Strategies used for childhood chronic functional constipation: the SUCCESS evidence synthesis

Alex Todhunter-Brown,[1*] Lorna Booth,[1] Pauline Campbell,[1] Brenda Cheer,[2] Julie Cowie,[1] Andrew Elders,[1] Suzanne Hagen,[1] Karen Jankulak,[3] Helen Mason,[4] Clare Millington,[3] Margaret Ogden,[3] Charlotte Paterson,[5] Davina Richardson,[6] Debs Smith,[3] Jonathan Sutcliffe,[7] Katie Thomson,[1,8] Claire Torrens[5] and Doreen McClurg[1]

[1]Nursing, Midwifery and Allied Health Professions (NMAHP) Research Unit, Glasgow Caledonian University, Glasgow, UK
[2]ERIC, The Children's Bowel and Bladder Charity, Bristol, UK
[3]PPI Representative, Glasgow, UK
[4]Yunus Centre for Social Business and Health, Glasgow Caledonian University, Glasgow, UK
[5]Nursing, Midwifery and Allied Health Professions (NMAHP) Research Unit, University of Stirling, Stirling, UK
[6]Bladder and Bowel UK, Manchester, UK
[7]Leeds Teaching Hospitals NHS Trust, Leeds, UK
[8]Department of Occupational Therapy, Human Nutrition and Dietetics, Glasgow Caledonian University, Glasgow, UK

[*]Corresponding author Alex.TodhunterBrown@gcu.ac.uk

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Andrew Elders has disclosed being an independent member of the steering committee for the NIHR-funded MAGIC2 trial of the TransiCap in paediatric constipation. All other authors have declared no competing interests.

Disclaimer: This report contains transcripts of interviews conducted in the course of the research, or similar, and contains language which may offend some readers.

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Scientific summary

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Background

Chronic functional constipation (CFC) in childhood is common; it is estimated to affect 5–30% of school-aged children, becoming chronic in around one-third of cases. CFC has negative effects on quality of life (QoL) of children, families and carers, with increasing impact as the child gets older. Although rarely life-threatening, CFC is an unpleasant and distressing condition, associated with a wide range of complications, including physical discomfort, missed school, poor school performance, social isolation and reduced involvement in group activities. More than a third of children with CFC will present clinically with behavioural problems as a result of the constipation. The healthcare costs of childhood CFC are significant. Treatments are usually directed at symptom control since limited diagnostics mean no underlying cause is identified in more than 95% of cases, thus limiting ability to stratify treatments. There are a number of different interventions available for the management of CFC; however, the optimal strategy for combining and implementing interventions for individual circumstances remain unclear. National Institute for Health and Care Research (NIHR) commissioned this work to address the question: '*What are the most effective interventions, and combinations and sequences of interventions, for childhood chronic functional constipation (CFC), and how can they best be implemented?*'

Objectives

Specific research questions (RQs) answered by this project were:

RQ1: What is the current evidence relating to management strategies for childhood CFC? (Scoping review).

RQ2: What are the most effective childhood CFC strategies and combinations of strategies in relation to outcomes of importance to stakeholders and/or cost to the patient/NHS? [Systematic review (SR) of evidence of effectiveness and cost effectiveness].

RQ3: What factors are associated with implementation success or failure of childhood CFC strategies and combinations of strategies for different subgroups? (SR of factors affecting implementation).

RQ4: What are the evidence gaps in childhood CFC management strategies?

Design

We conducted a three-stage pragmatic mixed-method study. In stage 1, we completed a broad, comprehensive scoping review. In stage 2, we conducted focused SRs evaluating effectiveness, cost effectiveness and factors affecting implementation. In stage 3, we integrated findings, generating interactive evidence maps, exploring complementarity between our findings and published clinical guidelines, and identifying evidence gaps.

Methods

Patient and public involvement

Stakeholder involvement was central to our project. We formed a stakeholder group (SG) from across the UK, comprising people with lived experience of childhood CFC, parents of children with CFC, healthcare

professionals and representatives of relevant charities. We adhered to key principles for research co-production. The SG provided continuous project oversight and completed specific activities. These activities included development of an intervention taxonomy and logic model, agreement on outcomes for the review, identifying evidence gaps and reaching consensus on clinical implications.

Scoping review

Our scoping review was based on a systematic search of several electronic databases including medical literature analysis and retrieval system online (MEDLINE), excerpta medica database (EMBASE) and Cumulative Index to Nursing and Allied Health Literature (CINAHL; January 2011 to March 2020), as well as searches of grey literature, contacting experts and forward citation tracking. We included papers, regardless of study design, which investigated, reported or discussed any strategy, delivered in any setting, aimed at improving any outcomes in children (aged 0–18 years) with a clinical diagnosis of CFC. We did not include studies of assessment/diagnosis. We included studies involving children with or without additional needs but excluded those with a recognisable cause of constipation such as anorectal malformation, Hirschsprung's disease, intestinal nerve abnormalities, metabolic or endocrine causes. Eligible abstracts and full texts were independently reviewed by two reviewers. Data were extracted by one reviewer and cross-checked by a second. Two reviewers independently applied descriptive codes to categorise the type of study, aim/focus of the study, outcomes, types of interventions/intervention combinations, and availability of data relating to effectiveness, economics or implementation factors. In keeping with scoping review methodology, we did not formally assess research quality. Data were summarised within an evidence gap map.

Systematic reviews of evidence of effectiveness

For our SRs of evidence of effectiveness, we considered all studies identified in the scoping review and 'tagged' them as studies of effectiveness. We included any studies investigating effectiveness of any intervention, or combination of interventions, aimed at improving outcomes in children with CFC. Informed by our stakeholders, we grouped studies according to whether the intervention was one that would be delivered by families/carers ('Level 0'), the wider children's workforce (e.g. general practitioner, health visitor) ('Level 1'), continence teams ('Level 2') or specialist consultant-led teams ('Level 3'). We also considered different models of service delivery, and complementary and psychosocial therapies. For each different intervention, we adopted a hierarchical, step-wise approach to inclusion of different study designs. If there was a comprehensive SR, judged to be low risk of bias (ROB) [using risk of bias assessment tool for systematic reviews (ROBIS) criteria, assessed by two independent reviewers], this was also included. Where we included a SR, we also included any randomised controlled trials (RCTs) published after the date of the search in the review. Where there was no SR, we included RCTs and other primary studies of intervention effectiveness. Data were extracted on study methods, participant characteristics, intervention characteristics [using template for intervention description and replication (TIDieR) framework], outcomes and key findings. ROB was judged using tools appropriate to the study design [e.g. Cochrane ROB tool for RCTs, critical appraisals skills programme (CASP) tools for cohort studies, Joanna Briggs Institute (JBI) tools for qualitative evidence, Ways of Evaluating Important and Relevant Data (WEIRD) tool for other study designs]. Relevant meta-analyses within included SRs were updated with any new RCTs following the methods reported in the SR. A narrative synthesis of evidence of effectiveness for each intervention, delivered within 'level' 0 to 3 was presented, with a process of considered judgement used to judge certainty in the evidence as high, moderate, low, very low or insufficient evidence.

Economic evaluation

For our SR of economic studies, we considered any economic evidence identified in our scoping review and conducted additional searching of electronic databases and citation tracking following best practice guidance. We included all types of study detailing costs related to interventions aimed at children with CFC that were published in English, regardless of study design. One reviewer extracted data, including details of economic evaluations, and these were checked by a second reviewer. Studies were categorised as cost-consequence, cost-effectiveness, cost-utility or cost-

benefit and their quality evaluated using the consensus health economic criteria (CHEC) checklist, and data were brought together into a narrative synthesis.

Systematic review of factors affecting implementation

For our SR of factors affecting implementation, we included studies which were identified in the scoping review as explicitly reporting data relating to key participant variables, barriers, facilitators, equity factors and adherence. One reviewer systematically identified, extracted and coded [using the consolidated framework for implementation research (CFIR)] barriers and facilitators, and a second reviewer checked this. We used a best fit framework synthesis approach combining deductive and inductive thematic approaches to identify barriers and facilitators. Data were brought together in a narrative synthesis organised around the CFIR domains.

Integration of findings

Our integration of findings from the SRs was informed by decisions taken by our stakeholders, including development of a logic model. We explored agreements between our findings and recommendations within previously published guidelines. We brought our findings together within interactive evidence maps, and systematically identified evidence gaps.

Results

The scoping review included 651 studies, including 190 RCTs and 236 primary studies. Forty-eight interventions (or combinations of interventions) were reported. Studies were mainly conducted in high-income countries; no studies from low-income countries were identified.

The most frequently reported interventions were delivered by carers, prior to healthcare professional involvement (22%); these were primarily lifestyle interventions focused on diet. The least frequently reported were psychosocial interventions (3%). Children were recruited from a variety of settings including hospitals, clinical outpatients, and other community settings. Interventions were generally delivered face to face either at home or within a variety of hospital settings such as the emergency department. Interventions were rarely delivered in education settings (e.g. school-based settings) (n = 5) or residential care/looked after population (n = 1) settings. The most frequently reported outcome measurement was defaecation frequency, which was reported in one-third of studies within the scoping review. School attendance or absenteeism was the least frequently reported outcome (n = 8 studies).

Our SRs of effectiveness included 32 studies (including 2 SRs) which explored effectiveness of interventions delivered by families/carers ('Level 0'); 21 studies (including 2 SRs) which explored effectiveness of interventions delivered by wider children's workforce ('Level 1'); 31 studies (including 1 SR) which explored effectiveness of interventions delivered by continence teams ('Level 2'); 42 studies (no SRs) which explored effectiveness of interventions delivered by specialist consultant-led teams ('Level 3'); 15 studies (no SRs) which explored effectiveness of different models of service delivery; 15 studies (2 SRs) which explored effectiveness of complementary therapies; and 4 studies (1 SR) which explored effectiveness of psychosocial interventions.

Interventions for which there was some evidence of potential benefit included, within Level 0: a trial of cows' milk-free diet, educational interventions for parents, selenium supplements. Within Level 1: laxatives, physical exercise focused on pelvic floor muscle, combined pharmacological, diet and behaviour programme. Within Level 2: combined oral and enema therapy, transanal irrigation, biofeedback (for children with abnormal defaecation dynamics), combined treatment programmes. Within Level 3: botulinum toxin, antegrade continence enema (ACE)/Malone antegrade continence enema (MACE), sacral modulation. Models of care delivery which may be beneficial included nurse-led clinics, an algorithm, or care pathway, used in primary care settings, specialist (Level 2) services and web-based information, following an appointment with a specialist. Complementary therapies for which there was some evidence of effectiveness included: connective tissue manipulation (CTM) for

children with cerebral palsy (CP), and some herbal/traditional medicines. There was some evidence in favour of behavioural therapy. Interventions which evidence suggests may not be beneficial include, probiotics, additional dietary fibre, increased fluid intake and biofeedback (for children with normal defaecation dynamics).

Evidence relating to probiotics was judged to be moderate quality, but for all other interventions was considered low to very low quality. There was insufficient evidence to support conclusions relating to several other interventions.

We identified 31 studies which reported some evidence relating to cost or resource use, of which 20 were cost-of-illness studies. Fewer than 30% of the studies employed a formal economic evaluation study design. Most studies were poorly reported with limited details. Data included in this review were insufficient to support any generalisable conclusions relating to cost or resource use.

One hundred and six studies described multiple barriers and facilitators across the five domains of the CFIR framework. The most commonly reported factors related to 'successfulness' of an intervention included; whether the intervention was adaptable, flexible and offered an advantage over an alternative solution; understanding the tension for change (i.e. why clinicians and families felt that the changes were needed now); the taboo nature of constipation and the reluctance of children, families, healthcare professionals and wider society to openly engage in discussion about constipation; a lack of understanding of what children and their families need; self-efficacy, coupled with individual knowledge and beliefs; and engagement of champions to support children.

Research gaps were identified through evidence maps and stakeholder discussions. Key topics considered priorities for future research relate to recognition of CFC; information provision; diet; laxatives and combinations of laxatives; behavioural therapy and psychological support. Future research studies should address what works for which individual child, and when, including children with and without additional needs. Research to explore the optimal delivery of services, including identification of key components and features of effective teams and criteria for referring children from one 'level' to the next, is needed.

Conclusions

We conducted a comprehensive review of all evidence relating to interventions, and combinations of interventions, for children with CFC. The finding from our review are generally in agreement with the current guideline recommendations, where recommendations exist. A significant proportion of interventions for which we found evidence had not been addressed within current guidelines.

This project has highlighted that research in this field often does not adhere to recognised standards for conduct and reporting or consider the complexities of interventions for CFC. We found no evidence which gave us high certainty in the findings; and we only had moderate certainty relating to one intervention (probiotics, with evidence demonstrating that probiotics may not have any beneficial – or harmful – effect). Our certainty about all other findings was low to very low or, in many cases, we judged that the evidence was insufficient to support any generalised conclusions. The current evidence base rarely measured outcomes deemed of highest priority to children and families, and many studies failed to describe the complex nature of the treatments that a child may be receiving. This limits the conclusions that can be made from the current evidence. Further, the limitations within the evidence base reduce confidence in recommendations and create a barrier to implementation of best practice, impairing progress in efforts to improve outcomes for this group of children.

Our findings do not indicate that changes are necessarily needed to the treatment recommendations within current clinical guidelines. However, management of childhood CFC is complex, and there is no simple 'one size fits all' approach. Clinical care and future studies must consider the individual

characteristics of each child with constipation, and the context – or environment – within which they live. Key goals of successful management of CFC should be early recognition of symptoms and delivery of interventions by families/carers, achieved by providing children and families/carers with effective education and support from members of the wider children's workforce (primary care services). Development, evaluation and implementation of strategies to enhance the delivery of services focused on individualised care, combining lifestyle and behavioural strategies with laxatives are a priority.

To avoid further research waste, it is essential that future research addresses the questions which are of the highest priority to key stakeholders and has the highest possible standards of conduct and reporting. Future research studies should address what works for which individual child, and when, including children with and without additional needs. Future research into any interventions for childhood CFC should take into account relevant evidence relating to the development and evaluation of complex interventions.

Study registration

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