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Efficacy and safety of non-pharmacological treatments for paediatric functional constipation: a systematic review and meta-analysis

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ABSTRACT

Background Recent studies have expanded the evidence on novel and existing non-pharmacological treatments for paediatric functional constipation (FC). This study aimed to systematically review the efficacy and safety of non-pharmacological therapies for FC in children.

Methods PubMed, MEDLINE, Embase, PsycINFO, Cochrane Library and trial registries were searched from inception to March 2025. Randomised controlled trials (RCTs), including children (0–18 years) with FC treated with non-pharmacological interventions compared with placebo, no treatment or other interventions, were included. Primary outcomes were treatment success, defecation frequency and withdrawals due to adverse events. Dual data extraction and appraisal was conducted. Certainty was assessed using Grading of Recommendations, Assessment, Development and Evaluations (GRADE).

Results 93 RCTs comprising 7787 children (50.4% female) were included investigating dietary, psycho-educational, physiotherapeutic interventions, various complementary and complementary medicine interventions, and electrical stimulation. A substantial part of the therapies provided evidence that was of very low certainty, meaning no conclusions could be drawn. Abdominal transcutaneous electrical stimulation plus pelvic floor muscle exercises (PFME) may improve treatment success and defecation frequency compared with PFME alone (risk ratio (RR): 1.75 (95%CI 1.25 to 2.44) and mean differences (MD): 1.85 (95%CI 1.28 to 2.43), moderate certainty). Percutaneous tibial nerve stimulation plus PFME leads to more treatment success (RR: 1.73 (95%CI 1.08 to 2.77), low certainty) and greater defecation frequency (MD: 1.82 (95%CI 0.82 to 2.82), moderate certainty). Behavioural therapy plus polyethylene glycol may not improve treatment success (RR: 0.83 (95%CI 0.62 to 1.12), low certainty) and probably reduces defecation frequency (MD: −1.80 (95%CI −2.88 to −0.72), moderate certainty).

Conclusions Imprecise data, poor reporting and substantial heterogeneity led to downgrading in GRADE assessments. Some non-pharmacological treatment options for children with FC show beneficial effects, and these may be considered in the management of children. Future trials should aim to improve methodological rigour.

PROSPERO registration number CRD42023416891.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Both non-pharmacological and pharmacological treatments should be considered in the treatment of paediatric functional constipation.

⇒ An up-to-date systematic review employing rigorous methods, including certainty assessment and all types of non-pharmacological treatments, is currently lacking.

WHAT THIS STUDY ADDS

⇒ There is low certainty evidence that a specific probiotic and synbiotic strain, abdominal transcutaneous electrical stimulation, percutaneous tibial nerve stimulation and pelvic physiotherapy may have beneficial effects. A substantial part of the evidence was of very low certainty, precluding any conclusions.

⇒ This systematic review reveals consistent methodological deficiencies within the included studies, for which recommendations for future research are provided.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This systematic review may serve as a reference for policymakers, guideline developers, healthcare professionals working with children, affected children and their families and caregivers. It may also help guide future research in this area.

INTRODUCTION

Functional constipation (FC) is a common condition in childhood and affects 8.6% of boys and 8.9% of girls worldwide.[1] As defined by the Rome IV criteria, FC is characterised by reduced defecation frequency, faecal incontinence, painful or hard bowel movements, and stool retention, in the absence of organic underlying causes.[2] These symptoms impact healthcare services significantly[3–5] and cause considerable distress to children and their families.[6 7]

According to the European / North American society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN/NASPGHAN) international guideline[8] for the treatment of FC in children, polyethylene glycol (PEG) is the first-line pharmacological treatment in conjunction with education, stool diaries and toilet training. Given the multifactorial pathophysiology of FC and the chronic nature in children, personalised management is essential. Both non-pharmacological and pharmacological treatments should be considered, as pharmacological treatment alone may not be sufficient in every child.[7 9 10] However, most non-pharmacological approaches have shown limited clinical benefit, and their use is primarily supported by expert opinion with a low level of certainty in the 2014 guideline.[8] A meta-analysis by Wegh *et al*,[11] which included 52 randomised controlled trials (RCTs), found some benefit on treatment success and/or defecation frequency with abdominal electrical stimulation, *Cassia Fistula* emulsion and cow's milk exclusion diet. However, a systematic certainty evaluation was not performed, which is critical when translating evidence into practice.

In recent years, a substantial number of new studies have been published on this topic, with new data on novel and existing non-pharmacological approaches. Therefore, we conducted an updated systematic review and meta-analysis on the efficacy and safety of non-pharmacological interventions for the treatment of FC in children, providing a comprehensive evaluation of evidence certainty to guide clinical decision-making.

METHODS

Literature search

Electronic searches were conducted in PubMed, MEDLINE, Embase, PsycINFO and the Cochrane Library from inception to March 2025 (online supplemental eAppendix 2). To identify unpublished and ongoing studies, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform Search Portal and the metaRegister of Controlled Trials were searched. Additionally, the reference lists of included articles were screened. No language restrictions were applied.

This review's protocol was registered in the International Prospective Register of Systematic Reviews in May 2023 (CRD42023416891) and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Publicly accessible data were used, thus ethical approval was not applicable.

Study selection

Inclusion criteria were limited to published or unpublished RCTs that were (1) in children aged 0–18 years old diagnosed with FC, as defined by authors; (2) treated with any non-pharmacological intervention with a minimal follow-up of 2 weeks; and (3) compared with placebo, sham therapy, no intervention or any other pharmacological or non-pharmacological treatment.

Primary outcomes, based on the core outcome set developed for childhood constipation,[12] were treatment success as defined by authors, defecation frequency and withdrawals due to adverse events. Given the heterogeneous definitions of treatment success across studies, harmonising these outcomes was not feasible, as doing so would have required multiple separate meta-analyses for each definition. Secondary outcomes were stool consistency, painful defecation, abdominal pain, faecal incontinence, quality of life, school attendance, tolerability/acceptability/compliance and total and serious adverse events. Abstracts were considered if they met the inclusion criteria. Corresponding authors were contacted when additional information was required.

Search records were imported into a web-based collaboration software (Covidence), where duplicates were removed, and title/abstract and full-text screening were performed by independent assessors (DANA, AdG, AT, SK and MK). Disagreements were resolved by consensus with a senior author (VS and MG). Protocol deviations are reported in online supplemental eAppendix 1.

Quality assessment and data extraction

Data extraction was conducted independently by pairs of authors (DANA, AdG, AT, SK and MK). Disagreements were resolved by a third senior author (VS and MG). Risk of bias was assessed using the Cochrane Risk of Bias tool.[13] The certainty of evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework and presented in summary of findings tables. Magnitude of effect thresholds measures were used to objectively assess imprecision of the results (online supplemental eTable 4).[14]

Statistical analysis

A random-effects meta-analysis was performed when two or more intervention studies were available and when the populations and outcomes were sufficiently comparable. Dichotomous outcomes were reported as risk ratios (RRs) with corresponding 95% CIs. Continuous outcomes were expressed as mean differences (MD) with 95% CI. If different scales were used in the same analysis, the standardised mean difference with 95% CI was estimated. Heterogeneity was quantified using the Higgins I^2 statistic, with thresholds prespecified according to the *Cochrane Handbook*.[15] Statistical analyses were conducted using Review Manager software, V.5.4.1 (The Cochrane Collaboration).

Data presentation

Given the large number of comparisons, it was decided in consensus with this review's authors (MG, VS, MAB and MT) to present only the results of the evidence with at least low certainty. If that was too extensive for inclusion in the main text, a selection was made based on the number of studies per comparison, certainty of evidence, magnitude of effect and clinical importance.

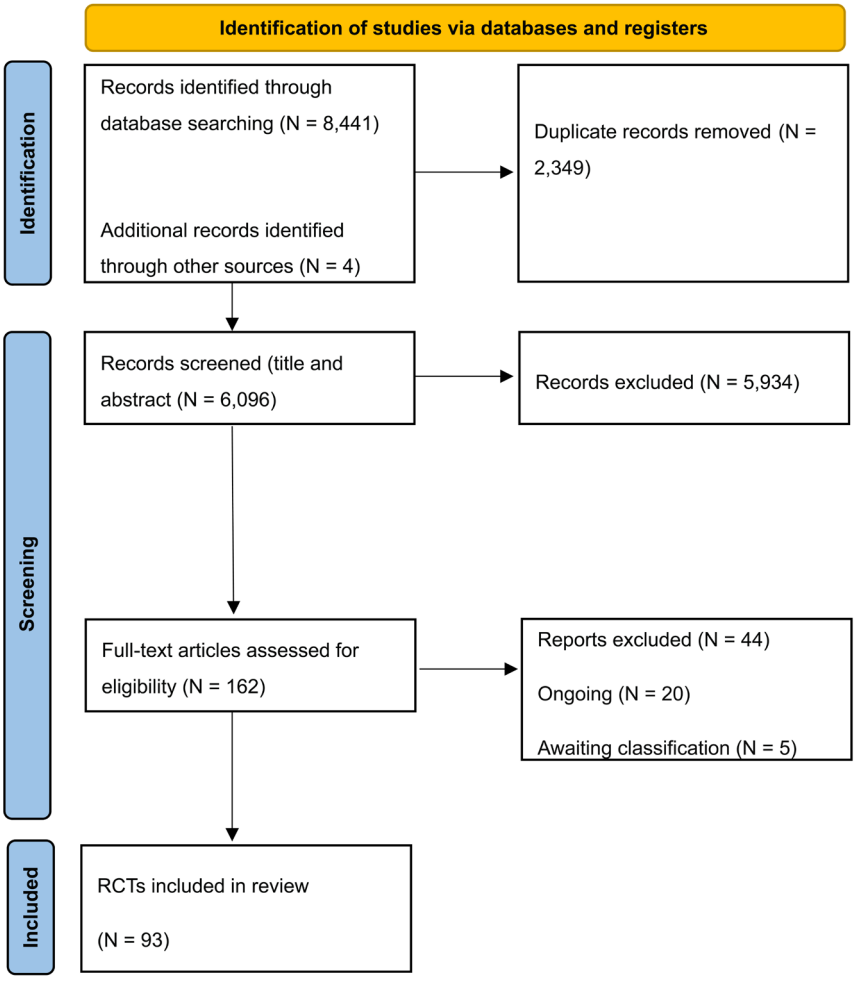

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram. RCT, randomised controlled trials

The remaining low certainty evidence is presented in a table within the main text.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research. Study outcomes were defined according to the FC core outcome set for therapeutic studies, developed with patient and caregiver input.[16]

RESULTS

Electronic searches identified 8441 records (inception to January 2025), reduced to 6096 after removing 2349 duplicates. Following the title, abstract and full-text screening, 162 were assessed in full-text (figure 1, online supplemental eTables 8–10). Finally, 93 records met the eligibility criteria for inclusion (online supplemental eTable 1).

Data from 7787 children (50.4% female) aged 0–18 years old were analysed. Mean age was reported in 70 studies (median of means: 6.1 years). 26 studies (28%) were conducted in Europe, 26 (28%) in the Middle East, 20 (21.5%) in Asia, 11 (11.8%) in North America and 1 each (1.1%) in North Africa and Oceania. Intervention duration ranged from 2 weeks to 6 months, while follow-up timepoints varied from 1 week to 6 years. Most studies used Rome III criteria (43.6%), followed by Rome IV (25.5%), Rome II (2.1%) and modified Rome criteria or other definitions (26.6%).

The included studies investigated 47 interventions, administered either alone or as an adjunct to laxatives, standard care or as adjunct to other non-pharmacological therapies. These interventions included probiotics (N=20), dietary fibre (N=13), complementary and complementary medicine (N=14), psycho-educational interventions (N=14), modified infant formulas (N=6), electrical stimulation (N=6), physiotherapeutic interventions (N=5), cow's milk free diet (CMFD) (N=4), synbiotics (N=4), massage (N=3), increased fluid intake (N=1), visceral manipulation (N=1), cryotherapy (N=1) and dry cupping (N=1). A total of 62 comparisons were identified, primarily against no treatment, placebo, laxatives, standard care or non-pharmacological approaches (online supplemental eTable 6).

The definition of treatment success varied considerably across studies. Most trials defined it using the following criteria: achieving a prespecified threshold of weekly bowel movements, no longer meeting Rome criteria for FC or resolution of symptoms.

Safety data were inconsistently reported across the included trials, with substantial variation in completeness between intervention categories. 45 studies reported withdrawals due to adverse events. In many studies, a conservative worst-case assumption was applied, classifying participants with unclear dropout reasons as withdrawals due to adverse events. Overall, most interventions showed no major differences in the incidence of adverse events between intervention and control groups. Probiotics were associated with minimal adverse events, mainly transient gastrointestinal symptoms such as mild abdominal pain[17–21] or diarrhoea that resolved with dose adjustment.[22] Serious adverse events were rare and generally unrelated to the intervention.[23] Dietary fibre demonstrated a favourable safety profile, with mild gastrointestinal effects including abdominal distension and flatulence.[24] Herbal products similarly produced mostly mild abdominal symptoms, such as diarrhoea,[25–27] vomiting[26 28 29] and abdominal pain.[25 29 30] For electrical nerve stimulation, one study[31] reported erythema, blisters and foot numbness associated with percutaneous tibial nerve stimulation (PTNS). Psycho-educational interventions, modified infant formulas, physiotherapy, CMFD, synbiotics, massage, increased fluid intake, visceral manipulation, cryotherapy and dry cupping either reported no adverse events or did not report safety outcomes.

Risk-of-bias assessment

A summary of the risk of bias for each study is provided in online supplemental eTable 5. Randomisation was judged at low risk in 55 out of 93 studies (59.1%), while 38 studies (40.9%) were judged to be at unclear risk. Allocation concealment was judged as low risk in 28 studies (30.1%), high risk in 4 studies (4.3%) and unclear in 61 studies (65.6%), primarily due to insufficient reporting.

54 RCTs (58.1%) had an open-label design and were rated high risk for performance bias, while in 17 studies (18.3%) the risk was unclear.

Attrition bias was at high risk in five studies (5.4%). 28 studies (30.1%) were rated unclear.

High risk of selective reporting was observed in 15 studies (16.1%) due to protocol deviation or lack of outcome reporting. 56 studies (60.2%) showed unclear risk of reporting bias.

4 studies (4.3%) reported unexplained imbalances in baseline participant characteristics that could have affected the results and were rated as high risk, 20 studies (21.5%) were rated as unclear risk and 69 studies (74.2%) as low risk.

Most of the comparisons were judged at very low certainty according to GRADE (online supplemental eTable 6). Table 1 presents all comparisons with at least low GRADE certainty for the primary outcomes.

Probiotics versus placebo

Nine RCTs[19 20 23 32–37] compared probiotics to placebo (N=722 participants, aged 0.5–18 years). Zaja *et al* [37] included only patients with anorexia nervosa; therefore, it was excluded from the meta-analysis. Four probiotic species were tested, with three studies[20 23 35] using a mixture of different strains. Six studies[19 20 23 32 34 36] (66.6%) reported treatment success, and seven studies reported mean defecation frequency per week.[19 20 23 32 33 35 36] Both outcomes were assessed as very low certainty due to serious risk of bias, inconsistency and imprecision, and no conclusions can be drawn (online supplemental eTable 6).

Withdrawals due to adverse events were reported for 22/352 children for probiotics versus 25/339 for placebo. GRADE analysis showed very low certainty of evidence due to risk of bias and imprecision.

Analysis by bacterial strain

When probiotic studies were subgrouped by bacterial strain, one study[20] showed that a probiotic mixture containing *L. acidophilus, B. longum* and *S. thermophilus* may lead to more treatment success compared with placebo (RR: 1.72 (95% CI 1.18 to 2.50); large magnitude of effect, low certainty) (figure 2), but showed no significant difference for defecation frequency (MD: 0.61 (95% CI −0.73 to 1.95), low certainty). The remaining analyses by bacterial strain were of very low certainty or did not show effect and are therefore not further discussed.

Probiotics in addition to laxative versus laxative

Nine studies investigated the additional effect of probiotics combined with laxatives compared with laxative monotherapy (N=691 participants, aged 0.5 to 16 years), of which four[21 38–40] used PEG, four[17 18 41 42] used lactulose and one[43] used magnesium oxide. Treatment success was reported in four studies[17 18 38 42] (44.4%), with GRADE rated as very low certainty owing to very serious risk of bias and serious imprecision.

Defecation frequency per week was reported in five studies[17 18 21 38 39] (55.5%), and meta-analysis showed there may be no difference between both groups (MD: 0.12 (95% CI −0.09 to 0.34), low certainty, downgraded twice because of very serious risk of bias) (figure 3).

Withdrawals due to adverse events were reported in 49/247 children in the probiotics and laxatives group and in 58/242 children in the laxative group. GRADE was rated as very low certainty due to very serious risk of bias and imprecision.

Analyses by bacterial strain were of very low certainty or did not show effect and are therefore not further discussed.

Synbiotics versus placebo

Two RCTs[44 45] compared synbiotics to placebo (N=245 participants, aged 3–18 years). One study[44] investigated a synbiotic consisting of a mixture of probiotics (*casei, L. rhamnosus, L. plantarum, B. lactis*) and prebiotics (*fibre,*

Table 1 Comparisons with outcomes rated at least low GRADE certainty

Outcome	No. of patients		Effect			GRADE certainty
	Intervention group	Control group	Relative (95% CI)	Absolute	Magnitude	
Abdominal transcutaneous electrical stimulation+pelvic floor muscle exercises versus pelvic floor muscle exercises						
Treatment success	45/62	25/62	RR: 1.75 (1.25 to 2.44)	302 more per 1000 (from 101 more to 581 more per 1000)	Large magnitude in favour (small in favour to large in favour)	Moderate ⊕⊕⊕⊖
Defecation frequency per week	N=62	N=61	MD: 1.85 (1.28 to 2.43)	1.85 more stools per week (1.28 more stools per week to 2.43 more stools per week)	Small magnitude in favour (small in favour to moderate in favour)	Moderate ⊕⊕⊕⊖
Behavioural therapy+laxative versus laxative						
Treatment success	35/67	42/67	RR: 0.83 (0.62 to 1.12)	106 less per 1000 (from 238 less to 75 more per 1000)	Small magnitude against (large against to small in favour)	Low ⊕⊕⊖⊖
Defecation frequency per week	N=67	N=67	MD: −1.80 (−2.88 to −0.72)	1.80 lower (from 0.72 lower to 2.88 lower)	Small magnitude against (trivial against to moderate against)	Moderate ⊕⊕⊕⊖
Withdrawals due to adverse events	0/67	1/67	RR: 0.33 (0.01 to 8.04)	10 less per 1000 (from 15 less to 108 more per 1000)	Small magnitude in favour (moderate in favour to large against)	Low ⊕⊕⊖⊖
Percutaneous tibial nerve stimulation+pelvic floor muscle exercises versus sham therapy+pelvic floor muscle exercises						
Treatment success	26/42	15/42	RR: 1.73 (1.08 to 2.77)	261 more per 1000 (from 29 more to 632 more per 1000)	Large magnitude in favour (trivial in favour to large in favour)	Low ⊕⊕⊖⊖
Defecation frequency per week	N=42	N=42	MD: 1.82 (0.82 to 2.82)	1.82 higher (from 0.82 higher to 2.82 higher)	Small magnitude in favour (trivial in favour to moderate in favour)	Moderate ⊕⊕⊕⊖
Withdrawals due to adverse events	3/42	3/42	RR: 1.00 (0.21 to 4.67)	0 more per 1000 (from 56 less to 262 more per 1000)	Trivial magnitude (large in favour to large against)	Low ⊕⊕⊖⊖
XiaojiDaozhi decoction (multi-herbal) versus placebo						
Treatment success	69/100	42/100	RR: 1.64 (1.26 to 2.14)	269 more per 1000 (from 109 more to 479 more per 1000)	Large magnitude in favour (small in favour to large in favour)	Low ⊕⊕⊖⊖
Defecation frequency per week	N=100	N=100	MD: 1.17 (0.68 to 1.66)	1.17 more stools per week (0.68 more stools per week to 1.66 more stools per week)	Trivial magnitude in favour (trivial in favour to small in favour)	Moderate ⊕⊕⊕⊖
Probiotics versus laxative						
Defecation frequency per week	N=82	N=106	MD: 0.36 (0.15 to 0.57)	0.36 more stools per week (0.15 more stools per week to 0.57 more stools per week)	Trivial in favour (trivial in favour to trivial in favour)	Low ⊕⊕⊖⊖
Probiotics+laxative versus laxative						
Defecation frequency per week	N=224	N=226	MD: 0.12 (−0.09 to 0.34)	0.12 stools more per week (0.09 lower stools per week to 0.34 higher)	Trivial magnitude in favour (trivial against to trivial in favour)	Low ⊕⊕⊖⊖
Synbiotics versus placebo						
Treatment success	48/77	21/78	RR: 2.32 (1.54 to 3.47)	355 more per 1000 (from 145 more to 665 more per 1000)	Large magnitude in favour (moderate in favour to large in favour)	Low ⊕⊕⊖⊖
Synbiotics versus dietary fibre						
Defecation frequency per week	N=36	N=36	MD: 0.66 (0.32 to 1.00)	0.66 more stools per week (from 0.32 more stools per week to one more stools per week)	Trivial magnitude in favour (trivial in favour to trivial in favour)	Low ⊕⊕⊖⊖
Synbiotics+laxative versus laxative						
Defecation frequency per week	N=37	N=29	MD: 0.02 (−0.56 to 0.60)	0.02 higher (from 0.56 lower to 0.60 higher)	Trivial magnitude in favour (trivial against to trivial in favour)	Low ⊕⊕⊖⊖
Cow's milk free diet+laxative versus normal diet+to laxative						
Defecation frequency dichotomous (number of patients with≥3 defecations per week)	67/70	50/70	RR: 1.34 (1.15 to 1.57)	243 more per 1000 (from 107 more to 407 more per 1000)	Moderate magnitude in favour (small in favour to large in favour)	Low ⊕⊕⊖⊖

Continued

Table 1 Continued

Outcome	No. of patients		Effect			GRADE certainty
	Intervention group	Control group	Relative (95% CI)	Absolute	Magnitude	
Telerehabilitation+laxative versus laxative						
Defecation frequency dichotomous (number of patients having≥3 defecation per week)	116/200	40/200	RR: 2.90 (2.15 to 3.92)	380 more per 1000 (from 230 more to 584 more per 1000)	Large magnitude in favour (moderate in favour to large in favour)	Low ⊕⊕⊖⊖
Internet-based programme+standard care versus standard care						
Treatment success	30/48	13/43	RR: 2.07 (1.25 to 13.42)	323 more per 1000 (from 76 more to 1000 more per 1000)	Large magnitude in favour (small in favour to large in favour)	Low ⊕⊕⊖⊖
Pelvic physiotherapy+standard care versus standard care						
Treatment success	24/26	12/27	RR: 2.08 (1.34 to 3.21)	480 more per 1000 (from 151 more to 990 more per 1000)	Large magnitude in favour (moderate in favour to large in favour)	Low ⊕⊕⊖⊖
Parasacral transcutaneous electrical nerve stimulation versus sham therapy						
Treatment success	16/20	6/20	RR: 2.67 (1.32 to 5.39)	501 more per 1000 (from 96 more to 1000 more per 1000)	Large magnitude in favour (small in favour to large in favour)	Low ⊕⊕⊖⊖
Xiao'er Biantong granules versus placebo						
Treatment success	195/360	4/120	RR: 16.25 (6.17 to 42.79)	508 more per 1000 (from 172 more to 1000 more per 1000)	Large magnitude in favour (moderate in favour to large in favour)	Low ⊕⊕⊖⊖
Defecation frequency dichotomous (number of children with≥3 bowel movements per week)	291/360	34/120	RR: 2.85 (2.14 to 3.81)	524 more per 1000 (from 323 more to 796 more per 1000)	Large magnitude in favour (large in favour to large in favour)	Low ⊕⊕⊖⊖
Sugarcane extract versus laxative						
Treatment success	35/45	42/47	RR: 0.87 (0.72 to 1.05)	116 less per 1000 (from 250 less to 45 more per 1000)	Small magnitude against (large against to trivial in favour)	Low ⊕⊕⊖⊖
Defecation frequency dichotomous (number of patients with≤2 bowel movements per week)	1/41	3/45	RR: 0.37 (0.04 to 3.38)	42 less per 1000 (from 64 less to 159 more per 1000)	Trivial magnitude in favour (trivial in favour to moderate against)	Low ⊕⊕⊖⊖
Cassia fistula's emulsion versus laxative						
Defecation frequency per week	N=89	N=91	MD: 4.22 (2.78 to 5.66)	4.22 more stools per week (from 2.78 more stools per week to 5.66 more stools per week)	Large magnitude in favour (moderate in favour to large in favour)	Low ⊕⊕⊖⊖
D. sophia seeds versus laxative						
Defecation frequency per week	N=56	N=53	MD: 0.00 (−0.98 to 0.98)	0 more stools per week (0.98 less stools per week to 0.98 more stools per week)	Null magnitude (trivial against to trivial in favour)	Low ⊕⊕⊖⊖
Red sugar versus fig syrup						
Defecation frequency dichotomous (number of patients having>3 faecal excretions a week)	30/30	30/30	RR: 1 (0.94 to 1.07)	0 more per 1000 (from 60 less to 70 more per 1000)	Null magnitude (trivial against to trivial in favour)	Low ⊕⊕⊖⊖
Z. jujube versus laxative						
Defecation frequency per week	N=49	N=62	MD: 0.4 (0.28 to 0.52)	0.4 more stools per week (0.28 more stools per week to 0.52 more stools per week)	Trivial magnitude in favour (trivial in favour of trivial in favour)	Low ⊕⊕⊖⊖

Green: results are in favour of the intervention group, yellow: there is no difference between both groups, red: results are in favour of the control group.
GRADE, Grading of Recommendations, Assessment, Development and Evaluations; MD, mean differences; RR, risk ratio.

polydextrose, fructo-oligosaccharides, galacto-oligosaccharides). One study[45] investigated a synbiotic consisting of a mixture of probiotics (*B. breve, B. breve, B. lactis, B. longum, L. casei, L. rhamnosus, L. salivarius* and *L. acidophilus*) and mixed-chain length prebiotic substrates. Subgroup analysis by probiotic strain showed one synbiotic[44] (*L. casei, L. rhamnosus, L. plantarum, B. lactis* plus prebiotics) may lead to more treatment success compared with placebo (RR: 2.32 (95% CI 1.54 to 3.47), large magnitude of effect, low certainty) (figure 4).

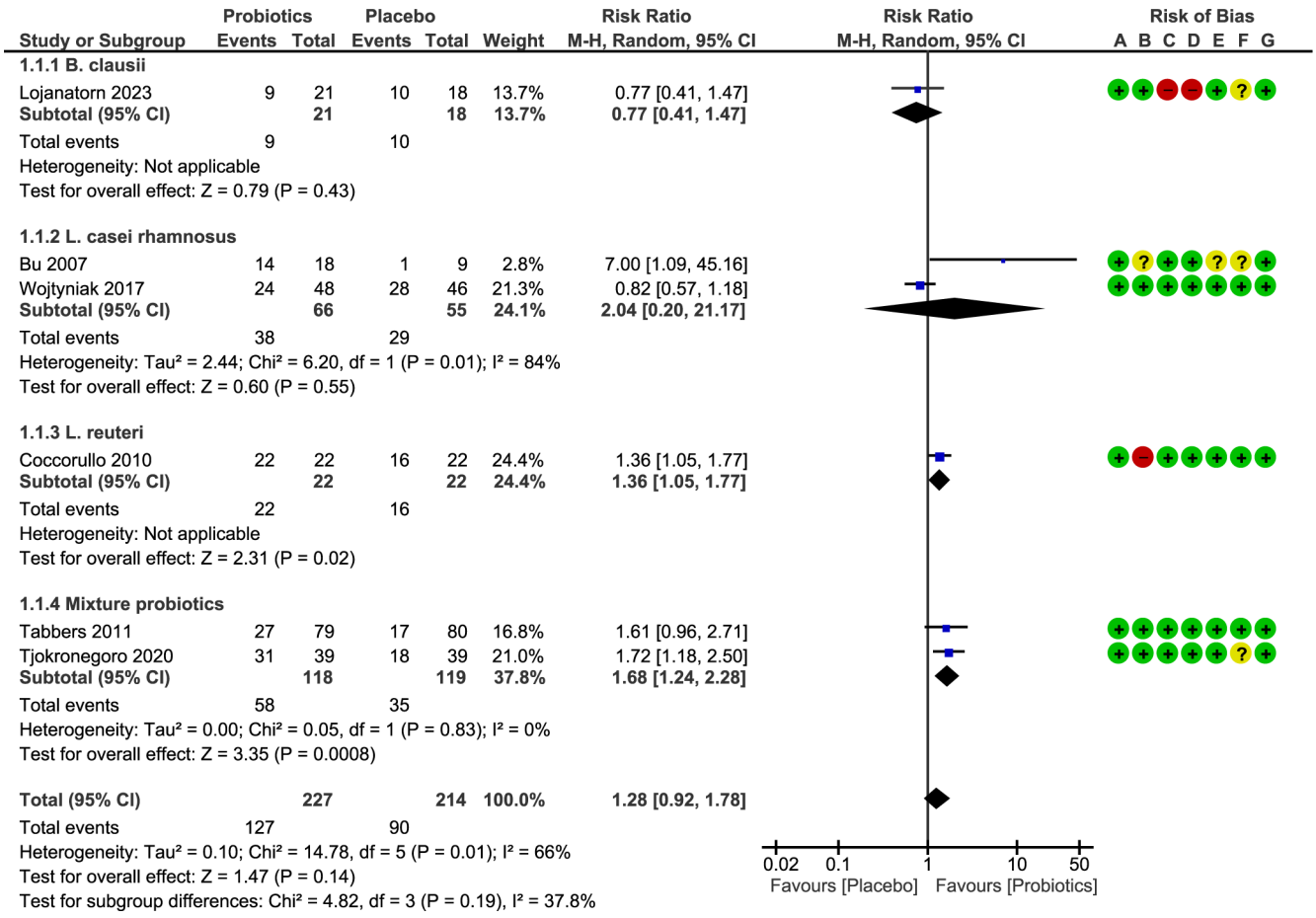

Figure 2 Treatment success for probiotics versus placebo. Green, yellow and red circles indicate low, unclear and high risk of bias, respectively. The risk of bias assessment is presented following order: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias. IV, inverse variance; M-H, Mantel–Haenszel; random, random effects.

CMFD in addition to laxative versus normal diet in addition to laxative

Two studies[46 47] assessed the addition of a CMFD to laxatives compared with laxatives plus a non-milk-restrictive diet. No conclusions could be drawn for treatment success due to very low certainty evidence. In Bourkheili,[47] results were reported only for children on CMFD before the trial and those on normal diet after the trial, and thus this study was not included in the meta-analysis.

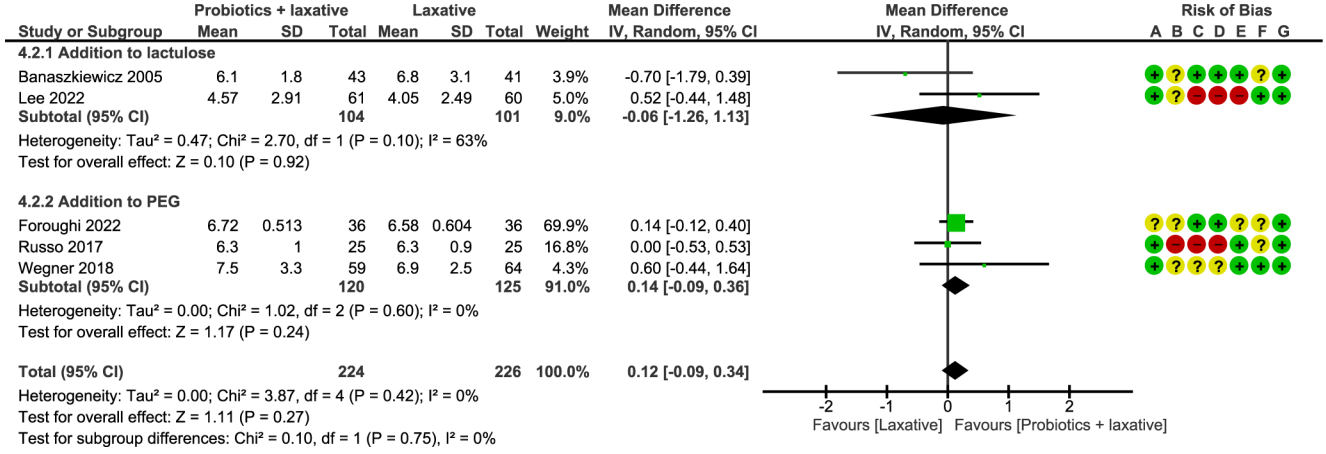

Figure 3 Defecation frequency of probiotics+laxative versus laxative. Green, yellow and red circles indicate low, unclear and high risk of bias, respectively. The risk of bias assessment is presented following order: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias. IV, inverse variance; PEG, polyethylene glycol; random, random effects.

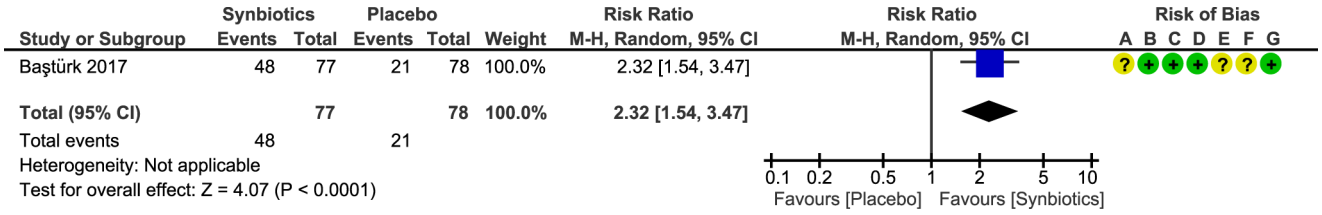

Figure 4 Treatment success of synbiotics versus placebo. Green, yellow and red circles indicate low, unclear and high risk of bias, respectively. The risk of bias assessment is presented following order: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias; IV, inverse variance; M-H, Mantel–Haenszel; random, random effects.

In Dehghani,[46] defecation frequency was reported as a dichotomous outcome in terms of number of individuals achieving three or more bowel movements per week. CMFD as an addition to PEG may lead to more children with three or more bowel movements, and GRADE certainty was rated as low due to very serious risk of bias (RR: 1.34 (95% CI 1.15 to 1.57), moderate magnitude of effect) (figure 5).

Withdrawals due to adverse events were rated as very low certainty due to very serious risk of bias and imprecision.

Abdominal transcutaneous electrical stimulation in addition to pelvic floor muscle exercises versus pelvic floor muscle exercises alone

Two studies[48 49] compared abdominal transcutaneous electrical stimulation (ATES) combined with pelvic floor muscle exercises (PFME) to PFME alone (N=124 participants, aged 5–13 years). In both RCTs, all participants received education on FC, dietary advice, toilet training and laxatives as rescue therapy. In Sharifi-Rad *et al*,[49] PEG was also administered daily to all patients. All primary outcomes were reported in both studies. Meta-analysis and GRADE assessment showed ATES+PFME probably leads to more treatment success compared with PFME alone (RR: 1.75 (95% CI 1.25 to 2.44), large magnitude of effect, moderate certainty due to risk of bias) (figure 6A). PFME+ATES also probably leads to higher defecation frequency per week (MD: 1.85 (95% CI 1.28 to 2.43), small magnitude of effect, moderate certainty due to risk of bias) (figure 6B).

There was only one withdrawal due to adverse events in the PFME group, for which no reason was provided. Withdrawals were very low certainty.

Percutaneous tibial nerve stimulation in addition to pelvic floor muscle exercises versus sham therapy and pelvic floor muscle exercises

One study[31] evaluated PTNS combined with PFME versus sham therapy+PFME in children with symptoms refractory to PEG (N=84 participants, aged 4–14 years). Treatment success was higher in the group receiving combination therapy (PTNS+PFME) (RR: 1.73 (95% CI 1.08 to 2.77), large magnitude of effect, low certainty due to very serious imprecision) (online supplemental eTable 6).

Defecation frequency was reported as change in spontaneous bowel movements per week from baseline, showing PTNS probably leads to higher defecation frequency (MD: 1.82 (95% CI 0.82 to 2.82), small magnitude of effect, moderate certainty due to serious imprecision) (online supplemental eTable 6).

Two participants withdrew from each group due to low compliance and one participant withdrew from each group due to having other treatments (RR: 1.00 (95% CI 0.21 to 4.67), low certainty owing to very serious imprecision) (online supplemental eTable 6).

Pelvic physiotherapy in addition to standard medical care versus standard medical care alone

One study[50] compared the combination of pelvic physiotherapy with standard medical care to standard medical care alone (N=53 participants, aged 5–15 years). Standard medical care consisted of education, demystification, dietary advice, toilet training, keeping track of bladder and bowel diaries, and when needed, prescription of PEG. The GRADE certainty for treatment success was rated as low due to serious risk of bias and serious imprecision (RR: 2.08 (95% CI 1.34 to 3.21), large magnitude of effect) (online supplemental eTable 6), indicating

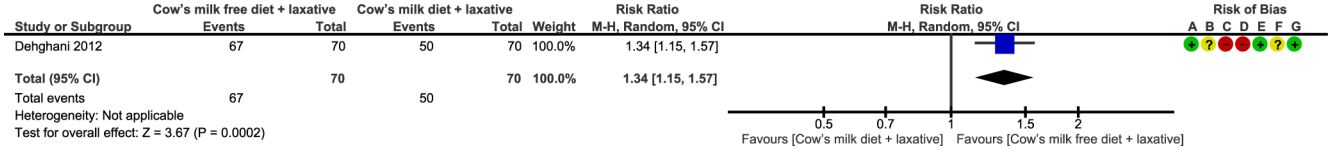

Figure 5 Treatment success of cow's milk-free diet+laxative versus normal diet+laxative. Green, yellow and red circles indicate low, unclear and high risk of bias, respectively. The risk of bias assessment is presented following order: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias; IV, inverse variance; M-H, Mantel–Haenszel; random, random effects.

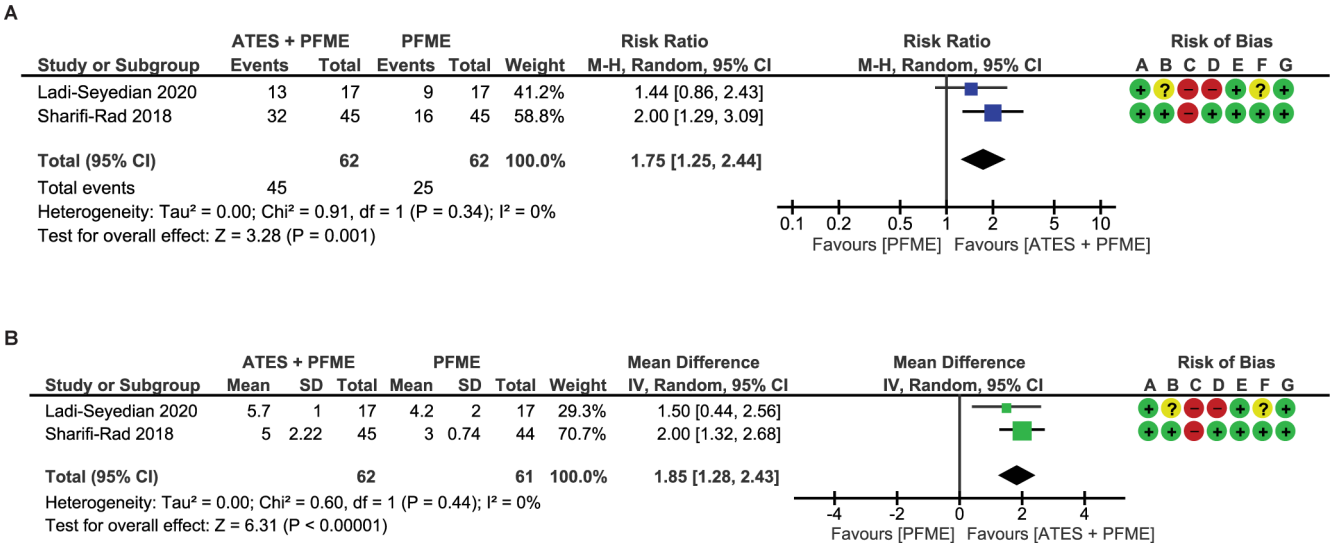

Figure 6 Forest plots of abdominal transcutaneous electrical stimulation+pelvic floor muscle exercises versus pelvic floor muscle exercises. (A) Treatment success; (B) defecation frequency per week. Green, yellow and red circles indicate low, unclear and high risk of bias, respectively. The risk of bias assessment is presented following order: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias. ATES, abdominal transcutaneous electrical stimulation, IV, inverse variance; M-H, Mantel–Haenszel; PFME, pelvic floor muscle exercises; random, random effects.

pelvic physiotherapy as an addition to standard care may lead to more treatment success.

Defecation frequency was inadequately reported and therefore not included in the analysis. No withdrawals due to adverse events were reported (very low certainty, due to serious risk of bias and very serious imprecision).

Behavioural therapy in addition to laxative versus laxative

The addition of behavioural therapy to PEG in comparison to laxatives alone was evaluated in one study[51] (N=134 participants, age 4–18 years). GRADE assessments showed that there may be no difference in treatment success for both groups (RR: 0.83 (95% CI 0.62 to 1.12), low GRADE certainty due to very serious imprecision) (online supplemental eTable 6) and that the addition of behavioural therapy probably leads to lower defecation frequency (MD: −1.80 (95% CI −2.88 to −0.72), small magnitude of effect, moderate certainty due to serious imprecision) (online supplemental eTable 6). One participant was lost to follow-up in the PEG group and there was low certainty evidence that there is no difference between groups for withdrawals due to adverse events (RR: 0.33 (95% CI 0.01 to 8.04), low certainty) (online supplemental eTable 6).

DISCUSSION

To our knowledge, this review represents the largest and most methodologically comprehensive synthesis of evidence on the efficacy and safety of non-pharmacological treatments for childhood FC, including 93 RCTs and 62 different pairwise comparisons. Summarising the results is challenging, as few conclusions can be drawn from the many analyses due to the very low certainty of evidence and the wide range of comparisons made, many of which included only a single study.

Among the few conclusions that can be drawn, combining probiotics with laxatives may not improve defecation frequency compared with laxatives alone. Subgroup analyses by bacterial strain suggested one specific probiotic mixture and one synbiotic preparation may lead to more treatment success than placebo. One study showed that a CMFD added to PEG treatment may lead to higher defecation frequency compared with PEG plus a normal diet. A meta-analysis of two studies indicated that the addition of ATES to PFME may improve treatment success and defecation frequency compared with PFME alone. One study showed PTNS combined with PFME may lead to more treatment success and probably leads to greater defecation frequency. One study showed pelvic physiotherapy added to standard medical care may lead to more treatment success than standard care alone. Behavioural therapy added to PEG may make no difference in treatment success and probably reduces defecation frequency. Across all comparisons, withdrawals due to adverse events were either of very low certainty or showed no difference between interventions.

Several systematic reviews have previously assessed the efficacy of non-pharmacological interventions for childhood FC, though most focused on a narrow subset of interventions, such as probiotics[52–54] or transcutaneous neuromodulation.[55] One methodologically well-performed review[11] included a wide range of non-pharmacological treatments, but like most others, did not assess certainty of evidence. Our inclusion of a wide range of interventions and GRADE assessment is therefore novel and allows us to identify common methodological

limitations across studies and provide guidance for the design and reporting of future trials.

The overall quality and completeness of evidence in childhood functional bowel disorders is known to be poor, with examples seen in our reviews of both functional abdominal pain[56 57] and pharmacological treatments of FC (unpublished manuscript). However, this review reveals even more systematic issues. The evidence comprises 62 comparisons due to the wide variability in the interventions and control groups, resulting in most comparisons including only one or two studies. This leads to significant imprecision in meta-analyses results. Chronic underpowering of trials, common in this field,[58 59] further compromises precision and overall certainty of the evidence.

While methodological limitations are frequently observed in individual studies,[60] this was a more significant and pervasive issue in the included trials. This could be related to the relatively limited governance surrounding non-pharmacological trials, particularly compared with pharmacological trials. Poor reporting in individual trials, such as lack of detail on allocation methods or trial registration, led to frequent downgrading for risk of bias in GRADE assessments. Due to the nature of many non-pharmacological interventions, more than half of the included studies were open label, resulting in a high risk of performance and detection bias. This raises concerns about the placebo effect, which is known to significantly influence treatment outcomes in children with other disorders of gut-brain interaction.[61 62] If the placebo effect was present in these trials, it may have concealed true differences between the active intervention and the comparator, especially in the context of underpowered trials. However, there is a notable lack of research specifically investigating the placebo effect in children with FC. In our analysis, we applied a less strict approach for downgrading GRADE assessments for risk of bias when the intervention could not be masked. In practice, downgrading for risk of bias was mainly driven by concerns related to the randomisation process, incomplete outcome data and selective reporting of outcomes.

A major overarching issue in research involving children with FC is the substantial heterogeneity of the included patient populations across studies (eg, disease severity and prior treatments received) and the lack of international consensus on the definition of therapy resistant constipation. Only recently has an evidence-based definition been proposed, and we recommend that future research adopt this definition when characterising study populations.[62 63] Additionally, there is often a lack of detail regarding both the studied interventions (eg, form and frequency of clinical follow-up) and other interventions provided during the trial period (eg, education, dietary advice, disimpaction, or concomitant therapy), likely contributing to unexplained heterogeneity.

Another key limitation affecting comparability of study results is the lack of universally accepted outcome measures. In 2017, a core outcome set was developed through consultation with healthcare professionals, parents and patients, to reduce heterogeneity and facilitate data pooling. Although more recent studies increasingly incorporate outcomes from this outcome set, the measurement methods still vary widely (eg, continuous vs dichotomous variables, different scales), which continues to hinder synthesis of results. Currently, no standardised guidelines exist on how these outcomes should be reported, highlighting a key area for future research.

Strengths of this systematic review include the use of rigorous methodology, including GRADE[64] assessments and the application of predefined outcome thresholds[14] to objectively evaluate imprecision and support interpretation of clinical relevance. In addition, no language restrictions were applied and abstracts were included, limiting publication bias.[65] To ensure a comprehensive and complete database and an accurate risk of bias assessment, study authors were contacted[66] when information was missing or unclear.

This study has several limitations. First, an inclusion criterion was FC as defined by the original study authors, meaning we were reliant on each study's definition of the patient population. Although most studies used the Rome criteria, these do not distinguish between FC and therapy-resistant constipation, meaning disease severity may have varied across studies. Secondly, one of the primary outcomes was treatment success, also as defined by the study authors. Variability in these definitions likely contributed to the heterogeneity observed across studies. Third, the predefined thresholds for imprecision assessment, established by the international guideline committee,[14] were based on 15 healthcare professionals and did not incorporate individuals with lived experience.

Despite limitations in the evidence synthesis and the predominance of very low certainty evidence, important conclusions can be drawn from this review to guide future research. Some interventions with at least low-certainty evidence showed beneficial effects as stand-alone treatments or as adjuncts to laxatives. Our systematic review on pharmacological treatments (not yet published) identified PEG as the most effective laxative; however, laxative treatment alone is not sufficient for all children. As most non-pharmacological interventions are likely to be used as adjuncts in clinical practice, we recommend that future trials evaluate them in this context, with appropriate sample size calculations. Greater clarity is also needed in defining patient populations, using standardised definitions for faecal impaction and therapy-resistant constipation, and in reporting of previously received interventions. Clinical trials should also consider reporting outcomes by patient subgroups (eg, age groups, sex, race, disease severity) to identify populations who may benefit more from specific interventions, potentially supporting individualised management approaches. Methods should explicitly report which concomitant therapies were allowed and if patients were provided general dietary advice, rescue therapy or disimpaction prior to starting the intervention. When

blinding is not feasible, measures such as sham therapies or blinded outcome assessment should be used to limit performance and detection bias. Protocols should be prospectively registered and all trials should follow the CONSORT 2025 guidelines.[67] Researchers should ensure adequate sample sizes through multicentre collaborations, research networks and standardised outcomes to enable data pooling and meta-analyses, highlighting the need for future research to establish definitions and outcome measures as a follow-up to the core outcome set.

CONCLUSION

There is a wide variety in non-pharmacological treatment options for children with FC, but due to systemic issues in study design and reporting, evidence of at least low certainty evidence remains limited. Some interventions show beneficial effects and may be considered in the management of children with FC; however, more high-quality RCTs are recommended on these interventions as the evidence is based on a limited number of mostly underpowered studies. Future trials should aim to improve methodological rigour, provide detailed descriptions of patient characteristics and interventions. Standardised outcome measures should be developed for the core outcome set.

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