and consequences of using oral macrogol 3350 plus electrodes compared to enemas/suppositories, manual evacuation, and NG administration of macrogol in treating paediatric faecal impaction in Australia	Economic analysis (decision model analysis)	Faecally impacted children	NR	Australia	Hospital	Oral macrogol 3350 plus electrodes compared to enemas/suppositories, manual evacuation, and naso-gasrto administration of macrologol lavage solution	Expected costs associated with each treatment
Guest (2007) (Guest, Candy et al. 2007)	To assess the clinical and economic impact of using macrogol 3350 in an outpatient setting compared to enemas and suppositories and manual evacuation.	Other primary study (retrospective chart review)	224 children (aged 2-11 years) with intractable constipation and initially disimpacted.	NR	United Kingdom	Hospital (outpatient)	Macrogol 3350, or enemas, or suppositories or manual evacuation	Costs and consequences of treatments
Hahn (2015) (Hahn 2015)	To provide evidence summary of side effects of laxatives used to treat childhood constipation	Narrative review	NR Identified 18 RCTs for inclusion	NR	More than one – international evidence	More than one category	Laxatives - PEG, Milk of Magnesia, and fibre mixtures	Side effects
Han (2017) (Han 2017)	Explored the association between Glucomannan use and different clinical measures	SR (and MA)	Children with constipation diagnosed using the Rome criteria. Identified 3 RCTs (122 participants) as relevant for inclusion.	NR	More than one – international evidence	Did not set any restriction for study regions	Glucomannan compared with that of placebo (or other alternatives).	Primary outcome: defecation frequency per week. Secondary outcomes: stool consistency and the rate of successful treatment.
Hankinson (2018) (Hankinson, Borden et al. 2018)	To evaluate the outcomes associated with providing medical and behavioural treatments in a specialty outpatient clinic consisting of a nurse	Other primary study ('quasi-experimental' design)	162 children aged 1 – 15 years a multidisciplinary chronic constipation clinic. Rome III criteria used.	Mixed	USA	Home and hospital	Disimpaction or stimulant laxative plus behavioural psychology evaluation and intervention. Psychoeducation about the rationale for combined medical and behavioural components of constipation, behavioural methods for skill building	Short-term outcomes in the overall symptom presentation associated with constipation, including a reduction in bowel accidents and/or pain, in children with constipation (with and without FI).

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	practitioner and behavioural psychologist.						and motivation, including toilet sit schedules, differential reinforcement, relaxation/pain management, and goal setting were provided. If patients presented with chronic AP, behavioural pain management training was also provided. *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	
Hannah (2008) (Hannah, Juffrie et al. 2008)	To evaluate the effectiveness of laxative synbiotics in constipation in children compared to that of fibre foods	RCT	43 children aged 6 months to 14 years with CFC using Rome II crtieria.	NR	Indonesia	Primary care / Community / Patient's home	Laxative synbiotics	Recovery rate, onset therapy and side effects
Hardikar (2007) (Hardikar, Cranswick et al. 2007)	To assess the safety and efficacy of a Macrogol 3350-based, electrolyte containing preparation in the treatment of chronic constipation in children	Other primary study (non-randomised)	81 children aged 24 months to 11 years with CFC. The existing constipation was either untreated or inadequately treated by laxatives. Duration of constipation symptoms was at least > 6 months. CFC was defined as fewer than three complete bowel movements per week over the previous 14 days, in association with either straining or passage of hard stools in at least a quarter of bowel movements	NR	Australia	Hospital	All children were given Macrogol 3350 plus electrolytes (Movicol, Norgine Ltd, Uxbridge, UK) for 12 weeks	Primary outcome: was the number of spontaneous complete defaecations per week. Secondary outcomes: faecal form amount of stool (rated as none, small, moderate or large), AP, rectal bleeding, pain on defaecation, straining on defaecation and FI, stool withholding, use of concomitant laxative treatment, investigator assessment of efficacy, and patient or parental assessment of efficacy. Safety assessments included adverse events, laboratory tests (full blood examination, urea and electrolytes and liver function tests) and changes in vital signs. Compliance was also assessed.
Hashemi (2015) (Hashemi, Javaheri et al. 2015) (IRCT201311241 5511N1)	This study was conducted to evaluate and compare the effect of PEG treatment and probiotic bacilluscoagulans and bifidobacterium and probiotic to enhance the	RCT	120 children aged 2-16 years with functional constipation	U	Iran, Islamic Rep.	U	PEG+placebo and Probiotics+placebo and PEG+probiotics *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	NOT REPORTED

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	growth of probiotics.							
Hoekman (2013) (Hoekman 2013)	To provide an overview of current and future pharmacological therapies for CFC	Narrative review	Children with constipation. Rome III Criteria was used.	U	More than one	More than one	Pharmacological interventions	NA
Horn (2012) (Horn 2012)	To define constipation, assess the pharmacist's role in identifying and treating constipation, and review clinical evidence for the efficacy, safety, and tolerability of PEG 3350	Narrative review	Unclear	U	More than one – international evidence	More than one category	Osmotic laxatives now available over the counter (OTC), across a variety of patient populations routinely encountered in pharmacy settings	NR
Hyman (2014) (Hyman 2014)	To evaluate the safety and effectiveness of lubiprostone in children with CFC	RCT (prospective, multicentre, open-label, safety and effectiveness study)	Children < 17 years or younger, 12 kg in weight, capable of swallowing capsules without chewing, and who met the Rome III diagnostic criteria for CFC	No	United States	Hospital and home	Patients received 4 weeks of open label Lubiprostone at doses of 12 mg once daily (QD), 12 mg twice daily (BID), or 24 mg BID based on age and weight.	Primary outcome: frequency of SBMs during week 1 compared with baseline. Secondary outcomes: included weekly patient reported SBM frequency (ie, other than the assessment at week 1), frequency of SBMs in the toilet, BM frequency, percentage of patients with SBMs within 24 and 48 hours of the first dose of lubiprostone, and time to first SBM following the first dose of lubiprostone. Weekly responder rates, frequency of faecal incontinence, the average degree of straining associated with SBMs, stool consistency of SBMs, painful SBMs, abdominal bloating, abdominal discomfort, constipation severity, and treatment effectiveness were also assessed.
Imanieh (2019) (Imanieh, Golpayegan et al. 2019)	To compare three therapeutic methods in the treatment of chronic constipation in CP (cerebral palsy) children.	RCT	52 children with CP and chronic constipation which was defined as hard/painful defecation, defecation frequency ≤ two times per week, large stool diameter, severe retention of stool, faecal incontinence (≥ once per week), and hard faecal mass on rectal examination. Children who met at least two of the above-mentioned	Yes	Iran, Islamic Rep.	Clinic and home	Randomly divided into three groups: group A received polyethylene glycol (PEG), group B received PEG with Motilium, and group C received Motilium for 2 weeks *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	Satisfactory outcome: defined as defecation > two times weekly, soft stool and no pain on defecation, no palpation of hard stool on abdominal examination, no FI, not palpating hard and large stool on rectal examination, and no blood in stool.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
			criteria for at least 2 months were eligible for inclusion					
IRCT20190717044239N (2019) (IRCT20190717044239N1 2019)	The effect of polyethylene glycol and lactulose in children with constipation	RCT (on-going)	Children aged between 1 -12 years with a diagnosis of CFC	NR	Iran, Islamic Rep.	NR	Intervention group 1: PEG 3 gr (for children of 6 months or less) or 6 gr (for children of above 6 months) orally in three divided doses daily for 4 weeks. Intervention 2: Lactulose (Darupakhsh Pharmaceutical Co.) 6 cc (for children of 6 months or less) and 12 cc (for children of above 6 months) orally in three divided doses daily for 4 weeks.	Primary outcome = Constipation.
Jarzebicka (2019) (Jarzebicka, Sieczkowska-Golub et al. 2019) (NCT03177434)	To compare the clinical efficacy and tolerance of PEG 3350 and lactulose for the treatment of functional constipation in infants and children.	RCT	102 children aged 6 months to 6 years who were 'newly recognised or ineffectively treated'. Diagnosis of functional constipation according to the Rome III criteria	NR	Poland	Hospital and home	PEG 3350 vs lactulose, 12 weeks of treatment *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	Primary outcome: number of BM per week after 12 weeks of treatment and improvement in stool consistency. Secondary outcome: the presence of adverse events.
Jagadisian (2018) (CTRI/2018/01/011262 2018) (CTRI/2018/01/011262)	Trial of PEG plus electrolyte solution with or/ without sodium picosulphate for home based disimpaction children with CFC	RCT (on-going)	Planned to recruit 94 children aged 1-12 years with CFC as diagnosed using Rome IV criteria	NR	India	Primary care / Community / Patient's home	PEG plus electrolyte solution with or/ without sodium picosulphate	Primary outcome: time to disimpaction (days). Secondary - Dose of PEG in sachets required for disimpaction, vomiting, abdominal distension necessitating drug discontinuation, pain abdomen, features of electrolyte abnormalities or intestinal obstruction, increase in encopresis, failure to disimpact after 7 days, compliance
Jordan-Ely (2012) (Jordan-Ely 2012)	Investigated the success of colonic disimpaction using high levels of laxatives	Other primary study	11 participants (aged 5 to 68 years) whose primary complaint was chronic constipation unresponsive to current treatment and who required disimpaction	NR	Australia	Hospital (Emergency department)	PEG in combination with stimulant laxatives	disimpaction
Jordan-Ely (2013) (Jordan-Ely 2013)	To review outcomes of oral bowel disimpaction with PEG administered in a nurse-led clinic using the MOTIVATE method.	Other primary study (retrospective cohort)	33 children aged 2-17 years with CFC who were referred to a surgeon at a tertiary hospital	NR	Australia	Hospital (tertiary referral)	Combined programme of patient education and engagement (called MOTIVATE). PEG+E (Movicol) combined with Sodium Picosulphate (Dulcolax SP). *This study is included in the effectiveness review. Further details*	Successful bowel disimpaction

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							about the intervention are profiled in Appendix 5, Table 20	
Jordan-Ely (2015) (Jordan-Ely 2015)	To assess the effectiveness of a high-dose oral protocol using PEG-E combined with sodium picosulphate (SP)	Other primary study	44 children aged 2 to 17 years with acute/chronic faecal impaction	NR	Australia	'Suburban clinic' and home	PEG with electrolytes (PEG + E) combined with sodium picosulphate (SP). Education modules (3 × 1 h sessions) consisted of how to administer the laxatives and how they work. Parents and children were given basic information about diet, toilet positioning, as well as how to estimate stool volume and consistency.	Disimpaction defaecation, soiling and food and water intake were recorded by parents/patients by daily diary for 7 days. Stool consistency was also reported.
Jordan-Ely (2016) (Jordan-Ely 2016)	To determine stool output and effect on faecaloma of combined PEG and SPS children with long established constipation.	Other primary study	94 children aged between 4 – 15 years with long-term constipation (>2 years chronic constipation), ongoing laxatives, palpable faecaloma confirmed by enlarged stool-filled rectum on x-ray and rectal: pelvic ratio (>0.6).	NR	Australia	Hospital and home	PEG with the stimulant sodium picosulphate (SPS)	Successful disimpaction
Katelaris (2016) (Katelaris 2016)	To assess the relative effectiveness of polyethylene glycol with (PEG+E) or without electrolytes (PEG) in the management of constipation in children.	SR (and network meta-analysis)	Children with constipation. Included 15 studies (1384 children)	U	More than one – international evidence	More than one category	Polyethylene glycol with (PEG+E) or without electrolytes (PEG)	Primary outcome: was the mean number of bowel movements per week. Secondary outcomes: related to safety, tolerability and compliance.
Koppen (2017) (Koppen, Broekaert et al. 2017)	To describe the mechanism of action, published studies on effectivity, and safety and recent developments concerning PEG, specifically focusing on its role in the treatment of childhood functional constipation.	Narrative review	Children with functional constipation	NR	More than one – international evidence	More than one category	PEG	Effect and safety
Koppen (2018) (Koppen, Van Wassenaer et al. 2018)	To assess treatment adherence in children with functional constipation and to evaluate the association	Other primary study (survey)	Children with CFC aged 0 to 18 years who were treated with PEG. A total of 150 families were included. CFC diagnosed using the Rome IV criteria	U	Netherlands	More than one	Laxatives: Polyethylene Glycol (PEG)	Treatment adherence and satisfaction with treatmetn assessed using questionnaires

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	with parental beliefs about medication, illness perceptions, treatment satisfaction, and satisfaction with information about medication.							
Ladenhauf (2012) (Ladenhauf 2012)	To report a case series of three children exhibiting severe hyperphosphatemia and hypocalcaemia after utilization of sodium phosphate-containing laxatives, necessitating intensive care services	Mixed methods (case series and literature review)	Case series of three children exhibiting severe hyperphosphatemia and hypocalcaemia after using sodium phosphate-containing laxatives, necessitating intensive care services in two of three cases. Additionally, we reviewed 32 case reports of similar occurrences. The cases described are pre-schoolers but evidence from the literature ranged from 8 days to 17 years	Mixed	Austria	Hospital	Laxatives: Sodium Picosulfate	Clinical examination, physical examination, laboratory workup and ultrasound examination of the abdomen
Lamanna (2018) (Lamanna 2018)	To determine the stool output and effect of a combined PEG and SPS regimen on faecaloma in children with severe CFC and impaction	Other primary study	120 children aged 4-18 years who have severe, chronic constipation and a palpable faecaloma	U	Australia	Hospital	Combined PEG and SPS regimen	Daily diary that was used to record laxative volume taken, stool volume produced, stool frequency, and consistency
Lee (2020) (Lee 2020)	To compare the clinical features, diagnostic findings, and medications of children with infrequent bowel movements or faecal soiling	Other primary study (retrospective cohort)	333 participants with CFC - 3 groups (infrequent bowel movement without fecal soiling [G3-a], infrequent bowel movement with fecal soiling [G3-b], and fecal soiling only [G3-c]). CFC diagnosed using the Rome III/IV criteria.	U	Korea, Rep.	Hospital	PEG 4000	Maintenance laxative dose, CTT, or CTT type.
Lee-Robichaud (2010) (Lee-Robichaud, Thomas et al. 2010)	To identify and review all relevant data in order to determine whether Lactulose or PEG is more effective at treating chronic constipation and faecal impaction.	SR	Patients diagnosed with chronic constipation (Rome III criteria) or faecal impaction, including both adults and children, treated with lactulose or PEG. Identified 10 trials enrolled a total of 868 participants (range 37 - 191), of which 322 were adults and 546 were children.	NR	More than one	More than one category	PEG or lactulose	Primary outcomes: change in frequency of defecation. Secondary outcomes: use of additional products, e.g., alternative laxative agents, enemas, percentage in global improvement of symptoms and relief of AP

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Loening-Baucke (2002) (Loening-Baucke 2002)	To determine the efficiency, accept-ability, and treatment dosage of PEG 3350	Other primary study (prospective)	49 children (4 years of age or older) with for functional constipation and encopresis.	No	United States	Hospital and home	PEG 3350 without added electrolytes, 12-month treatment period; 28 children treated with PEG without electrolytes were compared with 21 children treated with milk of magnesia. Regular stool sittings for 5 minutes after each meal were required for the initial months. The	Diary sheets to record each BM (number, consistency of stools, soiling episodes, AP episodes, medication use, and daytime or night-time urinary incontinence. A global assessment of whether the child was "doing well," "improved," or "not doing well" was also recorded.
Loening-Baucke (2004) (Loening-Baucke, Miele et al. 2004)	The aim of our study was to evaluate whether fibre supplementation 9 glucomannan) is beneficial in the treatment of children with CFC with or without encopresis.	RCT (double-blind, randomised, crossover study)	46 children (aged 4 years +) who had chronic functional constipation for 6 months with or without encopresis	No	More than one	Hospital and home	RCT comparing the fibre supplement glucomannan with placebo. Children were disimpacted with 1 or 2 phosphate enemas if a rectal impaction was felt during rectal examination. Patients continued with their pre-evaluation laxative. No enemas were given during each treatment period. Fibre and placebo were given as 100 mg/kg body weight daily (maximal 5 g/day) with 50 mL fluid/500 mg for 4 weeks each. Parents were asked to have children sit on the toilet 4 times daily after meals	Age, frequency of BM into the toilet and into the undergarment, presence of AP, dietary fibre intake, medications, and the presence of an abdominal and/or a rectal faecal mass were recorded. Children were rated by the physician as successfully treated when they had >3 bowel movements/week and <1 soiling/3 weeks with no abdominal pain in the last 3 weeks of each 4-week treatment period. Parents made a global assessment to whether they believed that the child was better during the first or second treatment period. Safety of the fibre supplement glucomannan was evaluated (parents and children) based on side effects.
Loening-Baucke (2006) (Loening-Baucke and Pashankar 2006)	To compare two laxatives, namely PEG 3350 without electrolytes and milk of magnesia, evaluating efficacy, safety, acceptance and 1-year outcomes.	RCT	79 children (aged 4 years+) with chronic constipation and faecal incontinence	U	United States	Hospital and home	Laxatives, namely polyethylene glycol 3350 without electrolytes and milk of magnesia.	Parents were instructed to keep a stool diary for the duration of the study, recording the bowel movements account and consistency, episodes of faecal incontinence, AP, and medication use. Primary outcome: improvement defined as >=3 bowel movements per week, <= episodes of faecal incontinence per month and no AP, with or without laxative therapy. Recovery was defined as >=3 bowel movements per week, <=2 episodes of faecal incontinence per month and no abdominal pain, with no laxative treatment for >=1 month. Other outcomes: 1) improvement in stool frequency per week, improvement

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								in episodes of faecal incontinence per week and resolution of abdominal pain; 2) safety profile and 3) patients' acceptance and compliance.
Lomas Mevers 2020 (Lomas Mevers, Call et al. 2020)	To replicate and extend the findings from Call et al. in a pilot randomized feasibility trial. The study also offered the opportunity to evaluate the preliminary efficacy of this multidisciplinary intervention of encopresis in children with ASD using a clinical trial.	RCT	20 children with ASD and encopresis.	Yes	United States	Hospital	Multidisciplinary Intervention for Encopresis (MIE). Reinforcement, scheduled toileting, liquid glycerin suppository, education	Feasibility focused on enrollment, attendance, attrition, treatment fidelity, and successful completion of study assessment and outcome measures. Bowel Continence and Bowel Independence. The Clinical Global Impression for Improvement. Parent Target Problem (PTP;
Lyseng-Williamson (2018) (Lyseng-Williamson 2018)	This article reviews the pharmacological, efficacy and tolerability profiles of macrogol 4000 without electrolytes.	Narrative review	Children and adults with chronic constipation	NR	More than one – international evidence	More than one category	Laxatives: PEG (without electrolyte)	NR
Masnata (2017) (Masnata 2017)	The aim of this study is to evaluate the connection between urinary and intestinal symptoms and the possible therapeutic approach in children affected by BBD.	Other primary study (cohort)	71 children aged from 4 to 10 years (mean age 7.5 years), with symptoms of the lower urinary tract (LUTS). Rome III criteria used.	U	Italy	Hospital and home	Treatment involved a comprehensive program, of laxatives – PEG plus diet and use of enemas (if needed) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	Not explicit but mention the Bristol Stool Form Scale as a "practical and extremely useful tool for the diagnosis and evaluation of response to therapy in constipation"
Michail (2004) (Michail, Gendy et al. 2004)	To determine safety, efficacy, and optimal dose of PEG powder for treatment of constipation in patients younger than 18 months.	Other primary study (chart review)	28 infants and children < than 18 months who were treated for constipation with PEG powder	No	United States	Hospital and home	Combination treatment: Diet therapy was tried before initiating PEG 3350 therapy. Families were educated on the pathophysiology of constipation and the rationale of therapy. PEG 3350 was administered orally. Caregivers for small infants mixed PEG 3350 in formula if it was the sole diet. The change in dose was permitted within 24 hours, if	Initial dose, effective maintenance dose, response to therapy, duration of therapy, and side effects were recorded.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							necessary. Duration of therapy and side effects were retrieved from the chart.	
Minguez (2016) (Minguez 2016)	To evaluate the evidence published so far on the use of PEG (with or without electrolytes), in the management of CFC and impaction	SR	Included studies on paediatric patients meeting diagnostic criteria of functional constipation and/or faecal impaction. Identified 58 studies (although 28 are children only)	No	More than one – international evidence	More than one category	PEG with or without electrolytes	NR
Mitra (2017) (CTRI/2018/01/011061 2018) (CTRI/2018/01/011061)	To compare the effectiveness, safety and acceptability of PEG	RCT (on-going) ('randomised open-label trial')	Planned recruitment of children aged 2-12 years old presenting to outpatient's department with a clinical diagnosis of CFC and FI	U	India	Hospital (outpatients)	PEG 3350 compared to Lactulose; four weeks treatment	Primary outcomes: weekly changes in frequency of stool passed and no. of painful bowel movement per week Secondary outcomes: monitoring of AEs and SAE s and assessment of acceptability
Modin (2018) (Modin, Walsted et al. 2018) (NCT01566409)	To investigate the long-term efficacy of PEG during maintenance treatment of CFC	RCT	102 children aged 2-16 years diagnosed with CFC according to Rome III	NR	Denmark	Home and hospital (outpatient)	PEG maintenance dose *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	Primary outcome: number of successfully treated children at 24 weeks. Successful treatment was defined as absence of any Rome III criteria, with or without use of medication. Secondary outcomes: number of children who needed rescue medication and presence of FI.
Mugie (2014) (Mugie 2014)	To determine the efficacy, safety, and tolerability of prucalopride compared with placebo for the treatment of CFC	RCT	215 children aged between 6 months and 18 years with a confirmed diagnosis of functional constipation based on the Rome III criteria were eligible for inclusion	U	More than one	U	Prucalopride versus Placebo	Primary outcome: Response was defined as a mean SBM frequency of >3/ week Secondary outcomes: SBM frequency, FI frequency, retentive posturing or excessive volitional stool retention, pain during defecation, stool consistency, abdominal pain, use of rescue medication, and HRQoL. Safety and tolerability were assessed throughout.
NCT02559570 (2015) (NCT02559570 2015)	To evaluate dose response of the safety and efficacy of linaclotide for the treatment of functional constipation (FC), in children age 6-17 years	RCT (reported as completed, and data on clinical trials website but cannot locate a full publication)	Target: 173 children aged 6-17 years Reported as completed. Results posted on the clinical trials website: 14/05/2019	NR	United Kingdom	Home and clinic (setting not reported)	Compared range of Linaclotide doses (9 ug or 18 ug; 18 ug or 36 ug; 36 ug or 72 ug; 145 µg) with placebo control Treatment: 4 weeks	Primary outcomes: change from Baseline in Spontaneous Bowel Movement (SBM) Frequency. Secondary outcomes: AP, Stool consistency, Abdominal Bloating Daytime Symptoms, overall complete SBM frequency
NCT02961556 (2016)	To evaluate the efficacy and safety of AJG555	Unclear – appears to be	Target: 39 children aged between 2-14 years.	NR	Japan	Home and clinic (setting not reported)	AJG555 orally administered for 2 weeks	Primary outcome: change in number of spontaneous bowel movements (SBMs).

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
(NCT02961556 2016)	orally administered for 2 weeks in paediatric participants with chronic constipation.	non-randomised primary study ('baseline-controlled, open-label, multicentre study')	Reported as completed. No results reported on the clinical trials website: date of last clinical trial update is. 24/10/2017					Secondary outcomes: change from the second week of the screening period in the number of SBMs at each week of the administration period, Change from the second week of the screening period in the number of complete SBMs (CSBMs) at each week of the administration period , Change from the screening period in the number of SBMs at two weeks after the initiation of the administration, Change from the screening period in the number of CSBMs at two weeks after the initiation of the administration, Number of days until SBM and CSBM, Change from the second week of the screening period in the total number of SBMs at each week of the administration period, Percentage of responders for SBM and CSBM at each week of the administration period, Stool consistency measured by the Bristol stool form scale, Usage of rescue medication, Number of pouches of AJG555 administered, Duration of administration of AJG555
NCT03120520 (2017) (NCT03120520 2017)	To evaluate efficacy, safety, and pharmacokinetics of oral Plecanatide 0.5, in adolescents with CFC	RCT (reported as completed)	Target: 124 adolescents (aged 12-17 years) diagnosed with CFC based on the Rome III criteria Reported as completed. Results posted on the clinical trials website: 19/9/2019 Cannot see a linked publication to the trial	U	United States	Home and clinic (setting not reported)	Oral Plecanatide 0.5, 1.0 and 1.5 mg tablets dosed once a day as compared to matching placebo, when administered for 8 weeks	Primary outcome: proportion of Overall Responders (An SBM responder is defined as a participant who had >3 SBMs per week). Secondary outcomes: weekly average Stool Consistency, weekly rate of SBM, Weekly rate of complete SBM
NCT04026113 (2019) (NCT04026113 2019)	To evaluate the safety, tolerability and efficacy of Linaclotide therapy	RCT (on-going)	Target: 426 children aged between 6 and 17 years. Participants who meet the modified Rome III criteria for Child/Adolescent FC. Study reported as currently	NR	United States	Home and clinic (setting not reported)	Linaclotide therapy in comparison with placebo 12 weeks treatment	Primary outcomes: change from baseline in 12-week SBM frequency. Secondary outcomes: change from baseline in 12-week stool consistency

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
			recruiting. Last updated in clinical trial register: 25/5/2022					
NCT04110145 (2019) (NCT04110145 2019) This trial is also linked to a EudraCT Number: 2019-002126-75	To evaluate the dose response, safety, and efficacy of linaclotide when compared with placebo in children	RCT (reported as completed)	Target: 35 children aged between 2-5 years. Participant meets modified Rome III criteria for FC. Reported as completed. Results posted on the clinical trials website: 26/4/2022. Cannot see a linked publication to the trial.	NR	United States	Home and clinic (setting not reported)	Linaclotide – different dosages; 4 weeks treatment	Primary outcome: change from baseline in 4-week overall spontaneous bowel movement (SBM) frequency rate (SBMs/week), Change from baseline in 4-week stool consistency reported by the caregiver, Change from baseline in 4-week straining reported by the caregiver, Proportion of days FI
NCT04166058 (2019) (NCT04166058 2019)	A study of Oral Linaclotide Administered to Paediatric Participants with CFC or Irritable Bowel Syndrome With Constipation (IBS-C)	RCT (on-going)	Target: 120 children aged 6- 18 years; mixed population of children with IBS-constipation and CFC alone. Participants meet modified Rome III criteria for child/adolescent FC Enrolling by invitation. Last updated in clinical trial register: 20/8/21 Study due to complete: 14/12/2023	NR	United States	Home and clinic (setting not reported)	Oral Linaclotide	Primary outcome: incidence of adverse events related to treatment
Pare (2014) (Pare 2014)	To review relevant research evidence from clinical studies investigating the efficacy and safety of commercially available pharmacological laxatives in Canada	SR	CFC. Identified 19 relevant studies.	U	Canada	NR	Commercially available pharmacological laxatives in Canada	NR
Pashankar (2001) (Pashankar and Bishop 2001)	To determine efficacy, safety, and optimal dose of PEG 3350, in children with chronic constipation	Other primary study (prospective)	24 children between the ages of 18 months and 12 years with CFC. Diagnosis of chronic constipation was based on symptoms of at least 3 months' duration including at least 2 of the following: hard stools, painful defecation,	U	United States	Home and hospital	At the start of the study all children received PEG solution, and administration of all other medications for constipation was stopped. he initial dose prescribed, based on our previous experience with this agent, was ~1 g/kg body weight per day (14	Detailed history. Daily diary forms to record stool frequency, stool consistency, soiling frequency, and associated symptoms, including fear or avoidance of defecation, blood in stools, and pain during defecation. The dose of PEG solution actually given, the beverage in which PEG was mixed,

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
			withholding of stools, faecal soiling, palpable faecal mass, and fewer than 3 bowel movements per week				mL/kg/d solution), given in 2 divided doses. Parents were asked to increase or decrease the volume of PEG solution by 20% every 3 days as required to yield two soft-to-loose stools (consistency score of 3-4) per day. Caregivers were given a detailed explanation about the pathophysiology of constipation and the rationale of therapy. Children of appropriate developmental status were advised to sit on the toilet for 5 minutes after each meal. The duration of study was 8 weeks.	any adverse effects, and the child's willingness to take the PEG solution were also recorded.
Pashankar (2003a) (Pashankar, Loening-Baucke et al. 2003)	To assess the clinical and biochemical safety profile of long-term PEG 3350	Other primary study	83 children (44 with chronic constipation, 39 with constipation and encopresis) receiving PEG therapy for more than 3 months. The diagnosis of chronic constipation was based on symptoms of at least 3 months' duration, including at least 2 of the following symptoms: hard stools, painful defecation, encopresis, or fewer than 3 bowel movements per week.	NR	United States	Hospital	PEG-3350	Clinical adverse effects related to PEG therapy and acceptance and compliance with PEG therapy. Serum electrolyte levels, osmolality, albumin levels, and liver and renal function test results were also measured. Parents were interviewed using a structured questionnaire and were asked about the dose of PEG given, medication compliance, beverage used to prepare PEG, and ease of mixing. Children were asked about liking the medication and preference compared with laxatives used in the past. Parents were asked about any possible adverse effects of PEG, and about overall improvement in BM pattern regarding stool frequency and consistency with PEG therapy.
Paul (2012) (Paul 2012)	This article focuses on the medical management of functional constipation and outlines some of the non-medical strategies which may help in the overall improvement of the	NR	CFC	NR		More than one category		disimpaction of hard faeces and restoration of regular bowel habits,

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	condition.							
Pensabene (2015) (Pensabene 2015)	To prospectively investigate the occurrence of postinfectious functional gastrointestinal disorders (FGIDs), diagnosed according to the Rome III criteria, in children with acute diarrhea of different infectious aetiology	Narrative review	Children with FI defined using Rome III criteria	U	More than one	More than one	More than one intervention: discusses all interventions in the guidelines	NA
Penuelas Calvo (2016) (Peñuelas Calvo, Sevilla Llewellyn-Jones et al. 2020)	Describes a clinical case of an 11-year-old girl, with a diagnosis of functional encopresis with constipation and overflow incontinence for 4 years.	Other primary study (single case study)	11-year-old female, with a diagnosis of functional encopresis with constipation and overflow incontinence for 4 years.	NR	Spain	Hospital	The program we designed consist of toilet training, establishment-token economy- of a diet high in fiber with a progressive remove of laxative medication and a family intervention with both parents *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	NR
Perkin (1977) (Perkin 1977)	To compare senna and lactulose	RCT (cross-over)	21 children (aged < 15 years) with a history of constipation treated at home for 3 months or more	U	United Kingdom	Home and clinic	Children were "told that a different type of laxative treatment would be given in each of two treatment weeks and that no treatment would be given in the intervening week. Dose varied according to the age of the patient. Lactulose was given in a dosage of 10 to 15 ml daily, while the senna syrup was given in a dose of 10 to 20ml daily. Patients were given lactulose or senna first according to a code list of random numbers	Diary card designed to cover the 3 weeks, day by day. A 4-point stool consistency (loose, normal, hard or non) was used. Number of stools each day was recorded.
Phatak (2014) (Phatak and Pashankar 2014)	To review the recently published paediatric literature on the efficacy, safety, and patient acceptance of PEG.	Narrative review	Childhood constipation. Limited details.	NR	More than one – international evidence	More than one category	PEG	Efficacy, safety, patient acceptance, and cost
Philichi (2018)	This review has multiple	Narrative	Children with constipation.	NR	More than	More than one	More than one intervention:	NA

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
(Philichi 2018)	objectives including explaining the criteria for functional constipation diagnosis and discussing management using the most current evidence-based recommendations.	review	Rome III Criteria was used.		one		Nonpharmacologic Therapy, Pharmacologic Therapy, Education.	
Pijpers (2009) (Pijpers, Tabbers et al. 2009)	Aim to investigate and summarise the quantity and quality of all current evidence for the effect of laxatives and dietary measures on functional childhood constipation in comparison to placebo, no treatment or alternative treatments.	SR	Children aged 0–18 years with CFC. Identified 28 relevant studies (1912 participants)	No	More than one	More than one	Osmotic, bulk-forming, stimulant or emollient laxatives, lubricating agents or dietary measures and were compared to placebo, no treatment or alternative treatment;	Outcome measures at least were either establishment of normal bowel habit (increase of defecation frequency and/or decrease of faecal incontinence frequency) or treatment success as defined by the authors of the study
Poddar (2019) (Poddar 2019)	To find the aetiological spectrum, clinical features to differentiate organic from CFC and the efficacy of polyethylene glycol (PEG) over lactulose in the treatment of CFC	Other primary study (cohort)	316 children with a diagnosis of constipation, managed in the paediatric gastroenterology department	NR	India	Home and clinic	Compare PEG with lactulose	'Successful outcome' defined as: a period of at least 4 weeks with three or more bowel movements per week, without pain during defecation, and two or fewer soiling episodes per month, with complete resolution of all associated symptoms such as retentive posturing, pain abdomen and bleeding per rectum
Price (2001) (Price and Elliott 2001)	To determine the effect of stimulant laxative treatment in children with CFC who may also suffer from soiling / encopresis.	SR	Children who have been diagnosed as having chronic constipation or soiling/ encopresis.	U	More than one	NR	Systematic review which included all RCTs comparing stimulant laxatives with either a placebo or an alternative treatment	Outcomes: cessation of soiling and establishment of normal bowel habit. Time to resolution of symptoms.
Qizilbash (2011) (Qizilbash and Mendez 2011)	To quantify the use of laxatives such as PEG 4000 and to test whether PEG laxative use has increased over time	Other primary study (Retrospective cross-sectional observational study)	Survey targeted 1200 GPs 100 Paediatricians. They must have treated children with constipation who had a prescription of Forlax at doses of 4 g and 10 g in subjects aged 0–18 years, at least once in each relevant year of the study	NR	France	More than one category	Hyperosmolar PEG laxative use (e.g., PEG 4000)	Laxative use
Pranoto 2016 (Pranoto,	To compare the effectiveness of oral and	RCT	99 children aged 8 – 17 years with CFC. Diagnosed as per	NR	Indonesia	Hospital and home	Oral bisacodyl vs rectal bisacodyl	Recurrence of constipation and frequency of defecation. Recovery was

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Supriatmo et al. 2016)	rectal laxatives in terms of recovery and recurrence in children with functional constipation		Rome III criteria.				*This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	defined to be an increase in defecation to more than 3 times/week. Recurrence was defined to be defecation frequency returning to less than two times/week after a period of recovery.
Rachel (2020)(Rachel, Griffith et al. 2020)	Rachel H, Griffith AF, Teague WJ, Hutson JM, Gibb S, Goldfeld S, Trajanovska M, King SK. Polyethylene Glycol Dosing for Constipation in Children Younger Than 24 Months: A Systematic Review. J Pediatr Gastroenterol Nutr. 2020 Aug;71(2):171-175. doi: 10.1097/MPG.0000000000002786. PMID: 32520829.	SR	Children Younger Than 24 Months 468 (5 studies)	NR	More than one – international evidence	More than one category	PEG3350, with or without electrolytes, vs PEG4000 *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	
Radwan (2015) (Radwan 2015)	To determine which dose and duration of senna-based laxatives (SBL) treatment are needed to achieve full defecatory control in children with overflow retentive stool incontinence	Other primary study (observational prospective)	72 children overflow retentive stool incontinence according to Rome III criteria with a contrast enema suggestive of faecal loading	NR	Egypt, Arab Rep.	Hospital	Senna-based laxative treatment	Full defecatory control
Rafati (2011) (Rafati 2011)	To evaluate the clinical efficacy and safety of PEG 3350 solution and liquid paraffin in the treatment of children with CFC	RCT	160 ambulatory children aged 2- 12 years with a history of functional constipation for at least 3 months. CFC was defined as less than 3 stools/week, more than 1 encopresis/week or palpable abdominal or rectal faecal mass on physical examination.	No	Iran, Islamic Rep.	Hospital and home	Patients were randomly assigned to receive either 1.0-1.5 g/kg/day PEG 3350 or 1.0-1.5 ml/kg/day liquid paraffin orally for 4 months	Clinical efficacy was evaluated by stool and encopresis frequency/week and overall treatment success rate. Adverse drug events were determined during examination or at the time of complain of patients and their parents.
Ratanamongkol (2009) (Ratanamongkol, Lertmaharit et al. 2009)	To compare two laxatives, polyethylene glycol 4000 without electrolytes (PEG) and milk of magnesia by	RCT	94 infants and children aged 1-4 years, who met the diagnostic Rome III criteria for CFC and had constipation symptoms for > 1 month	NR	Thailand	Hospital (paediatric outpatient clinic) plus home	PEG 4000 without electrolytes and milk of magnesia. Children received initially either PEG 0.5g/kg/day (PEG400 without electrolytes, 10g/ sachet) or MOM 0.5mL/kg/day (milk	Primary outcome: improvement rate, defined as the proportion of patients who had > three bowel movements per week, < two episodes of FI per month, and no painful defecation, with or

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	evaluating the effectiveness, adverse effects, and patient compliance						of magnesia suspension, 400mg/5mL) once daily.	without laxative therapy. Secondary outcomes: 1) improvement in stool frequency per week; 2) the proportion of the patients who had any adverse effects; and 3) the compliance rate, defined as the proportion of patients who received more than 80% of the medication. compliance rate.
Rezaie (2012) (Rezaie, Cheng et al. 2012)	To assess the efficacy and safety of prucalopride for the treatment of chronic constipation.	SR protocol (on-going)	Patients of any age or gender, with chronic constipation will be included in the study	NR	More than one – international evidence	More than one category	Prucalopride	Primary outcome: proportion of patients having three or more spontaneous bowel movements (SBM) per week. Secondary outcomes: will include: Proportion of patients having, on average, three or more spontaneous complete bowel movements per week during the trial period. Also planned to assess adverse events and QoL measures using self-reported questionnaires
Sadeghzadeh (2014) (Sadeghzadeh 2014)	To investigate the effectiveness of probiotics in childhood constipation	RCT	56 children aged 4–12 years old who fulfilled Rome III criteria for CFC	No	Iran, Islamic Rep.	Hospital and home	Randomly allocated into two groups who received lactulose (1 mL/kg/d) plus Protexin (probiotic) one sachet daily or lactulose plus placebo alone for four months	Questionnaire for symptoms of constipation including the frequency of defecation, stool consistency, AP, frequency of FI, and side effects in both groups.
Saha (2016) (Saha 2016)	The aim of this study was to find out the pattern of constipation in children attending a tertiary care hospital	Other primary study (prospective)	Children aged 1 month to 10 years old with constipation. Constipation was defined as per the NASPGHAN definition which states that“constipation is a delay or difficulty in defecation, present for two weeks or more, and suffi cient to cause signifi cant distress to the patient”	U	India	Hospital (outpatients)	Polyethylene glycol	Age, sex, duration of constipation, symptoms and signs such as bowel frequency and consistency, painful defecation, presence of bloody stool, fecal and urinary incontinence, presence of fecal impaction or an abdominal mass. A response was defined as passage of at least one semisolid stool without discomfort with use of PEG for at least 4 weeks.
Saneian (2012) (Saneian 2012)	To compare the efficacy of three laxatives: PEG, magnesium hydroxide, and lactulose.	RCT	75 children aged 1 to 6 years with CFC.	No	Iran, Islamic Rep.	Hospital and home	PEG vs magnesium hydroxide vs and lactulose in a standard dosage. Treatment was one month. The intervention conducted in four stages as the following: 1. Verbal education and pamphlet by paediatric resident; 2. Diet (prepared list), 3. Laxatives for a month and	Therapeutic result was evaluated as defecation equal or more than 3 times a week without pain and bleeding (smooth, relax and large diameter) in addition with FI < twice a month at the end of one-month treatment.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							disimpaction, if necessary and 4. follow-up (a week later and then monthly for 4-6 months.	
Savino (2012) (Savino 2012)	To compare the efficacy, tolerability, acceptance and compliance of anew PEG-only formulation compared to a reference PEG-electrolyte formulation in resolving faecal impaction and in the treatment of CFC	RCT	96 children aged between 2 and 16 years and had a diagnosis of CFC according to Rome III criteria or showed faecal impaction at physical examination.	No	Italy	Hospital and home	PEG-only laxative vs PEG-electrolyte. The duration of treatment was 4 weeks	Stool frequency over the 4 weeks of treatment. Secondary outcomes: occurrence and timing of faecal disimpaction, stool consistency, frequency of pain/difficulty in passing stools over 4 weeks, frequency of soiling episodes over 4 weeks, parent and child satisfaction, use of laxative, tolerability (episodes of nausea and AP), acceptability (palatability 5-point scale and ease of administration) and compliance.
Shatnawi (2019) (Shatnawi, Alrwalah et al. 2019)	To compare the safety, efficacy, tolerability of this therapy compared to a reference PEG formulation in resolving faecal impaction.	RCT	72 children aged between 1 and 14 years and had diagnosis of CFC according to Rome III criteria with evidence of faecal impaction.	No	Jordan	Hospital and home	Lactulose versus polyethylene glycol for disimpaction therapy *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	Age, gender, growth parameters (height and weight), day of disimpaction, possible adverse events, parents and child satisfaction, compliance and acceptability.
Soares (2009) (Soares, Tahan et al. 2009)	To analyse the effects of conventional treatment of CFC in patients attending a referral outpatient clinic	Other primary study (prospective case series)	34 children with CFC. Median age was 93.7 (74.3-107.4) months, range: 3-13 years)	U	Brazil	Hospital (outpatient clinic) and home	Disimpaction was performed if necessary with phosphate enema for 2 to 5 days. Patients were then prescribed a high-fibre diet and mineral oil at a dose of 1-3 mL/kg/day, in two divided doses. General instruction in the physiology of evacuation and bowel training including defecation in the toilet after meals were also part of the therapy regimen. At follow-up appointments, when necessary, mineral oil dose was adjusted. In the case of reimpaction, disimpaction procedures were repeated *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	Individual standardized form including the following clinical parameters was used: defecation frequency, pain during defecation, fear or effort during defecation, faecal retention, stool consistency and shape, presence of soiling, blood mixed with stools, and abdominal distension and pain. A complete physical examination, including a rectal examination, was also performed

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Sondheimer (1982) (Sondheimer and Gervaise 1982)	To assess the outcome of two groups of children with CFC treated in a highly supportive environment either with mineral oil, a stool lubricant, or Senakot	RCT	37 children aged 3 and 12 years with CFC. Diagnosis of CFC was made of the basis of historical features and a physical exam demonstrating a dilated rectum, excessive retained stool directly within the anal verge, and in most cases evidence of perianal soiling	No	United States	Hospital (outpatient clinic) and home	Mineral oil, a stool lubricant, or Senakot	3-day food diary, plain abdominal X-ray, parental record of medication, stool frequency, faecal soiling, 2nd 3-day diary, subject record of patient compliance was recorded at each telephone contact and clinic visit
Southwell (2015) (Southwell 2015)	To determine stool output produced by combined PEG and SPS in children with chronic constipation with a palpable faecaloma.	Other primary study (prospective cohort)	22 children (median age: 8 years) with CFC (> 2 years duration) and a palpable faecaloma confirmed by enlarged stool-filled rectum on x-ray	NR	Australia	U	Combined PEG and Sodium Picosulphate for disimpaction	Daily diary with laxative dose, defecation frequency, stool volume and consistency
Speridião (2003) (Speridiao, Tahan et al. 2003)	To determine dietary fibre and energy intake and nutritional status during the treatment of CFC	Other primary study (prospective cohort)	25 children aged 2- 10 years with CFC. Children presenting soiling or less than three bowel movements per week were included in the study irrespective of the elimination of hard stools.	No	Brazil	Hospital (outpatients)	Standardised diet therapy plus laxatives *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 20*	The anthropometric measurements, the 72-h food record, the food frequency inquiry and the evaluation of the clinical manifestations were repeated after 45 and 90 days of treatment.
Steiner (2011) (Steiner 2011)	To assess and analyze the treatment adherence of constipated children	Other primary study (chart review)	68 children with constipation. Mean age 74.4 +/- 42.3 months	NR	Brazil	Hospital (outpatients)	Polyethylene glycol versus milk of magnesia	Treatment adherence
Steiner (2014) (Steiner 2014)	The aim of the present study was to evaluate the treatment adherence of children with chronic functional constipation	Other primary study (prospective longitudinal study)	50 children (<16 years old; mean age : 77.6 +/-43.8 months) with CFC. CFC defined using Rome III criteria.	U	Brazil	Hospital (outpatients)	Polyethylene Glycol (PEG) without electrolytes, magnesium hydroxide, mineral oil	Ahderence
Okumura (2018) (Okumura, Tang et al. 2018)	To compare the efficacy of Linaclotide with other CFC medications for CC.	SR	Patients with CFC, including IBS-C and opioid-induced constipation (OIC). 52 studies included in this review	NR	More than one – international evidence	More than one category	Linaclotide compared to other medications. A total of 47 treatments/16 drugs (Lubiprostone, Plecanatide, PEG, Prucalopride, Lactulose, Bisacodyl, Ispaghula, Wheat (trticum), Lactitol, Methylnaltrexone, Alvimopan, Naloxegol, Naxalone, Tegaserod, Placebo)	NR

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Thomas (2013) (Thomas 2013)	To identify and review all relevant data in order to determine whether Lactulose or Polyethylene Glycol is more effective at treating chronic constipation and faecal impaction.	SR (and MA)	Chronic constipation. Included 12 studies, participant age ranged from 3 months to 70 years	NR	More than one – international evidence	More than one category	Comparing the use of lactulose and polyethylene glycol	Outcomes measured based on what was extracted from each study included stool frequency, consistency and AP.
Thomson (2007) (Thomson, Jenkins et al. 2007)	To assess the efficacy and safety of polyethylene glycol 3350 plus electrolytes (PEG+E) for the treatment of chronic constipation in children.	RCT	51 children aged 24 months to 11 years with CFC for at least 3 months. Chronic constipation was defined according to the Rome criteria as fewer than three complete BMs per week, and at least one of the following: pain on defaecation on at least 25% of days; at least 25% of bowel movements with straining; and at least 25% of BM with hard or lumpy stools.	U	United Kingdom	Hospital (outpatients) and home	PEG 3350 plus electrolytes (PEG+E)	Primary outcome: mean number of complete defaecations per week. Secondary outcomes: included the total number of complete and incomplete defaecations per week, pain on defaecation, straining on defaecation, faecal incontinence, stool consistency, and a global assessment of treatment by the investigator and by the child or his or her parent or guardian. Safety was monitored by adverse events recording, physical examination findings, and weight changes theoretically secondary to fluid shifts and gastro-intestinal fluid loss, however unlikely.
Tolia (1993) (Tolia, Lin et al. 1993)	To compare the efficacy and acceptability of the treatment of faecal impaction using either mineral oil or pineapple flavoured isotonic intestinal lavage solution containing PEG-3350	RCT	48 participants older than 2 years in age with constipation were potentially acceptable for the study. Constipation was defined as the passage of infrequent, large sized firm to hard stools with or without associated rectal pain or bleeding.	No	United States	Hospital and home	Group 1 received 2-8 tablespoons of mineral oil in two divided doses for two days. The dose of mineral oil was empirically determined by the formula of 30ml/10kg body weight. If the parents had any difficulties administering the oil, they were asked to disguise it by blending it with 120-180ml of orange juice. Patients in group 2 were assigned pineapple flavoured balanced oral lavage solution (sweetened with nutra-sweet) to drink in the dose of 20ml.kg/hour for 4 h once daily on two consecutive days. Maximum amount of lavage solution per hour was 1 litre. In addition, group 2 patients received a single oral dose of metoclopramide (0.1mg/kg) before drinking the lavage	Physical examination, bloods for polyethylene glycol (PEG) level was drawn from the patients before and after treatment. Parents were asked to keep a diary of the compliance of their child with the medication, the number of the first bowel movement after treatment, number of bowel movements each day, consistency of bowel movements, abdominal distention, cramps, nausea and vomiting.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							solution on both days to prevent nausea and vomiting. After the treatment of faecal impaction all the patients were advised on long-term maintenance stool-softening protocol with diet and behaviour modification with addition of lubricant as necessary.	
Torabi (2017) (Torabi, Amiraslani et al. 2017) (IRCT2014091618971N)	To compare the effect of oral paraffin and PEG for treatment of children with CFC	RCT	160 children aged 2-12 years with CFC for at least 6 months and without improvement after given suitable diet and toilet training. CFC diagnosed using Rome III criteria	NR	Iran, Islamic Rep.	Hospital and home	Oral paraffin vs PEG	Frequency of defecation per week, stool consistency, rectal bleeding, painful defecation, FI and AP
Tort (2016) (Tort 2016)	How does polyethylene glycol (PEG) compare with placebo and other interventions for the management of childhood constipation?	Narrative review	Cochrane clinical answer – see Gordon 2016 for more details about the review on which this summary is based.	NR	More than one – international evidence	More than one category	Osmotic laxatives	Frequency of defecation, rates of FI, adverse effects
Treepongkaruna (2014) (Treepongkaruna 2014)	To compare the efficacy of PEG 4000 to that of lactulose in the treatment of young children aged between 12 to 36 months with CFC	RCT	88 children aged between 12 to 36 months with a diagnosis of CFC based on a modification of the Rome II criteria for infants and preschool children	U	Thailand	Hospital (outpatients) and home	Osmotic laxatives: lactulose (3.3 g per day) or PEG (Polyethylene glycol (PEG, macrogol) 4000 (Forlax®; 8 g per day) for a period of four weeks	Primary outcome: stool frequency at week 4. Secondary outcomes: stool consistency, ease of stool passage and the occurrence of subjective symptoms associated with defecation, namely cramping, flatus and anal irritation at each visit. Adverse events (AEs) were assessed from discussion with the parents at Visits 3 and 4. Incidence of AEs and serious AEs (SAEs) was documented over the entire four-week study period.
Urganci (2005)	To determine and compare efficacy, safety and optimal dose of two laxatives: liquid paraffin and lactulose.	RCT	40 children aged 2–12 years old referred to the paediatric gastroenterology clinic for evaluation of constipation with evidence of faecal impaction were enrolled.	N	Turkey	Hospital	Liquid paraffin or lactulose was given for 8 weeks to children with constipation. They also met with a nutritionist, were given instructions to increase their daily fibre intake to an amount of grams equal to their age plus parents were asked to have children sit on the toilet four times daily after meals and to keep a stool diary, and received a calendar to	Daily diaries to record encopresis, AP, stool frequency, stool consistency and associated symptoms, including rectal bleeding, fear of painful defecation, encopresis and abdominal pain. Patients were also instructed to bring both empty and full containers and the amount of medication taken was calculated.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							record the occurrence of bowel movements.	
Ustundag (2010)	To see if partially hydrolysed guar gum (PHGG) can be used safely as a fibre source for treatment of CFC and to compare it with lactulose.	RCT	68 Children aged between 4 to 16 years who had at least two or more criteria for constipation: stool frequency of two or fewer per week, at least one episode of FI per week, history of retentive posturing or excessive volitional stool retention, history of painful or hard bowel movements, presence of large faecal mass in the rectum, and history of large diameter stool that may obstruct the toilet.	U	Turkey	Hospital (outpatients)	Hydrolyzed guar gum (PHGG) or lactulose	Defecation frequency, consistency of stool, frequency of FI and AP, and adverse reactions. Successful treatment was defined as soft to formed stool consistency, absence of pain, stool withholding and blood in the stool, and no palpable rectal or abdominal mass.
Valencia (2014) (Valencia 2014)	Which constipation management approaches are most effective for infants younger than 2 years?	Narrative review	Children <2 years old diagnosed with CFC using the Rome III criteria	U	More than one	More than one	Mineral oil, lactulose, sorbitol, PEG, and MOM	NA
Van Wering (2012) (Van Wering 2012)	A literature to evaluate the efficacy and safety of laxatives used in treatment of childhood CFC	Narrative review	Children aged 0-18 years diagnosed with CFC with or without FI in either the primary health or specialist setting.	No	More than one – international evidence	More than one category	Laxatives - osmotic laxatives, faecal softeners, stimulant laxatives. Enemas. Maintenance Treatment - dietary interventions, behavioural modification and laxatives.	Safety and effectiveness
Voskuijl (2004) (Voskuijl, de Lorijn et al. 2004)	To compare PEG 3350 with lactulose in children with CFC	RCT	100 children aged six months - 15 years were included in this study. Childhood constipation was defined as having at least two out of four of the following symptoms for the last three months: less than 3 bowel movements per week; encopresis more than once a week; large amounts of stool every 7–30 days (large enough to clog the toilet); and palpable abdominal or rectal mass on physical examination	No	Netherlands	Hospital and home	Children aged between six months and six years of age (inclusive) began treatment with one sachet of either PEG 3350 or lactulose per day (2.95 g or 6 g, respectively) while those older than six years of age were given two sachets per day (5.9 g PEG 3350 or 12 g lactulose). Toilet training after each meal (five minutes) was advised and incentives such as small gifts and praise were used to encourage compliance	Defecation and encopresis frequency, AP and stool consistency recorded. compliance.
Wang (2012)	To evaluate the efficacy and safety of PEG 4000	RCT	227 children aged 8-18 years of age Diagnosis based on	U	China	Hospital and home	Children in the PEG 4000 treatment group received 20 g of PEG 4000	Primary outcomes: weekly stool frequency and stool consistency.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	for the treatment of CFC		symptoms which consisted of weekly stool frequency of 2 or less and stool consistency type 1-3 (Bristol Stool Scale) for at least 2 weeks.				dissolved in a glass of water or drink each morning before breakfast for two weeks. Patients in the lactulose treatment group received 15 ml of lactulose (10 g) oral solution (Duphlac) per day after breakfast for the first 3 days, and then 10 ml (6.7 g) per day for the following 11 days.	Secondary outcomes: included the remission rate of abdominal pain and the rate of clinical remission.
Williams (2018) (Williams 2018)	To determine whether trace amounts of ethylene glycol (EG), diethylene glycol (DEG), or triethylene glycol (TEG) in PEG 3350 are associated with increased blood levels of EG, DEG, or TEG in children receiving daily PEG 3350 therapy.	Other primary study (cohort)	9 children (6-12 years old) who were being treated for constipation with PEG 3350	U	United States	Hospital (outpatients)	PEG 3350	PEG 3350, tap water, and blood samples
Winter (2013) (Winter 2013)	To evaluate the pharmacokinetics, efficacy, safety, and tolerability of Prucalopride oral solution.	Other primary study (non-randomised)	38 children aged 4 years to 12 years with a confirmed diagnosis of CFC defined as a history of faecal impaction occurring periodically during at least 2 months	No	United States	Hospital	Oral prucalopride. All children received a single dose of 0.03 mg/kg prucalopride in oral solution (0.2 mg/mL), together with 30 mL of water. A standardized snack of milk and cookies was served 2 hours after dosing. All of the children consumed age-appropriate meals and fluid volumes. Fluid intake was standardized and strictly monitored. 4-week interventional study	Blood samples, a daily diary to document frequency of bowel movements in the toilet, episodes of FI, the need for repeated disimpaction, and stool consistency.
Yachha (2018) (Yachha 2018)	To formulate practice guidelines for the management of childhood functional constipation that are relevant to Indian children.	Other primary study (questionnaire based survey)	Children with CFC	U	India	More than one	More than one intervention: Patient counseling, Toilet training, diet, Fibre and water intake. Medical therapy: Disimpaction, Maintenance theapy (Osmotic Laxatives - PEG, Lactulose. Stimulant Laxatives), Behavioural therapy and biofeedback, follow-up	Successful outcome of treatment: defined as (a) stool normalcy while on laxatives for a period of at least 4 weeks of initiation of therapy, and (b) achievement of stool normalcy for a minimum period of 6 months before tapering. Normalcy of stools should defined as daily, nothard, nor loose watery stools, with absence of pain, straining, bleeding, posturing or incontinence.
Yik (2018) (Yik 2018)	To identify indications of the use for Movicol	Other primary study	198 children with CFC	NR	Malaysia	Hospital	Movicol	Symptoms of constipation

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	and the effectiveness of Movicol in treating CFC in Malaysian children	(prospective, cross- sectional survey)						

Table 4. Level 2 – Continence teams: specialist community and secondary care-based services Level 2 interventions delivered by Continence teams

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Anderson (2019)(Anderson 2019)	To assess and compare the efficacy of the various enema solutions used in a paediatric ED	Other primary study (Online survey and retrospective chart review)	768 children based on electronic pharmacy or nursing order records which indicated that they received any type of liquid enema in the paediatric ED. The majority of patients seen in this ED are <18 years of age, but during the study period, paediatric subspecialty patients were eligible to be seen until their 25th birthdays	NR	United States	Hospital (Emergency Department)	Enema solutions: included sodium phosphate enemas, the locally compounded pink lady enema, and soap suds enemas. The pink lady enema consists of 100 mL docusate liquid, 60 mL magnesium citrate, 60 mL mineral oil, and 66 mL sodium phosphate enema solution.	Primary outcome: stool output after enema administration. Other outcomes: enema dose, chief complaint, comorbidities, side effects, use of additional enemas, patient disposition, and the use and findings of radiographs.
Awan 2016 (Awan and Masood 2016)		Prospective cohort	40		Pakistan?		Physical therapy for cerebral palsy *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	
Awan 2021 (Ahmed Awan, Masood et al. 2021) (NCT03379038)		RCT (crossover trial)	35	Yes	Pakistan?		Physical therapy for cerebral palsy *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	
Bae (2019)(Bae 2019)	Analysed clinical characteristics, the results of diagnostic tests, and treatments of pelvic floor dysfunction in children who had constipation	Other primary study (retrospective case note analysis)	13 children, median age was 10yrs (range 8-18yrs), who were diagnosed pelvic floor dysfunction with fluoroscopic defecography. median duration of constipation was 6.5 years (2-18yrs), and median age of onset of constipation was 3 years (0-11 years)	NR	Korea, Rep.	Hospital	Medical therapy with PEG 4000 plus biofeedback	Demographics, colon transit time and laxatives used.
Bekkali 2009 (Bekkali, van den Berg et al. 2009)	To evaluate the efficacy and tolerability of enemas versus high doses of oral PEG in disimpaction of children with functional constipation and rectal faecal impaction	RCT	90 children (mean age of 7.5±2.8 years. Eligible if they had evidence of rectal faecal impaction upon rectal examination and fulfilled at least one of the other Rome III criteria for CFC for at least 2 months.	NR	Netherlands	Hospital (tertiary institution)	Enema vs PEG One group received rectal enemas (dioctylsulfosuccinate sodium) once daily for 6 consecutive days, children < 6 years 60 ml and children ≥ 6 years 120 ml. The other group received oral PEG 3350 with electrolytes for six consecutive days. Maintenance treatment was started after 6 days disimpaction treatment and	Primary outcome was successful disimpaction. Secondary outcomes: defecation and faecal incontinence frequency per week, abdominal pain, watery stools, CTT values and the child's behaviour

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							consisted of oral PEG 3350 with electrolytes for at least 2 weeks (follow-up). *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	
Benninga (2005) (ISRCTN99089299) (ISRCTN99089299 2005)	The effect of additional use of enemas versus the standard treatment of chronic constipation in children	RCT (on-going)	100 children aged 8 to 18 years with constipation	NR	Netherlands	Multiple settings	Movicol	Primary outcomes: defecation frequency, Soiling/encopresis frequency, stool consistency and use of laxatives. Secondary outcomes: rectal compliance and sensation
Benninga (2006) (ISRCTN71579145) (ISRCTN71579145 2006)	Enema versus high doses of PEG 3350 in the treatment of rectal faecal impaction	RCT (on-going)	90 children aged 4 to 18 years with constipation and faecal impaction upon rectal exam	NR	Netherlands	Multiple settings	PEG 3350	Primary outcomes: rectal faecal impaction evaluated by rectal examination/abdominal x-ray. Secondary outcomes: defaecation frequency/week, FI frequency/week. Number of side effects, such as abdominal pain, bloating, flatulence, nausea, bad taste is documented. Total and segmental colonic transit time is measured.
Bischoff (2018)(Bischoff 2018)	Present a protocol to treat CFC	Other primary study (Online survey and retrospective chart review)	215 children aged between 11 months and 20 years with CFC. Duration of constipation symptoms was available for 148 patients: 55 (37%) of them had constipation symptoms since birth and 93 (63%) of them developed constipation after the newborn period, most commonly after the introduction of solid foods. The average duration of symptoms for patients that presented with constipation later in childhood was 54 months.	U	United States	Hospital	Individualised treatment regimen. Begin with a water-soluble contrast enema, without bowel preparation. The three enemas are: 1) normal saline + liquid glycerin, 2) normal saline + fleet enema, 3) normal saline + castile soap. If the child remains impacted, he/she is admitted to the hospital and receives Golytely® (25 ml/kg/h) through a nasogastric tube for 2 days in addition to the enemas. If faecal impaction persists, the child is then taken to the operative room for manual disimpaction under anaesthesia. Once the colon is confirmed clean on the abdominal radiograph, the trial and error protocol is started with a Senna based laxative. The initial dose is arbitrarily determined based on the magnitude of the colonic dilation as seen on contrast enema. The parents are instructed to record the number and consistency of bowel	A laxative trial was considered successful when the daily dosage of laxative required to empty the colon, as confirmed by a clean colon on abdominal radiograph, was reached, and the patient remained clean in his/her underwear.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							movements during the next 24 h. If there is no bowel movement in 24 h, the parents are instructed to give an enema to clean out the colon, and the laxative dose is increased by 15 mg on that same day. If the patient has multiple liquid bowel movements, the laxative dose is decreased by 7.5 mg of Senna.	
Bongers 2009 (Bongers, van den Berg et al. 2009)	To explore whether additional treatment with rectal enemas is clinically more effective than conventional treatment alone in severely constipated children.	RCT	102 children aged between 8 and 18 years with CFC for at least 2 years and unresponsive to conventional treatment were eligible. Functional constipation was defined as presence of at least 2 of the 4 following symptoms: (1) spontaneous defecation frequency 3 per week, (2) fecal incontinence episodes 2 per week, (3) passage of large-diameter stools that might obstruct the toilet, and (4) palpable abdominal or rectal mass on physical examination	No	Netherlands		Enema + PEG vs PEG All children underwent rectal disimpaction by rectal enema (120 mL sodium-dioctyl sulfosuccinate and sorbitol) on 3 consecutive days to achieve an empty rectum before starting the treatment trial. If rectal disimpaction was unsuccessful, rectal enemas were continued for a maximum of 7 days. Conventional treatment consisted of education, behavioural strategies, and oral laxatives.15 Oral laxative therapy consisted of polyethylene glycol, with a starting dose of 0.5 g/kg. If treatment was considered insufficient, the dose was optimized to a maximum of 1.5 g/kg. In the CG, a rectal enema or bisacodyl suppository of 5 mg was only prescribed in case of reoccurrence of faecal impaction. In the IG, children received, in addition to conventional treatment, 3 rectal enemas weekly during the first 3 months. Thereafter, this frequency was reduced by 1 enema per week every 3 months. *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	Visits to the outpatient clinic for evaluation of defecation pattern and laxative use were scheduled for all children at 2, 4, 6, 12, 26, 39, and 52 weeks. In addition, at week 52, subjective feelings about application of rectal enemas were assessed. Main outcome measures were defecation frequency per week, fecal incontinence frequency per week, and overall treatment success after 12, 26, 39, and 52 weeks of treatment. Overall success was defined as 3 bowel movements per week and 1 fecal incontinence episode per week, irrespective of laxative use. Secondary outcome measures were abdominal pain and painful defecation at 12, 26, 39, and 52 weeks and scores on the short questionnaire about regular application of rectal enemas after 1 year of treatment.
Borowitz 2002 (Borowitz, Cox et al. 2002)		RCT	87				Intensive medical therapy; intensive medical therapy plus enhanced toilet training; these combined with EMG biofeedback. *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	
CADTH (2015)	To answer the following questions: 1. What is the clinical effectiveness and	Narrative review (rapid response)	Patients presenting with constipation and fecal impaction in the emergency department.	NR	More than one – internationa	Hospital – Emergency department	Any type of enema	Clinical benefit (e.g., changes in bowel function), clinical harm Guidelines

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	harms of enemas for patients presenting with constipation and fecal impaction in the emergency department? 2. What are the evidence-based guidelines regarding the use of enemas for patients presenting with constipation and faecal impaction in the emergency department?		Identified 5 relevant studies.		l evidence			
Chumpitazi (2016)(Chumpitazi 2016)	To assess the efficacy and safety of soap suds enema (SSE) in the treatment of fecal impaction in children with abdominal pain within the pediatric emergency department (ED) setting	Other primary study (Online survey and retrospective chart review)	512 children with AP and clinically suspected of having a faecal impaction by the attending physician were included. Median age 7.8 years, range: 8 months-23 years	U	United States	Hospital – Emergency department	Soap suds enemas	The primary outcome was stool output following SSE. Secondary outcomes were adverse events, admissions, and return visits within 72 hours
Clarke (2009) (Clarke, Chase et al. 2009)	To determine the effects of interferential therapy on colonic transit	RCT	26 children aged between 7 to 18 years with STC diagnosed by NTS - nuclear transit studies	NR	Australia	Multiple settings	Transcutaneous electrical stimulation using interferential current (interferential therapy [IFT])	Primary outcome measure was nuclear scintigraphic assessment of colonic transit
Clarke 2012 (Clarke 2012)	To determine whether transcutaneous electrical stimulation using interferential current (IFC) applied to the abdomen increased colonic PS in STC children.	Other primary study						
Coulter (2002) (Coulter, Favreau et al. 2002)	To review evidence for the efficacy of biofeedback in the treatment of gastrointestinal problems.	SR	Gastrointestinal condition. 16 studies	NR	More than one – international evidence	Multiple settings	Biofeedback	Rsk ratio and treatment success
Croffie (2005) (Croffie, Ammar et al. 2005)	To determine whether biofeedback benefits children with dyssynergic defecation and constipation/encopresis, and whether home biofeedback improves long-term outcomes.	Unclear (clinical trial)	36 children with recalcitrant idiopathic constipation/encopresis who were referred for anorectal manometry by faculty paediatric gastroenterologists and were diagnosed with dyssynergic defecation. Age range was 6–14 years, with a mean age of 9.2 years. Constipation was defined as less	U	United States	Residential care/looked after child	Biofeedback therapy	Frequency of bowel movements, soiling, and laxative use before and after biofeedback were compared

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
			than 3 bowel movements per week, with or without overflow incontinence, and not improving, despite compliance with conventional therapy, including laxative and toilet behaviour modification, for at least 6 months					
Dale (2019) (Dale, Morgan et al. 2019)	This paper summarises Cedar's assessment report and how it was used to inform the NICE MTG on the Peristeen transanal irrigation system to manage bowel dysfunction (MTG36).	Narrative review (summary report)	People with bowel dysfunction in any setting. Identified 24 studies (11 studies with children) as relevant. CFC definition was NR.	NR	More than one – international evidence	Multiple settings	Peristeen transanal irrigation system; Control: comparator was defined as conservative bowel management, which can include treatments such as diet and bowel habit advice, medication, disposable pads and anal plugs, muscle/bowel training, biofeedback and electrostimulation, and digital stimulation and manual evacuation	Severity and frequency of incontinence, severity of constipation, quality of life, length and frequency of irrigation, device-related adverse events, frequency of UTI, incidence of stoma surgery and hospitalisations, staff time (including primary care and community care visits), and individual length of use/user satisfaction.
Desantis (2011) (Desantis 2011)	This study was undertaken to summarize available literature relating to the effectiveness of biofeedback for dysfunctional elimination syndrome in the paediatric population.	SR	Children aged < 18 years with dysfunctional elimination syndrome. Identified 27 relevant studies. CFC definition was NR but the RFI had to be diagnosed by the physician performing abdominal and/or rectal examination.	NR	More than one – international evidence	Multiple settings	Included papers assessing children younger than 18 years of age who were diagnosed with DES and underwent therapy with Biofeedback modalities performed by a qualified professional including pelvic floor muscles EMG (by direct tracing or interactive software).	Effectiveness of biofeedback treatment was determined by reduction in the two primary outcomes: urinary tract infections and daytime urinary incontinence. Secondary outcomes included nocturnal enuresis, constipation, urinary frequency, urinary urgency, vesicoureteral reflux (VUR), post-void residual (PVR) and uroflow parameters.
Dziechciarz (2015) (Dziechciarz, Wojtyniak et al. 2015)	The aim of this systematic review was to compare the effectiveness and tolerability of PEG versus enema in the management of rectal faecal impaction (RFI) in children with constipation.	SR	Children (up to 18 years old) with functional constipation and RFI were included. CFC definition was NR.	NR	More than one – international evidence	Multiple settings	The intervention had to be the administration of enema compared with oral administration of PEG	The primary outcome measure was the treatment success as defined by the investigators. The secondary outcome measures were frequency of stool defecations, tolerability of the medication, and adverse events. Other outcomes were included if relevant to the current review.
Eisenberg 2009 (Eisenberg, Zuk et al. 2009)	To explore the feasibility of using the HW device with children who have CP and are not ambulatory	Other primary study (Non-randomised study)	22 11 children with severe CP. Aged between 3.5 and 10 years at the first visit to the clinic, diagnosis of CP spastic quadriplegic and categorized by the gross motor function classification system (level 4), inability to stand and walk with	Yes	Israel	Hospital – outpatient clinic	Standing frame vs walker for cerebral palsy. Before the study began, all subjects were receiving physical therapy based on neurodevelopmental treatment of movement while working on motor functions (including lower-extremity weight-bearing activities). A standing program in a SF 4 times a week for 30 minutes	Not explicitly stated

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
			a traditional walker/rollator because of insufficient upper extremity control, attempts steps when in a supported standing position, and flexion contracture of the hips and the knees of less than 30°.				was part of the NDT treatment. Parents were encouraged to use a SF at home, for example during the time the child watches television. All the children in the study underwent the NDT treatment program. The control subjects continued with the program which included the standing sessions. Children in the study group, however, did not use the SF but practiced a standing and stepping program in the HW- gait trainer that provides support to allow the child to walk. The program began with 30-minute sessions, 4 times a week but the children as well as parents were encouraged to use the HW device. *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	
EUCTR2010-023538-22-IS (EUCTR2010-023538-22-IS 2011)	Lýsi sem hægðalyf fyrir born The primary objective of this trial is to investigate the laxative effect of Lysisstílar (Free Fatty Acids suppositories) as compared to Klyx	RCT (on-going)	Reported as completed but no data. https://www.clinicaltrialsregister.eu/ctr-search/search?query=2010-023538-22					
Farahmand (2007) (Farahmand 2007)	The aim of this study was to compare the clinical, efficacy and safety of liquid paraffin and lactulose in the treatment of functional childhood constipation	RCT	247 children with CFC (aged 2 -12 years). Diagnosis of chronic constipation was based on: having at least two out of four of the following symptoms, for the last 3 months: less than 3 bowel movements per week; faecal soiling, more than once a week, large amounts of stool every 7-30 days and palpable abdominal or rectal faecal mass on physical examination.	U	Iran, Islamic Rep.	Hospital	At the first, patients received one or two enemas daily for two days to clear any rectal fecal impaction. (30 cc / 10 kg weight of paraffin oil for enema). Medications were administered orally as 1-2 ml/kg at, twice daily for each drug, for 8 weeks. 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, 1 or 2, firm– loose, stools. They also, were given instructions to increase their daily fiber intake to an amount of grams equal to their age plus 10 (9). Toilet training after each meal (five minutes) was advised were used to enhance compliance.	Treatment success was defined as three or more bowel movements a week and encopresis episode less every two weeks. The incidence and severity of gastrointestinal adverse event were recorded.
Freedman 2014 (Freedman,	To determine whether enema administration is	Other primary study	877 2795 children <18 years old who	NR	Canada	Hospital – Emergency	Enema administered in the emergency department *This study is included in the effectiveness review.*	Primary outcome: 7-day ED revisit for persistent symptoms related

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Thull-Freedman et al. 2014)	associated with 7-day ED revisits for persistent symptoms of constipation	(Retrospective cohort)	presented to the ED and were assigned a diagnosis consistent with constipation by the treating physician.			department	*Further details about the intervention are profiled in Appendix 5, Table 21*	to constipation. Secondary outcomes: assessing associations between discharge laxative medications (any medication vs no medication) and revisits and identifying other predictors of ED revisits.
Garcia 2016 (Garcia 2016)	To validate COMREST, a structured management scheme for the treatment of faecal impaction	RCT	58 paediatric patients aged 2-18 years old admitted for faecal impaction. Diagnosis criteria for CFC was not reported.	Philippines		Hospital	Oral + enema therapy vs enema COMREST (Constipation management relief and support therapy) regimen. One-day novel combination of oral and rectal laxatives for the treatment of fecal impaction that consists of Fleet enema, bisacodyl suppository, and castor oil. *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	Primary outcome: proportion of successful disimpaction between the two treatment groups defined as relief of symptoms present prior to the disimpaction regimen and/or a Blethyn Score of 0 or 1.
Gil (2015)(Gil 2015)	We compared the effectiveness and complication of sigmoidoscopic enema between children and adult	A single-center, retrospective study	64 (43 children) patients with faecal impaction receiving sigmoidoscopy-assisted enema. Mean age 5.98 ± 3.64 years	NR	Korea, Rep.	Hospital	Sigmoidoscopic enema	Efficacy and safety
Gunawan (2017) (Gunawan 2017)	To determine proof of principle of whether a new home-based electrical stimulation device (Rhythm.IC) is safe and effective to reduce symptoms of chronic constipation in children after 4 months' stimulation.	Phase 3, single-cohort, open-label and single-center study comparing patient data before and after treatment	10 children aged 5 to 18 years with CFC which was defined as a > 6-month history of ≤ 2 "spontaneous complete bowel movements" per week for at least 6 months before recruitment and experiencing > 25% of the time at least one symptom of lumpy/hard stools, sensation of incomplete evacuation, need to strain during defecation, or sensation of anorectal obstruction/blockage,	NR	Australia	Primary care / Community / Patient's home	Home-based electrical stimulation device (Rhythm.IC)	Safety and efficacy to reduce symptoms of chronic constipation
Habib (2019) (Habib 2019)	To report an unusual side effect of milk of molasses enema in the form of anaphylactic reaction in a paediatric patient.	Other primary study (Single case study)	9-year-old boy with a known history of allergies, eczema and asthma presented to the ED for 4 days of lower abdominal pain, decreased appetite, and constipation.	No	Mexico	Hospital – Emergency department	Milk of molasses enema	Side effects
Hatori	The aim of this study was	Other primary	CFC. No other details	NR	Japan	Hospital	Diluted gastrografin enema. 1:1 to 1:5 diluted	Data collected electronically included

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
(2016)(Hatori 2016)	to review and assess the use of diluted gastrografin enema for management of fecal impaction.	study (multicentre retrospective chart review)				(multicentre - 18 hospitals)	gastrografin enema was effective within 24 hours after the enema solution was administered	indication for gastrografin treatment, identification of fecal impaction with X-ray imaging, period up to excretion of fecal impaction, and any complications.
Heymen (2003) (Heymen, Jones et al. 2003)	To critically review biofeedback and compare the various biofeedback treatment protocols for pelvic floor dyssynergia-type constipation used in this research	Narrative review (critical review)	Constipation. 11 child studies.	NR	More than one – international evidence	Multiple settings	Biofeedback	NR
Hodges (2017)(Hodges 2017)	To describe the techniques which we have developed to properly diagnose the constipation component of paediatric bowel and bladder disorders (BBD) in children and the treatment techniques that most rapidly and effectively resolve these issues.	Narrative review	BBD	NR	More than one – international evidence	Multiple settings	Enemas	NR – refer to "excellent results in treating pediatric voiding dysfunction with enemas directed at resolving rectal dilation"
Hutson (2015) (Hutson 2015)	Review of testing whether transcutaneous electrical stimulation (TES) could improve motility and (STC) symptoms,	Narrative review	Children with slow-transit constipation	U	More than one – international evidence	Multiple settings	Transcutaneous electrical stimulation	Motility and symptoms
Jarzebicka 2016 (Jarzebicka, Sieczkowska et al. 2016)	To evaluate the effectiveness of biofeedback therapy as assessed by clinical improvement as well as by changes in manometric parameters in children with constipation and pelvic floor dyssynergia (PFD).	Other primary study (Cohort)	44 children aged 7+ years with constipation and PFD. Rome III criteria were used.	NR	Poland	Hospital	Anorectal manometer to provide biofeedback *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	Clinical improvement was defined as an increased frequency of defecation, improved consistency of stools, and reduced number of encopresis episodes
Jordan-Ely (2013)(Jordan-Ely 2013)	To pilot a novel nurse-led method using combined high dose medication and TES	Other primary study (pilot)	33 children aged 4 to 16 years with moderate faecal loading (<3 BA/week)	NR	Australia	Primary care / Community / Patient's home	Nurse-led TES plus medical disimpaction, toilet training / posture Medication disimpaction (Movicol) plus TES.	Primary outcomes: total stool volume, frequency, consistency and soiling episodes per week.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							Patients were educated on stool description, medications and correct toilet posture for defecation	
Jorgensen 2017 (Jorgensen, Kamperis et al. 2017)	To evaluate the feasibility and efficacy of TAI in the treatment of functional faecal incontinence (FFI)	Other primary study (Retrospective cohort)	72 children (mean age 9.2 +/- 2.2 years, 47 males) with treatment-resistant FFI was performed. Rome III criteria were used.	NR	Denmark	Hospital	Transanal irrigation: Alterna TAI All children accepted treatment and 35% (n = 25) were titrated to daily sessions *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	Treatment success, reduction in FI episodes, safety and tolerance
Kajbafzadeh (2011) (Kajbafzadeh 2011)	We evaluated the efficacy of animated biofeedback urotherapy in bowel and voiding dysfunction in children with dysfunctional elimination syndrome.	RCT	80 children with DES were randomly assigned to undergo animated biofeedback (group A) or conservative therapy (group B); Group A: Mean: 8.5 +/- 2.7 years Group B: Mean: 9 +/- 2.3 years. CFC was diagnosed using the Paris Consensus on Childhood Constipation Terminology Criteria.	No	Iran, Islamic Rep.	NR	Group A - Animated Feedback; Group B - Conservative treatment	Number of diurnal incontinence episodes and wet nights per week, patients with urgency, patients with fecal soiling episodes during the week and urinary tract infections in the last 6 months, and VUR grade, presence of DVSS and uroflometry parameters were evaluated before and 6 months and 1 years after treatment
Koppen 2017 (Koppen, Kuizenga-Wessel et al. 2017)	The aim of this survey study was to explore the treatment efficacy and parental satisfaction in children with FC who are treated with Peristeen.	Other primary study (Survey study)	67 parents of children who were treated with transanal irrigation for intractable FC (with or without fecal incontinence). Rome III criteria used.	NR	Netherlands	Primary care / Community / Patient's home	Peristeen TAI. Children and their parents received information about Peristeen and were instructed on how to use this irrigation system conform the instructions of the manufacturing company. This included patient-tailored instructions on how to insert and inflate the balloon (eg, maximum amount of air inflations based on age). During the first time of irrigation, the balloon was inflated until there was no more water leakage from the anus, this indicates that the balloon seals the anal canal. The patients (and their parents) were then supported during outpatient clinic visits until they were able to use Peristeen at home, from then on follow-up by the pediatric gastroenterology nurse consisted mainly of telephone contacts.	Questionnaire involved 25 questions and consisted of multiple choice questions regarding gastrointestinal symptoms, use of Peristeen, concomitant medication use, and parental satisfaction with treatment.
Kuizenga-Wessel (2016)(Kuizenga-Wessel 2016)	Aim of this study was to assess the treatment efficacy and parental satisfaction in pediatric patients treated with TAI.	Cross-Sectional Survey	121 families Children with organic or functional constipation	NR	Netherlands	Multiple settings	Transanal irrigation (TAI) with Peristeen	Current gastrointestinal symptoms, concomitant medication use, school absence, hospitalizations and parental satisfaction
Ladi Seyedian	For the first time in this	prospective	60 children age older than 5 years	NR	Iran,	Hospital	Functional pelvic floor muscle therapy exercises	Patients' symptoms (daytime

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
(2014) (Ladi Seyedian, Sharifi-Rad et al. 2014)	study, we combined functional PFM exercises with Swiss ball exercises, to the behavioral urotherapy program, and compared treatment outcomes of this combination in the management of children with DV.	and randomized controlled trial pilot study.	with dysfunctional voiding.		Islamic Rep.		exercises (with and without Swiss ball) and behavioural urotherapy	incontinence, enuresis, urgency, and constipation) and signs (UF/EMG results, voiding pattern, pelvic floor activity during voiding, UTI, VUR, and PVR) were evaluated
Ladi-Seyedian (2021)(Ladi-Seyedian, Sharifi-Rad et al. 2022) IRCT20140527017876N4				NR				
Leong (2011)(Leong 2011)	To determine long-term outcomes for STC children treated by TES	Trial	42 children with slow transit constipation (STC)	NR	Australia	Unclear	Transabdominal electrical stimulation (TES) 2 groups receiving: (A) 1 month sham and 1 month stimulation or (B) 2 months of stimulation administered by physiotherapists (20-minutes, 3/wk) with 8 weeks between stimulation months in Group B.	STC symptoms
Librizzi (2017)(Librizzi, Flores et al. 2017)	The primary objective of this study was to evaluate practice patterns and patient outcomes for the hospital management of functional constipation in US children's hospitals.	Multicenter, retrospective cohort study	14243 children (aged between 0-18 years) with CFC. Patients were identified using one of the primary ICD-9-CM discharge diagnosis codes: 564.0 to 564.09 (constipation), 307.7 (encopresis), 306.4 (psychogenic constipation), or 560.32 (fecal impaction).	U	United States	Hospital		calculated percentage of hospitalizations due to functional constipation (including inpatient and observation hospitalizations), treatments administered (including electrolyte laxative, sodium phosphate enema, mineral oil enema, bisacodyl, glycerin suppository, senna, and docusate), LOS (in days, with a day defined as crossing midnight), and 90-day readmission rate for constipation.
Loening-Bauke (1989) (Loening-Baucke 1989)	To evaluate factors which might contribute to treatment failure in children with chronic constipation and soiling	Other primary study (non-comparative study)	97 consecutive children diagnosed with chronic constipation and overflow incontinence.	No	United States	Hospital	Laxatives, diet, toileting programme, rewards. Phosphate enemas, milk of magnesia, a high fibre diet, and instructions in bowel training techniques. Parents and children were instructed and encouraged to increase intake of high fibre or bran	Factors which are thought to contribute to treatment failure (e.g.severe constipation, external sphincter contraction during defecation attempts, inability to

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							containing cereals and breads, fruits, and vegetables. *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	defecate balloons, blunted rectal sensation, decreased ability of the internal anal sphincter to relax during rectal distension), and compliance with a treatment programme.
Loening-Baucke 1990 (Loening-Baucke 1990)	The aims of our study were to evaluate (1) what proportion of patients with abnormal contraction of the EAS during def- ecation attempts could learn relaxation of the EAS with biofeedback training, (2) whether relaxation of the EAS would persist for 5 to 6 months after the children success- fully learned it, and (3) whether learning relaxation of the EAS with biofeedback training would influence outcome.	RCT	43 children aged between 5-16 years, with chronic constipation and encopresis and with abnormal defecation dynamics. All children had faecal soiling for more than 1year.	No	United States	Hospital	External anal sphincter electromyographic (EMG) biofeedback Treatment protocol. All patients received conventional laxative treatment for encopresis and constipation similar to that used for the previous 10 years in our encopresis clinic plus A biofeedback training session included approximately 30 to 35 defecation trials and lasted approximately 45 minutes. At least two and up to six training sessions 7 _+ 2 days apart were given. The number of training sessions given de- pended on how soon the child learned to relax the EAS. Biofeedback training sessions were stopped after 10 relax- ations of the EAS without visual feedback could be accom- plished in each of two successive biofeedback training ses- sions. *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	Evaluated physiologic outcome at 7 months and clinical outcome at 7 and 12 months. Defecation studies and anoreetal manometry
Loening-Baucke 1993 (Loening-Baucke 1993)		Cohort	174		United States	Hospital	Education, disimpaction, and toilet training *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	
Loening-Baucke (1995) (Loening-Baucke 1995)	To evaluate if biofeedback treatment had improved long-term outcomes.		129 children with constipation, encopresis and abnormal defectatiopn dynamics were treated conventionally, 63 of them received additional biofeedback training directed towards teaching normal defecation dynamics		United States	Hospital		
Loening-	Biofeedback training in	Narrative		NR	More than	Multiple	Electrical stimulation therapy (EST)	

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Baucke (1996) (Loening-Baucke 1996)	children with functional constipation A critical review	review			one – international evidence	settings		
Lu (2015)(Lu 2015)	We have conducted this systematic review in order to better define the current state of knowledge about EST in the treatment of slow transit constipation in children.	SR	Children with slow tranist constipation (STC). Identified 6 relevant studies (range 8-39) The criteria for inclusion of studies in this systematic review were patients with slow transit constipation and patients treated with transcutaneous electrical stimulation, transabdominal electricalstimulation,orinterferential electricstimulation	NR	More than one – international evidence	Multiple settings	Neurostimulation	NR
Lu (2015)(Lu 2016)	Our objective is to review current applications of neurostimulation in the treatment of gastrointestinal disorders with an emphasis on the use of these treatment modalities in children.	Narrative review	Children with gastrointestinal symptoms refractory to medical treatment	NR	More than one – international evidence	Multiple settings		NR
Miller (2012) (Miller, Dowd et al. 2012)	This study aimed to compare efficacy of enema versus polyethylene glycol (PEG) 3350 for paediatric fecal impaction treatment.	RCT	79 children aged 1 to 17 years with CFC. A diagnosis of at least one of the following by the treating ED physician was required to be eligible: (1) fecal impaction (lower quadrant mass or dilated rectum with hard stool), (2) functional fecal retention (large diameter stools as determined by caregiver for less than twice per week and retentive behaviors), or (3) excessive stool in colon on abdominal radiograph as determined by radiologist or treating ED physician	No	United States	Hospital (Emergency Department)	Participants were randomized to a single milk and molasses enema in the ED (mixed 1:1, 10 mL/kg with maximum 500 mL, standard enema therapy at this institution) or oral high-dose PEG 3350 (1.5 g/kg/d, max dose of 100 g/d) for outpatient use for 3 days.11 Subjects in both groups were discharged with PEG 3350 for maintenance therapy (at 0.8 g/kg/d for 3 days)22; enema	The primary outcome was main symptom improvement. Additional outcomes were stool frequency, consistency, and ease of stool passage. Treatment failures (home enema, ED return, or hospital admission) were tracked. Before receiving an intervention, caregivers of subjects provided information on demographics and past medical history. Additionally, baseline data were collected from caregivers (and participants if appropriate) using questions from the Questionnaire on Gastrointestinal Symptoms (QGS).21

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							subjects were instructed to start maintenance within 24 hours after ED discharge and PEG 3350 subjects advised to start within 24 hours after taking the third cleanout dose. Participants received written instructions on their cleanout and maintenance regimens and also received enough complimentary PEG 3350 to complete this study. Subjects received additional, standard discharge information on constipation from the treating ED physician	The QGS instrument is now widely used to classify children's gastrointestinal symptoms into diagnostic groups. Development of this instrument was a collaborative effort that underwent multiple pilot tests and revisions.21 The QGS also allows for assessment of postYintervention symptoms and was used in modification for follow-up as well.Primary caregivers were contacted by telephone for followup on days 1, 3, and 5 to evaluate stool patterns, on-going symptoms, and symptom improvement. Structured surveys were conducted by the primary investigator (M.M.) or a research assistant and took 5 to 10 minutes to complete. Because of the difficulty in obtaining follow-up, we accepted responses up to 7 days after enrollment. If caregivers believed the subject was not tolerating the study treatment, they were instructed to contact the research coordinator (who would advise over-the-counter sodium biphosphate/sodium phosphate enema treatment or physician evaluation after consulting with a study principal investigator). Treatment failure was defined as a participant who received an enema at home, returned to the ED for evaluation, or was later admitted to an inpatient

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								service for treatment of fecal impaction.
Modin (2016) (Modin 2016)	To evaluate changes in behavioural difficulties in CFC with and without faecal incontinence	Other primary study (questionnaire)	116 children aged five to 16 years who fulfilled the Rome III criteria for FC and received conventional treatment	NR	Denmark	NR	Conventional treatment, including information and disimpaction (1.5 g/kg/day) and maintenance treatment (1 g/kg/day) with PEG 3350 *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	Primary - change in mean TDS (a total difficulties score) between inclusion and 12 months according to treatment outcomes. Secondary outcomes: SDQ (behavioural difficulties) sub scores, the presence of FI, AP and a number of Rome III criteria.
Muddasan (Muddasani, Moe et al. 2017)i (2017)	To determine the efficacy of physical therapy (PT) for faecal incontinence in children with pelvic floor dyssynergia (PFD).	Retrospective chart review	64 children with a mean age of 8.69 ± 3.19 (SD) years and a clinical diagnosis of FI	U	United States	United States	Physical Therapy	Compliance with PT visits was classified into the followingcategories: good (subjects had≤30% no-shows to PT visits); fair (subjects had 30%-50% no-shows to PT visits); poor (subject had frequent [>50%] no-shows to PT visits). The primary outcome was based on fecal incontinence frequency reported at the time of the subject's last documented PT visit compared with fecal incontinence frequency at the initial baseline PT visit. Fecal incontinence frequency was defined as the number of fecal accidents per week. Fecal incontinence outcome was categorized as excellent (complete continence), good (>50% decrease in frequency of fecal incontinence), fair (not worsening but <50% improvement), and poor (more frequent fecal incontinence). Excellent and good outcomes were categorized as favorable,and fair or poor outcomeswerecategorizedasbeingunfavorable.Thiswasbased primarily on expert recommendation that a ≥50% reduction infecalincontinenceepisodesisaclinicallymeaningfuloutcome measure.17 Secondary outcomes

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								includedimprovementinbowelmovement frequency at the time of the last PT visit vs baseline (in those with<3 bowel movements per week at baseline),medicationuseatthelastdocumentedPTvisitvsbaseline,andPFM functioning at the time of the last PT visit vs baseline.For assessment of a change in bowel movement frequency, categories included excellent (doubling or more of frequency),good (>50%-99% increase), fair (not worsening but <50% increase in frequency), and poor (decreased frequency).
Nader 2016 (Nader 2016)	: To analyze the outcome of biofeedback with a special emphasis on the evolution of need volumes and envy scores.	Other primary study (Retrospective cohort)	25 children aged between 7 and 17 years with FI (based on Rome III criteria)	NR	France	Hospital	External anal sphincter electromyographic (EMG) biofeedback initial management included enemas, PEG treatment and weekly biofeedback sessions after ano-rectal manometry to rule out Hirschsprung disease *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	envy score to defecate on a scale of 0 to 100 corresponding to the need volume. The outcome was considered a success when soiling completely disappeared,
Nasher 2014 (Nasher, Hill et al. 2014)	To evaluate the efficacy of the PeristeenD transanal irrigation system when treating faecal incontinence in children due to chronic idiopathic constipation	Other primary study (Retrospective cohort)	7 13 participants affected with FI referred to our centre for Peristeen D transanal irrigation treatment PeristeenD was offered to all patients who w. ere seeing no improvements on conventional medical therapy. No clear definition but they used "The faecal continence scoring system" (Table 1) used previously and validated by Rintala and Lindahl	No	United Kingdom	Hospital and home	Peristeen TAI We recommended using PeristeenD as described in the guidelines published by the manufacturing company Coloplast [11]. The families were then supported at home by the local paediatric community nurse who had been educated in the transanal irrigation system. The device was easily accessible to patients, as it is provided by the UK National Health Service on a free of charge prescription. If	A previously described and validated faecal continence scoring system was used to assess bowel function and social problems before and after treatment with PeristeenD

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
			[10] was used to assess bowel function and social issues before and after treatment with PeristeenD.				patients were unhappy with the procedure, they did not have to continue with it. The PeristeenD system consists of a control unit with a pump, a water bag, and a rectal catheter. Tap water is warmed (36–38∘ C) and introduced into the colon via the rectal catheter. Once the rectal catheter has been inserted, an inflatable balloon ensures that it remains in situ until the balloon is deflated. The water, along with the stools in the lower portion of the bowel, is then emptied into the toilet [11]. *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	
NCT01823848 (NCT01823848 2013)	A Trial of Three Types of Enemas Used to Treat Functional Constipation in Children		**Trial terminated early as there was insufficient staff to enrol** Planned to recruit 40 children aged 4 to 12 years	NR	United States		3 arms, a) PEG plus phosphate enema b) PEG plus normal saline enema and c) PEG plus mineral oil enema.	primary outcome = Change in pain scores following administration of enema, Secondary outcomes = patient's weight pre- and post-administration of the enema, satisfaction ratings on a visual analog scale from the treating physician and parental surveys on the day of administration and 3-5 days following discharge
Ng 2016 (Ng, Lee et al. 2016)	to evaluate the effectiveness and safety of TES when employed to improve bowel function and constipationrelated symptoms in children with constipation	SR (Cochrane review)	46 participants accepted various definitions of constipation in the included studies, including ROME III Check – identified 1 relevant studies (46 children)	U	More than one – international evidence	Multiple settings	TES *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	Primary - 1. Global or clinical improvement in constipation as defined by the included studies. 2. Spontaneous bowel movements (SBM) and complete spontaneous bowel movements (CSBM). Secondary - 1. Improvement in symptoms associated with constipation (e.g. perceived ease of defaecation, abdominal pain or distension, stool

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								consistency). 2. Improvement in bowel transit time, bowel activity or propagating contractions measured over a defined time period, for example, weekly. 3. Improvement in faecal soiling. 4. Improvement in growth (for example, weight in relation to centile or weight gain), measured at a defined intervals over the course of the study, for example, three monthly or six monthly. 5. The proportion of patients who experienced an adverse event. 6. The proportion of patients who experienced a serious adverse event.
Nolan 1998 (Nolan, Catto-Smith et al. 1998)	randomised controlled trial in medical treatment resistant and/or treatment dependent children with anismus using surface electromyographic (EMG) biofeedback training to determine whether such training produces sustained faecal continence.	RCT	29 68 children were eligible for study entry if: (1) they were aged 4 years or more and were judged to be of adequate maturity to cooperate with biofeedback treatment; (2) they had received three months or more of conventional multimodal therapy; (3) they had continuing soiling with or without laxative treatment (more than once a month) or had achieved remission from soiling but could not sustain continence without continued laxative treatment; and (4) they had anismus on EMG during anorectal manometry. Subjects were ineligible	No	Australia	Hospital	External anal sphincter electromyographic (EMG) biofeedback EMG BIOFEEDBACK TRAINING The aim of the biofeedback was to eliminate anismus during defecation attempts. No bowel preparation was required. The training procedure was conducted with the patient in the left lateral position. External anal sphincter activity was displayed using the EMG procedure described above, and abdominal pressure was displayed via a simple pressure gauge attached to a 12FG water filled Woodward catheter terminating in a balloon and incorporating a three way stopcock. The balloon was inserted into the rectum with its base 6 cm from the anal verge and was inflated with 40 ml warm water. The gauge was calibrated to read 0–50 mm Hg and was adjusted to zero for resting rectal pressure. Both recording devices could be seen by the patient but his attention was focused on the electromyograph recorder that indicated external sphincter contraction or relaxation both visually	The principal outcomes were remission of faecal incontinence and lack of need for laxative treatment at six months' follow up. Anorectal manometry was performed at baseline and six months after randomisation by a gastroenterologist (TCS). The gastroenterologist was blinded to the clinical details of the patient and group assignment at the time of the second anorectal manometry. Abdominal radiographs were also carried out before anorectal manometry. These were later scored blindly for faecal retention.14 Anorectal manometry was performed at least one hour after disimpaction with two Microlax enemas (one in

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
			if they had a known structural congenital or postoperative anatomical defect (such as spina bifida or anorectal malformation), or Hirschprung's disease (excluded by rectal biopsy only if clinically indicated). Sixty eight children referred from an encopresis or gastroenterology clinic were eligible and underwent anorectal manometry and EMG. Of these, 29 had anismus (aged 4.8–14.9 years) and had parents who consented to randomisation. A detailed report on the manometric and clinical characteristics of all clinically eligible subjects has been published elsewhere.6 Apart from failure to demonstrate anismus, four subjects were considered ineligible on other grounds, two of whom were judged to be too immature for biofeedback training. No parent of an eligible child refused consent				and aurally. Up to four sessions at weekly intervals were conducted for each patient, each session consisting of ~ 30–35 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 less than four sessions then biofeedback was discontinued. At the completion of biofeedback training, subjects were followed at monthly intervals by a single paediatrician, who gave verbal reinforcement of the skills learned during training. Both groups were telephone monitored monthly by the research assistant. Medication use was decreased to a level consistent with maintenance of continence as monitored in the diary following anorectal manometry for both groups, and both biofeedback and control subjects continued standard multimodal treatment and diary monitoring, as described above and elsewhere.2 Full remission was defined as no medication and no soiling for at least four weeks; full remission on medication was defined as on medication and no soiling for at least four weeks; partial remission was 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. *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	the evening before anorectal manometry, one in the morning) in the left lateral position (except balloon defecation into the toilet), using a pneumohydraulically perfused multilumen catheter with four sideholes at 0.5 cm intervals (Arndorfer hydraulic capillary infusion system; SDR Clinical Technology, New South Wales, Australia). Each lumen was connected connected to a pressure transducer and a multichannel polygraph recorder (Narco Biosystem MMS100 dynograph; SDR Clinical Technology). A terminal rubber balloon (size 2.5 ´ 6 cm) capable of distension to 200 ml was attached to the probe. The distances from the furthest (distal) and the nearest sideholes to the balloon base were 5.5 cm and 4 cm, respectively. Sphincter identification was by the slow station pull through technique. The catheter was withdrawn progressively in 0.5 cm increments until resting external anal sphincter pressure could be recorded by the distal channel. This resulted in the base of the balloon being positioned between 5.5 cm and 7 cm

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								from the anal verge. The midpoint of the resting oscillations of the manometric recording was taken as the baseline pressure. The extreme of the deviation from this baseline was recorded as the response to stimulus. EMG was carried out with an integrated electromyograph (Urolab model 1154; Life Tech, Houston, Texas USA) recording at 5 mm/second with a filter of either 20, 50, or 100 μV/cm, depending on the size of the signal. Three surface electrodes were used with two electrodes placed immediately adjacent to the anus and a reference electrode on the thigh. When recording electromyographic activity during straining, the accompanying increase in intra-abdominal pressure was monitored to ensure that the patient was pushing or squeezing correctly. Alterations in the balloon pressure were used to indicate changes in rectal (abdominal) pressure with a minimum increase of 50 mm Hg required for correct voluntary straining and no increase for correct squeezing. For balloon defecation, a

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								tube with an inflatable rubber balloon attached was inserted into the rectum with the patient in the left lateral position. The balloon was inflated with 100 ml warm water and the child then asked to defecate this into the toilet. If this did not occur within two minutes, 50 ml water was withdrawn and the attempt was repeated. Similarly, another 20 ml was withdrawn if defecation still did not occur (leaving 30 ml) and if this was still unsuccessful the equipment was removed. Anorectal manometry measures are described in detail elsewhere,6 and included the threshold for the recto-anal inhibitory reflex and transient sensation threshold, and threshold of lasting urge (30 seconds) to defecate. The procedure to determine whether anismus was present involved the use of a balloon filled with 50 ml warm water. After a tuition period to explain what was required to achieve correct straining and squeezing, the patient was asked to make five alternating attempts each to squeeze and strain. Normal strain

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								response was defined as a persistent decrease in external anal sphincter activity (measured by a decrease in amplitude of the electromyographic recording and an increase in rectal pressure of at least 50 mm Hg) in at least three of five attempts. A persistent increase in external anal sphincter activity with a corresponding increase in rectal pressure in at least four of five attempts were deemed as indicating anismus. The "child behaviour checklist" (CBCL)16 was completed by parents before randomisation, and at six months.
Ormarsson 2016 (Ormarsson, Asgrimsdottir et al. 2016)	to determine the efficacy of LP101 suppositories as a treatment for constipation in children referred to a paediatric emergency department and compare them to the standard treatment in our hospital, which is Klyx docusate sodium and sorbitol enemas	RCT	80 children (aged 1- 17 years) referred to the paediatric emergency department of Landspitali University Hospital, Iceland, with abdominal pain, and diagnosed with constipation	U	Iceland		Enema vs suppository study group, who received the LP101 suppositories, or the control group, who received Klyx enemas, *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	The primary endpoint of this study was the efficacy of LP101 free fatty acids suppositories, compared with Klyx, in children diagnosed with acute constipation. The secondary endpoint of this study was safety.
Pacilli (Pacilli, Ng et al. 2017)(2017)	to review the available literature and appraise the current results of this technique (transanal	SR and meta-analysis Protocol	Children (younger than 1 year) treated with transanal irrigation for constipation or incontinence	Mixed	More than one – international evidence	Multiple settings	Transanal colonic irrigations.	Response to colonic irrigations: number of patients with resolution of symptoms (constipation or incontinence); failure rate.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	colonic irrigation) in providing effective bowel management in children with incontinence or constipation and faecal soiling.							Complications.
Patel 2019 (Patel 2019)	was to evaluate the effectiveness of TAI Peristeen® device in children who failed to respond to conservative measures for stool incontinence and constipation	Other primary study (Cohort)	19 / 97 children who failed to respond to conservative measures for stool incontinence and constipation	NR	United States	Multiple settings	Peristeen TAI *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	Not specifically stated - may be symptoms before and after initiating TAI Peristeen device
Raffaele 2015 (Raffaele, Pasqua et al. 2015)		Cohort	25			Biofeedback	External anal sphincter electromyographic (EMG) biofeedback *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	
Rao (2015) (Rao 2015)	to provide evidence-based recommendations regarding the clinical utility and efficacy of biofeedback therapy for dyssynergic defecation, fecal incontinence, levator ani syndrome, solitary rectal ulcer syndrome and childhood constipation.	Narrative review	Children aged 5 years and above with a diagnosis of dyssynergic defaecation, afecal incontinence, levator ani syndrome, solitary rectal ulcer syndrome and childhood constipation. Identified 7 studies as relevant for childre with CFC.	NR	More than one – international evidence	Multiple settings	biofeedback	outcomes as per each included study
Rego (2019) (Rego 2019)	to assess the applicability and clinical outcomes of transcutaneous PTNS in children with functional intestinal constipation	Other primary study (single-center, prospective, longitudinal, and interventional study)	Diagnosis of intestinal constipation, according to Rome IV criteria. Estimated sample size is 28 patients, Children aged 7-18 years	U	Brazil	Hospital	Transcutaneous posterior tibial nerve stimulation (PTNS)	Adherence to treatment and related adverse events. bowel habits and quality of life.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Ruan (2018) (Ruan 2018)	To describe the usage of various enema therapies of children with AP and constipation in the ED and to determine the efficacy of various enema therapies which is defined by ED discharge	Other primary study (Retrospective cohort)	7178 children who received enema therapies in a large urban quaternary care ED	NR	United States	Hospital – Emergency department	Various enema therapies *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	Clinical presentation, diagnostic evaluation, enema type, arrival time, discharge time, and stool output following enema was systematically captured. Enema efficacy was defined by discharge from the ED
Satish (2019) (CTRI/2019/06/01959 2019) (CTRI/2019/06/019596)	Effectiveness Of conventional physical therapy along with structured physical therapy versus conventional physical therapy on constipation in children with neurodevelopmental disorders- A comparative study	RCT (On-going)	Target: 60 Inclusion criteria: Children diagnosed with a neurodevelopmental disorder. 2. Patients falling in the chronological age group of 2years - 7year 3. Patients of either gender. 4. Children having diagnosed with constipation by paediatrician or paediatric surgeon. 5. Parents willing to participate in the study. 6. Parents understanding English language. 7. Patients with a stool form of type 1 and 2 in Bristol Stool Form Scale	Yes	India	NR	Patients will receive conventional plus structured physiotherapy exercises versus conventional physiotherapy	Primary outcome: Defecation frequency Secondary outcome: Paediatric quality of life- gastrointestinal scale Bristol stool form scale
Savić (2020) (Savic, Zivkovic et al. 2020)	The aim of this review was to analyze the effects of physiotherapy interventions in childhood constipation.	Narrative review	Children with chronic functional constipation	NR	More than one – international evidence	Multiple settings	Physiotherapy interventions: Diaphragmatic breathing exercises Pelvic floor exercises and biofeedback Abdominal massage	NR

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Sharifi Rad 2018(Sharifi-Rad, Ladi-Seyedian et al. 2018) IRCT20160306 17876N	we assessed the efficacy of IF electrical stimulation as an adjuvant therapy in treating pediatric patients with functional constipation	RCT	90 Children aged 5 -13 years with functional constipation. Pediatric patients who had constipation, defecation frequency of less than three times per week, positive history for passing of hard stool, episodes of fecal soiling, abnormal stool form (Bristol Stool Form 1–3) (27), and painful defecation were enrolled in the study. Constipation was defi ned according to the Rome III criteria (28) as having at least two of the following symptoms for at least 2 months; a maximum of two defecation times per week, at least one episode of incontinence aft er toilet training, painful defecation, and passing of hard stool with large diameter, positive history of fecal impaction, or bowel movements that clogged the toilet. In addition, all included patients had failed to response to at least 6 months of conventional therapy such as dietary modifi cation and use of laxatives.	No	Iran, Islamic Rep.		Interferential electrical stimulation (IFS) plus pelvic floor muscles exercises. Case group (n =45) underwent PFM exercises plus IF electrical stimulation, whereas the control group (n =45) received PFM exercises plus sham IF electrical stimulation. TES *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	primary outcome was defi ned as the absence of functional constipation according to the Rome III criteria. Secondary outcomes were to measure an increase in defecation frequency of two times per week more than baseline, absence of fecal soiling episodes, absence of abnormal stool form, measuring the pain, and constipation scores. Changes in the constipation-related QOL scores were also compared between two groups
Sharma 2016 (Sharma, Gordon et al. 2016)	To evaluate the efficacy and safety of Peristeen for the rescue treatment of faecal incontinence in children with chronic idiopathic constipation who have not responded to long term laxative management	Other primary study (Cohort)	11 children with chronic idiopathic constipation who have not responded to long term laxative management. Mean age 12.2 years All children with faecal incontinence due to idiopathic chronic constipation who began Peristeen transanal irrigation at home were included. Duration of constipation was noted to be: 2–5 years in one child, 5–10 years in 8 children and more than 10 years in 2 children.	No	United Kingdom	Hospital	Peristeen TAI *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	Prospective data was collected on children who were still regularly soiling despite intensive input and laxative advice from the nurse-led constipation service

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Silva 2013 (Silva and Motta 2013)	The aim of the present study was to assess the effect of muscular training, abdominal massage and diaphragmatic breathing in patients with CFC	RCT	72 children and adolescents 4–18 years of age participated in the study. For inclusion in the study, patients with CFC should have demonstrated more than two of the following parameters in the basal period at least once a week, during the previous 2-month period, according to the Rome III criteria [16]: less than two bowel movements	No	Brazil	Hospital	Physiotherapy (including muscular training, abdominal massage and diaphragmatic breathing In the physiotherapy group, exercises including isometric training of the abdominal muscles, diaphragmatic breathing exercises and abdominal massage were used with conventional treatment including disimpaction, when necessary, a high fibre diet, laxatives and toilet training. Patients in the medication group were subjected to conventional treatment only. Disimpaction was conducted using phosphate saline solution (once a day, for 1–5 days according to patient need). During toilet training the patient was instructed to sit on the toilet for at least 5 min after the three main meals of the day [15]. Physiotherapy + medication group (intervention) Physiotherapy was conducted by a single generalist physiotherapist who was specially trained to perform the exercises over the 3 months prior to the study. Twelve individual 40-min sessions were held twice a week and adherence was confirmed only if patients attended all 12 sessions. A 1-min rest period was observed between each series of exercises. Isometric training of the abdominal muscles The aim of the training was to increase intra-abdominal pressure (which compresses the intestines) and the colonic propulsive force during voluntary effort [18,19]. Considering the indirect synergic activation between the	Defaecation frequency and retentive faecal incontinence were the primary outcome measures. Defaecation effort and pain with stool consistency and retentive behaviour were secondary outcome measures. During follow-up, parents or guardians kept a diary describing the childrens' intestinal habits.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							pelvic floor and the lower abdominal muscles, voluntary isometric contraction of the upper abdomen and the simultaneous relaxation of the lower abdomen improves muscle coordination and relaxes the pelvic floor and the external anal sphincter, thus optimizing defaecation [18–20]. This consists of contraction of the upper abdomen muscles and diaphragm and simultaneous *relaxation of the lower abdomen under the supervision of the physiotherapist [21]. Training was carried out in two ways. The patient was either lying down in a left lateral decubitus position with the hip and knee flexed at 90° or sitting or lying down. In the first case training began with two series of eight contractions and relaxations until the third week and was then increased to two series of 12 contractions and relaxations for 6 weeks. In the sitting method, training began with one series of three contractions and relaxations lasting 10 s which was increased to five repetitions in the third week until the sixth week. The exercise was considered successful when protrusion of the lower abdomen was visible, indicating the simultaneous relaxation of the lower abdomen and the pelvic floor, from which point the series was initiated [21].* *Breathing exercises*	

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							The aim was to achieve a regular pattern of abdominal breathing, strengthen the abdominal muscles and improve coordination between breathing, abdominal and anal muscle contraction and colonic propulsion [22]. Standard diaphragmatic breathing was achieved using a modified exercise under physiotherapist supervision with the patient in the seated position, with one hand placed on the abdomen and the other on the thorax; the patient was instructed to breathe in slowly, deeply and progressively for 6–8 s, retain the air for 10 s and exhale slowly for 6–8 s [22]. Two series of 10 repetitions were completed and the exercise was considered successful when greater mobility of the hand placed on the abdomen was achieved compared with minimal or no mobility of the hand on the thorax, from which point the series was initiated [22]. *Abdominal massage* *The aim was to perform propulsive abdominal massage to promote colonic and rectal motility to train intestinal function and defaecation [13,15]. The physiotherapist performed slow circular clockwise movements, along the line of the colon, applying constant moderate pressure to the abdomen with a regular tennis ball on each point for 1 min, beginning with the ascending colon and moving toward the sigmoid colon [13].* *Medication and guidance*	

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							Patients used a laxative (magnesium hydroxide) at a dosage according to individual needs (a minimum of 2 ml/kg) and received guidance regarding fibre dietary foods, water and toilet training during weekly consultations with a paediatric gastroenterologist who was unaware about which patient belonged to which treatment group. *Medication group (control)* *Patients in the control group were monitored on a weekly basis by a paediatric gastroenterologist who was unaware of the group to which the patient had been randomized since the patients were undergoing clinical follow-up only. All patients were prescribed a laxative (magnesium hydroxide) at a dosage according to individual need (minimum of 2 ml/kg) and received guidance regarding fibre dietary intake, water and toilet training, under the same conditions as the patients in the intervention group* *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	
Stephens (2018)(Stephens, Steiner et al. 2018)	We studied constipation-related health care among children before and after constipation admission.	Other primary study (retrospective cohort study)	780 patients ≤17 years of age with a first inpatient visit for constipation in the years 2010 to 2011.	Mixed population	United States	Hospital	Hospital treatments for CFC	Number of constipation-related outpatient visits and spending for those visits (ie, reimbursement to providers from Medicaid), both measured in the 12 months before and 12 months after the index admission for constipation. We also measured median

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								and mean spending for the index admissions and identified rehospitalizations for constipation in the following 12 months. Finally, filled prescriptions for constipation treatment after outpatient constipation visits during the study period were identified
Strisciuglio 2021 (Strisciuglio, Coppola et al. 2021) NCT02751411 EUCTR2015-005111-32-IT		RCT	158				Microenema vs PEG *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	
Van Biervliet (2019) (Van Biervliet, Van Renterghem et al. 2019)	To conduct a systematic review on long term results of transanal irrigations using a balloon catheter in children according to underlying disease	SR (on-going) Authors sent a draft version of the paper.	Planned to include studies with children (aged 4 -18 years) who have FI and constipation in children, irrespective of underlying pathology, for which transanal irrigation is used to obtain continence.	Planned	More than one – international evidence	Multiple settings	Long-term (> 12 months) transanal irrigations using a rectal balloon catheter with the intention to obtain continence.	Main outcome: Continence defined as no involuntary stool loss in the last 6 months, independence defined as being able to perform the complete procedure without help of a caregiver. Additional outcomes: Quality of life, complications, compliance, cost effectiveness
Van der Plas 1996 (van der Plas, Benninga et al. 1996)	A large, prospective, randomised study to evaluate the effect of biofeedback training and conventional treatment on defaecation dynamics and outcome in chronically constipated children.	RCT	192 children (aged 5 – 16 years) with chronic constipation referred by general practitioners, school doctors, paediatricians, and psychiatrists	No	Netherlands	Hospital	External anal sphincter electromyographic (EMG) biofeedback. Patients who were randomised to conventional laxative treatment (CT) had five outpatient visits lasting approximately 30 min during which laxative treatment and information from a diary containing defaecation frequency and encopresis and/or soiling episodes were discussed. A high-fibre diet was advised but additional fibre supplements were not prescribed and patients were instructed to try to defaecate on the toilet for 5 min immediately after each meal. (A high percentage of non compliance was reported by	Treatment was considered successful if the patients achieved three or more bowel movements per week and less than two soiling or encopresis episodes per month while not receiving laxatives for 4 weeks.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							parents if the child was asked to attempt toilet training 15–30 min after the meal to profit from the gastro—colic reflex.) During the first 3 days of conventional treatment, patients were instructed to use daily enemas (120 mL sodium dioctylsulfosuccinate, 1 mg sorbitol, 250 mg per mL, Klyx) at home. If, on day 3, enemas still resulted in large amounts of stool, enemas 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 5 g/10 kg body weight per day divided in two doses).31 Enemas were given whenever spontaneous defaecation was delayed for more than three days. Motivation was enhanced by praise and small gifts. The biofeedback group (CT+BF) had five outpatient visits, including the same conventional treatment as described above, in combination with five biofeedback training sessions. *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	
Van Engelenburg-Van Lonkhuyzen (2016) (van Engelenburg-van Lonkhuyzen 2016)	The objectives are as follows: To determine the effectiveness of physiotherapy or physiotherapy-related interventions, performed by any healthcare professional	SR protocol for a Cochrane review	Management of functional bladder, bowel dysfunctions, or concomitant BBD in neurologically normal and otherwise healthy children, aged between four to 18 years	No	More than one – international evidence	Multiple settings	Plan to compare the following 1. Motor control interventions versus no treatment, 2. Motor control interventions versus any other intervention, 3. Manual therapy techniques (abdominal massage) versus no treatment, 4. Manual therapy techniques (abdominal massage) versus any other intervention, 5. Electrotherapy (non-invasive) versus no treatment, 6. Electrotherapy (non-invasive) versus any other intervention, 7. Physiotherapy versus no treatment, 8. Physiotherapy versus any other intervention, 9. One type of a physiotherapy (intervention) versus another type of physiotherapy (intervention).	Protocol – still on-going
Van Engelenburg-Van Lonkhuyzen	Hypothesise that the combination of pelvic physiotherapy and standard medical care will be more	RCT	53 constipated children, aged 5 to 17 years diagnosed according to the Rome III criteria	No	Netherlands	Hospital and home	Standard Medical Care plus Pelvic Physiotherapy (PPT) (Or Standard Medical Care Alone) Physiotherapy (including core stability and balance training, relaxation and breathing	Web-based measurements include a structured patient reported outcome, which assesses the presence of the Rome III criteria and laxative use, co

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
(2017) (van Engelenburg-van Lonkhuyzen, Bols et al. 2017)	effective than standard medical care alone for treatment of CFC in children						exercises, sensory processing techniques, PFMT, and education). *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	morbidity (such as urinary problems and abdominal pain), the Strength and Difficulties Questionnaire (SDQ), the numeric rating scale (with regard to experienced burden) and a two weeks diary. At follow-up (M-WB 2 and M-WB 3) the web-based measurements are supplemented with the global perceived effect (GPE). At the last visit at the paediatrician, use of laxatives and the presence of Rome-III-criteria (primary outcome) are recorded.
Van Summeren 2020 (van Summeren, Holtman et al. 2020)	To determine the effectiveness of physiotherapy plus conventional treatment compared with conventional treatment alone for the treatment of functional constipation in children age 4-17 years in primary care.	RCT	134 children age 4-17 years diagnosed with functional constipation by their primary care physician using Rome III criteria.	No	Netherlands	Primary care	Physiotherapy (including knowledge, toileting behaviour and posture, awareness of sensation of needing to defecate, relaxation whilst defecating, pressure and straining during defecation). Physiotherapy that was carried out by specialist physiotherapists (i.e., with a master's degree in paediatric or pelvic physiotherapy and certified after additional postgraduate training in the treatment of bladder and bowel dysfunction in children) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	Treatment success was defined as meeting no more than 1 of the 6 Rome III criteria, with no laxative use for 4 weeks before measurement (absence of functional constipation without laxative use). Rome III criteria were assessed with the standardized Questionnaire on Paediatric Gastrointestinal Symptoms Rome III, adapted to evaluate symptoms over 4 weeks instead of 2 months, consistent with the new Rome IV criteria Main secondary outcome was treatment success over time, as defined for the primary outcome, but irrespective of recent laxative use (absence of functional constipation, laxatives allowed). Quality of life was measured by asking parents to complete the emotional and social functioning subdomains of the defecation disorder list. Global perceived effect of treatment was evaluated with the question "To what extent are the child's symptoms changed compared with the start of

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								the study?" A cost-effectiveness study is linked to this study – see (Van Summeren, Holtman et al. 2019) which is reported in more detail in Chapter 8.
Veiga (2013) (Veiga 2013)	To evaluate the efficacy of parasacral transcutaneous electrical nerve stimulation (TENS) for the treatment of constipation in children with lower urinary tract dysfunction (LUTD).	Other primary study	14 children over the age of 4 with LUTD and associated functional constipation diagnosed using the Rome III criteria were given and evaluated.	U	Brazil	Multiple settings	Parasacral TENS treatment. Electrical stimulation was applied by two experienced professionals in the field, and protocolised. The treatment consisted of 20 sessions at a frequency of 10 Hz and a pulse width of 700 ms. The intensity of the current was increased to the maximum level tolerated by the child, but without reaching the motor point, using two self-adhesive 3.5 cm electrodes placed to the side of S2 and S4. The electrical stimulation was performed three times weekly, for sessions of 20 min each.	Rome III criteria, stool consistency, and pain during defecation
Waingankar 2018 (Waingankar, Lai et al. 2018)		Other primary study (Retrospective cohort)	29				Sugar restriction (health professional supervised) *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	
Wald 1987 (Wald, Chandra et al. 1987)	To assess the efficacy of biofeedback to mineral oil therapy	RCT	50 children (aged 6- 15 years) with encopresis of at least 6 months duration (mean duration was 3.3 years)	U	United States	Multiple settings	Anorectal manometer to provide biofeedback vs conventional therapy Biofeedback therapy: Children were allowed to view the manometric recordings and given a simple explanation of the recording with specific attention to the responses of the external anal sphincter during contraction and simulated defecation. Children with normal expulsion patterns were simply asked to reproduce the pattern repeatedly, first with and then without visual feedback. All sessions lasted between 25 and 30 min. Following biofeedback, children were instructed to use the technique whenever they attempted to defecation after breakfast and dinner for at least 5-10 min. Reinforcement biofeedback sessions were conducted at 2,4 and 8 weeks. Progress was discussed at those sessions, which lasted approximately 30 min. Conventional treatment: ingesting mineral oil in grade amounts (range 1-4 tablespoons/ day)	Parents kept a written calendar indicating: 1) frequency of defecation; and b) number of episodes of soiling, designated as major and minor) smears or stains). A star was affixed to those days when no soiling occurred, but no other rewards were given. Calendars were submitted at each follow-up visits and at 12 weeks when repeat anorectal manometry and expulsion dynamics were performed.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							designed to induce a soft bowel movement daily. Children and parents were instructed on the goals of this regimen and the importance of having regular defecation. Defecations was attempted after breakfast and dinner, as with the biofeedback group. *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	
Wallaker (2014)(Wallaker 2014)	To describe current nursing practice and clarify the safest and most effective dose of milk and molasses enemas used to relieve constipation in paediatric patients	Other primary study	413 (patient records aged 2- 17 years) who were documented to have a discharge diagnosis of constipation or AP to determine whether a milk and molasses enema was administered.	U	United States	Hospital (Emergency Department)	Milk and molasses enemas	Main outcome: enema success rate based on nurse documentation of at least moderate stool and minimal side effects (including abdominal pain, vomiting and need for admission.
Whitehead (1992) (Whitehead 1992)	To provide a review of the expanding role that biofeedback plays in the management of gastrointestinal disorders,	Narrative review	Patients with gastrointestinal disorders	NR	More than one – international evidence	Multiple settings	Biofeedback Treatment	NR
Xinias (2015) (Xinias 2015)	The aim of this review is to provide the general paediatrician an overview of constipation in children discussing the etiology, differential diagnosis, signs and symptoms and patient evaluation.	Narrative review	Children with constipation. Rome III Criteria was used.	U	More than one – international evidence	More than one	More than one intervention: close medical supervision, dietary instructions, behavioral changes and instructions regarding toilet training (most preferably after meals). *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	NA
Yee (2011)(Yee 2011)	This retrospective audit aimed to determine if TES use affected appendicostomy-formulation rates and to monitor changes in practice.	Other primary (retrospective audit)	438 Children with intractable functional constipation (slow transit constipation (STC))	U	Australia	Hospital (tertiary institution)	Transcutaneous electrical stimulation (TES) therapy V appendicostomy operation (ACE)	Appendicostomy formation rate
Yik (2011) (Yik 2011)	This study examined if concurrent upper	RCT	46 children aged 8-18 years with slow transit constipation of > 2	No	Australia	Hospital (tertiary	Transcutaneous electrical stimulation (TES)	Bowel function (history, medical management, neonatal issues,

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	gastrointestinal dysmotility (UGD) affected response to TES.		years consistent with Rome II. All children were diagnosed with STC using NTS Rome III Criteria			institution)		existing bowel symptoms), weight, height, blood pressure, pulse rate and assessment of faecal loading by abdominal palpation were performed followed by 4 weeks recording of daily diary. The diary recorded defecation frequency, response to urge, consistency (Bristol Stool Scale), soiling, medications usage (laxatives, stool softeners) and abdominal pain
Yik (2012)(Yik 2012)	To determine if TES use affected appendicostomy-formation rates and to monitor changes in practice.	Other primary study (retrospective review)	40 children (aged > 2 years) with CFC – STC. STC was diagnosed by nuclear transit scintigraphy (NTS), as holdup of radioactivity in the transverse colon	NR	Australia	Hospital (tertiary institution)	appendicostomy and/or TES (transcutaneous electrical stimulation).	rates for appendicostomy
Yik (2012)(Yik 2012)	This study aimed to test the effectiveness of home transcutaneous electrical stimulation (TES) when patients with slow-transit constipation (STC) were trained by a naive clinician.	Other primary study (prospective study	38 children aged 3 - 17 years with chronic constipation and soiling for a minimum of 2 years and had failed to respond to conventional treatment. The diagnosis of STC was made by NTS.	U	Australia	Home	Home transcutaneous electrical stimulation (TES) Parents of the children and older children were trained to use the 9-V battery-operated, rechargeable interferential stimulator (INF 4160; Fuji Dynamics Ltd, Kowloon, Hong Kong) by YIY at a 1-hour clinic session with personal demonstration on the use of TES stimulator, proper placement of electrodes, appropriate connections of leads, and with reassurance on the safety of TES for home treatment. Stimulation was performed or monitored by the parent(s) at home (1 hour daily for 3-6 months) with frequent contacts with YIY, by telephone or e-mail, to ensure compliance of treatment and also to ensure continuous recording of bowel diary. Two self-adhesive 4-cm2 electrodes were placed on the anterior abdominal wall at the level of the umbilicus of the child, and 2 other electrodes were placed on the back between T9 and L2 on either side (Fig. 1) [9]. The current from the electrodes was crossed diagonally from front to back. Interferential treatments delivered a 4-kHz carrier frequency, a beat frequency of 80 to 160 Hz with	Bowel diary and PedsQL4.0 questionnaires were administered before and during treatment. Two groups were identified by defecation frequency before treatment: group 1, less than 3 bowel actions (BAs) per week, and group 2, more than 3 BAs per week. Careful instructions were given to patients and/or parents to record the bowel diary with details on soiling, defecation frequency, stool consistency based on Bristol Stool Scale (BSS), abdominal pain, and sensation to defecate before and during treatment. Primary end points were decreased soiling, increased defecation frequency, improved stool form, and increased sensation of defecation/urge-initiated defecation. As a secondary end point, colonic transit was measured by NTS before and after TES.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							an intensity of less than 33 mA as previously described [9].	
Yik (2016)(Yik 2016)	We performed a pilot study to test if TES can improve symptoms (defecation and soiling) in children with chronic constipation without STC and transit delay in the anorectum	Other primary study (Pilot study)	10 children aged 5-10 years with treatment-resistant constipation (> 6 months). Diagnosed with anorectal retention by NTS. All were on laxatives.	U	Australia	Home	Transcutaneous electrical stimulation (TES)	The primary outcome measure was defecation frequency. Fecal incontinence episodes/week, laxative use, episodes of abdominal pain/week, urge-to-defecate, and quality of life (PedsQL, parent and child-reported) and GIT measured by NTS before and after TES outcomes were secondary. The following changes were considered improvement: 1. defecation frequency of 3 BM/week; 2. reduced days of soiling and abdominal pain (measured as days/ week with symptoms); 3. reduced use or discontinued use of laxative; 4. increased PedsQL scores; and 5. faster colonic transit (with a higher GIT indicating faster transit) or increased excretion at 48 hours.
Yik (2018)(Yik 2018)	This study examined the effectiveness of stimulation (TES) for six months	Other primary study (Cohort) Study	62 children with slow transit constipation (STC) Inclusion criteria specified that the children had chronic constipation and soiling for greater than or equal to two years and had failed to respond to medical treatment (diet, behavior modification, laxatives/enemas) and had been investigated by NTS, where a diagnosis of STC was made as described previously (9–11). The specific criteria on NTS were that there was 40% of tracer retained in the transverse colon at 24 hours and/or 30% at 48 hours, or a mean geometric center of 3.0 and/or 4.2 at 24 and 48 hours, respectively. Exclusion criteria were patients with ventriculoperitoneal shunts or	NR	Australia	Home	Transcutaneous electrical stimulation (TES)	The primary outcome was defecation frequency (bowel actions/ day). Secondary outcomes included soiling, abdominal pain, sensation or urge to defecate, laxative use, and gastrointestinal transit. Soiling and abdominal pain were measured as days/week with symptom occurrence. Urge to defecate was measured using a visual analogue scale. The following changes were defined as an improvement: 1) defecation frequency 3/week. (for those who started<3 BA/week. at baseline); 2) reduced frequencies of soiling and abdominal pain (measured by days/week of occurrence); 3) reduced laxative use; 4) increased PEDSQL scores, and 5) faster colonic transit measured by NTS. short gastroinstesinal symptom score.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
			cardiac pacemakers, to avoid potential effects of electrical interference.					
Yoo 2017 (Yoo and Bae 2017)	Evaluated the efficacy and safety of combined oral and enema therapy using polyethylene glycol (PEG) 3350 with electrolyte solution for disimpaction in hospitalized children	Other primary study (Retrospective cohort)	28 children aged 2-17 years old with CFC. Rome III criteria used.	U	Korea, Rep.	Hospital	Combined oral and enema therapy using polyethylene glycol (PEG) 3350 with electrolyte solution *This study is included in the effectiveness review. Further details about the intervention are profiled in Appendix 5, Table 21*	Monitored for the development of adverse effects, and safety of the regimen was checked by observing clinical symptoms and assessment of laboratory blood tests including electrolytes and osmotic pressure, among others.
Zivkovic (2017) (Zivkovic 2017)	To evaluate the effects of interferential current (IC) stimulation and diaphragmatic breathing exercises (DBEs) in children with bladder and bowel dysfunction	Other primary study (Online survey and retrospective chart review)	79 children with bladder and bowel dysfunction.	U	Serbia	Clinic and Home	Interferential current stimulation and diaphragmatic breathing exercises	Evaluated the following clinical manifestations: daytime incontinence, enuresis, UTIs, voiding difficulties, number of defecations and episodes of FI.
Zollars (2019) (Zollars 2019)	To assess improvement in the quality of life, function, and colonic motility before and after visceral and neural manipulation in children with cerebral palsy and chronic constipation	Other primary study (case reports)	5 children with Cerebral Palsy (aged between 2 -18 years) with a diagnosis of constipation according to Rome II criteria modified for children with cerebral palsy.	Yes	United States	Therapists office	Visceral and neural manipulation – a hands-on therapy which works with specific tissues in the body, including nerves, fascia, joints, bones, organs and the vasculature. The treatments are gentle, and do not cause damage. Visceral and neural manipulation has clinically been used as a gentle, non-invasive treatment for constipation.	Quality of life and function were assessed using the CPCHILD and the WeeFIM

Table 5. Level 3 – Specialist consultant-led teams: highly specialist services, usually by tertiary care services

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Ahmadi (2013) (Ahmadi, Azary et al. 2013)	To determine the use of intra sphincteric injection of botox in children with refractory constipation	Other primary study (prospective case control study)	All children who suffered from chronic constipation for more than three months, and who had not responded to medical treatment, were referred to pediatric surgical clinic for interventions by pediatric gastroenterologist. Participant number not clearly reported but sample size based on statistical calculations is 88 patients (44 cases and 44 controls).	NR	Iran, Islamic Rep.	Hospital	Botulinum toxin plus stool softeners vs control group (stool softeners alone). Botox injection was carried out under general anaesthesia in three regions of the anal sphincter in lithotomy position. The botulinum toxin Dysport was injected in sphincter in 3, 6 and 9 o'clock. It was not injected in 12 o'clock to avoid the possibility of urinary incontinence. Total Dysport dosis was 160 units, half of it (i.e. 80 units) was injected in 6 o'clock and one-fourth (i.e. 40 U) in 3 o'clock and one-fourth in 9 o'clock, Injection was done simultaneously in both internal and external anal sphincters.	In the first month after injection, all patients were evaluated once a week and were investigated regarding the improvement or recurrence of symptoms and followed up monthly in the first six months. The response to botox injection six months after injection was compared with the control group. For evaluation of the patients' condition after the botox injection, patients were asked questions about the presence of the signs of constipation including painful defecation, vomiting, stool's consistency, soiling and defecation intervals.
Alqarni (2017) (Alqarni 2017)	To evaluate the 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) via a total endoscopic and anal irrigation management (TEAM®) approach in patients with myelomeningocele and neuropathic bladder and bowel who did not respond to conservative measures	Other primary study	14 mayelomeningocele patients with noncompliant neuropathic bladder and bowel, VUR, and urine/SI were prospectively enrolled in our trial of the TEAM® approach.	Yes	Saudi Arabia	Hospital	Botulinum toxin plus as well as trans anal irrigation to manage SI as a total endoscopic and anal irrigation (TEAM®) approach	Response criteria included a stable, compliant bladder with acceptable capacity given the patient age, VUR resolution, dryness between catheterization, and stool continence.
Azary (2011) (Azary, Khalifehsoltani et	To evaluate the outcome of injection of botulinum toxin into the	RCT	80 children who failed to respond to laxative treatment and were	NR	Iran, Islamic Rep.	Hospital	Botulinum toxin	Significant improvements in symptoms of constipation: soiling, pain and difficulty with defecation, delay in defecation, hard stool

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
al. 2011)	internal anal sphincter (IAS) for treatment of chronic idiopathic constipation		then referred to paediatric surgeons for follow-up management					and reduce impacted stool, general health and behavior, and fecal impaction of rectum.
Baeten (2011) (Baeten 2011)	To provide a brief update on the current data on and position of sacral neuromodulation (SNM) in the specialized management of refractory idiopathic constipation	Narrative review	Included 7 studies. Refer to several definitions of CFC including Rome II/III criteria.	U	More than one	Hospital	Sacral neuromodulation	NR
Basson (2014) (Basson, Charlesworth et al. 2014)	To evaluate outcomes of intrasphincteric botulinum toxin injection (ISBTI) in children with intractable constipation.	Other primary study (retrospective case-note Review)	43 children (aged < 17 years) undergoing injection of C. botulinum toxin type A injection to the anal sphincter for intractable constipation or faecal soiling	U	United Kingdom	Hospital	Botulinum toxin injection to the anal sphincter	Outcome was described as being successful when patients' symptoms had resolved with or without ongoing laxative use; improving when symptoms had improved but not resolved and failed when there was no change in symptoms.
Basson (2014) (Basson, Zani et al. 2014)	To evaluate our outcomes of ACEs and identify predictors of outcome.	Other primary study (retrospective case-note Review)	111 children (aged < 17 years) undergoing injection of C. botulinum toxin type A injection to the anal sphincter for intractable constipation or faecal soiling. This study may include participants reported in the other Basson 2014 paper.	U	United Kingdom	Hospital	Antegrade continence enema. Initially alternate day washouts are commenced with Bisacodyl (0.5–5 mg) and/or KleanPrep (10–20 ml/kg). Glycerin (10–30 ml) is our second-line agent of choice. Removal of the SILASTIC (Dow Coming, Midland, MI, USA) catheter is performed in the surgical outpatient clinic 6-weeks post operatively. Patients are closely monitored by our paediatric nurse specialists and followed up in gastroenterology/surgical outpatient department to establish individualised washout regimens. The type, dosage and frequency of washouts are adjusted so that patients achieve a successful washout. Successful washout is defined as the evacuation of faeces shortly after a washout without retrograde leakage from the stoma or soiling in-between washouts, and no palpable faecalomas on abdominal examination	Outcome was described as being successful when patients were totally clean or experienced the occasional leak and failed when patients described on going regular soiling and/or constipation.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Bellomo-Brandao (2018) (Bellomo-Brandao 2018)	To compare outcomes in children with refractory constipation and overflow retentive stool incontinence (ORSI) under conservative therapy or by antegrade continence enema (ACE) procedure.	Other primary study (retrospective study)	29 children (median age: 94 months; min: 27, max. 142 months) with refractory constipation and overflow retentive stool incontinence	U	Brazil	Hospital	Antegrade continence enema procedure compared with Conservative therapy (dietary fiber, oral osmotic laxatives, and rectal enemas)	1) ORSI control 2. Regular spontaneous evacuations, ACE or rectal enema were stopped.
Bigelli (2005) (Bigelli, Fernandes et al. 2005)	To standardize the methodology of anorectal manometry at our Institution and study the activity of anal sphincter in children	Other primary study	Children aged 4-12 years, with stool frequency of < 3 per week or the painful passage of bowel movements and stool retention with or without soiling even when the stool frequency was >3 per week for at least 1 month.	U	Brazil	Hospital	Anorectal Manometry plus standard care (education, faecal disimpaction, prevention of future impaction and promotion of regular bowel habits, toilet training)	
Bonilla (2013) (Bonilla, Flores et al. 2013)	To describe the rate of cecostomy failure in a cohort of paediatric patients with refractory constipation, and the long term outcome	Other primary study (retrospective cohort)	12 children with chronic refractory constipation that underwent cecostomy for administration of ACE	NR	United Kingdom	Hospital	Antegrade continence enema (ACE)	Detailed analysis of the subgroup of patients who failed to improve after cecostomy was performed including demographic variables, medical history, symptoms, subsequent treatment and clinical outcome. Clinical success was defined as frequency of defecation of ≥ 2 bowel movements per week and ≤ 1 episode of fecal incontinence per week and improvement in symptoms that have a significant impact on the patient's quality of life including abdominal bloating or pain, nausea, and vomiting
CADTH (2015) (Canadian Agency for Drugs and Technologies in Health (CADTH) 2015)	To determine the clinical benefits and harms of colonoscopy in patients < 50 years of age for investigating constipation and identify evidence-based guidelines for colonoscopy in patients	Narrative review (rapid summary of findings)	Patients under the age of 50 years with constipation, but with no family history of colon cancer, anaemia, or weight loss. Identified three relevant studies.	NR	More than one	Hospital	Colonoscopy	Clinical benefits and harms; Guidelines

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	< 50 years of age for investigating constipation							
CADTH (2018) (Canadian Agency for Drugs and Technologies in Health (CADTH) 2018)	To evaluate the clinical effectiveness of digital stimulation and manual disimpaction	Narrative review (rapid summary of findings)	Included a wide range of studies including patients with nerve damage preventing regular bowel movement (e.g., spinal cord injury patients, multiple sclerosis patients, flaccid bowel, neurogenic bowel, spina bifida). In order to answer Q2 and Q4 they included all patients with faecal impaction.	NR	More than one	Hospital	Digital stimulation and manual evacuation	Q1-2: Clinical effectiveness (e.g., clearing of bowel, change in symptoms, safety), Q3-4: Evidence-based guidelines
Carmo (2015) (Carmo 2015)	To assess clinical features and colonic transit patterns in children with refractory constipation	Other primary study (case study)	28 children aged 8-14 years wih refactory constipation with a median duration of symptoms longer than five years (ranging from 2 to 12 years). Rome II criteria used to define CFC.	U	Brazil	Hospital	Antegrade continence enema (ACE)	Adherence to therapy and clinical features on constipation symptoms were systematically evaluated
Cascio (2004) (Cascio, Flett et al. 2004)	To describe our experience with MACE and CB, aiming to compare the results, complications, and outcomes.	Other primary study (case note review)	49 children (aged 3-18 years) with an indication for surgery due to intractable constipation and faecal soiling that had failed conventional treatment	NR	United Kingdom	Hospital	MACE or CB	The success rate of the procedures was classified as full success, partial success, or failure, based on criteria specified by Curry et al. [3]. Surgical complications were classified as major or requiring operative intervention and minor or not requiring operative intervention.
Chaney (2017) (Chaney 2017)	To illustrate the importance of nursing input in the performance and interpretation of manometry testing for children with suspected gastrointestinal motility	Other primary study (case series)	3 children (aged 9, 12, and 16 years) who underwent manometry testing	NR	United States	Hospital	Manometry	Nurse observations

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	disorders.							
Chang (2013) (Chang 2013)	To collect data on the treatment practices from paediatric gastroenterologists.	Other primary study	Children > 12 months of age, who visited one of the 13 pediatric gastroenterology clinics due to prolonged constipation longer than 2 months and met the Rome III criteria for constipation.	NR	Korea, Rep.	Hospital	Digital rectal examination as an initial diagnostic tool, disimpaction as an initial treatment technique, types of drug treatments, and duration of treatments	Prevalence, clinical characteristics, and management
Cheng (2018) (Cheng 2018)	To review surgical options available for managing refractory constipation in children and provide guidance on how to choose the best procedure for a given patient	Narrative review	Children with refractory constipation using the Rome III criteria	U	More than one	Hospital	In addition to medical management, Surgical interventions included: anal procedures, antegrade enemas, colorectal resection, and intestinal diversion, anal procedures, Antegrade Colonic Enema, laparoscopic-assisted percutaneous endoscopic cecostomy (LAPEC), colorectal resection, intestinal diversion	NR
Chong (2016) (Chong, Featherstone et al. 2016)	To look at our patients 5 years after the formation of their ACE	Other primary study (retrospective case-note Review)	190 children (median age of 7 years at the time of ACE formation (range 6 months to 18 years) who were under the care of the departments of paediatric surgery and/or paediatric urology	NR	United Kingdom	Hospital	ACE procedure	NR
Church (2017) (Church, Simha et al. 2017)	To investigate the success of ACE in patients with encopresis in improving stooling habits and QOL.	Other primary study (retrospective case-note review)	10 children who had undergone placement of an appendicostomy or cecostomy tube and had antegrade continence enemas initiated with guidance by our pediatric colorectal program. Patients with a diagnosis of encopresis were also	U	United States	Hospital	ACE procedure	Variables of interest included demographic information, indication for operation, and age at procedure. Type of operation, comorbidities, length of stay, readmissions, and short and long-term complications.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
			included in the study. Mean age was 11.4±4.9 years old					
Clayden (2005) (ISRCTN24521269 2005) 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 ordinary needle versus control	RCT (Study was abandoned due to issues with eligibility)	80 children aged 3 to 15 years with idiopathic chronic constipation referred for anorectal manometry and inpatient bowel management programme.	NR	United Kingdom	Hospital	Botulinum toxin	Improvement in patients symptom severity score determined by parents completed questionnaire
Colares (2016) (Colares 2016)	To evaluate the impact of implementation of the bowel management program on the quality of life in children with FI	Other primary study	48 children > 3 years of age) with FI that were sent to our center and received the BMP. Mean age of 7.7 ± 3.1, range 3–12 years	U	Brazil	Hospital	Administration of daily enemas with saline solution alone or with glycerin and liquid soap	Quality of Life
Dolejs (2017) (Dolejs, Smith et al. 2017)	To elucidate the efficacy of ACE in the treatment of intractable constipation.	Other primary study (retrospective review)	93 children aged 3 to 18 years old who had undergone an ACE procedure for unremitting constipation and FI.	U	United States	Hospital	ACE procedure	The efficacy of the ACE procedure was based off of several measures. Normal bowel function after an ACE procedure was defined as no accidents, predictable bowel habits, and no pain with flush. Improvements in bowel function after ACE were based on subjective assessments from parents as well as objective measures of decreased episodes of fecal incontinence and fecal impaction. Postoperative morbidities and perioperative outcomes included hospital length of stay, surgical site infection (including rate and treatment required), bowel perforation, and thirty-day readmission. Several long-term outcomes were followed including stomal stenosis, small bowel obstruction, stomal prolapse, stomal leakage, recurrent impactions, pain with flushing, and any requirement for additional surgical procedures.
Firestone Baum (2013) (Firestone Baum, John et al. 2013)	To assess whether there was a sensory abnormality in patients who denied sensation	Other primary study (patient chart review)	participants with normal manometry and a diagnosis of functional	NR	United States	Hospital	Colon manometry	Colon pressure

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
			constipation					
Freeman (2014) (Freeman 2014)	To determine whether performance of appendicostomy/cecostomy prior to starting school (<6 years) would improve functional stooling and quality of life	Other primary study (survey and telephone interview)	14 children (6/14 with CFC diagnosis) aged 3 years+ who underwent appendicostomy/ cecostomy for bowel management	NR	United States	Hospital	Appendicostomy or cecostomy	Primary outcome was to compare the total stooling score and QOL score. Secondary outcome measures examined the subcategories of stooling pattern and their relation to QOL.
Gasior (2018) (Gasior, Reck et al. 2018)	To determine which patients will benefit from a colon resection with antegrade flush based upon bowel management, manometry, contrast enema and our multidisciplinary team.	Other primary study ('intermediate update of retrospective review')	31 children aged 4 to 18 years with CFC and failed medical management	NR	United States	Hospital	Laparoscopic sigmoid resection combined with Malone appendicostomy	Age, gender, associated medical conditions, pre-operative testing, post-operative complications, post-operative bowel regimens, and follow-up duration.
Gomez-Suarez (2016) (Gomez-Suarez, Gomez-Mendez et al. 2016)	To determine which preoperative clinical and both colonic and anorectal manometric features were associated with success of cecostomy in the treatment of constipation and faecal overflow incontinence.	Other primary study (retrospective review)	40 children (31 with CFC) patients who underwent an ACE procedure. Mean age at time of follow-up was 9.5 ± 4.4 years with a mean follow-up time of 12.2 ± 10.9 months	Mixed population	United States	Hospital	Manometry (colonic and anorectal) before cecostomy	Clinical outcomes were defined as good, if subjects had >3 bowel movements per week, <2 episodes of soiling per week, and absence of pain at the time of follow-up after cecostomy.
Gupta (2020) (Gupta 2020)	To review outcomes of children with IC who were managed surgically at a single tertiary care center.	Other primary study (retrospective case-note review)	67 children with IC who were managed surgically	NR	United Kingdom	Hospital	MDT protocol (including blood tests, upper and lower gastrointestinal endoscopies with mucosal biopsies, rectal biopsy, examination of rectum under anesthesia, anorectal and colonic manometry). Psychological evaluation was offered to most of these children as a part of workup or in preparation for surgery. ACE (antegrade colonic enema), colostomy, or ileostomy	Successful outcome was defined as adequate decompression (no longer fulfilling the Rome IV criteria for functional constipation in those without stoma, or having a functional stoma) without need for further unplanned surgical intervention
Hameed (2018) (Hameed 2018)	To determine the utility of intra-sphincteric injection of botox in the treatment of children with refractory constipation.	Other primary study (prospective case control)	50 children aged between 2-8 years with chronic constipation for more than three months, and who had not	NR	Iraq	Hospital	Botulinum toxin injection in addition to stool softners	Evaluation of the presence of the signs of constipation including painful defecation, vomiting, stool's consistency, and soiling and defecation intervals.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
			responded to medical treatment and were referred to pediatric surgical clinic for interventions. Rome III criteria used to diagnose CFC.					
Har (2013) (Har, Rescorla et al. 2013)	To determine if there is a change in the quality of life in pediatric patients with unremitting functional constipation and/or encopresis after undergoing a MACE procedure.	Other primary study (survey and questionnaire)	15 children, aged 5 to 18 years, with unremitting functional constipation and a normal evaluation, including both anorectal manometry and colonic manometry, who decided to undergo a MACE procedure were included	NR	United States	Hospital	MACE procedure	Quality of life
Heemskerk (2018) (Heemskerk, Rotteveel et al. 2018) NCT02961582	To assess the effectiveness, cost-effectiveness, and budget impact of SNM compared to personalized conservative treatment (PCT) in patients with idiopathic slow-transit constipation refractory to conservative treatment.	RCT (on-going)	Planned to recruit 64 participants (adolescents aged 14–17 years and adults aged 18–80 years) who have slow-transit constipation, defaecation frequency (DF) < 3 per week and meeting at least one other Rome-IV criterion.	NR	Netherlands	Hospital	Sacral neuromodulation versus personalized conservative treatment	Primary outcomes: treatment success defined as an average defecation frequency (DF) of ≥ 3 a week, based on a 3-week defecation diary. Secondary outcomes: proportion of patients with a 50% reduction in the proportion of defecations with straining, proportion of patients with a 50% reduction in the proportion of defecations with a sense of incomplete evacuation, constipation severity, fatigue, constipation specific (health-related) quality of life ((HR)QOL), generic (HR)QOL, adverse events and complications, resource use and costs, cost-effectiveness, and budget impact.
Hoekstra (2011) (Hoekstra, Kuijper et al. 2011)	To evaluate clinical success, complications, and quality of life of children with chronic defecation disorders with a MACE stoma.	Other primary study ('retrospective analysis')	23 patients with intractable constipation and/or FI who received a MACE stoma	Mixed population	Netherlands	Hospital	MACE Procedure (Malone antegrade continence enema)	Preoperative and postoperative data were evaluated. A specific questionnaire was used to assess patient satisfaction
Huber (2016) (Huber 2016)	To determine if the contrast enema findings could predict a final enema regimen in order	Other primary study (retrospective review)	83 children (34 with CFC) enrolled in the bowel management program included	Mixed population	United States	Hospital	Contrast enema	Contrast enema findings (including volume to completely fill the colon), and final enema regimen were collected.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	to simplify the trial-and-error process of bowel management.							
Husberg (2011) (Husberg 2011)	To evaluate the long-term functional results in a paediatric patient-group now reaching adulthood, who had been operated upon earlier with an ACE.	Other primary study (long-term follow-up)	27 children aged between 5 -21 years who had been operated upon earlier with an ACE because of gastrointestinal functional disturbances following surgery for inborn malformations or for intractable constipation. Of these only two had CFC.	NR	Sweden	Hospital	MACE procedure	Bowel function, rinsing technique and patient satisfaction.
Iacona (2019) (Iacona 2019)	To review the current literature on the application of the neuromodulation techniques in the management of chronic constipation and fecal incontinence in children.	SR	428 children with FI and / or CFC	U	More than one	Hospital	Neuromodulation techniques	Patient reported complaints, FI score, quality of life score, anorectal physiology results, and adverse outcomes.
Iacono (2006) (Iacono, Bonventre et al. 2006)	To evaluate the histology and manometry characteristics of the cases of constipation caused by CMI.	Other primary	36 consecutive infants and children with chronic constipation unresponsive to previous treatments.	No	Italy	Hospital	Manometry	Manometry and histology patterns
Jaffray (2009) (Jaffray 2009)	To perform an actuarial analysis of the outcomes of the ACE procedure in children consecutively referred to our unit for this procedure, who have idiopathic constipation, and who did not respond to 3 years of medically supervised conservative management.	Other primary study ('prospective actuarial analysis')	80 children (3.4- 18.7 years) underwent an ACE.	NR	United Kingdom	Hospital	Construction of an ACE	Ongoing lavage, failure, and cure. A minimum of 6 months follow-up was judged to be appropriate because a decision regarding “cure” would take no less than 6 months to determine.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Janssen (2018) (Janssen, Meyer et al. 2018)	To compare long-term results of SNM for FC between children and adults	Other primary	45 children aged 10 - 17 years who had failed conservative treatment prior to evaluation.	Mixed population	Netherlands	Hospital	Sacral neuromodulation (SNM)	Primary outcome: defaecation frequency of three or more times per week, Secondary outcome: QoL
Keohane (2019) (Keohane 2019)	To present a case report of an adolescent patient presenting to the emergency department with distended abdomen	Other primary study (case study)	Single case study of a 17-year-old male with abdominal compartment syndrome	U	Ireland	Hospital	Manual disimpaction	NR
Khoo (2017) (Khoo, Askouni et al. 2017)	To determine the natural history of the ACE in idiopathic constipation and factors predictive of closure.	Other primary study (retrospective case note review)	85 children with CFC selected for ACE on subjective clinical evaluation. Median age at ACE was 9.2 years (3.2–16.6 years)	U	United Kingdom	Hospital	Antegrade continence enema stoma (ACE)	Primary outcome: time to closure of ACE.
King (2005) (King, Sutcliffe et al. 2005)	To determine whether ACE are successful for idiopathic pediatric STC (slow transit constipation).	Other primary study (follow-up telephone interview study)	Patients who satisfied the Rome II criteria for CFC, with or without FI who also had the ACE procedure	NR	United Kingdom	Hospital	Antegrade continence enema (ACE) procedure	Information collected included (1) age at symptom onset and stoma formation, (2) indications for and mode of formation, (3) initial/current device, (4) formation complications, (5) initial/current ACE regimens, (6) abdominal pain pre-ACE/post-ACE, (7) soiling pre-ACE/post-ACE, (8) achievement of preformation aspirations, and (9) perceived quality-of-life changes. Evaluation of continence, using modified Holschneider criteria.
Koppen (2016) (Koppen 2016)	To assess the diagnostic and surgical approach of pediatric surgeons and pediatric gastroenterologists towards children with intractable FC.	Other primary study (survey)	74 physicians who specialised in the management of children with intractable functional constipation	NR	More than one	Hospital	Use of non-pharmacological and pharmacological treatment for FC and use of surgery in intractable FC	NR
Kuizenga-Wessel (2016) (Kuizenga-Wessel 2016)	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	Other primary study (literature review and survey)	Children and young people (aged < 25 years) with defecatory disorders when maximal behavioral, dietary, and medical therapies are not successful. 940	U	More than one	Hospital	Antegrade continence enema (ACE) Procedure	Unclear

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	worldwide regarding the use of the ACE.		participants were identified based on the literature review and 25 children were included in the survey					
Kuizenga-Wessel (2017) (Kuizenga-Wessel, Koppen et al. 2017)	To describe the surgical management of FC in children	Other primary study (Retrospective chart review with a cross-sectional parental questionnaire)	37 children aged between 0 and 18 years with intractable functional constipation (FC) who received surgical interventions.	U	Netherlands	Hospital	Surgical management: ileostomy, colostomy and sub(total colectomy	Complications classified as per the Calvien-Dindo classification.Post-surgical heath-related problems, parental satisfaction about surgery - yes-no question on a scale of 0-10, current bowel habits, constipation-associated symptoms according to the Rome III criteria, abdominal pain, school absences, current medications. Treatment success was defined as no longer fulfilling the Rome III criteria for FC in patients with stoma closure or having functional ostomy in children with ileostomy or colostomy, independent of pharmacological treatment.
Levitt (2011) (Levitt 2011)	To review surgical approaches to constipation and its role as a contributor to FI	Narrative review	Children with constipation	Mixed population	More than one	Hospital	More than one surgical interventions: Reoperation, antegrade enemas, permanent stoma, rectosigmoid resection	NR
Li (2018) (Li, Shanahan et al. 2018)	To review the evidence for Malone appendicostomy versus cecostomy tube insertion for children with constipation refractory to maximal medical management.	SR	Identified 3 studies with children with functional and pathologic causes of intractable constipation refractory to maximal medical management.	NR	More than one	Hospital	Malone appendicostomy versus cecostomy tube insertion	Primary outcomes: continence post-procedure and quality of life. Secondary outcomes: adverse events and complications.
Lu (2017) (Lu 2017)	To evaluate the efficacy of SNS in children with intractable constipation dependent on ACEs	Other primary study (Prospective patient registry)	24 children with intractable constipation (aged up to 21 years) and treated with ACEs who received SNS.	U	United States	Hospital	Sacral Nerve Stimulation (SNS)	ACE and medication usage, PedsQL Gastrointestinal Symptom Scale (GSS), Fecal Incontinence Quality of Life Scale (FIQL), Fecal Incontinence Severity Index (FISI), and Vancouver Dysfunctional Elimination Syndrome Score (DES)
Lu (2018) (Lu 2018)	To evaluate the long-term efficacy of sacral nerve stimulation (SNS) in children with constipation described patient benefit and parent satisfaction.	Other primary study ('prospective observational cohort study')	25 children and young people aged up to age 21 years with constipation (using the Rome III criteria) who underwent SNS initiation	Mixed population	United States	Hospital	Sacral Nerve Stimulation (SNS)	Patient symptoms, laxative and ACE usage, relevant diagnostic test results and complications of SNS. Patient-reported outcomes - PedsQL Gastrointestinal Symptom Scale(GSS), Fecal Incontinence Quality of Life Scale (FIQL), Fecal Incontinence Severity Index (FISI), and

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								Vancouver Dysfunctional Elimination Syndrome Score (DES)
Mousa (2006) (Mousa, van den Berg et al. 2006)	To report our 4-year experience with two different techniques of the cecostomy procedure and to compare the clinical outcome of cecostomy in children with defection disorders secondary to functional constipation, imperforate anus, and spinal abnormalities.	Other primary study ('reporting a 4-year experience')	31 children with functional constipation (n = 9), Hirschsprung's disease (n = 2), imperforate anus (n = 5), spinal abnormalities (n = 8), and imperforate anus in combination with tethered spinal cord (n = 7). anus, and spinal abnormalities. The median age at the time of cecostomy placement was 8 (range, 3–18) years	Yes	United States	Hospital	Placement of cecostomy following a colonic cleanout	Outcome measures were obtained by interviewing the parents to determine (1) complications, (2) type of antegrade enemas used, (3) effectiveness of treatment, and (4) quality of life. A standardized questionnaire was used to obtain data about the time taken to evacuation after antegrade out, the type and volume of enema solution used, and the child's health status before and after the cecostomy placement. Pre-cecostomy data were obtained retrospectively during the same interview. Bowel movement and faecal soiling frequency, number of medications, number of physician visits related to defecation problems, number of hospital admissions for disimpaction, number of missed school days per month, and quality of life.
Mousavi (2014) (Mousavi, Karami et al. 2014)	To assess the outcome of children who have been diagnosed with intractable chronic constipation and histopathologic condition	Other primary study ('prospective')	44 children presenting with intractable constipation that did not respond to classic conservative treatment (diet, laxatives or enema) over a period of 3 months or more were included. The age at operation ranged from 1 to 12 years (median: 4.6 years)	U	Iran, Islamic Rep.	Hospital	Anorectal myectomy	Bowel habits, complications and symptomatic improvement.
Mugie (2012) (Mugie, Machado et al. 2012)	To describe a single-centre, 10-year experience with the use of antegrade enemas	Other primary study ('retrospective analysis')	99 children (median age 8 years) who received a cecostomy for administration of antegrade enemas	NR	Netherlands	Hospital	Placement of cecostomy performed either percutaneously by an interventional radiologist or surgically with an open technique.	Medical history, symptoms, irrigation regime, complications, and clinical outcome were obtained and analysed. Clinical outcome after using antegrade enemas was classified in 4 groups: (1) full success, if the patient became totally symptom free; (2) partially successful, if the symptoms improved; (3) no difference, if the pre-existing symptoms persisted; and (4) failure, if the patient' symptoms worsened and the

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								cecostomy had to be removed. This outcome was based on the number of weekly bowel movements, number of weekly fecal incontinence episodes, number of hospital visits for disimpaction, number of oral medications, and complications, obtained from the clinical notes and letters in the medical charts.
NCT02255747(NCT02255747 2014)	To evaluate the effect of anal dilation in infants and children with constipation	RCT (on-going)	Planned to recruit 100 infants and children (aged 1 month to 14 years) with constipation	NR	China	Hospital	Anal dilatation and lactulose Recruitment status: unknown (3/10/2014)	Primary outcome: daily stool times. Secondary outcomes: frequency and amplitude of intestinal peristalsis waves
NCT02361749 (NCT02361749 2015) (Also registered as PACTR201408000857349)	To compare the results of botulinum toxin injection versus surgical myectomy to treat functional/ idiopathic constipation in children.	RCT (cross-over) (on-going)	Planned to recruit 40 children (aged 2- 12 years) with CFC	NR	Egypt, Arab Rep.	Hospital	Botulinum toxin injection versus surgical myectomy Recruitment status: unknown (30/01/2018)	Primary outcome: absence of insufficient Rome III Diagnostic criteria (0-1 criterion). Secondary outcomes: decrease in Rome III Diagnostic criteria score
NCT03593252 (NCT03593252 2018)	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 (on-going)	48 children aged 6 to 18 years who attend the Pediatric General Surgery service at McMaster Children's Hospital for elective colorectal surgery will be screened for inclusion in this study.	NR	Canada	Hospital	Combination bowel prep vs Oral antibiotics vs no prep Recruitment status: not yet recruiting (Last updated: 9/12/2021)	Primary outcome: Feasibility (recruitment rate). Secondary outcomes: superficial Incisional surgical site infection (SSI), Deep incisional surgical site infection (SSI), Organ space - Surgical site infection (SSI) , anastomotic leak - Surgical site infection (SSI), Length of hospital stay, Time to full enteric feed., Re-admission , Re-operation, electrolyte disturbance, electrolyte disturbance, Clostridium difficile infection,
NCT04182633 (NCT04182633 2019)	To evaluate Microbiota Transfer Therapy in children with ASD who	RCT (on-going)	Planned to recruit 70 children (aged 5 to 17 years) with a GI	Yes	United States	Hospital	Faecal microbiota transplantation Recruitment status: currently still recruiting	Primary outcomes: Childhood Autism Rating Scale (CARS), and Gastrointestinal Symptom Severity Scale (GSRS). Secondary

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	also have gastrointestinal disorders		disorder and a diagnosis of autism per the Childhood Autism Rating Scale 2 (CARS-2) and either the Autism Diagnostic Interview-Revised (ADI-R) or the Autism Diagnostic Observation Schedule 2 (ADOS 2). GI disorder as defined below that has lasted for at least 3 years. General good physical health aside from gastrointestinal problems				(Last updated: 30/12/2021)	outcomes: daily Stool Record, Social Responsiveness Scale 2, Aberrant Behaviour Checklist
NCT04246398 (NCT04246398 2020)	To evaluate FMT in children with autism and gastrointestinal symptoms	RCT (cross-over) (on-going)	Planned to recruit 50 children (aged 7 to 20 years) with ASD with gastro-intestinal symptoms and/or food selectivity that interfere with daily routine	Yes	Israel	Hospital	Faecal microbiota transplantation Recruitment status: not yet recruiting (Last updated: 5/02/2020)	Primary outcomes: incidence of treatment-emergent Adverse Events [Safety and Tolerability], significant change in GI symptoms. Secondary outcomes: change in food selection, improving ASD symptoms, diversity and variability of the gut microbiome
NCT03819062 (NCT03819062 2019)	To study if low level laser therapy will "do more harm for patients with severe chronic refractory constipation"	Single group (on-going)	Planned to recruit			Hospital		
NICE (2006) (NICE 2006)	To produce guidance about percutaneous endoscopic colostomy	Guidelines	Children with chronic refractory constipation	NR	More than one	Hospital	Percutaneous endoscopic colostomy	NR
Pal (2016) (Pal 2016)	To evaluate and quantify current use of surgical clinic time for CFC patients	Other primary study ('review of computerized records')	85 children with CFC	NR	United Kingdom	Hospital	Intervention either surgical or not surgical	Data obtained included referral source, waiting time and intervention (effectiveness and symptoms).
Peeraully (2014) (Peeraully, Lopes et al. 2014)	To retrospectively analyse the management and outcomes of children who underwent	Other primary study (retrospective review)	40 children < 16 years who had undergone an MACE procedure	U	United Kingdom	Hospital	MACE procedure	Using the continence scale described by Malone overall outcomes were categorised as full, partial or failure (full: totally clean or minor rectal leakage on night of washout;

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	MACE procedures at a regional pediatric surgery unit.							partial: clean but significant stoma or rectal leakage, occassional major leak and/ or still wearing protection but perceived by child or parent to be improvement; failure: regular soiling or constipation persisted, no perceived improvement, procedure was abandoned). As defined by Malone the overall success rate was calculated by combining the full and partial success rates.
Peyvasteh (2015) (Peyvasteh, Askarpour et al. 2015)	To evaluate the result of posterior myectomy in children with chronic constipation who underwent to this surgery	Other primary study (prospective)	48 children with refractory chronic constipation. Mean age of the cases was 4.41±2.58, ranged 1.5-11 years old	U	Iran, Islamic Rep.	Hospital	Surgery - Posterior Myectomy	Number of defecation, fecal consistency, straining, and diameter of feces were recorded after treatment. Stool consistency was defined as a normal (semi loose) and hard according to subjective report by parents or child. Diameter of feces was defined as large diameter (or with fecal soiling) versus normal diameter (or without fecal soiling) according to subjective reports by parents or child.
Quitadamo (2016) (Quitadamo, Thapar et al. 2016)	To prospectively evaluate the effect of preliminary bowel preparation on CTT measured by radio-opaque markers	Other primary study (prospective)	24 children (aged 4 to 16 years) with CFC referred for ROM-CTT	NR	Italy	Hospital	Preliminary bowel preparation	Reduction of total CTT
Randall (2014) (Randall, Coyne et al. 2014)	To assess the long-term outcomes of the ACE procedure performed in children	Other primary study (long-term follow-up)	203 children who had an ACE procedure to manage constipation and soiling.	NR	United Kingdom	Hospital	Operations to provide ACE / MACE	Outcomes included continued use of the ACE at last follow up, reasons for discontinuation, reversal of the ACE and further operations required for the underlying condition including stomas or resections. Frequency of ACE use, type of irrigant used and time taken to perform the enema were recorded.
Redkar (2012) (Redkar, Mishra et al. 2012)	To assess the role of diagnostic and therapeutic value of anorectal myectomy in cases of chronic refractory constipation	Other primary study (retrospective)	28 children presenting with chronic constipation and showing no response to rigorous medical management over a period of 1 month or more were included	NR	India	Hospital	Anorectal myectomy	Follow-up protocol included questionnaire regarding bowel habits, complications and symptomatic improvement.
Redkar (2018) (Redkar, Raj et al.	To assess the diagnostic role and therapeutic	Other primary study	107 children aged 7 months - 9 years with	NR	India	Hospital	Anorectal myomectomy	Clinical evaluation including postoperative bowel habits, the need for medication, relief

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
2018)	value of anorectal myomectomy in children with CRC.		chronic refractory constipation					of symptoms and dietary modifications.
Rodriguez (2013) (Rodriguez, Nurko et al. 2013)	To evaluate the relationship between colonic motility and response to the ACE	Other primary study (retrospective review)	40 children (age ranging from 11 months to 9 years) with constipation refractory to maximal medical therapy that required an ACE procedure, and that underwent a baseline colonic motility evaluation before surgery were reviewed	NR	United States	Hospital	Colonic manometry	Colon motility studies and reduction in ACE
Rybak (2016) (Rybak 2016)	To assess in children with intractable constipation whether any colonic manometry parameters could predict the outcome of the surgical ostomy formation	Other primary study ('retrospective analysis')	45 children with chronic constipation (n=42) and chronic intestinal pseudoobstruction syndrome (CIPO) (n=3) who had undergone high resolution colonic manometry completed prior surgery	NR	United Kingdom	Hospital	Surgical treatments - ACE formation, Colostomy and ileostomy	Clinical symptoms (soiling, abdominal pain, presence of faecal mass or anal fissure, feeding intolerance, urinary symptoms, failure to thrive, dyspeptic symptoms) before and after surgical management were assessed, as well as need for another surgery
Saikaly (2016) (Saikaly 2016)	To identify risk factors for surgical complications in children who undergo the MACE procedure.	Other primary study ('retrospective chart review')	97 children (median age 7.7 years) who underwent the Malone Antegrade Continence Enema (MACE)	U	United States	Hospital	Malone antegrade continence enema (MACE)	Patient information included patient age (preteen/teen), sex (male/female), patient BMI (obese/not obese-based on 95th percentile level on CDC BMI Calculator), and etiology of fecal incontinence (spina bifida, meningitis, spinal cord injury, spinal cord tumor, other). Surgical variables included stomal location (umbilical, right lower quadrant [RLQ], midline, left lower quadrant [LLQ], right upper quadrant [RUQ]), deliberate placement of a button/catheter through the stoma, and surgical technique (open/laparoscopic). Surgical complications were analyzed, including stomal stenosis, stomal site infection, leakage through stoma, complete

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								stomal breakdown, stomal prolapse, and false passage/stricture. Stomal stenosis was recorded if dilatation or surgical revision was necessary.
Siddiqui (2011) (Siddiqui, Fishman et al. 2011)	To present our center's long-term multidisciplinary experience with the use of an ACE in a diverse group of children with bowel movement difficulties	Other primary study	Children. No further details reported.	Mixed population	United States	Hospital	Antegrade continence enema (ACE)	ACE performance, irrigation characteristics (type of solution, irrigation dose, use of additives, frequency of use, and the duration of the infusion and of toilet sitting (time needed for complete defecation).
Siminas (2015) (Siminas 2015)	To systematically review all published studies and critically evaluates the outcomes of surgery for IC.	SR	Identidied 45 studies (1157 children)	NR	More than one	Hospital	Surgery: We categorized operations into 4 therapy groups according to the concept of the procedure: (1) anal and pelvic floor interventions, (2) colon resection with anastomosis and rectal operations, (3) operations that provided antegrade colon irrigation notably ACE, and (4) permanent or long-term stoma.	NR
Southwell (2020) (Southwell 2020)	To together systematic reviews and meta-analyses of electrical stimulation used to treat colonic disorders (faecal incontinence, constipation, slow transit constipation [STC], irritable bowel syndrome [IBS-C], and spina bifidaneurogenic bowel).	Narrative review (overview)	Colonic disorders including fecal incontinence (FI), constipation, slow transit constipation (STC), irritable bowel syndrome with constipation (IBS-C), and spina bifida-neurogenic bowel.	Mixed population	More than one	Hospital	Electro-Neuromodulation: Sacral nerve stimulation (SNS)/ Sacral Nerve Modulation (SNM), Transcutaneous Electrical Stimulation (TES) and Functional Electrical Stimulation (FES).	NR
Sparks (2018) (Sparks, Cooper et al. 2018)	To evaluate whether constipation in children with autism spectrum disorder (ASD) is associated with increased emergency department (ED) visits and inpatient admissions compared with constipation in children without ASD.	Other primary study ('retrospective cross-sectional study')	1.5 million visits of children aged 3 to 18 years to the emergency department were included in this study	Yes	United States	Hospital	Other interventions delivered by highly specialist tertiary care services in the ED	Primary outcome: proportion of ED visits that were constipation-related, the proportion of constipation-related ED visits that resulted in hospital admission, and characteristics of these ED visits (hospital charges and length of stay in admitted patients).

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Sulkowski (2015) (Sulkowski, Nacion et al. 2015)	To report the short-term results of SNS on patient-reported symptoms and medical management in children with BBD in order to begin to identify characteristics associated with better outcomes and guide future treatments.	Other primary study (prospective cohort)	34 children (median age 12.1 years) with bowel and bladder dysfunction who had a SNS placed	NR	United States	Hospital	Sacral nerve stimulation (SNS)	Cessation of antegrade enemas or surgical closure as markers of improvement after SNS. Symptom severity and quality of life. Frequency of interventions such as cecostomy flushes and bladder catheterisation. Clinical improvement was defined as termination of anti-cholinergic medications and improvement in at least 4 or the 7 categories from the 4 patient-reported outcome measures - fecal incontinence severity index, fecal incontinence quality of life scale (PEDsQL, Gastrointensintal symptom scale and Vancouver dysfunction elimination syndrome (DES) symptom score
Tambucci (2019) (Tambucci 2019)	To evaluate the clinical impact of colonic transit scintigraphic studies in children with FC	Other primary study (retrospective chart review)	31 children aged 1 to 18 years with CFC, with or without soiling. All children were unresponsive to standard medical treatment who underwent CTT with scintigraphy were included. CFC diagnosed using the Rome IV criteria.	NR	Italy	Hospital	Bowel empyting programme	NR
Tamura (2020) (Tamura and Jaffray 2020)	To present our accumulated experiences of colonic resection for chronic constipation, and in particular to contrast the outcomes of differing resectional techniques.	Other primary study (cohort)	22 children (median age 13.7 (2.9) years) with CFC undergoing colonic resection	NR	United Kingdom	Hospital	Three different types of resection are compared: pan-proctocolectomy with ileoanal pouch anastomosis (IPAA), total colectomy with ileorectal anastomosis (IR), and segmental resections and anastomosis	Outcomes were classified as Good: anal defecation with no soiling; Intermediate: anal defecation with occasional soiling or need for ACE; Poor: a permanent stoma. All complications were also recorded.
Thomas (2013) (Thomas 2013)	To review the evidence published on the use of SNS for chronic constipation	Narrative review	Chronic constipation. Included 13 studies, of which 3 focused on children only	U	More than one	Hospital	Sacral nerve stimulation (SNS)	Symptom improvement, quality of life and patient satisfaction scores.
Tran (2016) (Tran 2016)	To examine the long-term clinical outcomes of children with severe constipation, as defined by need for rectal	Other primary study (retrospective chart review)	175 Rectal biopsy and 350 controls (<21 years) were included. Children with severe constipation who	NR	United States	Hospital	Rectal biopsy	Successful outcome was defined as a period of at least 4 weeks with >3 bowel movements per week, without pain during defecation, and with <2 episodes of encopresis per month

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	biopsy (RB), and to determine which baseline characteristics were predictors of successful outcome.		underwent RB for evaluation of Hirschsprung disease at a tertiary medical center were eligible for inclusion.					
van den Berg (2005) (van den Berg, van Rossum et al. 2005)	To assess the outcome in children with functional constipation severe enough to require referral to a specialist to rule out Hirschsprung disease.	Other primary study ('a follow-up study')	53 children (<3 years) referred to the tertiary outpatient gastroenterology clinic of the Academic Medical Center, with a suspicion of having Hirschsprung disease and in whom constipation had started during the first year of life (n = 99), constituted the subjects of this study.	U	Netherlands	Hospital	We recommended elimination of the fecal impaction, when present, with enemas (sodiumducosate sorbitol or sodiumlaurylsulfoacatate) followed by the use of an adequate dose of oral laxatives (2 mL/kg per day lactulose or 0.5 g/kg per day polyethylene glycol). Treatment was managed by the primary care physicians according to our recommendations and their own preference.	Follow-up data were obtained by telephone, with the use of a standardized questionnaire. The questionnaire addressed the time of first passage of meconium, defecation frequency, stool consistency, straining and crying during defecation passage, bloody stools, the existence of fissures, age of onset of constipation, use of laxatives, medical and family history, and developmental benchmarks. Parents were asked to recall the clinical status of their child at the age of 6 months and 1, 2, 3, and 4 years. At these different ages, the number of months from presentation to the gastroenterology clinic to follow-up was calculated and categories of follow-up periods were plotted (3, 6, 9, 12, 18, 24, and 36 months). In addition to the clinical status at the specified ages, data about relapse were obtained within these time intervals. To assess clinical outcomes, three categories were defined. “Successful outcome” was defined as a period of at least 4 weeks with ≥3 bowel movements per week, without pain during defecation and without the use of oral or rectal laxatives (category 1). The second category of children had “success while using laxatives” (category 2), whereas the last group did not fulfill the clinical criteria for success (“unsuccessful outcome”), whether with or without the use of laxatives (category 3). A relapse was defined as a period of at least 4 weeks in which bowel movement frequency had decreased to <3 per week or, because of increasing symptoms, laxatives had to be reintroduced,

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								after a period of either “successful outcome” or “success while using laxatives.”
Van Der Wilt (2014) (Van Der Wilt 2014)	To assess the effectiveness of sacral neuromodulation (SNM) in this group.	Other primary	33 patients aged between 10-20 years with constipation refractory to conservative treatment according to the Rome III were included.	U	Netherlands	Hospital	Sacral Neuromodulation (SNM)	Primary outcome: frequency of defecation for 21 days as reported in a patient diary.
Van Der Wilt (2016) (van der Wilt, van Wunnik et al. 2016)	To evaluate whether the short-term effects of sacral neuromodulation (SNM) in children and adolescents with constipation are sustained over prolonged period of time.	Other primary study ('prospective cohort study')	30 children aged between 10 and 20 years of age, who were referred for chronic (>1 year) constipation refractory to conservative treatment	U	Netherlands	Hospital	Sacral Neuromodulation (SNM)	Primary outcome: frequency of defecation as recorded in the 3-week bowel diary. Treatment was considered successful when defecation frequency was at least three times per week. Secondary outcomes: change in Wexner constipation score, presence of abdominal pain, pain at defecation, straining, feeling of urge, incomplete evacuation, general comfort, and quality of life.
Van Der Wilt (2017) (van der Wilt, Groenewoud et al. 2017)	To assess the cost-effectiveness of sacral neuromodulation (SNM) compared with conservative treatment in children and adolescents with constipation refractory to conservative management.	Cost-effectiveness	30 children and adolescents aged 10–18 years with constipation refractory to conservative management who met ROME-3 criteria.	U	Netherlands	Hospital	Sacral Neuromodulation (SNM)	QALYs. Symptom severity was assessed by means of a 3-week bowel diary. Outcomes included defaecation frequency, ancillary treatment (laxatives, lavage, surgical procedures such as reoperation), complications and quality of life as measured by EQ-5D youth.
van Wunnik (2011) (van Wunnik, Baeten et al. 2011)	To review methods of neuromodulation used to treat constipation	Narrative review	Children, adolescents and adults. Rome III criteria used to define constipation.	U	More than one	Hospital	Sacral Neuromodulation (SNM)	"Both in clinical practice and in research studies, endpoints for constipation should include stool frequency and consistency, straining, incomplete evacuation, bloating and abdominal pain. The authors suggest a defecation frequency of three or more per week and/or >50% improvement in straining, incomplete evacuation and abdominal pain as minimal set of endpoints. Subjective improvement and satisfaction with therapy reported by the patient should at least be part of the total assessment. Cut-off points such as 50% improvement in symptoms are assessed with bowel habit diaries. Although subjective in nature, these

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								symptoms are part of the Rome III diagnostic criteria and constitute a major part of patient complaints. No studies are available assessing optimal cut-off values in relation to long term treatment results and patient satisfaction" For research purposes additional endpoints may be useful. The Rome foundation provides symptom-based diagnostic criteria for constipation and constipation-predominant irritable bowel syndrome. These criteria allow for defining sub-groups and assessing outcome in clinical trials. Quality of life assessment with for example SF-36 questionnaire provides additional information [35]. Use of additional interventions should be recorded. Diagnostic investigations, i.e. defecography, whole gut transit studies and manometry may show anatomical or physiological changes due to the intervention applied. Constipation severity may be rated using the Cleveland Clinic constipation score. This score, comprising eight factors, ranges from 0 to 30 with 0 indicating no symptoms and 30 indicating severe constipation as described by Wexner et al [36]. The authors suggest using this validated score to evaluate treatment.
Van Wunnik (2012) (van Wunnik, Peeters et al. 2012)	To describe the short-term results of sacral neuromodulation in adolescents with chronic functional constipation refractory to intensive conservative treatment.	Other primary study (retrospective review)	13 adolescents who underwent SNM therapy for constipation and who met the Rome III criteria for functional constipation, not responding to intensive conservative treatment (oral laxatives, enemas or colonic lavage, and behavioral approaches).	U	Netherlands	Hospital	Sacral Neuromodulation (SNM)	History taking, physical examination, whole-gut transit time study, defecography, MRI of the lower pelvic area, anorectal manometry, and rectal sensitivity measurement were performed. Evaluation included completion of a bowel habit diary during 21 consecutive days in which details on defecation frequency were recorded while the patient received optimal conservative therapy. The presence of abdominal pain, straining, and sensation of incomplete evacuation and constipation severity was rated with the use of the Cleveland Clinic constipation score. Other outcomes included use of additional

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								laxatives or enemas and absenteeism from school were documented. Adverse events.
Vriesman (2020) (Vriesman, Wang et al. 2020)	To compare antegrade continence enema (ACE) treatment and sacral nerve stimulation (SNS) in children with intractable functional constipation (FC) and fecal incontinence (FI).	Other primary study (retrospective review and prospective follow-up questionnaire)	42 children between 6 and 18 years with clinically confirmed FC and FI based on the Rome III criteria who were treated with either ACE or SNS	Mixed population	United States	Hospital	CYP treated with either ACE or SNS	We recorded symptoms at baseline, 6 months, 12 months, 24 months, and their most recent visit after starting treatment. We compared improvement in FI, bowel movement (BM) frequency, abdominal pain, laxative use, and complications. Patients were contacted to evaluate perceived benefit using the Glasgow Children's Benefit Inventory.
Wester (2013) (Wester 2013)	A paediatric surgeon's perspective of CFC	Narrative review	Children with functional constipation. Rome III criteria used to define constipation.	U	More than one	Hospital	Multiple interventions. The first step is to provide information and education to the family. Disimpaction - oral polyethylene glycol or rectal enemas. Maintenance Therapy - diet (fibre, balanced diet and fluid), Laxatives (Lactulose, PEG). Surgery - resection, antegrade enemas, botulinum toxin, colostomy.	NR
Wheeler (2019) (Wheeler, Blumenthal et al. 2019)	To describe an application of bedside AR manometry testing in a pediatric Motility Disorders Program, including diagnostic findings and outcomes	Other primary study ('electronic medical record review')	50 children aged 6-18 years	NR	United States	Hospital	Patients were treated with high dose stimulant laxatives or large volume enemas	Feasibility of performing bedside AR manometry
Wood (2016) (Wood 2016)	To review surgical approaches to children with severe constipation, including assessing the qualtiy and levels of evidence and the use of objective measures to determine outcomes.	Narrative review	Children with severe functional constipation. Rome III criteria used to define constipation.	U	More than one	Hospital	Surgical approaches: Anal and pelvic floor procedures: anal dilation, IAS myectomy and botox injection, Antegrade Enema Procedures, Colonic resections and rectal operations, Stoma formation and Sacral nerve stimulation.	NR
Wright (2017) (Wright 2017)	To summarise the evidence for non-invasive and invasive electroneurostimulation (ENS) modalities in bladder bowel dysfunction in children.	Narrative review (summary report)	Children with bladder and bowel dysfunction	Mixed population	More than one	Hospital	Other interventions delivered by highly specialist tertiary care services including: Non-Invasive Electroneurostimulation (ENS): Transcutaneous Electrical Nerve Stimulation (TENS), Functional Electrical Nerve Stimulation (FES) and Invasive END Techniques:Intravesical Electrical Stimulation (IVES), Percutaneous tibial	NR

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							nervie stimulation (PTNS) and Sacral Nerve Stimulation (SNM)	
Youssef (2002) (Youssef, Barksdale Jr et al. 2002)	To assess the benefit of antegrade enemas in children with severe constipation who were referred to a tertiary care center.	Other primary study ('electronic medical record review')	12 children (aged 8.7 ± 4.4 years) who had undergone cecostomy placement for administration of antegrade enemas and who had no evidence of neurologic handicap. These children had been referred to a tertiary motility center for further evaluation of intractable constipation.	No	United States	Hospital	Antegrade enemas through cecostomy catheter	Number of weekly bowel movements, number of weekly soiling episodes, number of medications used for constipation, weekly episodes of abdominal pain, number of missed school days each month, and numberof physician office visits each year because of constipation. Primary caretakers also rated their children's overall health and emotional state
Yuan (2016) (Yuan, Li et al. 2016)	To appraise the clinical efficacy and safety of Faecal microbiota transplantation (FMT) for the treatment of intestinal diseases (such as inflammatory bowel disease, Clostridium difficile colitis and so on).	SR protocol	Planned to include any patients with any type of intestinal diseases such as inflammatory bowel disease, Clostridium difficile colitis, slow transit constipation, short bowel syndrome and so on.	NR	More than one	Hospital	Faecal microbiota transplantation	Primary outcomes: remission rate of intestinal diseases treated with FMT. Secondary outcomes: comparison of the remission rate between different types of intestinal diseases, routes of instillation, choices of donor, volume of infused fecal suspension given and adjective/preparatory treatments.
Zar-Kessler (2018) (Zar-Kessler, Kuo et al. 2018)	To investigate botox, including response duration, symptom association and effectiveness in relation to sphincter dynamics.	Other primary study ('retrospective')	164 children receiving sphincter botox for severe constipation unresponsive to medication management	NR	United States	Hospital	Botulinum toxin injection	Primary outcome: response defined by a decreased pain with defecation or increase frequency of defecation at least 2 weeks after injection. Response information was based on parental description on a severity scale and/or frequency scale as noted in the physician note

Table 6. Complementary (and/or alternative) interventions

Abbreviations: BM: bowel movements, CFC: chronic functional constipation; FI: faecal incontinence; N: no; NA: not applicable; NR: not reported; RCT: randomised controlled trial; TCM: traditional Chinese medicine; U: unclear; Y: yes

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
Alcantara (2014) (Alcantara, Alcantara et al. 2014)	An integrative review of studies of chiropractic care in children with CFC	Narrative review	Identified 16 studies (14 case reports, 1 case series and 1 review) with children (0-18 years of age) with CFC who were receiving chiropractic care. 17 children reported across 16 studies.	NR	More than one – international evidence	U	Musculoskeletal manipulations	NR
Allen (2014) (Allen 2014)	Provides a summary of massage used to help children with digestive issues including constipation	Narrative review	Children – no other details.	Mixed	More than one – international evidence	U	Massage	NA
Aquino (2017) (Aquino, Perini et al. 2017)	Describes the use of osteopathic manipulative treatment in child with CFC	Other primary study (case study)	Single case study of 10-year-old male with Pitt-Hopkins Syndrome and CFC. Constipation for 6+ years Enema and abdominal/perineal massage routinely used for constipation. High fibre diet and/laxative regimens reported as not effective	Yes	Italy	NR	Musculoskeletal manipulations: osteopathic manipulative technique *This study is also included in the effectiveness review*	Constipation diary, Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III Version form and Bristol Stool form
Aslam (2021) (Aslam 2021)	To evaluate the role of genus cassia in the treatment of CFC	SR	Identified two RCTs (132 participants) children aged between 2 – 15 years	NR	More than one – international evidence		Herbal / traditional medicine – Cassia fistula *This study is also included in the effectiveness review*	Defecation <3 / week, incontinence, history of previous treatment, retentive posturing
Babaei (2018) (Babaei 2018)	To assess efficacy of behavioural modification plus herbal medicines based on traditional Persian medicine for treatment of CFC	Other primary study (case series)	Case series (n=6); aged 2-12 years Mean age (SD): 5 (2.7) years All children met 2+ criteria of ROME III and had not responded to conventional treatments for	No	Iran, Islamic Rep.	Department of Traditional Medicine	Herbal / traditional medicine - Traditional Persian Medicine (Senna Cascara, aloe, Rhubarb, Terminalia chebula, citrullus colocynthis, Ficus carica) *This study is also included in the*	Improvement in constipation symptoms

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
			CFC				*effectiveness review*	
Barber (2016) (Barber 2016)	Describe the application of chiropractic manipulative therapy (CMT) abdominal massage, and probiotic in a single case	Primary	31-month-old female patient previously diagnosed with vesiculoureteral reflux and CFC Treated with continuous antibiotic prophylaxis plus laxatives with little effect.	No	United States	Hospital	Musculoskeletal manipulations	Improvement in constipation symptoms
Bishop (2003) (Bishop, McKinnon et al. 2003)	Explored the efficacy of reflexology in CFC	Primary	50 children with CFC and encopresis Aged 3-14 years Existing medications were not changed	NR	United Kingdom	Outpatient clinic	Reflexology	Number BM, incidences of soiling, Parental attitudes
Bromley (2014) (Bromley 2014)	Describes a service development initiative	Other primary study (non-comparative)	28 children (aged 3 months to 19 years) with a known disability and/or learning needs who had a history of chronic constipation (> 8 weeks). Children all treated with a variety of laxative medications	Yes	United Kingdom	Multiple: special schools, community hospital, health centre and home	Massage (abdominal) *This study is also included in the effectiveness review*	Stool diary, study evaluation. Economic data were also collected on medication costs and the cost of implementing the service initiative.
Cai (2018) (Cai, Ma et al. 2018)	To confirm the effect and safety of Xiao'er Biantong (XEBT) granules for treating chronic constipation in children Trial register: ChiCTR-TRC-13003326	RCT	480 children aged 1-14 years diagnosed using ROME IV criteria Children were randomized to receive XEBT or placebo Other laxatives or other treatments were not allowed during the trial.	No	China	Hospital (7 centres across China)	Herbal / traditional medicine - Xiao'er Biantong (XEBT) versus placebo *This study is also included in the effectiveness review*	Primary outcome: frequency of BM; Other: effectual time, score of main symptoms, effect of constipation, disappearance rate of accompanying symptoms, and recurrence rate.
Canbulat Sahiner (2017) (Canbulat Sahiner and Demirgoz Bal 2017)	To determine the effectiveness of reflexology in treating functional constipation in children	RCT	37 Children aged 3–6 years with a diagnosis of CFC by the paediatric surgeon 40 children were randomized to received combination of education of parents (about toilet, diet, motivation training) plus reflexology 10 mins session x5	NR	Turkey	Hospital	Reflexology *This study is also included in the effectiveness review*	Questionnaire, number of BM, stool consistency and information about the child's compliance with the education.

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
			weeks for 4 weeks) or control (information alone)					
Cao (2012) (Cao, Wang et al. 2012)	To assess the efficacy and safety of acupuncture therapy for chronic constipation	SR protocol	Any age with a diagnosis of CFC (based on ROME II or ROME III)	NR	China	NOT REPORTED	Acupuncture	Primary outcomes: global improvement of clinical symptoms and improvement. Several planned second outcomes plus cost-effectiveness
Chase (2011) (Chase 2011)	To establish the efficacy of non-pharmacological, non-surgical and non-behavioural treatments of functional chronic constipation in children. A secondary aim was to identify any of nonpharmacological, non-surgical and non-behavioural treatments of functional chronic constipation, used either alone or in combination with pharmacological, surgical and behavioural interventions.	SR	Children aged 0–18 years, with a diagnosis of functional chronic constipation for longer than eight weeks not related to congenital abnormalities or disease. CFC diagnosed using the Rome III criteria. Identified 6 relevant studies, of which 3 studies (87 participants) were children	U	More than one – international evidence	More than one	More than one intervention: Non-pharmacological, non-surgical and non-behavioural treatments *This study is also included in the effectiveness review*	NR
Cheng (2009) (Cheng, Bian et al. 2009)	to determine the efficacy and safety of CHM (Chinese herbal medicine) for the treatment of FC	SYSTEMATIC REVIEW	Patients of both sexes and of any age or any ethnic group with diagnosed FC according to the Rome criteria (Rome I, II or III)	Not reported	More than one – international evidence	NOT REPORTED	Herbal / traditional medicine	The responder rate of patients with a mean increase of ≥ 1 complete spontaneous bowel movement (CSBM) per week was considered a primary outcome. Secondary - symptoms, examination indices, such as blood nitric oxide (NO) and substance P (SP) levels, total colon transit test (TCTT) and anorectal pressure. QOL, adverse events
Connor, 2014 (Connor, Hunt et al. 2014)	This article describes the introduction of abdominal massage techniques by a community team as part of a total bowel management	OTHER (PLEASE SPECIFY)	People with learning disabilities	Yes	United Kingdom	NOT REPORTED	Massage	positive and negative aspects of abdominal massage and to gain some informal feedback on the experiences of people with learning disabilities and

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
	programme for people with learning disabilities							their carers.
CTRI/2018/02/012194 (2018) (CTRI/2018/02/012194 2018)	To see the effect of naraca churna in constipation among children without any underlying diseases	RCT (on-going)	Target sample: 30 children with CFC aged 5-15 years. Diagnostic criteria for CFC not reported on the clinical trial registry *Trial is currently listed as 'not-recruiting'. Clinical trial register was last updated on 24/11/2021*	No	India	NR	Herbal / traditional medicine. Appears to be a 3-arm RCT which will compare the following: 1. Naraca churna: NIL 2. ntervention2: Naracha churna: Ingredients - Trivrit Mula, Pippali and Khanda Sarkara. Dose- as per age for 7 days 3. Control:Triphala Churna: Ingridents - Haritaki, Vibhitaki and Amalaki.	"There will be significant result of Naraca churna in the management of functional constipationTimepoint: 3,5,7 and 15 days after starting treatment."
CTRI/2018/12/016752 (2018) (CTRI/2018/12/016752 2018)	A Comparitive Clinical Study on role of Haritaki Draksha Avaleha and Aargwadh phalmajja Avaleha in the management OF Malvibandh with speacial reference to Functional Constipation in Children(5-10 YEARS	RCT (on-going)	Children with CFC aged 5-10 years	No additional support needs	India	NOT REPORTED	Herbal / traditional medicine	To study the role of Haritaki-draksha avaleha and aaragwadha phalmajja avaleha in the management of malvibandha. 1)To study the effect of Haritaki-Draksha avaleha 2)To study the effect of Aaragwadha phalmajja avaleha 3)To observe the adverse effect of haritaki-Draksha avaleha and Aaragwadha phal majja avaleha , if any.
CTRI/2019/03/018241 (2019) (CTRI/2019/03/018241 2019)	Comparison of Haritaki pippali avaleha and Aargwadha phalamajja avaleha in the treatment of constipation in the age group of 3 to 6 years.	RCT (on-going)	Children with constipation Inclusion criteria: 1.children fullfilling ROME3 CRITERIA 2.must include 2 or more of following symptoms a.2 or fewer defecations in toilet/week b.atleast 1 epi of fecal incontinence/week c.h/o painful or hard bowel movements d.presence of large fecal mass in rectum e.h/o large diameter stool which may obstruct	UNCLEAR	India	NOT REPORTED	Herbal / traditional medicine	Primary: role of Haritaki pippali avaleha and aargwadha phalamajja avaleha in the management of malavibhandha.Timepoint: 15 days with follow up on 5th,10th and 15th day Secondary: 1 To study the efficay of haritakipippali avaleha 2To study the efficay of aargwadhaphalamajja avaleha 3.to study the adverse effect if anyTimepoint: 15 days

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
			the toilet 3.Abdominal pain 4.Anorexia Exclusion criteria: 1.k/c/o other organic disorder as Hirschsprungs disease 2k/c/o other systemic illness like HIV TB etc 3k/c/o hormonal diseases as hypothyroidism etc 4.k/c/o irritable bowel syndrome					
CTRI/2019/06/019692 (2019) (CTRI/2019/06/019692 2019)	To identify the prevalence and effectiveness of Siddha management in children with CFC	Other primary study (on-going)	Target sample: 100 Children diagnosed based on ROME-III criteria	NR	India	NR	Herbal / traditional medicine	Prevalence Effectiveness
Duymaz (2020) (Duymaz 2020)	To investigate the effects of reflexology on constipation severity, defecation frequency, pain and quality of life in the treatment of children with cerebral palsy (CP) with constipation	RCT	50 children with CP	Additional support needs	Turkey	EDUCATION (SCHOOL / UNI)	Reflexology *This study is also included in the effectiveness review*	Gross Motor Function Classification System, BSS, Visual Analogue Scale (VAS) was asked to mark a suitable point on a horizontal line with an actual length of 10 cm in order to determine the degree of impact of constipation severity and Functional Independence Measure for Children (WeeFIM)
Elbasan (2018) (Elbasan and Bezgin 2018)	This study was planned to investigate the effects of reflexology combined with neurodevelopmental therapy on constipation and motor functions in children with cerebral palsy.	Other primary study (non-randomised)	40 children between the ages of 3 and 15 years with cerebral palsy within levels 3/4/5 according to the Gross Motor Function Classification System (GMFCS) were included in the study. Children with GMFCS levels of 3/4/5, without any open wounds in the reflexology application area of the foot were included in the study. However, children who	Yes	Turkey	HOSPITAL	Reflexology *This study is also included in the effectiveness review*	Medications used by the child and the doses of these medications were recorded. Constipation was evaluated using the Modified Constipation Assessment Scale (MCAS) and motor evaluation was done with the Gross Motor Function Measure (GMFM).

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
			received Botulinum injections within the last six months, who had undergone a surgical intervention in the lower extremities, who received reflexology or any other alternative medicine modality, and who had treatment-resistant epilepsy were excluded					
Erdrich (2020) (Erdrich, Reid et al. 2020) (CRD42018096644)	To systematically review the literature and analyse the methodological quality of all included studies, and to provide an overall level of evidence analysis. CRD42018096644	SR	Participants (age 12 years +) with a diagnosis of constipation. Identified 7 studies for inclusion but no studies in children were included.	NR	More than one – international evidence	NOT REPORTED	Manual therapies were defined as "techniques such as: mobilisation, manipulation, high-velocity low amplitude thrusts, myofascial techniques, balanced ligamentous tension techniques, massage, stretching, passive articulation, soft tissue techniques, and practitioner-resisted movements. In addition to this, studies that employed non-manual approaches often used by manual therapists (such as exercise prescription, muscle strengthening and breathing exercises) in addition to application of a manual technique were included for review."	Not explicit
Field (2019) (Field 2019)	This narrative review on pediatric massage literature from the last decade suggests that massage therapy has positive e↵ects on several pediatric conditions	NARRATIVE REVIEW	Children with gastrointesinal conditions	UNCLEAR	More than one – international evidence	UNCLEAR	Massage	NOT REPORTED
Gardiner (2005)(Gardiner and Kemper 2005)	For GI complaints Which herbs and supplements spell relief?	OTHER (PLEASE SPECIFY)	constipation	NOT REPORTED	More than one – international evidence	Primary care / Community / Patient's home	Herbal / traditional medicine	Treatment of constipation
Gurol (2019) (Gurol, Sener Taplak et al. 2019)	to determine the herbal supplement product(s) frequently used by mothers to cope with some health problems among children.	PRIMARY STUDY	NR	NOT REPORTED	Turkey	Primary care / Community / Patient's home	Herbal / traditional medicine	The answers to the following research questions were sought: 1 For which health problems of their children do mothers use the

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
								herbal supplement products? 2 Which herbal supplement products do mothers use? 3 What is the sources of information of mothers about herbal supplement products? 4 Where herbal supplement products do mothers obtain from?
Huang (2018) (Huang, Zhao et al. 2018) (CRD42018108415)	To determine whether foot reflexology is an effective intervention to treat functional constipation?	SR protocol	Patients with a definite diagnosis of FC. No restrictions were imposed on the age of the participants.	NR	More than one – international evidence	NR	Foot reflexology	primary - Stool number, intensity, bowel movements, symptoms of constipation and cure rates., secondary - Anxiety, quality of life (QOL) and attitude towards reflexology
IRCT20151217025575N1 (IRCT20151217025575N2019)	Effect of Rosa damascena hydroalcoholic extract and polyethylenglychol in treatment of chronic constipation in children	RCT (on-going)	Age > 12 years	NR	Iran, Islamic Rep.	NR	Rosa damascene hydroalcoholic extract vs PEG	Primary outcome: Frequency of defaecation per week
IRCT2017072535304N (2017) (IRCT20170725535304N2017)	Evaluation of the anti-constipation effects of abdominal application of olive oil ointment in children 1-4 years old: A double-blind, randomized clinical trial	ON-GOING (RCT)	Inclusion criteria: The presence of two or more of the NASPGHAN, Rome III criteria for at least one month: Two or fewer defecations in the toilet per week At least one episode of faecal incontinence per week History of retentive posturing or excessive volitional stool retention History of painful or hard bowel movements Presence of a large faecal mass in the rectum History of large diameter stools which may obstruct the toilet.	NR	Iran, Islamic Rep.	NR	Intervention: An ointment containing 85% olive oil is massaged for 5 minutes twice daily on abdominal area for two weeks Placebo: ointment containing liquid paraffin will be is massaged for 5 minutes twice daily on abdominal area for two weeks	Primary outcome: change in stool frequency
IRCT20190614043891N (2019) (IRCT201906	Effect of visceral manipulation on children with chronic functional constipation	ON-GOING (RCT)	Inclusion criteria: All children with Functional constipation aged 5 to 18 years At least 3 months have passed	TYPICAL DEVELOPMENT	Iran, Islamic Rep.	NOT REPORTED	Musculoskeletal manipulations	Primary outcomes = Bristol scale score that measure the consistency and shape of the stool. Number of defecation

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
14043891N 2019)			since they occurred Exclusion criteria: Endocrine and Metabolic disorders (eg, Hypothyroidism, Hypercalcemia, Diabetes mellitus) Neurologic and Psychiatric disorders(Spina bifida, Cerebral palsy, Autism) Hirschsprung'sdisease and Down's syndrome Congenital anorectal malformation					per week. Score of abdominal pain. Score of defecation pain. Secondary outcomes = Dosage of laxative drug.
IRCT2019072 2044310N (2019) (IRCT201907 22044310N 2019)	Comparison of response to Quchi point massage therapy versus standard treatment in children with functional constipation	ON-GOING (RCT)	nclusion criteria: Children Aged more than 4 years with Functional constipation Based on ROME 4 Criteria Exclusion criteria: Unable to re-access children to record therapeutic response Organic Causes of Constipation	NOT REPORTED	Iran, Islamic Rep.	NOT REPORTED	Massage	Primary outcome = Painful stool disposal. Stool consistency. Times of stool disposal. Secondary outcomes = Feelings of incomplete deification. Thick stool disposal.
Lakshmeesh (2019) (CTRI/2019/0 8/020576 2019) CTRI/2019/08 /020576	To Evaluate the Efficacy and Safety of HCLX031706 (Herbal Syrup) for the symptomatic relief of Functional Constipation in Pediatric Population Email from authors confirm trial complete but results yet to be published	ON-GOING (RCT)	clinically diagnosed with Functional Constipation as per ROME III criteria	NOT REPORTED	India	Primary care / Community / Patient's home	Herbal / traditional medicine	primary - stool consistency and frequency. Secondary - Global assessment of efficacy based on the evaluation of severity of functional constipation. Improvement in the associated symptoms like irritability, loss of appetite and abdominal bloating at the end of the study or the early satiety(which disappear following the passage of a large stool
Lee (2013) (Lee and Rickards-Tilley 2013)	Describes the treatment of a 32-month-old male who had suffered from idiopathic chronic constipation for the past 2 years	PRIMARY STUDY	32-month-old male	No additional support needs	United Kingdom	OTHER (STATE)	Acupuncture	Bowel frequency
Madhale (2018) (CTRI/2018/0	EFFECT OF MATRIX RHYTHM THERAPY (MaRhyThe)IN LONG-	RCT (on-going)	56 children aged 4 to 11 years diagnosed with chronic functional constipation using Rome III	NR	India	Multiple settings	Type of dance therapy	1. Constipation Severity Index 2. Patient Assessment of

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
8/015415 2018) CTRI/2018/08 /015415	STANDING CONSTIPATION IN CHILDREN		criteria					Constipation Quality of Life (PAC-QOL) 3. Bristol Stool Scale 4.Seven - day bowel diary (Frequency of bowel movement, stool consistency, defecation time)
Martin-Marcotte (2018) (Martin-Marcotte 2018)	The purpose of this case report is to evaluate the safety and efficacy of the chiropractic adjustment vs the use of laxatives in the treatment of functional constipation	Other primary study (single case study)	21 month female infant with chronic constipation	TYPICAL DEVELOPMENT	Canada	UNCLEAR	Musculoskeletal manipulations *This study is also included in the effectiveness review*	Following the first chiropractic treatment, and with no further laxatives, the bowel movement improved to once every day or second day. There was no adverse reaction to adjustment reported at this point
Mostamand (2019) (Mostamand 2019)	Our goal is to evaluate the effects of abdominal massage on colonic motility in patients receiving colonic manometry testing for various indications.	Other primary study (prospective cohort)	Patients undergoing colonic manometry	UNCLEAR	United States	Hospital	Massage *This study is also included in the effectiveness review*	Three pediatric gastroenterologists skilled in manometry independently reviewed manometric tracings for objectively defined motility patterns including :low amplitude propagating contractions(LAPC,amplitude<50-60mmHg,duration≥10seconds and propagating distance≥ 30 cm), high amplitude propagating contractions (HAPC; amplitude ≥80mmHg,duration≥10seconds and propagating distance≥30 cm) and non-propagative colonic motor activity (segmental contractions) using “yes” or “no” qualifiers... Subjective findings such as cramping, passage of flatus or stool, were also documented by the bedside nurse.

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
Motaharifard (2016) (Motaharifard, Jafari et al. 2016)	to find the most cost- and therapeutically-effective methods to relieve the symptoms of chronic functional constipation in children - ITM Iranian traditional medicine	NARRATIVE REVIEW	pediatric constipation	NOT REPORTED	More than one – international evidence	UNCLEAR	Herbal / traditional medicine	treatment
Nath (2017) (Nath 2017)	examines some common complementary and alternative treatments used in the management of behavioral and gastrointestinal symptoms associated with autism including food selectivity, abdominal pain, nausea, gastroesophageal reflux, constipation, and diarrhea.	PRIMARY STUDY	A 5-year-old boy with autism presented to a pediatric gastroenterology clinic at a large nonprofit teaching hospital for constipation follow-up	ATYPICAL DEVELOPMENT	United States	HOSPITAL	More than one complementary therapy	safety and efficacy of these treatments
NCT03751267 (2018) (NCT03751267 2018)	to investigate the efficacy of pediatric tuina (massage) on the functional constipation of pre-school aged children.	ON-GOING (RCT)	Suffered from functional constipation (base on Rome IV criteria) d. Currently receiving rehabilitation service in the pediatric service unit run by Yan Chai Hospital Social Service Department (e.g. Early Education and Training Centre (EETC), Special Child Care Centre (SCCC), On site Pre-school Rehabilitation Service team.)	NOT REPORTED	Hong Kong SAR, China	HOSPITAL	Massage	Primary = Defecation frequency per week, Defecation frequency per week, Fecal incontinence frequency per week , Overall treatment success after 4 weeks of treatment (Treatment success was defined as bowel movements ≥ 3 times per week and fecal incontinence ≤ once per 2 weeks). Secondary = Frequency of abdominal pain and painful defecation, Abdominal pain and painful defecation, The children's subjective level of pain: pictorial scale, The children's subjective level of pain during bowel movement in pictorial scale, Score of child behavior

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
								questionnaire, Score of care-giver's perceived stress level
Nimrouzi (2014) (Nimrouzi, Sadeghpour et al. 2014)	To somewhat help the anxious. "to find a definition for constipation in traditional Persian medicine as well as in conventional medicine" academics to achieve proper findings in the field of gastroenterology, in pursuit of the traditional Persian medicine advices.							
Nimrouzi (2015) (Nimrouzi, Sadeghpour et al. 2015)		RCT	120 constipation	NOT REPORTED	Iran, Islamic Rep.	Primary care / Community / Patient's home	Herbal / traditional medicine - PEG vs Flixweed (Descurainia sophia) *This study is also included in the effectiveness review*	to find related works concerning ‘‘children constipation’’ and ‘‘laxative’’ herbs.
Orhan (2018) (Orhan, Kaya Kara et al. 2018)	to investigate the effects of CTM and KT on the symptoms of constipation including defecation frequency, the duration of defecation, stool type, the feeling of incomplete evacuation, and pain in children with CP.	RCT	45 children with chronic constipation and CP. Children were primarily recruited from rehabilitation centers. free for laxative medications and enemas for at least 4 weeks before the study,	ATYPICAL DEVELOPMENT	Turkey	HOSPITAL	Musculoskeletal manipulations - Connective tissue manipulation and kinesiotaping *This study is also included in the effectiveness review*	Primary outcome = Defecation frequency was chosen as the primary outcome measure. Secondary outcomes - the duration of defecation (in minutes), feeling of incomplete evacuation, and changes in food and liquid consumption, straining during defecation, painful defecation, and withholding behavior, Bristol Stool Form Scale (stool consistency), constipation severity, QOL, improvement of overall perception of constipation, Compliance with lifestyle advice
Paknejad (2019) (Paknejad, Motaharifard	to evaluate the efficacy and safety of a variety of complementary and alternative medicine	SYSTEMATIC REVIEW	CFC	NOT REPORTED	More than one – international evidence	NOT REPORTED	More than one complementary therapy	does not specifically state but mentions in the aims about efficacy and safety

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
et al. 2019)	subtypes in childhood constipation.							
Parnell Prevost (2019) (Parnell Prevost 2019)	to evaluate the use of manual therapy for clinical conditions in the pediatric population, assess the methodological quality of the studies found, and synthesize findings based on health condition. We also assessed the reporting and incidence of adverse events within the included studies. Additionally, we compared conclusions to Clar et al.'s UK Update manuscript [	RCT	children under the age of 18 who were treated with manual therapy of any type from any health care professional for any condition.	UNCLEAR	United States	MORE THAN ONE CATEGORY	Manual therapy	either: "improvement" (manual therapy appeared to be effective in the intervention group), "no improvement" (manual therapy did not appear to be effective in the intervention group), or "no difference" (results appeared to be the same in the intervention group as compared to a different intervention, sham intervention or control group).
Qiao 2021(Qiao, Wang et al. 2021) (NCT03186079)	To explore the clinical efficacy and safety of Chinese herbal medicine Xiaojidaozhi Decoction in the treatment of childhood constipation.	RCT	200 Clinical diagnosis of childhood constipation Criteria of constipation meets the Rome IV criteria(H3a) Must be able to swallow capsules	NR	China	Primary care / Community / Patient's home	Chinese herbal medicine (XiaojiDaozhi Decoction) vs placebo *This study is also included in the effectiveness review*	Primary = Percentage of overall efficacy, Change of constipation score. Secondary = Incidence of Treatment-Emergent Adverse Events
Radha (2020) (CTRI/2020/01/022916 2020) CTRI/2020/01/022916	Clinical evaluation of the effect of aynkaaya chooranam for the treatment of kattu mantham	ON-GOING (RCT)	Children with Abdominal pain Abdominal distension Constipation Oliguria Anorexia Low grade fever Consumption of less milk, food, and feeling of fullness of stomach Tirednes Exclusion: Anal fissure Anal stricture Intestinal parasitosis Intestinal obstruction Rectal bleeding Intussuseption Hyperpaeristalsis condition	NOT REPORTED	India	Unclear	Herbal / traditional medicine	Primary: Peristaltic movements Number of defecation per day. Secondary: bowel movement that are hard dry and difficult to pass stool
Sahana (2017) (CTRI/2017/03/008095 2017)	Open labeled single arm non-randomized prospective clinical trial to study the effect of Haritaki Khanda	ON-GOING (non-RCT)	Children with Vibandha (constipation) Inclusion:	UNCLEAR	India	HOSPITAL	Herbal / traditional medicine	The primary outcome measures will be relief from constipation and improvements in the

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
CTRI/2017/03/008095	given at a dose of 6grams bid with warm milk for 14days in children with Vibandha (constipation		1 Children either of both genders between the age group of 03 to 06 years. 2 Children fulfilling the diagnostic criteria of constipation. 3 Parents willing to give assent for the Research study Exclusion: 1 Children having constipation secondary to any of other disorder like hypothyroidism, hirschprung's disease and structural anamolies of anal canal will be excluded					diagnostic tool ROME III criteria. Secondary outcome: Improvement in overall health and nutrition Improvement in digestion
Sathya (2017) (CTRI/2017/03/008145 2017) CTRI/2017/03/008145	In balavagadam and gunapadam mooligai vaguppu there is a sastric siddha formulation Ingi Ennai for kattumantham The drug is more cost effective and also efficacy is not yet scientifically validated ,so i selected the medicine Ingi Ennai as a trial drug for the treatment of kattumantham	ON-GOING (RCT)	Children with constipation indigestion stomach pain fever cough yawning Exclusion Criteria: High temperature >102F Intolerable stomach pain.	NOT REPORTED	India	Unclear	Herbal / traditional medicine	Primary: clinical efficacy of the trial drug assessed by modified vesikari scoring system
Shahamat (2016) (Shahamat, Daneshfard et al. 2016)	This study was designed to evaluate the efficacy of dry cupping therapy of the abdominal wall in children with functional constipation.	RCT	118 children diagnosed with functional constipation. The children with diagnosis of functional constipationbased onRome III criteria(Inalooet al.,2014),for at least 3monthsbefore diagnosis andagebetween 4-18 years oldwere considered for inclusioninthe study. Childre nhavingtheRome III criteriafor Inflammatorybowel disease or organic causes of defecation disorders such as Hirschsprung's disease, spina bifida occulta, hypothyroidism, cystic fibrosis,	UNCLEAR	Iran, Islamic Rep.	MORE THAN ONE CATEGORY	Other complementary therapy Dry-cupping therapy vs laxative *This study is also included in the effectiveness review*	The primary outcome was number of patients who had responded to the treatment. Response to the treatment was defined as improvement of constipation for at least three bowel movements, soft stool and convenient defecation, no soiling and bloody stool per week as well as not fulfilling the Rome III criteria for constipation after the 2nd,4 th,8 thand 12thweeks of intervention. Secondary outcomes were frequencyof defecation, presence of fecal soiling

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
			neurologic abnormalities, intestinalpseudo-obstruction,anddiabetesmellitusw ereexcludedfromthestudy.					(encopresis), hard stool consistency, retention posturing and abdominal pain,atthementionedtimeperi ods
Sinclair (2011) (Sinclair 2011)	This article reviews scientific evidence from 1999 to the present, regarding abdominal massage as an intervention for chronic constipation.	NARRATIVE REVIEW	Children with chronic constipation.	NOT REPORTED	More than one – internationa l evidence	NOT REPORT ED	Manual therapy	NOT REPORTED
Soo (2018) (Lee, Kim et al. 2018)	The objective of this review will be to assess the clinical evidence for or against massage as a management for symptoms of constipation	ON-GOING (SR PROTOCOL)	People with constipation symptoms based on the Rome II and III criteria regardless of age and sex	NOT REPORTED	More than one – internationa l evidence	Unclear	Massage	Main outcomes: 1. Stool frequency and colonic transit time. 2. Patient Assessment of Constipation-Symptoms (PAC-SYM) Additional outcomes: 1. Patient Assessment of Constipation-Quality of Life (PAC-QOL). 2. Adverse events (Aes
Tavassoli 2021(Tavassol i, Eftekhari et al. 2021) IRCT2018030 5038968N1		RCT	120				PEG vs Viola flower syrup *This study is also included in the effectiveness review*	
Vakili (2018) (Vakili 2018)	This review was conducted to report the medicinal plants effective for constipation	NARRATIVE REVIEW	Children with constipation	UNCLEAR	Iran, Islamic Rep.	NOT REPORT ED	Herbal medicine	NOT REPORTED
Wang (2019) (Wang, Zhang et al. 2019)	To provide evidence of whether Tuina is an effective and safe intervention for FC.	ON-GOING (SR PROTOCOL)	Patients who were diagnosed as FC according to ROME II, III, or IV criteria will be included, without limits on gender, age, race, nationality, and medical units	NOT REPORTED	More than one – internationa l evidence	NOT REPORT ED	Massage	Primary - defecation frequency and stool consistency. Secondary - treatment success rates, quality of life, proportion of patients using laxatives, and adverse effects.
Woodward (2009)	to attempt to answer the question:Does reflexology	ON-GOING (SR	chronic idiopathic constipation	NOT REPORTED	More than one –	MORE THAN	Reflexology	primary - global or clinical improvement

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
(Woodward, Norton et al. 2009)	decrease physical or psychologicalmorbidity and symptomdistress and improve quality of life in patients with a diagnosis of chronic idiopathic (functional) constipation? The primary objective is to assess the efficacy and safety of reflexology for the treatment of chronic idiopathic constipation	PROTOCOL)			internationa l evidence	ONE CATEG ORY		as defined by the included studies (e.g. clinical symptoms frequency of defecation, straining, lumpy or hard stools, sensation of incomplete evacuation, sensation of anorectal blockage,manual manoeuvres to facilitate defecation, pain, and bloating). Secondary - anxiety and depression; - quality of life; - need for rescue medication such as laxatives or rectal evacuants; - transit time measurement (radio-opaque markers), functional recto-anal evaluation (proctoscopy, ano-rectal manometry, defecography) or electromyography; - cost effectiveness; and - any adverse events.
Yue (2019) (Yue and Sun 2019) CRD42019142719	Can aromatherapy benefit functional constipation patients?	ON-GOING (SR PROTOCOL)	Patients with a definite diagnosis of FC. No restrictions were imposed on the age of the participants.	Not reported	More than one – internationa l evidence	NOT REPORT ED	Other complementary therapy	Stool number, intensity, bowel movements, symptoms of constipation and cure rates
Zadpe (2020) (Zadpe, Rathi et al. 2020)	Study on the effectiveness of Shunthyadi Syrup in Children with Vibandha (Constipation)	Other primary study (non-comparative)	30 patients of constipation with complaints of abdominal pain (abdominal pain), Kshudhamandya (lack of appetite), hard stool, difficulty in evacuation , flatuence.	NOT REPORTED	India	Primary care / Commun ity / Patient's home	Herbal / traditional medicine - Shunthiyadi Syrup (ginger, dried fruit of the Haritaki tree, long pepper plant) *This study is also included in the effectiveness review*	Primary - Udarshool(abdominal pain), Kshudhamandya(lack of appetite), Frequency of defecation, Defecation, Flatuence. Secondary - No reoccurence
Zhong (2015) (Zhong, Bian et al. 2015)	Review question Whether integrative medicine (IM), mainly including Chinese medicine	ON-GOING (SR PROTOCOL)	Patients of both sexes and of any age or any ethnic group with diagnosed FC according to the Rome criteria	NOT REPORTED	More than one – internationa l evidence	NOT REPORT ED	Herbal / traditional medicine	primary - The responder rate of patients with a mean increase of >= 1 complete spontaneous bowel

First Author (year)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Country	Setting	Type of intervention	Main outcomes
CRD42015016260	and conventional medicine has better effectiveness and safety than conventional medicine or Chinese medicine alone for constipation patients							movement (CSBM) per week. Secondary - the overall effectiveness assessment according to the references of Criteria of Diagnosis and Therapeutic Effect of Diseases and Syndromes in Traditional Chinese Medicine, Guidelines for Clinical Research on New Chinese Herbal Medication, Guidelines for Clinical Research on New Chinese Herbal Medication (Draft) or criteria made by the authors with details and comparable definitions.

Table 7. Psychosocial (including behavioural) interventions

Author (year) (ref)	Aim	Study design code	Participant characteristics	Additional support needs?	Country	Setting	Type of intervention	Main outcomes
Berg (1983) (Berg, Forsythe et al. 1983)	To see whether behaviour therapy alone is better than behaviour therapy plus a laxative for the treatment of severe and persistent faecal soiling.	RCT	44 children with soiling as a main complaint	No	United Kingdom	Hospital (outpatient)	More than one psychosocial intervention: combination of psychotherapy, incentives, positive reinforcement) Randomised to three arms: A. Behavioural (toilet training, rewards, counselling) plus Senokot B. Behavioural (toilet training, rewards, counselling) plus Placebo C. Behavioural (toilet training, rewards, counselling) alone	Improvement in faecal soiling
Brazzelli (2011) (Brazzelli 2011)	To conduct a SR of RCTs on the effects of behavioural (including biofeedback training) and cognitive therapies with or without other treatments for the management of children defaecation disorders.	SR	Children (as defined by trials' authors) with a history of FI (with and without constipation). Review identified "19 trials assessing children with functional faecal incontinence, fourteen trials studied children with a history of constipation and/or faecal impaction, four trials children with "primary and secondary encopresis" and one trial children with "faecal soiling with or without constipation".	NR	More than one – international evidence	More than one	More than one psychosocial intervention: combination of behavioural and cognitive interventions)	"1. Children's symptoms: • number of children cured or improved • number of voluntary bowel movements per week • number of soiling episodes per week • number of self-initiated trips to the toilet • number of parent-initiated trips to the toilet • number of self-toileting episodes per week • rate of improvement in incontinence status (by means of continence scales)• self-reported defaecation pain• parent-rated defaecation pain• adjunctive use of medication such as laxatives, suppositories, and enemas. 2. Anorectal physiology: resting anal pressure maximum squeeze pressure • sensory threshold • rectal inhibitory reflex • defaecation dynamics • saline retention test 3. Health status measures: • psychological measures (e.g. Child Behavior Checklist, Achenbach 1987) 4. Health economics • resource implications resources required to provide the intervention resource consequences of long-term care • costs of intervention costs of resources cost falling on health services cost falling on patients, families or

Author (year) (ref)	Aim	Study design code	Participant characteristics	Additional support needs?	Country	Setting	Type of intervention	Main outcomes
								carers • cost-effectiveness of interventions cost per episode of soiling avoided cost per unit of health gain/preference (e.g., cost per QALY, Weinstein 1977) 5. Other outcomes: • outcome measures quoted in individual trials and judged to be important by the reviewers."
Call (2017) (Call 2017)	To investigate whether a combined behavioural and medical regimen could improve encopresis in three participants with developmental disabilities.	Other primary study	Three children diagnosed with developmental disabilities (2 cases of ASD and one with developmental delay and expressive language disorder) All of the children had a history of encopresis	Yes	United States	Hospital	More than one psychosocial intervention: combination of behavioural therapy, toilet training plus provision of individual bathroom with all necessary supplies/equipment available	Continent and incontinent BM served as the primary dependent variables for this study. Medication use including number of doses and type of medication. Number of times participants sat on the toilet and the duration of each sitting.
Coulter (2001) (Coulter, Hardy et al. 2001)	To evaluate the efficacy of mind-body therapies for the treatment of GI disorders	Narrative review	Children and adults with GI problems including irritable bowel syndrome, FI or encopresis, CFC, nausea or vomiting, ulcers, ulcerative colitis, AP and GI distress. Identified evidence from 53 RCTs and controlled studies	NR	More than one – international evidence	More than one	More than one psychosocial intervention: "mind-body therapies" i.e. biofeedback, relaxation therapy, behavioural therapy, cognitive therapy, guided imagery, hypnosis, placebo as therapy and multimodal (combination) therapies	Physical and psychological test outcomes.
Freeman (2014) (Freeman, Riley et al. 2014)	To synthesise the effects of behavioural interventions in children with FI and CFC	SR	Children aged 4–18 years with FI and CFC. Identified 10 relevant studies (562 participants)	NR	More than one – international evidence	More than one (8 studies were in “ambulatory practices” and 2 studies were online)	More than one psychosocial intervention: behavioural interventions (single or combined) *This study is included in the effectiveness review*	Outcomes included: number of children who had an 80% increase in accident- free days; number of children with ≤1 soiling accident per month; number of children with ≥50% increase in BM in the toilet per week; number of children defecating ≥3 times per week; number of children who met 'Author-Defined Success'; frequency of soiling accidents and

Author (year) (ref)	Aim	Study design code	Participant characteristics	Additional support needs?	Country	Setting	Type of intervention	Main outcomes
								frequency of BM in the toilet.
McGrath (2000) (McGrath, Mellon et al. 2000)	To review the empirical research examining behavioural and medical treatments for constipation and FI	Narrative review	Children with constipation	NR	More than one – international evidence	More than one	More than one intervention	NA
NCT03197922 (NCT03197922 2022)	To evaluate MIE (multidisciplinary intervention for encopresis) compared to TAU (treatment as usual) and determine the optimal treatment length	RCT (on-going)	Planned recruitment: 138 children diagnosed with ASD aged between 5 -12 years *Currently recruiting and estimated completion date is July 2022*	Yes	United States	Outpatient clinic	More than one psychosocial intervention: multidisciplinary intervention includes behaviour (positive reinforces) and toilet training plus suppositories if required. Intervention will be delivered over two weeks. *NB. There were plans to deliver the intervention to a sample for 7 days, but this was discontinued in Oct 2019.*	Number of children achieving continence, Clinical Global Impression Scale, Change in Parenting Stress Index Short Form Score, Change in Caregiver Strain Questionnaire
Person (2019) (Person 2019)	To discuss current knowledge of brain-gut therapies in paediatric functional gastrointestinal disorders (FGID) and inflammatory bowel disease	Narrative review	Children with paediatric functional gastrointestinal disorders and inflammatory bowel disease	NR	More than one – international evidence	NR	More than one psychosocial intervention: brain-gut therapies: Cognitive behavioural therapy, hypnotherapy, mindfulness-based therapy, and exposure-based therapy	NR
Santos Calmon (2016) (Santos Calmon 2016)	To gather and present scientific evidence on the use of diaphragmatic breathing exercise as a therapeutic strategy in childhood diseases	SR	Children with diseases	NR	More than one – international evidence	NR	More than one psychosocial intervention: diaphragmatic breathing exercise	NR
Santucci (2020) (Santucci 2020)	To determine the effect of the visit to a paediatric gastroenterologist on self-efficacy for defecation.	Other primary study	130 children aged 8 – 16 years with CFC as defined by ROME III criteria	Mixed	United States	Hospital	More than one psychosocial intervention: self-efficacy (i.e., belief that an individual can succeed at a goal, and short-term treatment outcome following a clinical visit *This study is included in the effectiveness review*	Primary outcome: at least three BMs into the toilet and no episodes of FI. Other outcomes: stool consistency, Self-Efficacy for Functional Constipation Questionnaire. School Absenteeism reported at baseline.
Santucci (2018) (Santucci 2018)	To assess the effectiveness of guided mastery	RCT (pilot)	21 children aged 7-16 years who met the ROME IV criteria for CFC	NR	United States	NR	More than one psychosocial intervention: Guided therapy plus psychotherapy Randomized to receive either guided mastery, a therapeutic method of raising a person's perception to accomplish a task or information on dietary changes	Primary outcome: included symptoms on the Rome IV criteria checklist
Shepard (2017)	To identify and classify	Narrative review	Paediatric	U	More than	U	More than one psychosocial intervention:	NR

Author (year) (ref)	Aim	Study design code	Participant characteristics	Additional support needs?	Country	Setting	Type of intervention	Main outcomes
(Shepard 2017)	interventions used to treat paediatric elimination disorders, according to the guidelines set forth by the Task Force on the Promotion and Dissemination of Psychological Procedures		elimination disorders (enuresis and encopresis).		one – international evidence		Biofeedback, toilet training	Authors extracted the key outcomes from each included study.
Silver (1998) (Silver, Williams et al. 1998)	To conduct a retrospective audit of the therapy outcomes of children with soiling and their families	Other primary study (retrospective cohort)	108 children and families based on referrals over a four-year interval	Mixed (details were limited)	United Kingdom	U	More than one psychosocial intervention: externalizing treatment, whole family therapy or other treatments included conventional behavioural treatments *This study is included in the effectiveness review*	Further soiling incidents (and number) since they were last seen and whether treatment was helpful of unhelpful. Parents were also asked from their experience in dealing with their child's soiling what advice they would give to other families
Taitz (1986) (Taitz, Wales et al. 1986)	To test the effectiveness of fairly modest programmes of behaviour therapy or psychotherapy (or both)	Other primary study (survey)	47 children with faecal soiling (with or without constipation). None had previously been treated by psychotherapy or behaviour modification techniques.	No	United Kingdom	Hospital (outpatient)	More than one psychosocial intervention: Incentive based behavioural modification, plus or minus psychotherapy Children were usually seen once a month by a child psychiatrist over 2-12 months. Parents were also seen to discuss their feelings about bowel problems *This study is included in the effectiveness review*	Questionnaire: child cured, improved, or unchanged and asked how often the child defecated; whether and how often soiling occurred; and whether and how often laxatives were needed.
Turner-Bowker (2015) (Turner-Bowker 2015)	To assess the use of a Paediatric Functional Constipation Daily Diary	Other primary study	22 interviews and 36 concept elicitation were conducted with children and parents of children aged 6 months to < 18 years	NR	United States	Primary care / Community / Patient's home	More than one psychosocial intervention: Electronic diary which focuses on clinical symptoms and the impact of CFC	Most important and relevant signs, symptoms, and impacts associated with the CFC
van Dijk (2008) (van Dijk, Bongers et al. 2008)	To assess clinical effectiveness of behavioural therapy with laxatives compared to conventional treatment in treating CFC	RCT	134 children aged 4-18 years with CFC who referred by general practitioners, school doctors, and paediatricians to the outpatient clinic	NR	Netherlands	Hospital	More than one psychosocial intervention: protocolised behaviour therapy included two age-related modules based around five steps: Know, Dare, Can, Will and Do. Conventional treatment was typically laxatives – PEG 3350 or enemas or bisacodyl suppositories. "Praise and small gifts" were also given to encourage children not to withhold stools.	Primary outcome: defecation frequency per week, faecal incontinence frequency per week and successful treatment. Secondary outcome: stool-withholding behaviour and, behaviour problems.
van Dijk (2007) (van Dijk, Benninga et al.	To release a newly protocolized behavioural intervention program for	Narrative review	Children aged 4–18 years with CFC	NR	More than one – international	NR	More than one psychosocial intervention: Psychotherapy, positive reinforcement, comprehensive behaviour	NR

Author (year) (ref)	Aim	Study design code	Participant characteristics	Additional support needs?	Country	Setting	Type of intervention	Main outcomes
2007)	children with CFC				evidence		(psycho)therapy. Detailed description of a protocolized intervention reported in van Dijk (2008) (van Dijk, Bongers et al. 2008)	

Table 8. More than one intervention

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Agarwal (2013)(Agarwal 2013)	To review literature with regard to epidemiology, clinical features, investigation and management of chronic constipation in children.	Narrative review	Children with constipation. Used the NASPGHAN criteria to define CFC.	NR	More than one	More than one	More than one intervention: Counselling, Behavioural therapy, Diet modification, Pharmacological therapy, Disimpaction, Maintenance treatment	NA
Allen (2019) (Allen 2019)	This article discusses functional constipation in children 1 year of age and older.	Narrative review	Children with constipation aged >1 year. Functional constipation is a term used to describe a condition in which patients have hard, infrequent bowel movements that are often difficult or painful to pass	U	More than one	More than one	More than one intervention	NA
Arbelo (2004) (Arbelo, Lorenzo et al. 2004)	To review the topic of constipation in the child, including the definition of constipation, encopresis and fecal incontinence	Narrative review	Children with chronic constipation, with or without encopresis. Defined as the delay or difficulty in defecation, present for 2 or more weeks, with modifications in the frequency, volume, weight, consistency, or difficulty in passing stool.	NR	More than one	More than one	More than one intervention: 1) teaching, 2) disimpaction, 3) preventing stool from accumulating and 4) reconditioning normal bowel habits. non-surgical treatment includes various forms of behavioural modification and psychological methods. Diet, laxatives,	NA
Baskin (2015) (Baskin, Copp et al. 2015)	General overview of constipation	Narrative review	Children with constipation	U	More than one	More than one	More than one intervention: clean out and maintenance, including medication	NA
Bernal (2018) (Bernal 2018)	This review aims to provide an evidence-based guide on the evaluation and management of constipation in children.	Narrative review	Children with constipation. Rome IV Criteria was used.	U	More than one	More than one	More than one intervention: Education, pharmaceutical therapy, disimpaction, maintenance (laxatives), behavioural interventions, dietary interventions, Antegrade Continence Enema Procedure, Botox, Sacral Nerve Stimulation	NA
Brooks (2000) (Brooks, Copen et al. 2000)	To review the literature of treatments for encopresis, functional constipation, and stool-toileting refusal	Narrative review	Children with constipation and /or encopresis; pre-school and school-age children. Several definitions for CFC. No set criteria. 9 relevant studies identified.	NR	More than one	More than one	More than one intervention: medical, behavioural, psychological, and biofeedback	NA
Brown (2013) (Brown 2013)	Not explicit. Provides a general overview of constipation	Narrative review	Children with constipation	U	More than one	More than one	More than one intervention: Behaviour and dietary modification, disimpaction, Maintenance therapy (lactulose, a synthetic disaccharide, or sorbitol, an osmotic laxative, polyethylene glycol added to water (Movicol® or Klean-Prep®). If conventional treatment fails, further options can be considered, including relaxation of the internal	NA

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							sphincter with persistent surgical dilatation, an injection of botulinum toxin or a sphincterotomy, resection of an enlarged localised rectosigmoid distended loop, or an antegrade colonic washout via an appendicostomy (Malone procedure).	
Burgers (2013) (Burgers 2013)	We present a consensus view of members of the International Children's Continence Society (ICCS) together with pediatric gastroenterologists, experts in the field of functional gastrointestinal disorders, on the management of functional constipation in children with lower urinary tract symptoms.	Guidelines/ Consensus Study (Expert Opinion)	Children with lower urinary tract symptoms. CFC defined using Rome III Criteria	U	More than one	More than one	More than one intervention Education, Demystification and Behavior Modifications, disimpaction, maintenance treatment (laxatives), dietary interventions, oral laxatives, enemas, antibiotic therapy, behavioral Therapy and Biofeedback Training, surgery, neuromodulation (sacral, TES)	NA
Campeotto (2019) (Campeotto 2019, Campeotto, Barbaza et al. 2020)	To estimate in France the prevalence of each disorder in infants and to describe the management of such troubles.	Other primary study (cross-sectional)	1722 infants with FGIDs (mainly regurgitation, colic, constipation, and diarrhoea). CFC defined using Rome IV criteria.	U	France	Hospital (outpatients)	Management of FGIDs included changes to milk diet, adapted infant formula or physicians prescribed a specific treatment in 51% to 66% of FGID infants. Probiotics were often prescribed (from 35% in the case of regurgitation up to 64% for diarrhoea).	NR
Ciullo (2015) (Ciullo 2015)	To examine how Italian Paediatricians approach FC and how closely their approaches adhere to the guidelines - in 2014 ESPGHAN and NASPGHAN	Other primary study	147 Paediatricians who treat children diagnosed with CFC	NR	Italy	Hospital	Non-pharmacological intervention.	Adherence
Coffey (2017) (Coffey 2017)	To investigate methods of diagnosis and recommendations for first line treatment in the management of common FGIDs in infants 0–6months and then to further assess the attitudes of healthcare professionals towards the effect that FGIDs have on the quality of the infant's and the wider family's life	Other primary study (cross-sectional)	76 Healthcare professionals (general practitioners (26), public health nurses (29), practice nurses (13) and other (8)) who treat infants 0-6 months old with common functional gastrointestinal disorders (FGIDs). Rome criteria was used.	U	Ireland	More than one	More than one intervention: most prevalent first line treatment for colic, constipation and reflux in both formula fed (FF) and breast fed (BF) infants was parental reassurance. The most common secondary treatment for FF infants was a change in formula while for BF infants it was medicinal treatment	Quality of Life
Coury (2012) (Coury 2012)	A symposium which addressed 4 major areas of concern for children with ASDs: reflux, constipation, diarrhoea, and nutrition.	Narrative review (Symposium with review updates)	Children With Autism Spectrum Disorder and gastrointestinal conditions	Yes	More than one	More than one	More than one intervention	NA

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
Davis (2019) (Davis 2019)	Not explicit. Review of management strategies in CFC	Narrative review	Children with constipation. Rome IV Criteria was used.	NR	More than one	More than one	More than one intervention: addition of sorbitol-containing juices (see below) and dietary fibre to the diet should be followed by close monitoring to ensure that constipation is resolved. Occasional use of glycerine suppositories Treatment of functional constipation requires a comprehensive approach that includes education of parent and child, behaviour interventions, dietary changes, pharmacotherapy and frequent close follow-up to ensure that movements occur at regular intervals with good evacuation.1,5 In toddlers with constipation, toilet training should be postponed as it may not be effective until rectal awareness is restored and defaecation is pain-free. Education and behaviour changes, disimpaction (osmotic/ stimulant laxatives, enemas, suppositories), dietary changes, pharmacological treatment, maintenance therapy (laxatives and behaviour therapy), tapering.	NA
Dos Santos (2017) (Dos Santos 2017)	To provide recommendations for the diagnosis and treatment of BBD in children based on an updated, thorough discussion of relevant studies in the field and experts opinions.	Narrative review	Children with bladder and bowel dysfunction (BBD). Rome III Criteria was used.	U	More than one	More than one	More than one intervention: four phases: 1) education; 2) disimpaction; 3) prevention of re-accumulation of faeces; and 4) followup. Pharmacological, surgical - ACE.	NA
Eicher (2007) (Eicher, Vitello et al. 2007)	Part of a series of article to focus on medical, motor and behavioural influences on feeding and swallowing issues in children	Narrative review	Children with constipation	NR	More than one	More than one	More than one intervention: four components including care providers education, dis-impaction of the retained stool, if needed, maintenance therapy, and for older children behavior modification	NA
ERIC campaigns (2015)(ERIC 2015)	Describes a national campaign to raise awareness of childhood constipation among parents of 2–4-year olds and health and education professionals working with this age group.	Narrative review	Children (up to age 4 years) with constipation	NR	More than one	More than one	National campaign to raise awareness - intervention is website, resources.	NA
Giannetti (2011)(Giann	A narrative summary of the NASPGHAN four-step approach	Narrative review	Children with constipation	NR	More than one	More than one	More than one intervention: primary treatment, disimpaction, maintenance	NA

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
etti 2011)	involving education, disimpaction, prevention of reaccumulation and behavioural therapy to managing CFC						treatment, behavioural treatment, non-pharmacological treatments	
Gibas-Dorna (2014)(Gibas-Dorna 2014)	To describe the most important aspects of diagnostic and therapeutic processes regarding functional constipation in neonates and toddlers	Narrative review	Children with constipation and soiling (encopresis). Rome III Criteria was used.	NR	More than one	More than one	More than one intervention: non-pharmacological and pharmacological	NA
Gould (2011)(Gould 2011)	Not explicit. Presents a narrative summary of NICE guidelines for nocturnal enuresis and constipation in children and young people	Narrative review	Children with constipation and/or nocturnal enuresis	NR	More than one	More than one	More than one intervention: discusses several treatments in general	NA
Han (2018) (Han, Iragorri et al. 2018)	To comprehensively evaluate the cost effectiveness of treatments for CC	SR	Studies eligible for inclusion represented full economic evaluations [i.e. cost-effectiveness analyses (CEAs), cost utility analyses (CUAs), or cost-consequences analysis (CCA)] that evaluated a treatment for CFC. Identified 10 relevant studies - adults only.		More than one	More than one	More than one intervention described	Costs and outcomes of treatments for CC and cost effectiveness methods
Ho (2020)(Ho and How 2020)	Present a short vignette and an overview of management of this case	Narrative review (with CPD learning outcomes)	Children with constipation		More than one	More than one	More than one intervention	NA
Howarth (2016)(Howarth and Sullivan 2016)	To give the reader a clear guide to diagnosis, investigation, pharmacological and non-pharmacological management of CFC	Narrative review	Children with constipation. Rome III Criteria was used.	NR	More than one	More than one	More than one intervention: discusses pharmacological and non-pharmacological treatments	NA
Jang (2019) (Jang, Chung et al. 2019, Jang 2019)	To investigate the awareness and application of ROME IV criteria for functional constipation (FC) in real-world practices and assessed differences between pediatric gastroenterologists (PGs) and general pediatricians.	Other primary study (survey)	239 Paediatricians who treat children diagnosed with CFC. The Rome IV criteria was employed.	NR	Korea, Rep.	More than one	More than one intervention: pharmacologic and non-pharmacologic treatment. - In the age ≥ 1-year group, we included the medications polyethylene glycogen (PEG) 4000, PEG 3350, lactulose, magnesium, lactitol, and probiotics. In the age < 1-year group, we included formula changes, PEG 4000, PEG 3350, lactulose, and probiotics. We asked about diet modification, toilet training, defecation diaries, and multidisciplinary approaches that included	Awareness and application of the definition for pediatric FC, use of various diagnostic methods, management duration and follow-up patterns, rate of relapse, and pharmacologic and non-pharmacologic treatment.

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							dieticians and pediatric psychologists.	
Jurgens (2011)(Jurgens 2011)	To review the literature with respect to assessment and management of CFC	Narrative review	Children with constipation. Identified 33 relevant studies.	NR	More than one	More than one	More than one intervention: discusses several treatments in general	NA
Karami (2013)(Karami 2013)	To present a useful guide to the organization of pediatric constipation and appraise the current suggestion for treatment regimens, to help the clinician in treating a situation that can be distressing and has a significant influence on affected families.	Narrative review	Children with constipation	Mixed population	More than one	More than one	More than one intervention: discusses several treatments in general, laxatives, diet etc	NA
Koppen (2015) (Koppen 2015)	This review focuses on the current approach to management of FC in the pediatric population and provides practical guidance, including a summary of drug treatment options	Narrative review	Children with constipation. Rome III Criteria was used.	NR	More than one	More than one	More than one intervention: Education Toilet training, reward system and defecation diary. Dietary fibre, fluid and physical activity. Behavioural therapy. Biofeedback training. Pharmacological Treatment (disimpaction, maintenance treatment and weaning.) Osmotic laxatives - PEG, lactulose, lactitol, magnesium hydorxide). Stimulant laxatives - Diphenylmethanes, antraquinones. Lubricants - Mineral oil, ducosate. Enemas. Rectal irrigation. Novel therapies - Lubiprostone, linaclotide and prucalopride. Probiotics.	NA
Koppen (2016) (Koppen 2016)	To provide an update on nonpharmacological interventions and other novel diagnostic and therapeutic tools related to childhood constipation	Narrative review	Children with constipation	NR	More than one	More than one	Nonpharmacological interventions	NA
Koppen (2018) (Koppen, Vriesman et al. 2018)	The aim of the study was to assess whether physicians approach children with functional constipation according to the 2014 European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN)/North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) guideline.	Other primary study (survey)	328 Physicians who treat children diagnosed with CFC. The Rome IV criteria was used.	NR	Netherlands	More than one	More than one intervention: based on guidelines	Questions assessed factors related to the works etting, familiarity with the 2014 ESPGHAN/NASPGHAN guideline, and the diagnostic and therapeutic approach toward children with FC. The self-reported frequency with which items from the medical history and physical examination were put into practice was scored ona 5-point Likert scale

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
								(never-rarely-sometimes-oftenalways).
Kuizenga-Wessel (2015) (Kuizenga-Wessel, Benninga et al. 2015)	To systematically assess how definitions and outcome measures are defined in therapeutic randomized controlled trials (RCTs) of infants with CFC	Narrative review	Infants and young children (≤4 years old) with constipation. Rome III Criteria was used.	NR	More than one	More than one	More than one intervention ('any used in therapeutic RCTs')	NA
Kuizenga-Wessel (2016) (Kuizenga-Wessel, Heckert et al. 2016)	To systematically assess how definitions and outcome measures are defined in therapeutic randomized controlled trials (RCTs) of children with CFC	Narrative review	Children(aged 1-18 years) with constipation	NR	More than one	More than one	More than one intervention ('any used in therapeutic RCTs')	NA
Lancioni (2001) (Lancioni, O'Reilly et al. 2001)	To provide a general picture of the research work performed in faecal soiling in people with intellectual disabilities, and to discuss outomes of the studies and treatment packages in relation to characteristics of soiling problems.	Narrative review	Children with Learning disabilities and encopresis. 21 studies identified.	Yes	More than one	More than one	More than one intervention	NA
Levy (2017) (Levy 2017)	This review intends to update what is known about and what is still a challenge in functional constipation (FC) in children regarding epidemiology, pathophysiology, diagnosis, and management.	Narrative review	Children with constipation. Refer to The Paris Consensus on Childhood Constipation Terminology (PACCT) and Rome II Criteria.	NR	More than one	More than one	More than one intervention: normal intake of fibers and fluids, normal physical activity, and an additional pharmacologic treatment for fecal disimpaction (PEG with or without electrolytes) followed by a pharmacologic maintenance therapy.	NA
Lu (2018) (Lu 2018)	To summarise recent advancements in the evaluation and treatment of children with FC and discusses their clinical applications, particularly to children with continued symptoms despite conventional treatment.	Narrative review	Children with constipation. Rome Criteria was used.	NR	More than one	More than one	More than one intervention: Conventional treatment: Education, toilet training, oral medications (osmotic and stimulant laxatives). Novel pharmacologic treatments: osmotic laxatives (PEG), stimulant laxatives or lubricants (lubiprostone, linaclotide, prucalopride). Biofeedback Therapy. Anal spincter bolulinum toxin injection. Surgical treatment - ACE, neurostimulation, colonic resection, stoma formation and bowel diversion.	NA
Madani (2016) (Madani	In this review, we discuss the epidemiology, causes, evaluation, and management of children with	Narrative review	Children with constipation. Rome III Criteria was used.	Mixed population	More than one	More than one	More than one intervention: four-pronged approach: education, disimpaction (PEG, Enema, Glycrine suppositories),	NA

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
2016)	functional constipation.						maintenance therapy (laxatives in adequate doses for requisite duration, dietary supplementation with fiber, and behavioral modifications.2 PEG 3350 is the recommended laxative to be used for maintenance therapy, with lactulose as the preferable alternative and behavioural modification), and long-term follow up. Rescue Therapy (stimulant laxatives - Senna).	
Mahon (2017) (Mahon, Lifschitz et al. 2017)	To estimate the cost of FGIDs and related signs and symptoms in infants to the third party payer and to parents.	SR (also includes a cost-of-illness calculation)	Included infants (aged birth to 24 months) with FGID - with colic, regurgitation and/or functional constipation. CFC diagnosed using the Rome III criteria. Identified 31 studies.	NR	More than one	More than one	More than one intervention: OTC colic remedies and special infant formulas. Laxatives for constipation.	Publicly funded healthcare resource use. Prescription data (use and costs), Primary and community care costs, Hospital care costs.
Meyer (2017) (Meyer 2017)	To provide an overview of management in children with CFC	Narrative review	Children with constipation. The Paris Consensus on Childhood Constipation Terminology (PaCCT) Group has proposed a simplified terminology that clearly defines the criteria for chronic constipation, which also informs the Rome IV criteria for functional constipation and diagnosis.	NR	More than one	More than one	More than one intervention:divided into three stages of therapy, i.e. disimpaction, maintenance therapy - Removal of pain-associated defaecation (laxatives), establish regular bowel movements (osmotic and stimulant laxatives), dietary modification (fluid, fibre, carbohydrates, removal cow milk) and behavioural modification. (normalise and sustain toilet routines, discourage stool withholding and improve understanding of defecation dynamics amongst the children and their caregiver). Caregiver and patient education. Long-term monitoring.	NA
Mugie (2011) (Mugie 2011)	To provide a summary of the current knowledge of the clinical aspects of childhood constipation, including pathogenesis, diagnosis and treatment	Narrative review	Children with constipation		More than one	More than one	More than one intervention	NA
NHS GGC (2019) (NHS GGC 2019)	Present a summary of local Paediatric Guidelines for managing childhood constipation	Guidelines (local)	Children with constipation. CFC defined using Rome III Criteria	U	United Kingdom	More than one	Laxative maintenance and disimpaction regimes	NA
NICE guidelines (2010) (NICE 2010)	The National Institute for Health and Clinical Excellence (‘NICE’ or ‘the Institute’) has commissioned the National Collaborating Centre for Women’s and Children’s	Guidelines	Children aged 0-18 years with idiopathic constipation in primary and secondary care. Included the following (number of studies): Disimpaction (5) Maintenance	U	More than one	More than one	More than one intervention: Disimpaction, Maintenance Therapy, Laxatives (PEG3350, PEG4000+electrolytes, PEG3350+electrolytes, Senna, Lactulose, liquid parafin, mineral oil, magnesium	NA

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	Health to develop a clinical guideline on the diagnosis and treatment of idiopathic childhood constipation for use in the NHS in England and Wales.		Therapy (15) Laxatives (14) Diet and Lifestyle (20), Psychological Interventions (10), Complementary Therapies (1), Antegrade Colonic Enema Procedure (6) and Information and Support (8). CFC defined using Rome III Criteria				oxide), Diet and Lifestyle, Psychological Interventions, Complementary Therapies, Information and Support and Antegrade Colonic Enema Procedure (ACE)	
Nierengarten (2017) (Nierengarten 2017)	An expert review of the latest guidelines	Narrative review	Children with constipation	NR	More than one	More than one	More than one intervention: Discusses laxatives, Suppositories and rectal enemas,	NA
Nurko (2011) (Nurko 2011)	A review of current concepts about faecal incontinence associated with constipation in both pediatric and adult populations.	Narrative review	Children with constipation and/or incontinence	NR	More than one	More than one	More than one intervention: laxatives, behavior modification and other techniques mentioned	NA
Nurko (2014) (Nurko 2014)	Not explicit. Provides a general overview of constipation and management in children and adolescents	Narrative review (with CPD learning outcomes)	Children and adolescents with constipation. CFC defined using Rome III criteria.	NR	United States	More than one	More than one intervention: education and behaviour modification, dietary changes, disimpaction, maintenance therapy with laxatives.	NA
Orhan (2012) (Orhan 2012)	To provide a review of issues including as irritable bowel syndrome, constipation, gastroesophageal reflux, esinophilic esophagitis, celiac disease, inflammatory bowel disease, hepatitis, and pancreatitis.	Narrative review	Children / adolescents with constipation. Rome III Criteria was used.	NR	More than one	More than one	More than one intervention: Discusses laxatives, Suppositories and rectal enemas,	NA
Ostaszkiewicz (2005) (Ostaszkiewicz, Ski et al. 2005)	To evaluate the relationship between constipation or faecal impaction and urinary incontinence (UI) and other lower urinary tract symptoms (LUTS).	SR	Any age in any setting with the dual diagnoses of constipation or faecal impaction (or the simulation of these conditions) and UI and/or other LUTS were included. Identified 6 relevant studies (386 participants); 4/6 were children only (300 participants)	U	More than one	More than one	More than one intervention: Education, PEG 3350, Multi-faceted indivudalised non-invasive intervention, Colonic manometry and urodynamics	Changes in the frequency or severity of UI and/or changes in other LUTS (e.g. bladder emptying, frequency, urgency) and/or changes in QoL
Panaite (2016)(Panaite 2016)	The aim of this audit was to assess the adherence of paediatricians from University Hospital Kerry (UHK) to current international guidelines for idiopathic constipation – in order to avoid unnecessary tests (especially abdominal x-rays) and to offer up to date recommendations of	Other primary study (retrospective chart audit)	76 children admitted for constipation. CFC diagnosed using the Rome III criteria.	NR	Ireland	Hospital	More than one intervention: as per current international guidelines for idiopathic constipation	NR

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	management.							
Paul (2016) (Paul 2016)	To provide a review of CFC in children clinical practice guidelines	Narrative review	Children with constipation. Followed NICE guidelines and the joint ESPGHAN/NASPGHAN guidelines.	NR	More than one	More than one	More than one intervention: discusses all interventions in the guidelines	NA
Poddar (2016) (Poddar 2016)	Conducted a review to examine the epidemiology, clinical features, and management of constipation	Narrative review	Children with constipation. Rome III Criteria was used.	NR	More than one	More than one	More than one intervention: treatment plan, Dietary modification: Toilet training: Laxatives.	NA
Prynn (2011) (Prynn 2011)	This article focuses on current views on definition, epidemiology, pathophysiology, red flag questions, evaluation and management strategies for CFC	Narrative review	Children with constipation Identified one relevant study (preschool aged 2-5 years). Rome III Criteria was used.	NR	More than one	More than one	Macrogol 3350 (polyethylene glycol 3350 plus electrolytes)	NA
Rajindrajith (2011) (Rajindrajith 2011)	Focuses on current views on definition, epidemiology, clinical features, evaluation and management strategies of constipation in children	Narrative review	Children with constipation. Rome III Criteria was used.	U	More than one	More than one	More than one intervention: education and demystification, treatment of fecal impaction, maintenance therapy and close follow-up.	NA
Rajindrajith (2013) (Rajindrajith 2013)	To review the epidemiology, pathophysiology, clinical evaluation and management of functional faecal incontinence in children	Narrative review	Children with FI. Rome III Criteria was used.	NR	More than one	More than one	More than one intervention	NA
Rajindrajith (2016) (Rajindrajith 2016)	To review current data on the epidemiology, predisposing factors, healthcare burden, and effects of constipation on the child and the family	Narrative review	Children with constipation. Rome III Criteria was used.	NR	More than one	More than one	More than one intervention	NA
Rogers (2011) (Rogers 2011)	Provides an overview of the management of functional or idiopathic constipation in childhood while reflecting on the NICE guidelines and discussing the keys to successful treatment.	Narrative review	Children with constipation	NR	More than one	More than one	More than one intervention: Maintenance therapy, Diet/fluid advice, Education and support.	NA
Rogers (2012) (Rogers 2012)	To update nurses on the assessment and management of constipation in children.	Narrative review	Children with constipation	NR	More than one	More than one	More than one intervention: maintenance therapy, Behavioural modification, Diet and fluid, Prebiotics and probiotics.	NA
Rogers (2014) (Rogers 2014)	Addressing continence in children with disabilities	Narrative review	Children with disabilities who have constipation	Yes	More than one	More than one	More than one intervention: enemas, laxatives, fluid intake, and regular toileting.	NA
Romano (2017)(Romano 2017)	To develop uniform guidelines for the management of the gastroenterological and nutritional problems in children with	Guidelines for children with neurologica	Children with disorders that primarily relate to the central nervous system, composed of the brain and spinal cord, affecting an individual's speech,	Yes	More than one	More than one	More than one intervention: ESPGHAN WG recommends in children with NI with constipation to use standard treatments as in typically developing children, unless	NA

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
	neurological impairment.	l impairment	motor skills, vision, memory, muscle actions, and learning abilities. Diagnosed using a careful history, abdominal, perineal, and if necessary rectal digital examination.				there is a risk of aspiration of polyethylene glycol or liquid paraffin	
Rowan-Legg (2011) (Rowan-Legg 2011)	To discuss the management of functional constipation in children	Narrative review	Children with constipation. Rome III Criteria was used.	NR	More than one	More than one	More than one intervention: Education, behavioural modification, daily maintenance stool softeners and dietary modification. Polyethylene glycol.	NA
Scarpato (2017) (Scarpato 2017)	The present study was aimed to assess the diagnostic and therapeutic approaches to children with suspected FGIDs by general pediatricians from different Mediterranean countries.	Other primary study (prospective multicenter survey)	278 Paediatricians who treat Infants (0–6 months and children/adolescents (4–18 years) diagnosed with CFC patients with symptoms suggestive of FGIDs (functional constipation (FC), functional regurgitation (FR), and irritable bowel syndrome (IBS)). Rome criteria was employed.	NR	More than one	More than one	More than one intervention: Dietary intervention - increasing fibre and water intake, reducing milk consumption. Laxatives (most commonly used), fecal softeners, stimulant laxatives. Parental behavioural advice.	NR
Silverman (2013) (Silverman 2013)	To evaluate the prevalence of FI in children with FC defined by Rome III criteria and to compare the current management practices for the two conditions.	Other primary study (Prospective multicenter observational/crosssectional study)	410 children referred to paediatric subspecialty practices across the US. CFC defined using Rome III criteria.	NR	United States	Hospital (outpatients)	More than one intervention: Medications used included polyethylene glycol in 75%, senna in 30%, mineral oil in 8%, milk of magnesia in 8%, bisacodyl in 4%, and lactulose in 4% of the subjects. Up to 40% patients had received rectal treatment with enemas or suppositories.	Age of onset of symptoms, age of medical help sought by parents, history of abdominal pain, urine incontinence, retentive behavior and treatment
Sobhani Shahmirzadi (2014) (Sobhani Shahmirzadi 2014)	Not explicit. Presents a summary of the management approaches to CFC	Narrative review	Children with constipation	NR	More than one	More than one	More than one intervention: Biofeedback, Tegaserod, Pre and Probiotics: Surgery:	NA
Sood (2018) (Sood 2018)	To identify gaps and unmet medical and educational needs in PFC.	SR	Children with functional constipation. Age range not specified. Identified 51 relevant studies.	NR	More than one	More than one	More than one intervention: Pharmacological therapies: Oral laxatives for faecal disimpaction and maintenance therapy (polyethylene glycol (PEG) with or without electrolytes or lactulose) or prucalopride. Dietary fibres, traditional medicine, and probiotics. Non-pharmacological interventions - sacral neuromodulation, enemas. Surgical approaches e.g. antegrade enemas	NR
Tabbers	We conducted a systematic review	SR	Infants and children < 16 years of age	Mixed	More	More	More than one intervention described	Treatment success: includes pain;

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
(2010) (Tabbers, Boluyt et al. 2010)	and aimed to answer the following clinical questions: What are the effects of treatments for children with chronic constipation? What are the effects of treatments for clearing the bowel in children with faecal impaction?		with CFC. Diagnosed using the Rome III criteria Identified a total of 14 relevant studies.	population	than one	than one	aimed at disimpaction of the impacted faeces and restoration of regular bowel habits	faecal incontinence; defecation three times or more a week; soiling fewer than twice a week/frequency of soiling; no laxatives for at least 4 weeks; gut transit time as measured by timing the passage of radio-opaque pellets; difficulty with defecation; worsening constipation. Quality of life. Outcomes for harms of stimulant laxatives: cancer, tolerance, dependence.
Tabbers (2011) (Tabbers 2011)	To discuss two evidence-based guidelines (the Netherlands and Great Britain) have been developed concerning the diagnostic and therapeutic approach for childhood constipation	Narrative review	Children with constipation. Rome III Criteria was used.	NR	More than one	More than one	More than one intervention: (1) education, (2) disimpaction, (3) prevention of re-accumulation of faeces and (4) follow-up	NA
Tabbers (2011) (Tabbers 2011)	To summarise the evidence and assess the reported quality of studies concerning nonpharmacologic treatments for childhood constipation	SR	Children with CFC. Identified 9 relevant studies (640 participants)	NR	More than one	More than one	More than one intervention: fiber, fluid, physical movement, prebiotics, probiotics, behavioral therapy, multidisciplinary treatment, and forms of alternative medicine	Outcome measures were either establishment of normal bowel habits (increase in defecation frequency and/or decrease in fecal incontinence frequency) or treatment success as defined by the authors of the study, adverse effects, and cost).
Tabbers (2014) (Tabbers 2014)	The present guidelines provides recommendations for the dignostic evaluation of children with functional constipation. It is intended as a general guideline and should not be considered a substitute for clinical judgement or used as a protocol applicable to all patients.	Guidelines (Evidence based recommendations from ESPGHAN and NASPGHAN)	Children aged 0-18 years old where functional constipation was diagnosed, treated or its course followed. CFC defined using Rome III Criteria	U	More than one	More than one	More than one intervention: Non-pharmacological treatments: Fibre, fluid, physical activity, prebiotics, probiotics, behavioural therapy, biofeedback. Multidisciplinary treatment (Pediatrician or pediatric gastroenterologist, dietitian, psychologist and physical therapist) Alternative medicine (including acupuncture, homeopathy, mind-body therapy, musculoskeletal manipulatiojns such as osteopathic and chiropractice and yoga). Pharmacologic Treatment: Lactulose, PEG. Disimpaction: PEG, Enemas. Maintenance Therapy: Lactulose, milk of magnesia, mineral oil, PEG. Novel therapies: Lubiprostone, linaclotide, prucaolopride. Surgery: ACE Transcutaneous Nerve Stimulation (TNS)	NA

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
The Royal Childrens Hospital Melbourne (2017) (The Royal Childrens Hospital Melbourne 2017)	A summary of local guidelines for a hospital based in Melbourne, Australia	Guidelines (local)	Children with constipation. CFC defined using Rome IV Criteria	U	Australia	Hospital	More than one intervention: Behaviour Modifications, Dietary modification, Medications, First line treatment options (oral laxatives), Rectal medications, disimpaction (outpatient and inpatient), Mainenance medications.	NA
Thomson (2011) (Thomson, Tighe et al. 2011)	To provide a practical guide for paediatricians and primary care physicians, to outline the current diagnostic criteria and provide an evidence-base for the medical management of idiopathic constipation in children, in the light of recent National Institute of Clinical Excellence (NICE) guidelines on constipation	Narrative review	Children with constipation. Rome III Criteria was used.	U	More than one	More than one	More than one intervention: Education, diet, Disimpaction, Maintenance therapy (laxatives and enemas)	NA
Torres (2015) (Torres 2015)	To analyze the knowledge, approaches, and practices of pediatricians participating in a regional pediatric conference regarding CFC to identify knowledge gaps	Other primary study (cross-sectional regional study based on a semistructured questionnaire)	264 Paediatricians who treat children diagnosed with CFC. CFC defined using Rome III criteria.	NR	Brazil	NA	Prescribed drugs	Type and amount of prescribed drugs
Traslaviña (2015) (Traslavina 2015)	Present the case of a six-year old child with acute urinary retention and constipation	Other primary study (single case study)	6 year old child with acute urinary retention and constipation	No	Brazil	More than one	More than one intervention: Faecal disimpaction: 12% glycerin enema solution. Mineral oil (1 mL/kg/day orally, divided into two doses) plus recommendations for modification of the child's eating habits, aiming mainly at increasing the intake of water and fiber-rich foods.	Episodes of acute urinary retention, evacuating twice daily without difficulty, stool consistency.
Trinkley (2015) (Trinkley	To identify patterns in pharmacologic and nonpharmacologic treatment of	Other primary study	Children aged < 18 years with constipation, irritable bowel syndrome-related constipation (IBS-	NR	United States	Hospital	More than one intervention: pharmacologic and nonpharmacologic treatment of constipation	Primary outcome: proportion of office visits in which each therapy was prescribed. Secondary

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
2015)	constipation and associations between treatment and other variables across age groups	(retrospective cross-sectional study)	C), and opioid-induced constipation					outcomes: assessment of differences in time periods and predictors of prescribing
Van Ginkel (2003) (van Ginkel, Reitsma et al. 2003)	Report the long-term clinical outcome of a large cohort of constipated children followed-up in a single center over the past 10 years. Specific research questions are: (1) Does childhood constipation continue into young adulthood or will the majority of children overcome constipation during adolescence? and (2) Are there clinical characteristics associated with persistent constipation or relapse of symptoms after initial success?	Other primary study (longitudinal cohort study)	418 patients were referred to our tertiary center gastrointestinal motility program by family practitioners, pediatricians, psychiatrists, and school doctors.	U	Netherlands	Hospital	More than one intervention: therapy consisted in all cases of a standard conventional treatment protocol including enemas, oral laxatives (started with lactulose 5 g/10 kg body weight/day, increasing the dose until soft stools were obtained), high-fiber diet, completion of diary cards, and education about constipation. Motivation was enhanced by praise and small gifts. Additional treatment, consisting of 5 biofeedback training sessions or 2 anorectal manometric sessions as part of the treatment regimen of the randomized trial in which they participated. Laxative therapy was continued until successful treatment was achieved and then tapered over a period of 3 months. Subsequently, laxative therapy was discontinued over a 4-week period while monitoring defecation frequency and encopresis episodes	Treatment success: defined as 3 or more bowel movements per week for a period of 4 weeks with less than 2 encopresis episodes per month, while not receiving laxatives in the previous 4 weeks. Defaecation frequency, large stools, consistency of stool, painful defaecation, encopresis frequency (day and night), abdominal pain, and laxative use were based on a 6-week period before the moment of follow-up. In addition to this 6-week period, all relapses between the previous and current follow-up time were documented.
Van Mill (2019) (van Mill 2019)	To discuss the evidence for new treatments in these children, including pre- and probiotics, pelvic physiotherapy, prucalopride, sacral nerve stimulation, and surgery, and to highlight the controversies surrounding them.	Narrative review	Children with constipation		More than one	More than one	More than one intervention: pre-and probiotics, pelvic physiotherapy, prucalopride, sacral nerve stimulation, and surgery,	NA
Vande Velde (2018) (Vande Velde 2018)	To give an overview on bowel problems in cerebral palsy children and to suggest a stepwise treatment approach	Narrative review	Children with CP and constipation / bowel problems	Yes	More than one	More than one	More than one intervention: stepwise approach	NA
Vandenplas (2019) (Vandenplas 2019)	The aim of this paper is to provide a critical and updated review on the management of FGIDs and their impact on the health of the infant and family to health care physicians.	Narrative review	Infants with Functional Gastrointestinal Disorders (FGIDs) . Rome Criteria was used.	U	More than one	More than one	More than one intervention: Nutritional intervention. A formula with a (partial whey) hydrolysate, a(a mixture of) prebiotics, probiotics, synbiotics, and beta-palmitate and/or formula with high magnesium content (but within normal	NA

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
							ranges, palm oil, laxatives (lactulose, polyethylene glycol, paraffin oil).	
Vash-Margita (2019) (Vash-Margita 2019)	The present article will review the current literature regarding the cause, pathophysiology, diagnosis, and treatment of lower urinary tract dysfunction and abnormal bowel habits in young and adolescent girls.	Narrative review	Young and adolescent girls with coexisting urinary symptoms and defecatory disorders, Bladder Bowel Dysfunction (BBD)	U	More than one	More than one	More than one intervention: Education, implementation of diaries, timed toileting, positive reinforcement, foot stool and sitting on the toilet facing a wall. Dietary modifications (fibre and hydration). Biofeedback therapy. Pelvic floor therapy - incorporation of interactive computer games. Neuromodulation therapy. Medications: anticholinergic medications, B3-adrenoceptor agonist mirabegron. Medical treatment 2 phases - evaluation and maintenance therapy - polyethylene glycol, lactulose, milk of magnesia, mineral oil, enemas.	NA
Vriesman (2020) (Vriesman 2020)	Provide an overview of the literature on childhood and adult functional constipation and discuss current and future diagnostic and therapeutic management strategies.	Narrative review	Children with constipation. Rome IV Criteria was used.	Mixed population	More than one	More than one	More than one intervention: Nonpharmacological management is the first step in the treatment of functional constipation. Dietary interventions: fibre and fluid, prebiotics and probiotics, FODMAP diet. Educational and behavioural therapy: counselling, structured toileting programme with reward system. Biofeedback training and physiotherapy. Pharmacological interventions - 2 steps - disimpaction (PEG or enemas) followed by maintenance therapy - laxatives (PEG, mineral oil, milk of magnesium), stimulant laxatives (bisacodyl or senna). New pharmacological interventions: lubiprostone, serotonergic agents (prucalopride). Bile acids. Cholinesterase inhibitors, transanal irrigation. Surgical interventions: Antegrade Continence Enemas (ACE), ostomies and resection. Neuromodulation - SNS, TES, PTNS.	NA
Vuletic (2017)(Vuletic 2017)	Present the latest findings within this area of paediatric gastroenterology - encopresis	Narrative review	Children with constipation and encopresis. Rome III Criteria was used.	NR	More than one	More than one	More than one intervention: Education, toilet training, and positive motivation, laxatives, biofeedback, gifts.	NA
Walia (2013)(Walia	This review summarizes the current evidence and aims to	Narrative review	Children with constipation	U	More than one	More than one	More than one intervention: A four-step approach involving education,	NA

Author (year) (ref)	Aim	Study design code	Participant characteristics	Did participants have additional needs?	Geographical region	Setting	Type of intervention	Main outcomes
2013)	provide practical advice in primary care.						disimpaction, maintenance therapy and behavioural therapy. Dietary education - fibre. Disimpaction - oral/ and or rectal medications (Polyethylene glycol (PEG) 3350, mineral oil, magnesium hydroxide, magnesium citrate, lactulose, sorbitol, senna, and bisacodyl are potential treatments available). Maintenance therapy may be achieved with behavioral modification, daily regimen of laxatives, good hydration, regular exercise and a balanced diet consisting of whole grains, fruits, and vegetables. Behavioural modification (daily toileting regimen with reward) and biofeebdback therapy. Emerging therapies: Selective serotonin uptake agonists (5HT-4), chloride channle activator (lubiprostone), alvimopan, guanylate cyclase activators (linactolide).	
Widodo (2018)(Widodo 2018)	To assess the knowledge of general paediatricians throughout Indonesia about the diagnosis and treatment of CFC	Other primary study (comprehensive questionnaires)	100 Paediatricians who treat children diagnosed with CFC	NR	Indonesia	NA	More than one intervention: fibre and fluid, toilet training, massage, pharmacalogical treatments, rectal pharmacological treatments	NA
Windell (2020)(Windell 2020)	Describes the stigma surrounding constipation and impact on management	Narrative review	Children with constipation	U	More than one	More than one	More than one intervention: fibre and fluids, lifestyle changes, laxatives, toileting routine	NA
Yang (2015)(Yang 2015)	To examine how paediatricians approach functional constipation and how closely their approaches adhere to the guidelines. - NASPGHAN Guidelines	Other primary study (questionnaire-based survey)	1202 Paediatricians who treat children diagnosed with CFC	NR	United States	More than one	More than one intervention: fluid increase, fibre increase, prune fruit juice, behavioural interventions, regular follow-up, reducing constipating foods, maintenance medications, cleanouts and stimulants	NA
Zaffanello (2019)(Zaffanello 2019)	The aim of the present review is to look at the management of constipation in children with CFC or DES in reducing the risk of recurrent UTIs.	Narrative review	20 children with UTIs or dysfunctional elimination syndromes (DES) and constipation. Rome III Criteria was used.	NR	More than one	More than one	More than one intervention: laxatives, enemas, high fibre diet, biofeedback therapy, pelvic floor muscle exercises, sacral neuromodulation, regular voiding, pharmacotherapy etc.	NA

Table 9. Table of excluded studies

Reasons for exclusions	Excluded studies (refs)
Not CFC or wrong population	N=490 records (Gleeson 1990, Fox, Sylvestre et al. 1991, Dalrymple and Ruble 1992, Anonymous 1996, Badiali, Bracci et al. 1997, Glia, Gylin et al. 1997, Emly, Cooper et al. 1998, Ernst 1999, Heymen, Wexner et al. 1999, Ausubel 2000, Chapman, Hewett et al. 2001, Dobbs 2001, Bellomo-Brandao, Collares et al. 2003, Chang, Myung et al. 2003, Granato 2004, Chiarioni, Whitehead et al. 2006, Canadian Agency for Drugs and Technologies in Health (CADTH) 2007, Canadian Agency for Drugs and Technologies in Health (CADTH) 2007, Canadian Agency for 2007, Evans Beti, Clark Wendy et al. 2007, Hale, Smith et al. 2007, Heymen, Scarlett et al. 2007, Canadian Agency for Drugs and Technologies in Health (CADTH) 2008, Canadian Agency for Drugs and Technologies in Health (CADTH) 2008, Chiarelli 2008, Dudding, Lee et al. 2008, Guest, Clegg et al. 2008, Christensen, Andreasen et al. 2009, Enck, van der Voort et al. 2009, Faried, El Nakeeb et al. 2009, Hintringer and Wild 2009, Canadian Agency for Drugs and Technologies in Health (CADTH) 2010, CTRI/2010/091/001106 2010, Faried, El Nakeeb et al. 2010, Holma, Hongisto et al. 2010, Ameh, Lukong et al. 2011, Canadian Agency for Drugs and Technologies in Health (CADTH) 2011, Canadian Agency for Drugs and Technologies in Health (CADTH) 2011, Cheng, Bian et al. 2011, Cook, Yik et al. 2011, Demirogullari, Yilmaz et al. 2011, Flageole, Ouahed et al. 2011, Ford and Suares 2011, Grasshoff-Derr, Backhaus et al. 2011, He and Kang 2011, Herman 2011, Huang, Su et al. 2011, Belghazi, Skalli et al. 2012, Conzo, Allaria et al. 2012, Deshpande, Craig et al. 2012, Dwyer and Reinberg 2012, Ellen, Kevin et al. 2012, Groves 2012, Hart, Lee et al. 2012, Horvath, Dziechciarz et al. 2012, Hsu 2012, Akca and Yilmaz 2013, Altınbas, Aktas et al. 2013, Ambartsumyan and Nurko 2013, Amira, Dusan et al. 2013, Bian, Cheng et al. 2013, Borch, Hagstroem et al. 2013, Borg, Holmdahl et al. 2013, Burgers, Reitsma et al. 2013, Bush, Shah et al. 2013, Bustos Fernández, Prizont et al. 2013, Cavusoglu, Karaman et al. 2013, Chen, Ke et al. 2013, Choi, Shin et al. 2013, Cinca 2013, Corsetti and Tack 2013, Di Lorenzo 2013, Di Lorenzo 2013, Dwyer, Vandersteen et al. 2013, Eirini 2013, Eradi, Hamrick et al. 2013, Filce and Lavergne 2013, Hryhorczuk, Lee et al. 2013, AHRQ 2014, All Wales Medicines Strategy 2014, Anonymous 2014, Ba-Bai-Ke-Re, Wen et al. 2014, Bellini, Gambaccini et al. 2014, Bergmann, Caubet et al. 2014, Bernstein, Hull et al. 2014, Bonnert, Ljotsson et al. 2014, Canadian Agency for Drugs and Technologies in Health (CADTH) 2014, Canadian Agency for Drugs and Technologies in Health (CADTH) 2014, Carr 2014, Clement 2014, Cobb, Dumont et al. 2014, Collins, Hibberts et al. 2014, Corbett, Denny et al. 2014, Dughetti, Jordan-Ely et al. 2014, Engels and Brinckmann 2014, Ford, Quigley et al. 2014, Ghoshal, Srivastava et al. 2014, Gijsbers, Kneepkens et al. 2014, Hui, Min et al. 2014, Hussain and Hyman 2014, Hussain, Whitehead et al. 2014, Accomando, Sciarrabone et al. 2015, Adriaansen, van Asbeck et al. 2015, Asgarshirazi, Shariat et al. 2015, Barnes and Yeh 2015, Canadian Agency for Drugs and Technologies in Health (CADTH) 2015, Canadian Agency for Drugs and Technologies in Health (CADTH) 2015, Chogle and Saps 2015, Choi, Han et al. 2015, de Souza Lima Sant'Anna, Rodrigues et al. 2015, Dynan, Jordan-Ely et al. 2015, Emami Alorizi, Fattahi et al. 2015, Farinelli, Zenzeri et al. 2015, Fukudo, Hongo et al. 2015, Gursen, Kerem Gunel et al. 2015, Heckmann, De La Fuente et al. 2015, Horrocks, Bremner et al. 2015, Huiyi and Kirsten 2015, Adragna, Carlucci et al. 2016, Agarwal, Mehrotra et al. 2016, All Wales Medicines Strategy 2016, Amatya, Elmalik et al. 2016, Arya, Gupta et al. 2016, Bosques, Martin et al. 2016, Caffarelli, di Mauro et al. 2016, Canadian Agency for Drugs and Technologies in Health (CADTH) 2016, Carbon and Kolber 2016, Chumpitazi and Shulman 2016, Dassow and Fox 2016, Dos Santos 2016, Fernandez 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Palsson, Heymen et al. 2004, Medical Advisory Secretariat 2005, Ramkumar and Rao 2005, Migeon-Duballet, Chabin et al. 2006, Quigley 2006, Naftali, Feingelernt et al. 2008, National Horizon Scanning 2008, Quigley 2008, Li Hong, Li Yi et al. 2009, Lin, Fu et al. 2009, Quigley 2009, Rao 2009, ISRCTN26938218 2010, Krassioukov, Eng et al. 2010, Lamas, Lindholm et al. 2010, Listernick 2010, Patel, Schimpf et al. 2010, Picon, Picon et al. 2010, Pourmomeni, Emami et al. 2010, Rao, Valestin et al. 2010, ISRCTN25945941 2011, ISRCTN33023013 2011, Jibaly, LaChance et al. 2011, Kaminski 2011, Kaselas, Philippopoulos et al. 2011, Klosterbuer, Roughead et al. 2011, Koenig and McKenna 2011, Lembo 2011, Leung, Patafio et al. 2011, Liang, Wei et al. 2011, McClurg, Hagen et al. 2011, Mugie and Di Lorenzo 2011, NCT01495806 2011, Ok 2011, Ong, Koeglmeier et al. 2011, Park 2011, Partovi, Ghane Shearbaf et al. 2011, Pollack, Smith et al. 2011, Pourmomeny, Emami et al. 2011, Ramacciati 2011, Rangel, Lawal et al. 2011, IRCT201205219825N1 2012, ISRCTN44563324 2012, Kajbafzadeh, Sharifi-Rad et al. 2012, Li, Zheng et al. 2012, Loftus 2012, McDougall 2012, Meredith, Blair et al. 2012, Muley, Mhapsekar et al. 2012, NCT01570673 2012, NCT01684319 2012, Ortiz, de Miguel et al. 2012, Riezzo, Orlando et al. 2012, Rohr-Kirchgraber 2012, International Braz 2013, Iturrino, Wong et al. 2013, Jazayeri 2013, Jen and Pimpalwar

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Groeneweg 2015, Lecompte, Hery et al. 2015, Lee, Hung et al. 2015, McKenna 2015, NCT02419534 2015, NCT02613078 2015, NICE 2015, Nili 2015, Ozgediz and Poenaru 2015, Pacheco A 2015, Jadresin, Hojsak et al. 2016, Jadresin, Hojsak et al. 2016, Kajbafzadeh 2016, Korterink, Ockeloen et al. 2016, Kovacic, Chelimsky et al. 2016, Kraus, Wong et al. 2016, Lama, Noor et al. 2016, Lehmberg, Hnatow et al. 2016, Li, Fu et al. 2016, Lombardi, Garrisi et al. 2016, Marzheuser, Karsten et al. 2016, Mason, Stephany et al. 2016, NCT02977858 2016, Nelson 2016, NTR6110 2016, Olympia and Brady 2016, Ouelbani 2016, Palmer 2016, Paquette, Varma et al. 2016, Phipps, Wrogemann et al. 2016, Rabah, Elnour et al. 2016, Rao, Kashinath et al. 2016, Rodriguez 2016, Iwanczak and Iwanczak 2017, Iyer, Skokos et al. 2017, Kim 2017, Kolber and Ng 2017, Kovacic, Hainsworth et al. 2017, Lalouni, Ljotsson et al. 2017, Laouni, Scaillon et al. 2017, Leonard, Gaffin et al. 2017, MacDonald 2017, Martin, Newlove-Delgado et al. 2017, Miner 2017, Moroni and Eugenicos 2017, Morris, Michael et al. 2017, Murata 2017, Newlove-Delgado 2017, NICE 2017, Ojetti, Petruzziello et al. 2017, Payne 2017, Poillucci, Degrassi et al. 2017, Reis, Saiovici et al. 2017, Jain 2018, JPRN-UMIN000033113 2018, Kamuda and Mazzola 2018, Karunanayake, Devanarayana et al. 2018, Khan 2018, Kumagai 2018, Lee, Kwon et al. 2018, Liwanag, Ang et al. 2018, Liz and John 2018, Lizarondo 2018, Lizi, Qingyang et al. 2018, McCann and Ponnambalam 2018, Moshiree 2018, NCT02813148 2018, NCT03148002 2018, NCT03764995 2018, Ness 2018, Niemczyk, Wagner et al. 2018, Partty, Rautava et al. 2018, Pennington 2018, Radojicic, Milivojevic et al. 2018, Raedsch 2018, Rao, Valestin et al. 2018, Jain and Karaviti 2019, James 2019, Jie 2019, Kirgizov, Minaev et al. 2019, Luthra 2019, Mallett, Hart et al. 2019, Miner 2019, Mingmin, Lu et al. 2019, Montero 2019, Nicole, Franziska et al. 2019, Ozturk and Kilic 2019, Pengfan, Yue et al. 2019, Phakanant, Paul et al. 2019, Qiang 2019, Rao, Go et al. 2019, Lallemant-Dudek, Cretolle et al. 2020, NCT04247100 2020, Pawliuk, Widger et al. 2020, Reed and Shores 2020, Ren, Zhang et al. 2020) (Weitzenkamp 1998, van Ginkel, Benninga et al. 2000, Salkeld, Bagia et al. 2004, Schneider 2007, Tod, Stringer et al. 2007, van Tilburg 2008, Wang, Tsai et al. 2008, Sansome 2011, Sohn, Chang et al. 2011, Stashinko, Frutchey et al. 2011, Suares and Ford 2011, Tan, Shah et al. 2011, Tan, Merenstein et al. 2011, Vandenplas, Veereman-Wauters et al. 2011, Vesna, Milica et al. 2011, Smith, Taintor et al. 2012, Steiner 2012, Suo, Gu et al. 2012, Thom, Campigotto et al. 2012, Yeung and Di Lorenzo 2012, Shah 2013, Shaoul and Bader 2013, Udani and Bloom 2013, Velde, Biervliet et al. 2013, Velde, Pratte et al. 2013, Videlock, Cheng et al. 2013, von Gontard 2013, Zhang 2013, Santos Jasso and Ruiz 2014, Sathe and Megison 2014, Schmier, Miller et al. 2014, Sewell, Eastwood et al. 2014, Sheu 2014, Shin 2014, Sobhani Shahmirzadi, Fadaei et al. 2014, Sopo, Arena et al. 2014, Sorser, Konanki et al. 2014, Szymanski, Keenan et al. 2014, Taibi and Comelli 2014, Utokpat and Chongsrisawat 2014, Wu, Liu et al. 2014, Xhafa, Shaipi et al. 2014, Xiong, Wang et al. 2014, Zar-Kessler, Kuo et al. 2014, Shin, Acosta et al. 2015, Somi, Bagheri et al. 2015, Spring, Anderson et al. 2015, Sullivan, Hounchell et al. 2015, Thomas, Duelund-Jakobsen et al. 2015, Wilson and O'Donnell 2015, Xue, Li et al. 2015, Shah and Lee 2016, Siggaard, Kamperis et al. 2016, Smith, Neville-Jan et al. 2016, Turan and Aşt 2016, Yektas, Cansiz et al. 2016, Santos-Jasso, Arredondo-Garcia et al. 2017, Tian, Ge et al. 2017, Walsh, Bloch et al. 2017, Yang, Liu et al. 2017, Zar-Kessler, Belkind-Gerson et al. 2017, Zigelmann and Reinberg 2017, Schwartz, Hillman et al. 2018, Shaunak and Kelly 2018, Spina Bifida Association 2018, Van Biervliet, Hauser et al. 2018, Waheed, Malone et al. 2018, Weir, Shu et al. 2018, Yang, Li et al. 2018, Zhang, Xia et al. 2018, Zhang, Bach et al. 2018, Schletker, Edmonds et al. 2019, Shirakura, Nagata et al. 2019, Tan, Wells et al. 2019, Tuppin, Riviere et al. 2019, Wang, Halleran et al. 2019, Wang, Hsieh et al. 2019, Yang, Yibo et al. 2019, Zar-Kessler, Kuo et al. 2019, Zeng 2019, Zheng, Chen et al. 2019, Shahrokhi and Nagalli 2020)
Wrong study design (e.g. commentary, editorial, overview)	N=137 records (Anonymous , Salvioli 1984, Ross 1996, Healthcare Insurance Board/College voor 1997, Ecri 1998, MacIntosh 1998, Bellenir 2000, Canadian Agency for Drugs and Technologies in Health (CADTH) 2001, Feudtner 2001, Medical Technology Unit - Swiss Federal Office of Public 2001, Bayne 2002, Canadian Agency for Drugs and Technologies in Health (CADTH) 2002, Anonymous 2007, Anonymous 2007, Smith 2007, Southern Health Board 2008, Koe, O'Neill et al. 2009, Jang 2010, Ali, Ahmed et al. 2011, Allan, Kolber et al. 2011, Anonymous 2011, Armstrong 2011, Bangels 2011, Chang 2011, Mobberley 2011, Quigley 2011, Rogers 2011, Southwell 2011, Tatsuki 2011, Vitito 2011, Wiwanitkit 2011, Anonymous 2012, Anonymous 2012, Armocida 2012, Camarero-Temiño 2012, Canning 2012, Dudding 2012, Greenhill 2012, Herguner and Herguner 2012, Hospital for Sick Kids 2012, Kratimenos 2012, Macleod 2012, NIHR Horizon Scanning Centre 2012, Shepherd 2012, Swanson 2012, Vivatvakin 2012, Wilby and Dobson 2012, Christophersen and VanScoyoc 2013, Darragh 2013, Elitsur 2013, Friman 2013, Luciano 2013, McBride 2013, Nicholson 2013, Patel and Pashankar 2013, Rajindrajith and Devanarayana 2013, Rogers 2013, Anonymous 2014, Anonymous 2014, Anonymous 2014, Anonymous 2014, Anonymous 2014, Benninga 2014, Dean 2014, Kundu 2014, Petersen 2014, Saps 2014, Southwell, Catto-Smith et al. 2014, Van der Speck 2014, Woolacott 2014, Alberta Health Services 2015, Anonymous 2015, Borch 2015, Cheer 2015, Dickens 2015, Favero 2015, Feagen 2015, Nimrouzi 2015, Ortiz and Stratis 2015, Patel and Pratt 2015, Pipan 2015, Sidaway 2015, Turkoglu, Bilgic et al. 2015, Wallis 2015, Benninga 2016, Chau, Kennedy et al. 2016, Favero 2016, Hayes and Inc 2016, López, Fernández et al. 2016, Lu, Ren et al. 2016, Luiz 2016, MacNeily 2016, Sarmiento, Quintero et al. 2016, van der Steeg 2016, Vandenplas and Salvatore 2016, Anonymous 2017, Born 2017, Canning 2017, Chan and Lee 2017, Chase 2017, Dean 2017, Dipasquale, Catena et al. 2017, Ferrara and Saccomano 2017, Gold 2017, Lam 2017, Nierengarten 2017, Peacock, Chase et al. 2017, Perth Children's Hospital 2017, Rondanelli, Faliva et al. 2017, Shields 2017, van Drimmelen 2017, van Summeren, Dekker et al. 2017, Engels and Brinckmann 2018, Green, Carroll et al. 2018, Health Service Executive 2018, Ofei and Fuchs 2018, Rajindrajith,

	Devanarayana et al. 2018, Shirvani Samani, Lam et al. 2018, Velasco-Benitez 2018, Yik Yee 2018, Anonymous 2019, Bhatnagar 2019, Flemming 2019, Gijsbers 2019, HealthLink BC 2019, Hojsak 2019, Hutson 2019, Jianhong, Junyan et al. 2019, Levin 2019, Mello 2019, Petros 2019, Prentis 2019, Vandenplas and Devreker 2019, Vandenplas and Savino 2019, Velasco-Benitez and Garcia-Perdomo 2019, Slomski 2020, Southwell 2020)
No intervention	N=98 records(Cucchiara, Coremans et al. 1984, de Lorijn, van Wijk et al. 2004, Lee, Choe et al. 2007, Lakshminarayanan, Kufeji et al. 2008, Meyer 2008, Sabirin 2008, Sabirin 2010, Bongers and Benninga 2011, Candy and Paul 2011, Choung, Shah et al. 2011, Indonesian Society of 2011, Kim, Lee et al. 2011, Lamont 2011, Maeda, Matzel et al. 2011, Reich 2011, Yik, Cain et al. 2011, Barrett and Macken 2012, Benninga 2012, Lukens, Monroe et al. 2012, Mohammed and Mekael 2012, Mugie, Bates et al. 2012, Perelló, Vega et al. 2012, Yik, Cook et al. 2012, Belkind-Gerson, Goldstein et al. 2013, Egritas Gurkan, Dalgic et al. 2013, Karami, Miri et al. 2013, Saliakellis, Borrelli et al. 2013, Wolfe-Christensen, Manolis et al. 2013, Ansari, Ansari et al. 2014, Beal, Asad et al. 2014, Bowen and Bowen 2014, Gieselman and Mezoff 2014, Indrio, Di Mauro et al. 2014, Kerur, Kantekure et al. 2014, Kilincaslan, Abali et al. 2014, Zachariassen and Fenger-Gron 2014, Bassily and Bowen 2015, Bigliardi, Ditaranto et al. 2015, Hardy and Goliath 2015, Infante, Rayo et al. 2015, JPRN-UMIN000017786 2015, Kloss and Diescher 2015, Kurowski, Kaur et al. 2015, Long 2015, Racaniello, Terzoni et al. 2015, Aranda-Lopez, Siancas-Pacheco et al. 2016, Bae and Kim 2016, Beinvogl, McSweeney et al. 2016, Benninga 2016, Fernandez, Carrizo et al. 2016, Hernani, Sanchez et al. 2016, Isabelle 2016, May, Marta Roqué i et al. 2016, Van Summeren 2016, Vieira, Negrelle et al. 2016, Barnes, Coleman et al. 2017, Barrie 2017, Beaudry-Bellefeuille, Booth et al. 2017, Beinvogl, Sabharwal et al. 2017, Bouzios, Chouliaras et al. 2017, Cullen, Riches et al. 2017, Foreman, Raju et al. 2017, Infante, Rayo et al. 2017, Ituku and Nduhiu 2017, Koppen, Lu et al. 2017, Macaulay, Spicer et al. 2017, Malamisura, Ciarlitto et al. 2017, Marler, Ferguson et al. 2017, Rodriguez, Sood et al. 2017, Sadjadei, Hosseinmardy et al. 2017, Abhishek, Nabeel et al. 2018, Barnes, Coleman et al. 2018, Chen, Tsao et al. 2018, Cross and Rawlins 2018, CTRI/2018/05/014058 2018, Koppen, Saps et al. 2018, Philichi 2018, Sangalli, Dos Santos Leffa et al. 2018, Sherburne 2018, Timmerman, Trzpis et al. 2018, Van Summeren, Holtman et al. 2018, Yilmaz, Tas et al. 2018, Beaudry-Bellefeuille, Lane et al. 2019, Harter 2019, Heitmann 2019, Kheirandish, Moghtaderi et al. 2019, Lee and Park 2019, MacGeorge, Williams et al. 2019, Medaer, Hoffman et al. 2019, Shaposhnikov 2019, Tappin, Grzeda et al. 2019, Tigapuram, Seetharaman et al. 2019, Vriesman, Rajindrajith et al. 2019, Vriesman, Rajindrajith et al. 2019, Wang, Dong et al. 2019, Woolf and Langhan 2019, Chen and Fujitake 2020, Krasaelap, Kovacic et al. 2020)
Awaiting assessment	N=174 records (Unknown , Sculati 1984, Kolko 1989, Trunnel 1991, Bleijenberg and Kuijpers 1994, Mellon 1996, Currie 2000, Pieczarkowski and Fyderek 2005, Cheng, Li et al. 2007, Demirogullari, Bagbanci et al. 2007, Melo 2007, Potapov, Komarova et al. 2007, Riveros García 2007, Soler 2007, Tsvetkova, Nechaeva et al. 2007, Cueto Rua and Miculan 2008, Privorotskiy and Luppova 2008, Gorelov, Shevtsova et al. 2009, Khavkin 2009, Komarova and Gundobina 2009, Li 2009, Morais and Tahan 2009, Shakhtakhtinskaya 2009, Shariff, Aboumarzouk Omar et al. 2009, Komarova 2010, Korniyenko 2010, Montero 2010, Privorotskiy and Luppova 2010, Raahave 2010, Wang 2010, Bautista Casasnovas, Arguelles Martin et al. 2011, Beradze, Sherozia et al. 2011, Blesa Baviera 2011, Bosman and Kruisinga 2011, Classen 2011, Gomes, Duarte et al. 2011, Gomes 2011, Gomes 2011, Hoehl 2011, Infante Pina, Miserachs Barba et al. 2011, Keller 2011, Khemakhem, Ben Dhaou et al. 2011, Lu, Huang et al. 2011, Nevoral 2011, Reinberg, Meyrat et al. 2011, Remes Troche, Chavez Barrera et al. 2011, Ryzko 2011, Troche, De La Cuesta et al. 2011, Tsymbalova 2011, Tsymbalova 2011, Vandenplas 2011, Wang and Wang 2011, Zurad and Johanson 2011, Barbosa Davim, Elza Oliveira de MendonÃ§a et al. 2012, Burghard, Tabbers et al. 2012, Chouraqui 2012, Du, Yu et al. 2012, Duo Uriarte 2012, Komarova 2012, Kornienko, Komarov et al. 2012, Leão 2012, Li, Jiang et al. 2012, Netsch 2012, Neves and Calais 2012, Polishchuk, Erdes et al. 2012, Smeets and Vandenplas 2012, Wang, Li et al. 2012, Xu, Jia et al. 2012, Zhang, Wang et al. 2012, Alvarez-Calatayud, Perez-Moreno et al. 2013, Anonymous 2013, Atay 2013, Bautista-Casasnovas, Martin-Martinez et al. 2013, Calle Palomino 2013, Dowling and Nightingale 2013, Ejerskov Pedersen, Jonsson et al. 2013, Eremeeva 2013, Faleiros-Castro and de Paula 2013, Kornienko 2013, Nam, Bang et al. 2013, Noviello, Romano et al. 2013, Oshima and Miwa 2013, Pakhomovskaya and Potapov 2013, Peng, Wang et al. 2013, Zakharova, Elezova et al. 2013, Zhang, Chon et al. 2013, 박지 and 손 정 2013, De la Torre Mondragón and Hernández Vez 2014, DeFreest, Smith et al. 2014, Ding, Xu et al. 2014, Dudekula and Bielefeldt 2014, Erdes and Matsukatova 2014, Fagundes-Neto 2014, Hlouskova 2014, Hou 2014, Infante Pina, Segarra Canton et al. 2014, Ivanovic, Siegel et al. 2014, Khavkin, Bel'mer et al. 2014, KilinÇAslan, Abali et al. 2014, Maffei 2014, Malczyk, Jarzumbek et al. 2014, Mitchell 2014, Steger, Hollwarth et al. 2014, Tang, Huang et al. 2014, Tanriverdi and Senel 2014, Torres 2014, Van Geluwe, Stuto et al. 2014, Wang, Yu et al. 2014, Wu, Zhang et al. 2014, You, Yan et al. 2014, Zakharova, Sugyan et al. 2014, Bezgin and Elbasan 2015, Campeotto 2015, Claßen 2015, Colombo, Wassom et al. 2015, Darragh 2015, Gasilina and Belmer 2015, Kholodova, Rubtsova et al. 2015, Liu, Zhou et al. 2015, Mao 2015, Mata Jorge and da Cuna Vicente 2015, Mirzaei 2015, Reis 2015, Torres and Gonzalez 2015, Usta 2015, Wei 2015, Xu 2015, Zakharova, Sugyan et al. 2015, هاشمی, جواهری et al. 2015, Babayan 2016, Bulatov and Kamalova 2016, Campos Navarro 2016, Chouraqui and Lasfargue 2016, Corrales Gonzalez, Torralbo Carmona et al. 2016, Davis 2016, Jprn 2016, Kamalova and Shakirova 2016, Llerena, Varea Calderon et al. 2016, Mouterde 2016, Rotteveel, Dirksen et al. 2016, Tyazheva and Pechkurov 2016, Zwiauer 2016, Benninga, Nurko et al. 2017, Bu, Ruan et al. 2017, CTRI/2017/06/008801 2017, Duymaz and Eker 2017, Garcia, de Luna et al. 2017, Iwanczak and Iwanczak 2017, Meents 2017, Pecl, Jabandziev et al. 2017, Sezer Bayam, Arıkan Ayyıldız et al. 2017, Shen 2017, Vivas Colmenares, Moya Jimenez et al. 2017, Wu 2017, Bastos 2018, Bellu and Condo 2018, Belousova and Hanzii 2018, Bogdanova 2018, Guerrero-Tinoco 2018, Katzemich 2018, Kumar 2018, Maffei 2018, Molina and Marzet 2018, Moola 2018, Nyankovska 2018, Zakharova, Osmanov et al. 2018, Anderson 2019, Basharkhah, Huber-Zeyringer et al. 2019, CTRI/2018/04/013492 2019, Diego 2019, Malhotra, Slade et al. 2019, Marin 2019, Marks and Nightingale 2019, Yangyi 2019)
Duplicated studies or studies that are linked to main study included	N=262 records (Loening-Baucke 1990, Ernst 1995, Brooks, Copen et al. 2000, Capra 2003, ISRCTN28937219 2005, Brazzelli and Griffiths 2006, ISRCTN43733247 2006, Canadian Agency for 2007, ISRCTN25185569 2007, Enck 2009, CenterWatch 2010, Gordon, Blakeley et al. 2010, Bekkali, Liem et al. 2011, Brazzelli, Griffiths

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