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Rehabilitative management of back pain in children: protocol for a mixed studies systematic review

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ABSTRACT

Introduction Little is known about effective, efficient and acceptable management of back pain in children. A comprehensive and updated evidence synthesis can help to inform clinical practice.

Objective To inform clinical practice, we aim to conduct a systematic review of the literature and synthesise the evidence regarding effective, cost–effective and safe rehabilitation interventions for children with back pain to improve their functioning and other health outcomes.

Methods and analysis We will search MEDLINE, Embase, PsycINFO, CINAHL, the Index to Chiropractic Literature, the Cochrane Controlled Register of Trials and EconLit for primary studies published from inception in all languages. We will include quantitative studies (randomised controlled trials, cohort and case–control studies), qualitative studies, mixed-methods studies and full economic evaluations. To augment our search of the bibliographic electronic databases, we will search reference lists of included studies and relevant systematic reviews, the WHO International Clinical Trials Registry Platform and consult with content experts. We will assess the risk of bias using appropriate critical appraisal tools. We will extract data about study and participant characteristics, intervention type and comparators, context and setting, outcomes, themes and methodological quality assessment. We will use a sequential approach at the review level to integrate data from the quantitative, qualitative and economic evidence syntheses.

Ethics and dissemination Ethics approval is not required. We will disseminate findings through activities, including (1) presentations in national and international conferences; (2) meetings with national and international decision makers; (3) publications in peer-reviewed journals and (4) posts on organisational websites and social media.

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INTRODUCTION
Rationale

A significant proportion of children over 10 years of age suffer from back pain.[1–5] The prevalence of back pain in children ranges between 4% and 74%; the wide range is due to heterogeneous populations studied, outcome measurements and methodologies

used.[6 7] Data from the WHO Global Burden of Disease study in 2017 shows that low back pain is the leading cause of global years lived with disability.[8] Back pain begins early in life with physical, mental and social consequences (eg, impact on school-related and sporting activities, general physical activity and well-being) that extend into adulthood.[9–11] Most episodes of spinal pain are brief; however, in a 3-year prospective cohort study of 1465 school children in Denmark, up to 25% of children had three or more episodes over 1 year, and approximately 13% of children reported episodes lasting 5 or more weeks.[12]

Two recent systematic reviews assessed the effectiveness of manual therapy to treat a number of conditions including back pain in children, but low-quality evidence precludes drawing conclusions.[13 14] A previous systematic review and meta-analysis which evaluated the effectiveness of conservative interventions for low back pain in children under 18 years of age reported that exercise interventions may be promising for improving pain scores in children compared with no

treatment; however, the evidence was very limited and of low-quality.[15] This evidence also needs updating. Additionally, to our knowledge, no integrative systematic review—one that incorporates both quantitative and qualitative studies—has been conducted regarding the rehabilitative management of back pain in children. Compared with traditional systematic reviews of quantitative studies, combining evidence of the effectiveness and efficiency of interventions with qualitative understanding from people's lived experiences can better inform clinical practice guidelines and policy.[16]

This comprehensive knowledge synthesis can inform clinical practice for decision makers involved with caring for children with back pain including healthcare professionals in a variety of clinical, rehabilitation or community settings (eg, physicians, nurses, physiotherapists, chiropractors, psychologists, occupational therapists, registered massage therapists). Moreover, the knowledge gaps that we identify can inform future research agendas.

Objectives
To support clinical practice for children with back pain, we aim to conduct an integrative systematic review of quantitative, qualitative and economic evidence regarding the rehabilitative management of back pain (including mid-back and low back pain) in children aged 19 years and under. Our review will address the following questions:
1. What is the effectiveness and safety of rehabilitation interventions for improving functioning and other health outcomes in children with back pain?
2. What are the patients', caregivers' and providers' experiences, preferences, expectations and valued outcomes regarding rehabilitation interventions for back pain?
3. What is the cost–effectiveness of rehabilitation interventions for improving functioning and other health outcomes in children with back pain?
4. What can be hypothesised from the integration of the quantitative, qualitative and economic evidence about the effectiveness, cost–effectiveness and safety of rehabilitation interventions for low back pain in children?

We are targeting decision makers (clinicians, health managers/administrators, policy makers, patients and caregivers) involved in implementing, delivering or receiving rehabilitation interventions or programmes of care. We aim to provide them with knowledge regarding effective, acceptable and positively experienced interventions for children with back pain and their caregivers.

METHODS
We developed this systematic review protocol using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Protocols (PRISMA-P)[17] (see online supplemental additional file 1) and using methods already reported in detail elsewhere.[18] We registered our protocol on the International Prospective Register of Systematic Reviews (PROSPERO).[19] We will report our

systematic review according to the PRISMA statement,[20] and the Enhancing Transparency in Reporting the Synthesis of Qualitative Research reporting guideline.[21]

Eligibility criteria
Population
We will target studies including children (aged 19 years or younger)[22] with non-specific low back or thoracic spine pain of any duration and severity. We define low back pain as pain and discomfort below the costal margin and above the inferior gluteal folds, with or without radiculopathy (referred leg pain).[23] Radiculopathy refers to inflammation, injury/dysfunction or compression of spinal nerve roots that can present as pain, weakness or altered sensation in a myotomal or dermatomal distribution. Lumbar radiculopathy is commonly attributed to lumbar disc herniation (localised displacement of disc material beyond the normal margins of the intervertebral disc space).[24] We define thoracic spine pain as pain within the region bounded superiorly by the first thoracic spinous process, inferiorly by the last thoracic spinous process and laterally by the most lateral margins of the erector spinae muscles.[25] We will include studies investigating diagnoses including low back pain, mid-back pain, mechanical back pain, lumbago, lumbar sprain or strain, back sprain or strain, lumbopelvic pain, lumbar radiculopathy, lumbar disc herniation, sacroiliac syndrome, sciatica, dysplastic or isthmic spondylolisthesis or spondylolysis, musculoskeletal or non-specific chest wall pain (pain referred to the chest wall from the thoracic spine).

We will exclude studies of children with back pain attributed to major structural or systemic pathology (eg, fracture, acute traumatic or pathological spondylolisthesis or spondylolysis, infection, tumour, osteoporosis, inflammatory arthritides, cauda equina syndrome, neuromuscular disease, myelopathy and scoliosis); (2) studies of children with back pain attributed to a non-spine-related condition that might refer pain to the chest wall (eg, heart, lung or oesophagus conditions) and (3) studies that target asymptomatic children at baseline and assess interventions that aim to prevent the incidence of back pain.

Intervention
We will include studies that investigate the effectiveness and safety of rehabilitation interventions or programmes of care for children with back pain, including education and self-management strategies, exercise, manual therapies, passive physical modalities, acupuncture, pharmacological interventions, psychological interventions, environmental modifications, assistive devices and complementary therapies. Interventions may be delivered in any manner such as in-person, or remotely using technology such as telehealth. The WHO defines rehabilitation as a set of interventions that assist individuals who experience, or are likely to experience, disability to achieve and maintain optimal functioning when interacting with their environments (as described in detail

previously).[18] [26] Rehabilitation interventions include rehabilitation medicine/therapy, which aims to: (1) improve function through the diagnosis and treatment of health conditions, reducing impairments, preventing or treating complications and (2) restore and compensate the loss of functioning, and prevent or slow deterioration in functioning in every area of a person's life.[26] It may also include assistive devices, which refers to any item, piece of equipment or product used to increase, maintain or improve functional capabilities.[26] Various healthcare providers may provide interventions including, but not limited to, general practitioners, nurses, physiotherapists, chiropractors, occupational therapists, psychologists and registered massage therapists (table 1).[18] We will exclude studies assessing surgical interventions, and interventions solely conducted at the societal level, such as barrier removal initiatives (eg, fitting a ramp to a public building).

Comparison

The quantitative component of this review will consider comparisons, including other interventions, placebo or sham interventions, wait list, standard care and no intervention.

Outcomes

Our primary outcome of interest is a child's functioning. Secondary health outcomes of interest are pain (eg, pain intensity, frequency or duration), psychological outcomes (eg, anxiety and depression), health-related quality of life, adverse events, qualitative outcomes and economic outcomes (table 2). We are interested in both short-term (<3 months) and long-term (≥3 months) outcomes. We selected these outcomes because they are important to children, their caregivers and decision makers and they are reflected in the WHO's framework for health and disability (International Classification of Functioning, Disability and Health (ICF)) (as described in detail previously).[18] [27] The ICF provides a standard language and framework for the description of health and health-related states, and organises information into two components—'body functions and body structures' and 'activities and participation'.[27] Our primary outcome of interest, functioning, aligns with the 'activities and participation' component of the ICF. Examples of *activities* include walking, running, jumping and lifting. *Participation* refers to involvement in life situations such as with one's family, school and community. Common methods to measure *functioning* include the Modified Oswestry Low Back Pain Disability Questionnaire,[28] Roland Morris Disability Questionnaire,[29] return to school and participation in sports or other recreational activities. Pain and psychological outcomes fit within the 'body functions and body structures' component of the ICF. Common methods to measure *pain* include the Visual Analogue Scale (VAS),[30] Numerical Rating Scale (NRS),[31] and Faces Pain Scale—Revised.[32] [33] Common methods to measure *psychological outcomes* (eg, anxiety and depression) include

Revised Child Anxiety and Depression Scale[34] and State-Trait Anxiety Inventory for Children.[35] We will also assess *health-related quality of life*, which is not definable in the ICF framework.[36] It is commonly measured with the KIDSCREEN-52,[37] Pediatric Quality of Life Inventory[38] and Patient-Reported Outcomes Measurement Information System Pediatric Self Report Scale.[39] We defined *adverse events or harms* as any unfavourable sign, symptom, or disease temporarily associated with the treatment, whether or not caused by the treatment.[40] [41] We will consider indirect harms (where the use of an intervention delays a diagnosis or treatment, and such delay holds a potential harm),[42] number of adverse events, severity of adverse events (ie, mild, moderate or severe) and number of participant withdrawals from the study due to adverse events. *Qualitative outcomes* include the experiences, preferences, expectations and valued outcomes (of children, caregivers and providers). Lastly, *economic outcomes* include direct costs (eg, resources saved by an intervention), indirect costs (eg, time freed by an intervention), economic health outcomes (eg, quality-adjusted life-year, incremental cost–effectiveness ratio, net monetary benefit) and intangible outcomes (eg, pain or suffering saved by an intervention).

Types of studies

We will include randomised controlled trials of any type (eg, superiority, non-inferiority and equivalence), cohort studies, case–control studies and mixed-methods studies (quantitative component) including any secondary analyses of eligible studies for question 1 (effectiveness and safety of interventions); qualitative and mixed-methods studies (qualitative component) for question 2 (users' experiences, preferences, expectations and valued outcomes of interventions) and trial-based and model-based full economic evaluations for question 3 (cost–effectiveness of interventions) (table 2).

We will exclude the following types of studies: cross-sectional studies, pilot studies assessing feasibility, protocol studies, case reports, case series, studies assessing only prevention of back pain and incidence outcomes, systematic reviews (although their reference lists will be searched for potentially relevant studies) and other review papers, clinical practice guidelines, biomechanical studies, laboratory studies, cadaveric or animal studies, conceptual papers, letters, editorials, commentaries, books and book chapters, conference proceedings, meeting abstracts, lectures and addresses, consensus development statements, guideline statements and studies reviewing solely partial economic evaluations (eg, cost of illness studies).

Context and setting

We will consider rehabilitation interventions/programmes of care delivered in any healthcare system within an urban or rural area and in any healthcare setting (eg, acute care, hospital, primary healthcare, rehabilitation clinics), or in the community (as described in detail previously).[18] Community-based rehabilitation is implemented through

Table 1 Examples of rehabilitation interventions

Intervention	Definition	Examples
Patient or caregiver education and self-management strategies (structured or unstructured)	Teaching patients skills that they can use to manage their health condition	► Learning disease-specific information ► Learning general managing skills (eg, problem-solving, finding and using community resources, working with healthcare team) ► Learning strategies to increase confidence (ie, self-efficacy) in ability to engage in behaviours that are needed to manage their condition on a daily basis ► Adequate peer role models and support networks that facilitate the initiation and maintenance of desired behavioural changes
Exercise	A subcategory of physical activity that is planned, structured, repetitive and purposeful; can be supervised (eg, by a healthcare professional) or unsupervised	► Stretching ► Strengthening ► Range of motion exercises ► Aerobic (eg, swimming, cycling, walking, running) ► Anaerobic (eg, jumping, sprinting, weight lifting) ► Yoga, Qigong
Manual therapies	► Manipulation: Techniques incorporating a high-velocity low-amplitude impulse or thrust applied at or near the end of a joint's passive range of motion ► Mobilisation: Techniques incorporating a low-velocity and small or large amplitude oscillatory movement, within a joint's passive range of motion ► Traction: Manual or mechanically assisted application of an intermittent or continuous distractive force ► Soft tissue therapy: A mechanical form of therapy where soft-tissue structures are pressed and kneaded, using physical contact with the hand or mechanical device	► Lumbar manipulation, mobilisation or traction ► Massage ► Muscle energy technique ► Strain-counterstrain
Passive physical modalities	A form of cold, heat or light application affecting the body at the skin level or ultrasonic or electromagnetic radiation affecting structures beneath the skin surface: ► Passive assistive devices: Device to encourage immobilisation in anatomic positions or actively inhibit or prevent movement	► Heat application: heat pack, hydrotherapy ► Cryotherapy: cold pack, vapocoolant spray ► Low-level laser ► Electrical muscle stimulation ► Pulsed electromagnetic therapy
Acupuncture	Any body-needling, moxibustion, electric acupuncture, laser acupuncture, microsystem acupuncture and acupressure	► Traditional needling ► Dry needling ► Burning of specific herbs ► Electro-acupuncture ► Photo-acupuncture
Pharmacological interventions	A substance used in treating disease or relieving pain	► Acetaminophen ► Nonsteroidal anti-inflammatory drugs ► Muscle relaxants ► Antidepressants

Continued

Table 1 Continued

Intervention	Definition	Examples
Psychological interventions	Activities used to modify behaviour, emotional state or feelings	► Cognitive behavioural therapy ► Counselling ► Social network and environment-based therapies ► Psychoeducational interventions ► Mindfulness meditation
Modifications to environment		► Ergonomic interventions at school or work
Assistive devices	Any item, piece of equipment or product system, used to increase, maintain or improve the functional capabilities of people with disabilities	► Walking aids ► Orthoses ► Braces ► Wheelchairs
Complementary therapies	Medical products and practices that are not part of standard medical care	► Homeopathy ► Traditional Chinese Medicine ► Naturopathy ► Products (eg, herbs, dietary supplements, probiotics)

the combined efforts of individuals with disabilities, their families and communities and relevant government and non-government health, education, social and other services (eg, advocacy programme).[43]

Information sources

We will develop the initial search strategy in MEDLINE, in consultation with an experienced health sciences librarian. A second experienced health sciences librarian will review the search strategy assessing its appropriateness and comprehensiveness using the Peer Review of Electronic Search Strategies Checklist.[44 45] We will conduct electronic searches of the following databases from database inception to the present: MEDLINE (Ovid), Embase (Ovid), PsycINFO (Ovid), CINAHL (Cumulative Index to Nursing and Allied Health Literature, EBSCO*host*), the Index to Chiropractic Literature (Chiropractic Library Collaboration), the Cochrane Controlled Register of Trials (Ovid) and EconLit (EBSCO*host*). We will augment our search of the bibliographic electronic databases to identify additional relevant studies, and mitigate the potential impact of publication bias and selective outcome reporting bias.[46] We will search reference lists of included studies from the database searches and relevant systematic reviews; and we will consult with content experts. We will ask experts to suggest up to three targeted websites that may contain relevant studies and other potentially relevant studies not captured by our search strategy. Lastly, we will search the WHO International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/). For studies only reported in the registry, we will contact first authors by email (with two reminders over 1 month) to obtain full study reports, or additional study or outcome data. We will include studies in any language and will use professional medical translation services where required. If 12 or more months elapse between the search date and submission for publication, we will update the search.

Search strategy

The searches will include a combination of subject headings specific to databases (eg, MeSH in MEDLINE) and free text words to capture the key concepts of rehabilitative management of back pain in children (see online supplemental additional file 2).

Patient and public involvement

Patients were not involved in the design of our study. However, we will seek patient and public consultation during the development of clinical practice guidelines, which will be the next phase of this project.

Data management

We will download the electronic search results into EndNote V.X9 reference manager software (Clarivate Analytics, Pennsylvania, USA). We will remove duplicates and upload the remaining references to the Evidence for Policy and Practice Information and Coordinating (EPPI) Centre Reviewer software for the data extraction stages (EPPI-Reviewer V.4, UCL Institute of Education, University of London, UK). EPPI-Reviewer software stores references, manages and monitors the data extraction process and provides an audit trail for the review.[47]

Screening for eligibility

Using the inclusion and exclusion criteria, pairs of reviewers will independently screen titles and abstracts, and subsequently the full text of each selected article in order to confirm inclusion into the study (as described in

Table 2 Research questions, outcomes and study types

Research question	Outcomes	Study types
What is the effectiveness and safety of rehabilitation interventions for improving functioning and other health outcomes in children with back pain?	Primary 1. Functioning: for example, Modified Oswestry Low Back Pain Disability Questionnaire, Roland Morris Disability Questionnaire, return to school, participation in sports/other recreational activities	Randomised controlled trials
	Secondary	Cohort studies
	2. Pain (including pain intensity, frequency, duration): for example, VAS, NRS, Faces Pain Scale—Revised	Case–control studies
	3. Psychological outcomes (including anxiety and depression): for example, Revised Child Anxiety and Depression Scale, State-Trait Anxiety Inventory for Children	Mixed-methods studies (quantitative component)
	4. Health-related quality of life: for example, KIDSCREEN-52, Pediatric Quality of Life Inventory, PROMIS Pediatric Self Report Scale	
	5. Adverse events: any unfavourable sign, symptom, or disease temporarily associated with treatment, indirect harms (eg, delayed diagnosis/treatment), number of adverse events, severity of adverse events (ie, mild, moderate, severe), number of participant withdrawals from study due to adverse events.	
What are the patients', caregivers' and providers' experiences, preferences, expectations and valued outcomes regarding rehabilitation interventions for back pain?	6. Qualitative outcomes: experiences, preferences, expectations, valued outcomes	Qualitative studies (eg, phenomenology, grounded theory, ethnography, action research, descriptive qualitative studies)
		Mixed-methods studies (qualitative component)
What is the cost–effectiveness of rehabilitation interventions for improving functioning and other health outcomes in children with back pain?	7. Economic outcomes	Full economic evaluations (trial-based and model-based): cost–effectiveness, cost–utility, cost–benefit, cost–consequences
	Direct costs: resources consumed or saved by an intervention	
	Indirect costs: productivity gains or losses (eg, time consumed or freed by the intervention)	
	Economic health outcomes: QALY, ICER, NMB	
	Intangible: for example, pain or suffering saved or brought on by an intervention	

ICER, incremental cost–effectiveness ratio; NMB, measure of net monetary benefit; NRS, Numerical Rating Scale; PROMIS, patient-reported outcomes measurement information system; QALY, quality adjusted life years; VAS, Visual Analogue Scale.

detail previously).[18] Titles and abstracts will be classified as possibly relevant or irrelevant. Subsequently, full-text articles of abstracts classified as possibly relevant will be retrieved, reviewed and classified as relevant or irrelevant.

We will conduct training exercises prior to initiating the screening process to ensure reliability between reviewers. Reviewers will first screen a random sample of 50 records based on titles and abstracts. Paired reviewers must reach 90% agreement before completing title and abstract screening for the remaining studies.[48] If this threshold is not reached for all review teams, all team members will discuss differences in classification to clarify and potentially modify the eligibility criteria prior to completing title and abstract screening. Next, reviewers will screen a random sample of 25 full-text articles. All paired reviewers must again reach 90% agreement before completing full-text article screening for the remaining studies. If not, all team members will discuss to clarify eligibility criteria and resolve disagreements prior to completing full-text article screening. On completing full-text article screening, paired reviewers will discuss disagreements and reach consensus related

to the inclusion of any article, involving a third reviewer if necessary.

Risk of bias in individual studies

We will critically appraise studies according to study design using appropriate checklists (see online supplemental additional file 3) (as described in detail previously).[18] We will assess the quality of studies using the Scottish Intercollegiate Guidelines Network (SIGN) criteria for randomised controlled trials (RCTs), cohort and case–control studies[49]; the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for qualitative studies[50]; the Mixed Methods Appraisal Tool (MMAT) for mixed-methods studies[51] and the Drummond checklist for economic evaluations.[52] The SIGN checklists allow reviewers to assess internal validity by considering the impact of selection bias, information bias and confounding on study results. The JBI checklist allows reviewers to assess the possibility of bias in qualitative studies' design, conduct and analysis. The MMAT allows reviewers to assess the interdependent qualitative and quantitative components of the study and criteria to consider, such as justification for mixing evidence, and appropriate ways of integrating the data. The Drummond checklist allows reviewers to identify elements that demonstrate a sound economic evaluation such as the assessment of both costs and effects of interventions, accurate measurements of costs and effects and allowances made for uncertainty in the estimates of costs and effects. We will contact the authors of papers to request missing or additional data for clarification where required. Paired reviewers will independently assess the eligible studies for quality. Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer. Since some of the reviewers have published within this area, the review coordinator will ensure that reviewers will not be assigned their own studies for risk of bias assessment. Additionally, reviewers will recluse themselves from any discussion and decision-making that involves their paper. We will clearly describe this in our final systematic review report.

Using these established checklists and notes to guide our assessment, we will categorise the validity or credibility of each study as either high, low, or unclear risk of bias. We will not use a quantitative cut-off score to determine study quality and will not pre-define weights for the checklist items. Rather, we will make an overall quality judgement by considering the impact of selection bias, information bias and confounding on study results throughout the conduct of each study.[53] We will report detailed results of the critical appraisal in a narrative form and in a 'risk of bias' table. All studies, regardless of their methodological quality, will be extracted and synthesised (where possible). The overall methodological quality of relevant studies will be considered in the individual synthesis of quantitative, qualitative and economic data and the integration of these findings. The results of the risk of bias assessment will be used in a sensitivity analysis to ensure that studies judged to be at 'high risk of bias' do not affect the robustness of our results.

Data items and data extraction process

Paired reviewers will independently extract the data from all eligible studies. For the quantitative studies, we will extract data on the study and participant characteristics; intervention and comparator intervention characteristics using the Template for Intervention Description and Replication (TIDieR) checklist[54]; all pre-determined outcomes including multiple measures if used; key findings; and methodological quality. The TIDieR checklist[54] consists of items to help readers better understand the interventions and how they were delivered (ie, name of intervention, why, what (materials), what (procedure), who provided, how, where, when and how much, tailoring, modifications, how well (planned), how well (actual)).[54] We will use the PerSPEcTIF question formulation framework to guide data extraction for the qualitative studies regarding the items: perspective, setting, phenomenon of interest, environment, timing and findings (eg, themes).[55] We will also extract data describing the qualitative approach used and methodological quality of studies. For both quantitative and qualitative studies, we will extract data on the ICF categories 'environmental factors' (contextual factors that make up the physical, social and attitudinal environment in which people live and conduct their lives) and 'personal factors' (internal contextual factors that influence how disability is experienced by the individual) to add context to the interventions and outcomes.[27] For the economic evaluations, we will use the Consolidated Health Economic Evaluation Reporting Standards statement[56] and extract data on the analytic approach (trial-based or model-based), evaluation type, the analytic perspective, time horizon adopted for costs, main cost items, setting, key findings and methodological quality of studies.

Paired reviewers will pretest the data extraction form and revise as needed. We will use EPPI-Reviewer software to manage the data extraction process. Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer. We will contact authors of papers to request missing or additional data, if required.

DATA SYNTHESIS

We will use a sequential approach at the review level to synthesise and integrate the data (as described in detail previously).[18 57] This will involve separate quantitative, economic and qualitative findings synthesis followed by integration of the resultant quantitative, economic and qualitative evidence.

Quantitative synthesis

We will stratify studies to conduct separate comparisons according to study design, population, intervention, comparison, outcome and methodological quality and

Table 3 Categories to guide the analysis (meta-analysis or qualitative synthesis)

Study design	Primary synthesis: Design: RCTs vs non-RCTs (ie, cohort, case–control) Subgroup analysis: Specific RCT: for example, superiority, non-inferiority or equivalence
Population	Primary synthesis: Pain duration: acute/subacute pain (ie, <12 weeks' duration) vs persistent pain (≥12 weeks' duration) Age range: infants (aged<1 year), children (aged 1–9 years), or adolescents (aged 10–19 years) Type of back pain: thoracic spine pain with/without radiculopathy, low back pain with/without radiculopathy, musculoskeletal chest wall pain, spondylolisthesis/spondylolysis Subgroup analysis: Pain severity: mild, moderate or severe
Intervention	Primary synthesis: Intervention type: education/self-management strategies, manual therapy, passive physical modalities, acupuncture, pharmacological intervention, psychological intervention, multimodal care, environmental modifications, assistive devices and complementary medicine Subgroup analysis: Specific intervention type: for example, type of exercise (eg, stretching vs aerobic) and type of manual therapy (eg, mobilisation, manipulation, traction, soft tissue therapy)
Comparison	Primary synthesis: Comparator type: active (other intervention) vs inactive (eg, placebo/sham intervention, wait list, standard or usual care, or no intervention)
Outcome	Primary synthesis: Outcome type: functioning (eg, ODI, RMDQ), pain (eg, VAS, NRS), psychological (eg, Revised Child Anxiety and Depression Scale), health-related quality of life (eg, KIDSCREEN-52), or adverse events (eg, number, severity) Time of outcome assessment: short-term (<3 months) or long-term (≥3 months) Type of effect estimate:* for example, mean difference, relative risk, OR, or HR
Methodological quality	Primary synthesis: Methodological quality assessment: low or unclear risk of bias Sensitivity analysis: low, unclear and high risk of bias

*If data are unavailable to re-express effect estimates into a common effect estimate (if applicable).
NRS, Numerical Rating Scale; RCTs, randomised controlled trials; RMDQ, Roland Morris Disability Questionnaire; VAS, Visual Analogue Scale.

further conduct subgroup analyses within categories (table 3). Specifically, we will stratify results to conduct separate comparisons between RCTs versus non-RCTs targeting, for example, children with acute low back pain without radiculopathy, treated with a specific intervention (eg, manual therapy) compared with an active comparison, and assessed by the mean difference in functioning score (eg, Oswestry Disability Index score) at 3 months.

We will assess clinical, methodological and statistical heterogeneity among studies (as described in detail previously).[18] Differences in populations, interventions, comparators or outcomes across studies may result in clinical heterogeneity. Methodological and statistical heterogeneity may result from differences in risk of bias and differences in outcomes across studies beyond what could be expected by chance alone. We will assess the methodological heterogeneity across studies using our assessments from the SIGN checklist as either high, low, or unclear risk of bias. We will assess statistical heterogeneity using the I^2 statistic, whereby I^2 of <25%–50% will be considered low to moderate (homogeneous), and ≥50% considered high (heterogeneous).[58] If two or more studies are clinically homogeneous (ie, similar populations, interventions, comparators and outcomes) and statistically homogeneous (ie, I^2 <25%–50%), we will perform a random effects meta-analysis using EPPI-Reviewer software using the relative risk (or OR for rare events) effect measure for dichotomous data, mean differences for continuous data, hazard rate ratios for time-to-event data and rates or rate ratios for count data. For studies that used multiple measures to assess the same outcome and at multiple time points, we will select the most prevalent measure and time point used across the studies to maximise the comparability of the findings. We will attempt to summarise the results in a similar way if possible. We will contact study investigators to obtain the data if it is not reported. If the data are unavailable, we will summarise the data in three ways: by entering the means as continuous outcomes, the counts as dichotomous outcomes and by entering all of the data in text form as 'other data' outcomes.[59] We may also use statistical approaches to re-express ORs as standardised mean differences (and vice versa), allowing us to combine dichotomous and continuous data.[59] For our primary analysis, we will analyse the studies with low and unclear risk of bias. We will then explore the impact of methodological heterogeneity through sensitivity analysis by analysing all studies together, including those with a high risk of bias, and comparing our primary analysis with our sensitivity analysis. If the results of the primary and sensitivity analyses differ, we will give precedence to the primary analysis because high risk of bias studies are known to be at risk of overestimating effect sizes.[60]

If the studies are heterogeneous (ie, if there is clinical, methodological and statistical heterogeneity), we will narratively summarise the characteristics and findings of all eligible studies according to the Synthesis Without Meta-analysis reporting guideline.[61] To quantify the effectiveness of interventions, we will use the data provided in the studies to compute effect measures and 95% CIs (ie, OR or relative risk for dichotomous outcomes, mean differences for continuous outcomes, hazard rate ratios

for time-to-event outcomes and rates or rate ratios for count outcomes).[62]

We will assess the potential impact of reporting biases on the results of our review or meta-analysis by attempting to identify study protocols through the trials registry (WHO International Clinical Trials Registry Platform http://apps.who.int/trialsearch/), and through the use of funnel plots. After studies are stratified (table 3), outcomes that are reported in at least 10 studies will be assessed for publication bias by visually inspecting funnel plots for asymmetry.[63 64]

We will interpret the quality of the evidence for each outcome according to the Grading Recommendations Assessment, Development and Evaluation system (GRADE).[65] The quality of evidence ratings are *very low* (ie, the true effect is probably markedly different from the estimated effect), *low* (ie, the true effect might be markedly different from the estimated effect), *moderate* (ie, the true effect is probably close to the estimated effect) and *high* (highly confident that the true effect is similar to the estimated effect). Assessment of the quality of the evidence is determined by considering the risk of bias, inconsistency, indirectness, imprecision and publication bias. We will use established minimal clinically important differences to determine the clinical importance of effect sizes when possible. Similar to any meta-analysis we may conduct, we will give precedence to the primary analysis consisting of studies with low and unclear risk of bias.

Economic synthesis
We will report the main findings of economic studies, first stratified by high, low or unclear risk of bias. We will further stratify findings by study design (ie, cost–effectiveness, cost–utility, cost–benefit or cost–consequences). We will then stratify findings by type of intervention, outcome and cost measure.

To indicate whether an intervention might be judged favourably (or unfavourably) from an economic perspective,[66] we will use the Dominance Ranking Matrix to classify the interventions into one of three options.[67] *Strong dominance* for the intervention will be selected when the incremental cost–effectiveness measure shows the intervention as: (1) more effective and less costly than the comparator; or (2) effective and less costly; or (3) equal cost and more effective. In this case, from an efficiency perspective, decision makers should favour the intervention over the comparator (in circumstances similar to those of the evaluations). *Weak dominance* for the intervention will be selected when the measure shows the interventions as: (1) equally costly and effective as the comparator; or (2) more effective and more costly; or (3) less effective and less costly. In this case, no conclusion may be drawn about whether the intervention is preferable from an efficiency perspective without further information on the priorities or preferences of decision makers in a particular context. Decision makers must determine whether the cost/benefit trade-offs are worth the implementation of an intervention in their particular context. Lastly, *non-dominance* for the intervention will be selected when the measure shows the intervention as: (1) more costly and less effective; or (2) equally as costly and less effective; or (3) more costly and as effective. In this case, we will interpret the evidence as suggesting the comparator is favourable from an efficiency perspective (in circumstances similar to those of the evaluations).

Qualitative synthesis
We will stratify the qualitative findings similar to the quantitative and economic findings. We will first stratify the findings by risk of bias (ie, high/low/unclear), then by study approach or design (eg, qualitative descriptive, ethnography, grounded theory) and by intervention type and outcome.

Additionally, we will stratify findings according to individual perspective (ie, patient (children), caregivers (parents/guardians), healthcare providers, community service providers or others involved with the rehabilitation of back pain in children). We will use thematic synthesis to synthesise the qualitative research findings.[68 69] First, we will enter all the text labelled as 'results' or 'findings' of the primary studies verbatim into EPPI-Reviewer. Then, pairs of trained reviewers will independently code each line of text according to its meaning and content, and group codes hierarchically into descriptive themes, including the *a priori* themes (intervention type and outcomes). Reviewers will also generate themes *a posteriori* to answer our review question (ie, experiences, preferences, expectations and valued outcomes regarding rehabilitation interventions for back pain in children). Reviewers will finalise the themes through discussion. We will give precedence to studies with low or unclear risk of bias.[70]

Integration of quantitative, qualitative and economic evidence
Various methods can be used to integrate diverse study types including: (1) juxtaposing findings in a matrix, (2) using logic models/conceptual framework, (3) analysing programme theory, (4) testing hypothesis derived using subgroup analysis and (5) qualitative comparative analysis.[57] We will integrate the evidence by juxtaposing findings in a matrix to generate hypotheses regarding the effectiveness, cost–effectiveness and safety of rehabilitation interventions for back pain in children. We selected this methodology because it is suitable for comparing and contrasting the findings across the individual quantitative, qualitative and economic evidence syntheses in our review.[57] The use of a matrix will allow us to explore heterogeneity in the findings of the quantitative studies and may indicate why some interventions may be effective, cost-effective and safe and some may not.[57] For example, we may list themes from the qualitative synthesis along one side of the matrix, and then plot the interventions evaluated in the quantitative synthesis against the themes as either a match (when the intervention matched a theme) or a mismatch (when the intervention was the opposite of a theme) (as described in detail previously).[18] We will also

plot the economic evaluation findings against the corresponding intervention and theme. We will identify gaps in knowledge if a particular theme for an intervention does not match with any of the interventions evaluated in the quantitative studies.

ETHICS AND DISSEMINATION

Ethics approval is not required for this mixed studies review. Knowledge translation activities will include presentations to clinicians and researchers at national and international conferences; meetings with national and international decision makers (clinicians, health managers/administrators, policy makers and patients); publications in peer-reviewed journals; clinician and patient/caregiver resources; posts and lay language summaries on organisations' websites (open access) and other social media platforms.

DISCUSSION

Findings from this mixed studies review will advance our knowledge of the effectiveness, safety, user experience and cost–effectiveness of a wide range of rehabilitation interventions for children with back pain. This work will provide the evidentiary basis to develop clinical practice guidelines and care pathways outlining the evidence-based management of back pain in children, which can be adapted for specific settings (eg, hospitals, rehabilitation clinics and schools) and geographical regions. Specifically, decision makers should consider interventions that are identified as effective, safe, efficient and positively experienced by patients and caregivers. Mapping findings to the ICF framework will allow decision makers to use standardised language in the assessment and management of children during their care programme. This may further facilitate improvements in functioning and health outcomes in this patient population.

A potential limitation of our review is that our search strategy may miss potentially relevant studies, however, we have mitigated this by expanding our search strategy to include content experts and searching relevant websites. A potential risk is that there may be too little evidence available to answer our review questions.

Findings from this review will guide future research by identifying methodological limitations and knowledge gaps in the available literature. Future studies can be designed to address these limitations and gaps. This novel interpretation of quantitative, qualitative and economic evidence according to the ICF framework serves as a model for how outcomes related to functioning and health can be prioritised in future research.

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