Mapping the evidence and gaps of interventions for pediatric chronic pain to inform policy, research, and practice: A systematic review and quality assessment of systematic reviews

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ABSTRACT

Background: Reviews in pediatric chronic pain often focus on only one intervention or population, making it difficult for policymakers and decision makers to quickly synthesize knowledge to inform larger-scale policy and funding priorities.

Aims: The aims of this study were to (1) create an evidence and gap map of interventions for pediatric chronic pain and (2) identify gaps between existing evidence and recently identified patient-oriented research priorities.

Methods: We performed a systematic review of English-language peer-reviewed systematic reviews or clinical practice guidelines of pediatric chronic pain intervention published in the past 20 years. Database searches of Medline, Embase, PsycINFO, Web of Science, CINAHL, and SCOPUS were conducted inclusive to June 3, 2019. Review quality was assessed using the AMSTAR-2.

Results: Of 4168 unique abstracts, 50 systematic reviews (including 2 clinical practice guidelines) were included. One third were rated high quality, with half rated low to critically low quality. The largest proportion of reviews addressed psychological and pharmacological interventions, followed by interdisciplinary, other (e.g., dietary), and physical interventions. Most common outcomes included pain, physical, emotional, and role functioning and quality of life. Treatment satisfaction and adverse events were less common, with minimal report of sleep or economic factors. Most patient-oriented research priorities had not been investigated.

Conclusions: Sufficient quality evidence is available to guide evidence-informed policies in pediatric chronic pain, most notably regarding psychological and pharmacological interventions. Numerous evidence gaps in patient-oriented research priorities and treatment outcomes should guide prioritization of research funds, as well as study aims and design.

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ARTICLE HISTORY
Received 18 February 2020
Revised 9 April 2020
Accepted 15 April 2020

KEYWORDS
pediatric; chronic pain; treatment; systematic review; policy; knowledge translation; evidence map

Accepted 15 April 2020

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Chronic pain is a leading cause of disability and morbidity for children and adults. Despite this, chronic pain was only recently recognized as its own disease through the inclusion of new chronic pain diagnostic codes in the World Health Organization’s International Classification of Diseases, 11th revision, in 2018. The classification of chronic primary pain as a disease in its own right facilitates the progress of large-scale national policies to improve chronic pain management across the life span, many of which are underway in countries around the world. Furthermore, an evidence-based policy focus on improved chronic pain management is critical alongside policy efforts to address the opioid epidemic.

The development of effective health policies is informed by both scientific evidence and stakeholder experience to ensure relevance and tailored implementation to the local context. Our group recently completed a national priority-setting partnership that engaged people with lived experience with pediatric chronic pain, family members, and treating health care providers across Canada to identify the top priorities for pediatric chronic pain research and care. The final top ten identified patient-oriented priorities direct the need for more evidence on prevention and treatment, as well as an improved understanding of the impact of pediatric chronic pain, delivery, access to care, and coordination of care. On its own, this priority-setting work provides a guided call to action for policymakers, decision makers, and researchers—from basic science to clinical research to health systems design—to address identified patient-oriented priorities; however, the uptake of these priorities may be limited by a lack of information about what research already exists in these areas. Current systematic reviews in pediatric chronic pain are often very niche and focus on one type of intervention. This makes it difficult for policymakers and decision makers to quickly synthesize knowledge across a variety of intervention modalities to inform clinical practice policy and research funding priorities. This is problematic given the current recommendation for multimodal care to thoroughly address biopsychosocial contributors to pediatric chronic pain.

Although pediatric pain research is growing rapidly, there remains a disconnect between existing scientific evidence and current clinical practice, a further challenge to developing pediatric chronic pain policy. Estimates suggest that it can take up to 17 years for research to impact patient care, and many children and adolescents with chronic pain struggle to access evidence-based treatment. There is an identified need for more effectual and efficient knowledge mobilization in pediatric pain. The availability of high-quality evidence synthesis is a key step in the process of moving generated scientific knowledge into sustainable action, as outlined in the knowledge-to-action framework. Evidence and gap maps have emerged as an effective knowledge translation evidence synthesis tool to inform evidence-informed policymaking and the development of strategic research agendas. Like other evidence synthesis methods, such as a Cochrane reviews, evidence and gap maps are rigorous in their search for and assessment of research evidence; however, they differ in their primary goal, which is to review the breadth and quality of available evidence compared to determining the efficacy of single specific interventions. This shift in focus facilitates the strategic identification of key gaps where little or no evidence exists or areas currently with only poor quality research. The use of schematic visual representation of findings in evidence and gap maps also makes research evidence more easily accessible and usable to researchers and decision makers.

Our primary goal was to create a contemporary evidence and gap map of systematic reviews of all interventions for pediatric chronic pain. Our secondary aim was to identify gaps between existing evidence and recently identified patient-oriented research priorities for pediatric chronic pain. Given that many pediatric chronic pain interventions have limited evidence, we expected many priority areas to be lacking high-quality research evidence.
Methods

Protocol and Registration

This review adheres to PRISMA reporting guidelines for systematic reviews. A protocol was registered for this review in February 2018 on PROSPERO: CRD42018086817. The current review presents a minor modification from our original review protocol that outlines our initial intent to conduct a traditional overview of systematic reviews. The decision to modify the current review to an evidence and gap map was made following consultation with an international expert in evidence-informed health policy (Dr. John Lavis, personal communication, April 17, 2019) and in response to emerging national chronic pain policy efforts through the development of the Government of Canada’s Canadian Pain Task Force. It was felt that an evidence and gap map would better achieve our primary goal of uptake of evidence and patient priorities by policymakers and decision makers and identify clear gaps to guide research efforts in key areas identified by patients and clinicians as priorities.

Evidence and gap maps provide an overview of the availability and quality of evidence of a sector, in this case interventions for pediatric chronic pain. Recommended evidence and gap map methodology includes completion of six primary steps: development of scope, inclusion criteria, systematic review of the literature, data extraction, analysis, and visualization. Evidence and gap maps are underpinned by a rigor similar to that of other systematic review methodology. As such, reporting of the evidence and gap map methods in this article adhere to the PRISMA statement for reporting of systematic reviews and meta-analyses. The current review adheres to our original protocol with regards to the stated review question, search strategy, type of study, participants/population, interventions, risk of bias/quality assessment, narrative synthesis, and report by type of intervention modality. The current review diverges only from that outlined in our original protocol in that the current review now is restricted to publications within the past 20 years (since 1999), no longer extracts specific efficacy findings for intervention outcomes, and does not conduct subgroup analyses by type of chronic pain condition; additionally, the review now includes an evidence and gap map.

A completed evidence and gap map provides a simple and accessible visual summary of existing systematic review evidence for various types of interventions in pediatric chronic pain across selected outcome domains. The rows of the evidence and gap map list the types of interventions and the columns list the outcome domains. Each cell shows the number and quality of systematic reviews that contain evidence on that combination of intervention and outcome domain. In doing so, evidence and gap maps identify areas where little or no evidence exists (“absolute gaps”) and areas where there is systematic review evidence is available but is either out of date and/or of poor quality (“synthesis gaps”). Evidence and gap maps can be used to inform strategic research investment by highlighting intervention and outcome areas where new primary studies and/or systematic reviews can add value. They can also be used to inform decision making by capturing best available evidence that can then be compared against existing policy or programming to inform discussions about areas of prioritizing future research, policy, or investment.

Eligibility Criteria

Papers were eligible for inclusion if they

1. were peer-reviewed published systematic review or clinical practice guidelines;
2. were published in English;
3. included at least 50% or more reviewed studies focused on children or adolescents ≤18 years old or reported findings from pediatric studies separately;
4. included randomized and nonrandomized studies focused on any intervention for any type of chronic pain (defined as pain lasting at least 3 months or longer and/or pain described as “chronic,” “recurrent,” or “persistent”); and
5. reported on at least one primary or secondary outcome included in PedIMMPACT recommended for clinical trials in pediatric chronic pain (that is, pain intensity, physical functioning, emotional functioning, role functioning, quality of life, sleep, global treatment satisfaction, economic factors, and/or adverse events).

Systematic reviews were excluded if they focused exclusively on chronic pain diagnosis or assessment and/or only reported prevalence. Prior iterations of eligible reviews were also excluded, as well as reviews/clinical practice guidelines published >20 years ago, given the availability of more current up-to-date evidence. Reviews including any type of intervention study design were included given recognized difficulty in conducting randomized controlled trials (RCTs) for some intervention modalities in pediatric populations (e.g., pharmacological) and given that interventions needed to
address identified patient-oriented research priorities may not lend themselves easily to randomized study designs (e.g., school-based interventions).

Given variability in evidence synthesis methodology, requirements for being defined as a systematic review and/or clinical practice guideline were drawn from those used by the James Lind Alliance. Thus, a systematic review was defined as a review that attempts to identify, appraise, and synthesize all of the empirical evidence that meets prespecified eligibility criteria to answer a given research question. Therefore, a systematic review typically states identifies a research question, provides search terms, searches multiple scientific databases, and reviews titles, abstracts, and full-text publications against some identified inclusion criteria. Clinical practice guidelines are clearly defined as such and include a systematic review to inform development of the guidelines. If multiple iterations or updates of the same systematic review or clinical practice guideline were found and identified as such, only the most recently published version of the systematic review or clinical practice guideline meeting the eligibility criteria was reviewed to reflect the most up-to-date evidence.

**Search Strategy and Conduct**

Searches were conducted in Medline, Embase, PsycINFO, Web of Science, CINAHL, and SCOPUS from database inception to June 3, 2019. Database search strategies were developed in collaboration with a pediatric medical librarian and experts in pediatric chronic pain care and research. A sample comprehensive search strategy for Medline is available in Supplementary Online Material 1.

**Study Selection**

Database search results were imported into Covidence for study selection. Initial abstract screening was conducted independently by two review authors (K.A.B. and T.D.A.), and full-text screening was independently performed by two review authors (C.O. and T.D.A.), with conflicts resolved by a third author (K.A.B.).

**Data Extraction and Quality Ratings**

Data were independently extracted by two review authors (K.A.B. and T.D.A.). Extracted data items included review sponsor (country, author, primary review objective, inclusion/exclusion criteria, date of literature search, inclusion of meta-analysis, types of reviewed studies (RCT or nonrandomized study [NRS]), total number of reviewed studies, number of reviewed studies focused on pediatric chronic pain intervention, population of reviewed studies (type of chronic pain/disease), setting of reviewed studies (e.g., outpatient, inpatient, emergency, etc.), type of intervention (pharmacological, psychological, physical, interdisciplinatory, other), comparator groups, inclusion of quality of evidence rating, inclusion of PedMMPACT recommended outcomes (pain intensity, physical functioning [e.g., mobility, disability], emotional functioning [e.g., anxiety, depression], role functioning [e.g., school attendance], quality of life, sleep, global treatment satisfaction, economic factors [e.g., cost, health care utilization, parent missed workdays], and/or adverse events), and time of outcome assessments.

When eligible systematic reviews included nonrelevant data (that is, pertaining to adults and/or nonchronic pain pediatric samples), only data relevant to reviewed studies focused on pediatric chronic pain were extracted. Supplementary material was accessed to inform data extraction and quality assessment if cited in published eligible systematic reviews. Separately reported systematic reviews that informed eligible clinical practice guidelines were accessed online (published and unpublished) and informed data extraction and quality assessment.

Risk of bias/quality of assessment of all eligible systematic reviews was conducted using the AMSTAR-2. The AMSTAR-2 critical appraisal tool includes 16 items that are rated to assess the quality of systematic reviews that include randomized or nonrandomized studies of health care interventions or both. Items address the review’s reporting of review criteria including elements of PICO (Population, Intervention, Comparator group, and Outcome), a priori review protocol registration, justification of study design selection, adequacy of literature search, study selection and data extraction in duplicate, justification for excluding individual studies, adequate description of included studies, risk of bias from individual studies included in the review, report of funding of included studies, appropriateness of meta-analytical methods (if applicable), consideration of risk of bias when interpreting the review results, and assessment and likely impact of publication bias (italics denote critical domains). Quality assessments for all eligible systematic reviews were rated independently by two authors (K.A.B. and C.O.), with disagreements resolved by consensus. Each systematic review was summarized by an single overall quality rating reflecting confidence in the results of review. Overall quality ratings are described as follows:

- **High**: No or one noncritical weakness; the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest.
- **Moderate**: More than one noncritical weakness; the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review.

- **Low**: One critical flaw with or without noncritical weaknesses; the systematic review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest.

- **Critically Low**: More than one critical flaw with or without noncritical weaknesses; the systematic review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.

Eligible systematic reviews and clinical practice guidelines were also independently coded by two authors (K.A. B. and C.O.) for relevance to each of the top ten patient-oriented research priorities for pediatric chronic pain identified in the Partnering For Pain priority-setting partnership. In brief, Partnering For Pain engaged hundreds of diverse Canadians with lived experience with pediatric chronic pain, family members, and multidisciplinary health care providers across four priority setting phases using the James Lind Alliance Priority Setting Partnership methodology. The James Lind Alliance methodology is recognized as being robust, strategic, objectively based and inclusive, and promoting equity in patient voices. In phase 1, 215 Canadians (86 patients [40.0%], 56 family members [26.0%], and 73 health care providers [34.0%]) submitted 540 potential priorities that were developed into 112 unique research questions (phase 2). Of the 112 questions, 63 were rated for importance by 57 participants (19 patients [33%], 17 family members [30%], and 21 health care providers [37%]) in phase 3. In phase 4, 20 participants (6 patients [30%], 6 family members [30%], and 8 health care providers [40%]) discussed the 25 most highly rated questions and reached consensus on the final top ten. The participant group was diverse with regards to age, sex, ethnicity, geographic location, chronic pain condition, care setting, and health care profession. A thorough discussion about the rationale, methodology, findings, and limitations of the Partnering For Pain priority-setting partnership is available in our previous peer-reviewed publication.

**Results**

**Study Selection**

Database searches identified 5077 records. After duplicates were removed, 4168 unique abstracts remained for review. Of these, 3897 were deemed not eligible. A total of 261 full texts were reviewed and 211 were excluded. Fifty full texts met inclusion criteria. See Figure 1 for the PRISMA review flowchart, including reasons for full-text exclusion.

**Study Characteristics**

Of the 50 full texts meeting review inclusion criteria, 2 reported a related systematic review and clinical practice guideline for pediatric chronic abdominal pain and 2 reported a related systematic review and clinical practice guideline for pediatric chronic widespread pain. Data extraction and quality assessment were combined for each pair of related systematic reviews and clinical practice guidelines. One additional paper was a summary of 3 other included systematic reviews. Data extraction and quality ratings were not conducted for the summary review because information was obtained from the original included systematic reviews. Thus, data and quality ratings are reported for 47 unique reviews/clinical practice guidelines. Of these, 24 (51.6%) included meta-analyses. Almost half of the reviews reported no funding or sponsorship (n = 22; 46.8%). See Tables 1 and 2 for characteristics and outcomes for each included review.

**Types of Populations**

Most reviews (n = 19; 40.4%) included variations of mixed chronic pain populations (e.g., abdominal pain, headaches or migraines, widespread pain/fibromyalgia, complex regional pain syndrome, neuropathic pain, sickle cell disease, cancer pain, back pain, and/or pelvic pain). Reviews focused on single populations most frequently examined abdominal pain (n = 10; 21.3%), headaches or migraines (n = 5; 10.6%), rheumatological conditions (e.g., juvenile idiopathic arthritis, lupus; n = 4; 8.5%), cancer-related pain (n = 3; 6.4%), cerebellar palsy (n = 1; 2.1%), endometriosis (n = 1; 2.1%), or joint hypermobility/ Ehlers-Danlos/osteogenesis imperfecta (n = 1; 2.1%).

Reviews included children 2–18 years old. Most reviews included studies crossing childhood and adolescence (n = 45; 95.7%), with two reviews (4.3%) focused on adolescents (>12–18 years old). Five reviews also included studies with adults (>18 years old).

**Types of Settings**

Reviews included studies conducted in a variety of settings, including primarily tertiary care or hospital settings (inpatient, day treatment, outpatient clinics,
and emergency departments), followed by primary care or community-based clinics and, rarely, schools. Three reviews (6.4%) focused exclusively on “e-health” or remotely delivered interventions.\textsuperscript{47,56,75} The setting was not clearly reported in 12 (25.5%) reviews.

**Types of Studies Included**

The majority of reviews exclusively included RCTs or reviews of RCTs ($n = 26$; 55.3%). The remaining reviews included a variety of study designs, including nonrandomized intervention studies, cohort or observational studies, retrospective chart reviews, and case studies or case series ($n = 21$; 44.6%). Most reviews included at least one study with a comparator group ($n = 41$; 87.2%). Comparator groups included usual/standard medical care, waitlist controls, placebo or sham interventions, or other active interventions.

**Types of Interventions**

Though some reviews focused on singular types of intervention, others focused on varied types of treatment for a particular pain population or setting. Almost half of the reviews examined psychological interventions ($n = 23$; 48.9%), with 19 (40.4%) reviewing pharmacological interventions, 12 (25.5%) reviewing interdisciplinary interventions, 11 (23.4%) reviewing “other” interventions, and 7 (14.9%) reviewing physical interventions. The “other” types of treatments reviewed were primarily dietary (e.g., fiber, lactose avoidance), botanicals (e.g., peppermint oil, herbal therapy), and surgical interventions.
### Table 1. Characteristics of included reviews.

| Author, year                           | Aim                                                                 | No. and type of relevant studies | Age and chronic pain population(s)                                      | Setting(s)                                                                 | Type of intervention(s)                        | AMSTAR-2 quality rating |
|----------------------------------------|----------------------------------------------------------------------|---------------------------------|--------------------------------------------------------------------------|---------------------------------------------------------------------------|-----------------------------------------------|------------------------|
| Abbott et al., 2017                    | To determine the effectiveness of psychosocial interventions for reducing pain in school-aged children with recurrent abdominal pain | 18 RCTs                        | 6–18 years                                                               | Gastroenterology and pain outpatient clinic, community                     | Psychological                                   | High                   |
| Abujaradeh et al., 2018                | To determine the benefits/efficacy of mindfulness-based interventions implemented among adolescents with chronic diseases in clinical settings | 8 RCTs and NRS                  | 12–18 years                                                              | Tertiary care multidisciplinary pain clinic or hospital setting            | Psychological                                   | Low                    |
| American Academy of Pediatrics, 2005   | To examine the diagnostic and therapeutic value of a medical and psychological history, diagnostic tests, and pharmacological and behavioral therapy for chronic abdominal pain | 8 RCTs and NRS                  | Abdominal pain                                                           | Psychological Pharmacological Other                                       | Psychological                                   | Low                    |
| Anie and Green, 2015                   | To examine the evidence that psychological interventions improve the ability of people with sickle cell disease to cope with their condition | 4 RCTs                          | 6–18 years+ Sickle cell disease                                         | “Urban setting”                                                          | Psychological                                   | Moderate               |
| Arruda et al., 2018                    | To review the comorbidities and treatment of chronic migraine in children and adolescents in the last ten years, summarizing evidence-based recommendations for disease management | 4 RCTs and NRS                  | 7–17 years Headsaches, migraine                                         | Inpatient, outpatient headache clinics                                    | Pharmacological                               | Critically low         |
| Badawy et al., 2018                    | To (1) review the types of technological tools used for self-management of sickle cell disease, (2) discover and describe what self-management activities these tools were used for, and (3) assess the efficacy of these technologies in self-management    | 5 RCTs and NRS                  | 13–18 years+ Sickle cell disease                                        | e-Health                                                                  | Psychological Interdisciplinary                | Low                    |
| Bailey and McManus, 2008               | To evaluate which treatment could be effective in the emergency department for children with migraine and status migrainous | 14 RCTs                         | 4–18 years Migraines                                                    | Emergency department, outpatient neurology clinics ??                     | Pharmacological                               | Critically low         |
| Barnes, 2015                           | To examine treatments for acute attacks and the effects of pharmacological prophylaxis for migraine headache in children | 23 RCTs and reviews of RCTs      | 3–18 years Migraines, headaches                                         | ??                                                                        | Pharmacological                               | Moderate               |
| Bredlau et al., 2013                    | To review the use of ketamine in the treatment of cancer-related pain in adults and children | 5 NRS                           | 4–19 years Cancer pain                                                  | ??                                                                        | Pharmacological                               | Low                    |
| Brent et al., 2009                     | To evaluate behavioral and psychological treatments applied to pediatric functional gastrointestinal disorders | 12 RCTs and NRS                  | Recurrent abdominal pain, IBS, functional abdominal pain, functional dyspepsia, stomachache, stomach pain 10–18 years Patellar tendon pain, Osgood-Schlatter’s | Outpatient, community Psychological Other Interdisciplinary               | Pharmacological                               | Critically low         |
| Cairns et al., 2018                    | To evaluate interventions for patellar tendon-related pain in children and adolescents | 3 RCTs and NRS                  | Patellar tendon pain, Osgood-Schlatter’s                                 | University physical therapy, secondary care orthopedics, orthopedic surgery department ? | Physical Interdisciplinary                     | Moderate               |
| Cohen et al., 2017                     | To assess the effects of psychosocial therapies on pain and function in children with rheumatic diseases | 5 RCTs and NRS                  | Juvenile fibromyalgia, juvenile arthritis                               | ?????                                                                    | Psychological                                   | Low                    |
| Cooper, Wiffen, et al., 2017           | To assess the analgesic efficacy of antiepileptic drugs used to treat chronic non-cancer pain in children and adolescents | 2 RCTs                          | 7–18 years Fibromyalgia, CRPS-I or neuropathic pain                     | Tertiary care centers Pharmacological                                   | Psychological                                   | High                   |
| Cooper, Heathcote, et al, 2017         | To assess the analgesic efficacy of nonsteroidal anti-inflammatory drugs used to treat cancer-related pain in children and adolescents | 0 RCTs                          | <18 years Cancer-related pain                                           | Pharmacological                                                           |                                               | High                   |

(Continued)
| Author, year | Aim | Meta-analysis | Search date | No. and type of relevant studies | Age and chronic pain population(s) | Setting(s) | Type of intervention(s) | AMSTAR-2 quality rating |
|-------------|-----|--------------|-------------|---------------------------------|----------------------------------|-----------|------------------------|------------------------|
| Cooper, Fisher, et al., 2017<sup>53</sup> | To assess the analgesic efficacy of opioids used to treat chronic non-cancer pain in children and adolescents; To evaluate the efficacy of psychological therapies that include parents of children and adolescents with chronic illnesses | Yes* | 09/2016 | 0 RCTs | <18 years Chronic non-cancer pain | Outpatient clinics, community | Psychological | High |
| Eccleston et al., 2015<sup>54</sup> | To assess the analgesic efficacy of nonsteroidal anti-inflammatory drugs used to treat chronic non-cancer pain in children and adolescents | Yes* | 09/2016 | 7 RCTs | 2–18 years Chronic non-cancer pain | Pediatric rheumatology tertiary care units, pediatric centers, clinical centers | Pharmacological | High |
| Egunsola et al., 2019<sup>55</sup> | To examine the efficacy and safety of gabapentin and pregabalin for pain in children and adolescents | No | 11/2017 | 2 RCTs | 7–18 years CRPS, neuropathic pain, fibromyalgia | Pharmacological | High |
| Fellas et al., 2017<sup>56</sup> | To review the evidence for physical and mechanical interventions for lower-limb problems in juvenile idiopathic arthritis | Yes | 06/2015 | 2 RCTs | 5–19 years Juvenile idiopathic arthritis | Hospitals, pediatric rheumatology clinics | Physical | High |
| Horvath et al., 2012<sup>57</sup> | To evaluate the effect of dietary fibers for treating abdominal pain-related functional gastrointestinal disorders in children | No | 12/2011 | 3 RCTs | 3–16 years Abdominal pain | Hospitals, community clinics | Other | Low |
| Huertas-Ceballos 2008<sup>58</sup> | To determine the effectiveness of medication for recurrent abdominal pain in school-age children | Yes* | 12/2006 | 3 RCTs | Abdominal migraine, recurrent abdominal pain, IBS | Community, outpatient clinic | Psychological | High |
| Huertas-Ceballos 2008<sup>59</sup> | To determine the effectiveness of psychological interventions for recurrent abdominal pain or IBS in school-age children | Yes* | 12/2006 | 6 RCTs | Recurrent abdominal pain | Community, outpatient clinic | Physical | High |
| Kichline and Cushing, 2019<sup>60</sup> | To evaluate the effect of exercise on pediatric chronic pain | Yes | 12/2016 | 11 RCTs and NRS | 6–16 years Arthritis, fibromyalgia, low back pain, cancer, mixed | Community, outpatient clinic | Psychological | High |

(Continued)
| Author, year | Aim | Meta-analysis | Search date | No. and type of relevant studies | Age and chronic pain population(s) | Setting(s) | Type of intervention(s) | AMSTAR-2 quality rating |
|-------------|-----|---------------|-------------|-------------------------------|-----------------------------------|------------|------------------------|------------------------|
| Liossi et al., 2019 | To review the effectiveness of interdisciplinary interventions in the management of pediatric chronic pain | Yes | 03/2018 | 28 RCTs and NRS | 6–21 years Mixed (headache, abdominal pain, back, migraines, CRPS, pelvic, neuropathic, widespread/ fibromyalgia, musculoskeletal), oncology (tumors, leukemia), arthritis | Inpatient, day treatment, outpatient | Interdisciplinary | High |
| Lonergan, 2016 | To examine the effectiveness of cognitive behavioral therapy in the treatment of chronic pain in children and adolescents | Yes | 12/2014 | 9 RCTs | 6–18 years Recurrent abdominal pain, fibromyalgia, headache or migraine | Outpatient, university, patient home | Psychological | Critically low |
| Martin et al., 2017 | To review the effectiveness of pharmacological interventions for recurrent abdominal pain in school-age children | Yes* | 06/2016 | 16 RCTs | 5–18 years Recurrent abdominal pain “Children” | Hospital pediatric outpatient clinics | Pharmacological | High |
| Michel et al., 2011 | To review relevant pediatric buprenorphine data, particularly in children suffering chronic pain | No | ?? | 12 NRS | | | Pharmacological | Critically low |
| Newlove-Delgado et al., 2017 | To examine the effectiveness of dietary interventions in improving pain in school-age children with recurrent abdominal pain | Yes* | 06/2016 | 19 RCTs | 4–18 years Recurrent abdominal pain, functional gastrointestinal disorders, IBS | Pediatric gastroenterology clinics, primary care pediatric practices, community clinics | Other | High |
| Ng et al., 2017 | To review the efficacy of cognitive–behavioral therapy for pediatric migraine | Yes | 05/2016 | 17 RCTs | 7–18 years Migraine | Medical setting, school | Psychological | Critically low |
| Nijhof et al., 2018 | To review the evidence for nonpharmacological treatment for chronic musculoskeletal pain in pediatric rheumatic disease | No | 10/2017 | 11 RCTs and NRS | 5–18 years Juvenile idiopathic arthritis, systemic lupus erythematosus <18 years | Hospital, outpatient clinic | Physical | Low |
| Ostojic et al., 2018 | To determine the efficacy of interventions for the management of pain in children and adolescents with cerebral palsy | No | 04/2018 | 50 RCTs and NRS | Cerebral palsy (postoperative, hypertonia, cerebral palsy spastic hip disease) | Hospital or clinic | Psychological | Moderate |
| Palermo et al., 2010 | To examine the efficacy of psychological interventions for pain and emotional and physical functioning in children | Yes | 08/2008 | 18 RCTs | 4–18 years Headache, migraine, abdominal pain, fibromyalgia | Hospital or clinic | Physical | Moderate |
| Scheper et al., 2013 | To review state of the art of diagnostics and treatment of generalized joint hyper mobility and joint hyper mobility syndrome in children and young adults | No | ?? | 3 RCTs | Osteogenesis imperfecta, generalize joint hyper mobility, joint hyper mobility syndrome, Ehlers-Danlos “Children” Migraine, headache, neuropathic, postoperative, cystic fibrosis, sickle cell, juvenile idiopathic arthritis, head, abdomen, fibromyalgia, CRPS, phantom limb, back, chest, cancer | Inpatient, outpatient settings | Pharmacological | Critically low |
| Shah et al., 2016 | This review the role of interventional procedures in the treatment of chronic pain in children and adolescents | No | 03/2013 | 133 NRS | | Inpatient, outpatient settings | Pharmacological | Critically low |
| Sprenger et al., 2011 | To examine the effectiveness of psychological therapies for children with recurrent abdominal pain | Yes | 11/2009 | 10 NRS | 4–18 years Recurrent abdominal pain | ? | Psychological | Critically low |
| Tomé-Pires and Miro, 2012 | To review hypnotic treatments for chronic and cancer procedure-related pain in children | No | 05/2010 | 2 RCTs | 6–18 years Headache, abdominal pain | ? | Psychological | Critically low |

(Continued)
| Author, year | Aim | Meta-analysis | Search date | No. and type of relevant studies | Age and chronic pain population(s) | Setting(s) | Type of intervention(s) | AMSTAR-2 quality rating |
|--------------|-----|---------------|-------------|---------------------------------|-----------------------------------|------------|-------------------------|-------------------------|
| Trautmann et al., 2006<sup>26</sup> | To describe the state of evidence in the treatment of pediatric headaches | Yes | 07/2004 | 23 RCTs | 7–18 years Headache | Outpatient clinic, school | Psychological | Low |
| Velleman et al., 2010<sup>26</sup> | To review the use of computerized cognitive behavioral therapy with children and adolescents with pain | Yes | ??/2008 | 4 RCTs | Headaches, recurrent abdominal pain, musculoskeletal | Via computer in outpatient clinic, community | Psychological | Low |
| Weydert et al., 2003<sup>27</sup> | To review treatments for recurrent abdominal pain in children | No | ??/2001 | 10 RCTs | 3–18 years Recurrent abdominal pain, IBS, abdominal migraine | Primary and tertiary care, community | Psychological | Critically low |
| Wicksell et al., 2015<sup>28</sup> | To provide an overview of research on acceptance and commitment therapy for youths with physical concerns | No | ?? | 8 RCTs and NRS | 7–18 years Chronic pain | ?? | Interdisciplinary Psychological | Critically low |
| Wiffen et al., 2017<sup>29</sup> | To assess the analgesic efficacy of opioids used to treat cancer-related pain in children and adolescents | Yes* | 02/2017 | 0 RCTs | Chronic pain <18 years | — | Pharmacological | High |
| Yeung et al., 2017<sup>29</sup> | To review characteristics and management of endometriosis in adolescents | No | ?? | 8 NRS | Cancer-related pain 10–25 years Endometriosis | ?? | Other Interdisciplinary Psychological Physical Pharmacological | Critically low |
| Zernikow et al., 2012<sup>27</sup> and Häuser et al., 2012<sup>26</sup> | To provide a definition, diagnosis, and therapy of chronic widespread pain and so-called fibromyalgia syndrome in children and adolescents | No + CPG | 12/2010 | ?? RCTs and NRS | “Children and adolescents” Chronic widespread pain, fibromyalgia | Inpatient, outpatient | Physical Pharmacological Interdisciplinary | Moderate |

* = Cochrane review; RCT = randomized controlled trial; IBS = irritable bowel syndrome; NRS = nonrandomized study; CPG = clinical practice guideline; ?? = unclear/unknown; CRPS = complex regional pain syndrome; — = no studies.
| Author, year | Intervention(s) | Longest follow-up time | PedIMMPACT outcomes |
|-------------|-----------------|------------------------|---------------------|
| Abbott et al., 2017 | CBT, hypnosis, written self-disclosure, yoga | >1 year | ✔️ ✔️ ✔️ ✔️ ✔️ |
| Abujaradeh et al., 2018 | Mindfulness-based interventions | 6 months | ✔️ ✔️ ✔️ ✔️ ✔️ |
| American Academy of Pediatrics, 2005 and Di Lorenzo et al., 2005 | CBT, coping skills, famotidine, pizotifen, peppermint oil, fiber supplement, lactose-free diet, surgery | 3 years | ✔️ ✔️ ✔️ ✔️ |
| Anie and Green, 2015 | Education, various psychotherapies, art therapy | 1 year | ✔️ ✔️ ✔️ ✔️ ✔️ |
| Arruda et al., 2018 | Amitriptyline, corticoid infusion, peripheral nerve blocks, onabotulinumtoxin injections, pharmacological + CBT | 7 months | ✔️ ✔️ ✔️ ✔️ ✔️ |
| Bailey and McMahon, 2008 | Acetaminophen, ibuprofen, zolmitriptan, sumatriptan, rizatriptan, dihydroergotamine, ketorolac, prochlorperazine | 24 hours | ✔️ ✔️ ✔️ |
| Barnes, 2015 | Almotriptan, ibuprofen, topiramate, flunarizine, sumatriptan, rizatriptan, zolmitriptan, eletriptan, propanolol, flunarizine | 4 months | ✔️ ✔️ |
| Bredlau et al., 2013 | Ketamine | 75 days | ✔️ |
| Brent et al., 2009 | Relaxation, hypnotherapy, CBT, psychoeducation, dietary (fiber), psychological + diet | 1 year | ✔️ ✔️ ✔️ |
| Cairns et al., 2018 | Shockwave treatment + light activity, other physical exercises, local anesthetic, surgery + physical therapy | 2–3 years | ✔️ ✔️ |
| Cohen et al., 2017 | CBT, coping skills, relaxation, education, distraction | 4 months | ✔️ ✔️ ✔️ ✔️ ✔️ |
| Cooper, Wiffen, et al., 2017 | Antiepileptics (pregabalin, gabapentin) | 15 weeks | ✔️ ✔️ |
| Cooper, Heathcote, et al., 2017 | NSAIDs | — — — — — — — — — — |
| Fisher, et al., 2017 | Opioids | — — — — — — — — — — |
| Eccleston et al., 2015 | CBT, behavioral intervention | 1 year | ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ |
| Eccleston et al., 2017 | NSAIDs | 1 year | ✔️ ✔️ ✔️ ✔️ ✔️ |
| Egunsola et al., 2019 | Antiepileptics (pregabalin, gabapentin) | 15 weeks | ✔️ ✔️ ✔️ |
| Fellas et al., 2017 | Foot orthotics, neoprene inserts | 6 months | ✔️ ✔️ ✔️ |
| Ferro and Speechley, 2008 | Relaxation, herbal therapy (Tripterygium wilfordii), massage therapy | 6 months | ✔️ ✔️ |
| Fisher et al., 2018 | CBT, relaxation with or without biofeedback, coping skills, problem-solving therapy, intensive inpatient rehabilitation | 1 year | ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ |
| Fisher et al., 2019 | CBT (CD-ROM, Internet) | 1 year | ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ |
| Hechler et al., 2015 | Variations of combined pharmacological, psychological, physical | 2 years | ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ |
| Horvath et al., 2017 | Dietary fiber | ?? | ✔️ ✔️ ✔️ ✔️ |
| Huertas-Ceballos 2008 | Pizotifen, famotidine, peppermint oil capsules | ?? | ✔️ ✔️ ✔️ ✔️ ✔️ |
| Huertas-Ceballos 2008 | CBT, family therapy, dietary fiber, psychological + fiber | 1 year | ✔️ ✔️ ✔️ |
| Kichline and Cushing, 2019 | Aerobic exercise | 6 months | ✔️ ✔️ |
| Liossi et al., 2019 | Variations of combined pharmacological, psychological, physical, and other | 2 years | ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ |
| Lonergan, 2016 | CBT, family therapy | 1 year | ✔️ ✔️ ✔️ ✔️ ✔️ |
| Martin et al., 2017 | TCAs, antibiotics, 5-HT4 receptor agonists, antispasmodics, antihistamines, H2 receptor antagonists, serotonin antagonists, SSRI, dopamine receptor antagonist | 4 months | ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ |
| Michel et al., 2011 | Buprenorphine | ?? | ✔️ ✔️ |

(Continued)
| Author, year | Intervention(s)                                                                                                                                                                                                 | Longest follow-up time | Pain | Physical functioning | Emotional functioning | Role functioning | Quality of life | Sleep | Economic factors | Treatment satisfaction | Adverse events |
|--------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|------|----------------------|-----------------------|------------------|----------------|-------|-----------------|------------------------|----------------|
| Newlove-Delgado et al., 2017<sup>70</sup> | Probiotic-based interventions, fiber-based interventions, low FODMAP diets, fructose-restricted diet, CBT, relaxation, biofeedback, education, physical conditioning, Pilates, resistive underwater exercises, physical therapy + biofeedback | 4 months               | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Ng et al., 2017<sup>65</sup> | CBT, relaxation, biofeedback, education, physical conditioning, Pilates, resistive underwater exercises, physical therapy + biofeedback                                                                 | 1 year                 | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Nijhof et al., 2018<sup>59</sup> | Physiotherapy, massage, TENS, intrathecal baclofen, botulinum toxin A, cyclic intravenous administration of pamidronate, fentanyl, clonidine, indomethacin, intrathecal morphine, amitriptyline, gabapentin, bupivacaine, ketamine, blocks/epidural, butorphanol, magnesium sulfate, laser therapy, surgery, physiotherapy + pharmacological | 6 months               | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Ostojc et al., 2018<sup>40</sup> | CBT, relaxation, biofeedback, education, physical conditioning, Pilates, resistive underwater exercises, physical therapy + biofeedback                                                                 | 2 years                | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Palermo et al., 2010<sup>53</sup> | CBT, relaxation, biofeedback, education, physical conditioning, Pilates, resistive underwater exercises, physical therapy + biofeedback                                                                 | 1 year                 | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Scheper et al., 2013<sup>61</sup> | Physical training, Bobath treatment                                                                                                                                                                           | 18 months              | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Shah et al., 2016<sup>54</sup> | Neuroaxial blocks, peripheral blocks, sympathetic blocks, Bier blocks, neurostimulation, intrathecal baclofen, intra-articular steroids                                                                                                                   | ✔                    | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Sprenger et al., 2011<sup>65</sup> | CBT, family-based, relaxation, biofeedback, yoga                                                                                                                                                               | ✔                    | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Tomé-Pires and Miró, 2012<sup>65</sup> | Hypnosis                                                                                                                                                                                                   | ✔                    | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Trautmann et al., 2006<sup>66</sup> | CBT, biofeedback, relaxation, stress management                                                                                                                                                              | ✔                    | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Velleman et al., 2010<sup>16</sup> | CBT (CD-ROM, Internet)                                                                                                                                                                                      | ✔                    | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Weydert et al., 2003<sup>37</sup> | CBT, famotidine, pizotifen, botanicals (peppermint oil), diet (fiber, lactose avoidance), CBT + biofeedback + fiber                                                                                          | ✔                    | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Wicksell et al., 2015<sup>68</sup> | Acceptance and commitment therapy                                                                                                                                                                            | ✔                    | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Wiffen et al., 2017<sup>33</sup> | Opioids                                                                                                                                                                                                   | ✔                    | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Yeung et al., 2017<sup>70</sup> | NSAIDs, TCAs, SSRIs, trazodone or amitriptyline, cyclobenzaprine, laparoscopy, laparoscopic excision or treatment, surgical ablation or excision, surgery + postoperative hormones | ✔                    | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |
| Zernikow et al., 2012<sup>17</sup> and Häuser et al., 2012<sup>90</sup> | CBT, trauma therapy, family therapy, other psychotherapy, aerobic exercises, qi-gong, psychological + physical therapy                                                                                     | ✔                    | ✔    | ✔                   | ✔                     | ✔                | ✔              | ✔     | ✔               | ✔                      | ✔             |

CBT = cognitive–behavioral therapy; — = no studies; NSAID = nonsteroidal anti-inflammatory drug; ?? = unclear/unknown; TCA = tricyclic antidepressants; SSRI = selective serotonin re-uptake inhibitor; FODMAP = fermentable oligosaccharides, disaccharides, mono- and polyols; - = no studies.
Types of Outcomes
Three reviews of pharmacological interventions found no eligible studies for inclusion; as such, extraction of assessed outcomes was not possible for those reviews. Of the remaining 44 reviews, all (100%) reported on pain intensity, 27 (61.3%) reported on physical functioning, 20 (45.5%) reported on emotional functioning, 20 (45.5%) reported on role functioning, 21 (47.7%) reported on quality of life, 8 (18.2%) reported on sleep, 5 (11.4%) reported on economic factors, 13 (29.5%) reported on treatment satisfaction, and 20 (45.5%) reported on adverse events. Time points for outcome reporting ranged from immediately postintervention to hours, days, weeks, months, or up to 5 or more years later. Most reviews included some sort of risk of bias or quality ratings of included studies (n = 32; 72.7%).

Quality of Systematic Reviews
See Figure 2 for a summary of the AMSTAR-2 quality ratings for the included reviews. Of the 47 reviews, the greatest number were rated as high quality (n = 16; 34.0%), followed by critically low quality (n = 13; 27.7%) and low quality (n = 11; 23.4%), with the fewest rated as moderate quality (n = 7; 14.9%). Reviews were primarily downgraded in quality for failing to register a review protocol or demonstrate clear evidence of review methods established a priori or failing to provide a list of excluded studies with justification, with fewer studies failing to use a comprehensive literature strategy, failing to include a satisfactory technique for assessing risk of bias, or failing to account for risk of bias in the interpretation of review results.

Synthesis of Results
See Figure 3 for the evidence and gap map summarizing the quality and number of included reviews relevant to each extracted treatment outcome of interest.

Additional Analyses: Mapping to the Top Ten Patient-Oriented Research Priorities
See Figure 4 for a summary of the quality and number of included reviews relevant to each of the top ten patient-oriented research priorities for pediatric chronic pain. All but two priorities had at least one relevant review and/or clinical practice guideline. Priority 3 (physical and psychological interventions) had the greatest number of relevant reviews (n = 9; 19.1% and n = 24; 51.1%, respectively), albeit primarily from reviews of low and critically low quality. Priority 1 (prevention of chronic pain) and priority 4 (improved access and delivery) were addressed by four reviews each (8.5%), and priority 2 (impact on education and vocational planning), priority 8 (managing acute pain flares), and priority 9 (treatment of co-occurring mental health symptoms) were addressed by only two to three reviews each (4.3–6.4%). Priority 5 (increase health care providers’ knowledge) and priority 10 (timing of interventions) had only one relevant review each (2.1%), and priority 6 (increase government and organization financial support) and priority 7 (educating school personnel) had no relevant reviews. Almost one third of included reviews and clinical practice guidelines did not address any of the patient-oriented research priorities (n = 15; 31.9%).

Discussion
Summary of Evidence
This systematic review offers a rigorous synthesis of available systematic reviews and clinical practice guidelines of interventions of any modality for pediatric chronic pain. The resulting evidence and gap map offers a succinct but thorough data visualization to effectively convey the current state of the evidence for use by key stakeholders, including members of the public, policymakers and decision makers, health care providers, and researchers alike. The broad scope of this review across intervention modalities and pediatric chronic pain populations, as well as its evidence and gap map methodology, uniquely positions its findings to be quickly and easily utilized.

This review reveals much about the contemporary state of synthesized evidence of interventions for pediatric chronic pain. It is promising for policymakers that many high-quality reviews exist to guide decisions (most of which were Cochrane reviews); however, more than half (55%) of included reviews were rated to be of low or critically low quality. It was surprising that only two clinical practice guidelines were identified. Most systematic reviews examine psychological interventions only, followed closely by pharmacological interventions. The sizable study of psychological interventions for pediatric chronic pain is promising given its prioritization among patients, family members, and treating health care providers but stands in stark contrast to the generally poor access to specialized multidisciplinary pediatric chronic pain intervention or mental health treatment. Three reviews focused on the remote or computerized delivery of psychological interventions. Far fewer systematic reviews examined interdisciplinary interventions despite this being the recommended approach to chronic pain management, followed by reviews of other interventions such as alternative diets, herbal supplements, and surgeries. The fewest...
reviews examined physical interventions, which highlights this as a key area for further research given its prioritization by patients and families, as well as the evidence for multimodal interventions, of which physical interventions are included. Possible contributing factors for less evidence in these areas could be their greater difficulty in studying with traditional clinical trial methodologies and fewer professionals in areas outside of medicine and psychology with advanced training to conduct research.

The largest proportion of reviews included diverse pediatric chronic pain populations. This suggests the applicability of many interventions across types of chronic pain and aligns with an all-encompassing primary chronic pain diagnosis. Reviews with medically
complex children and adolescents were largely absent, with the exception of cerebral palsy. No reviews obviously addressed interventions for children with cognitive or intellectual disabilities or those who are nonverbal, which is of concern given their greater risk for undertreated and poorly recognized pain. When reviews focused on single patient groups, headaches and migraines or abdominal pain were the most common, possibly reflecting their higher prevalence rates. Reviews of interventions for pediatric migraines and headaches offered unique contributions and alignment with patient-oriented priorities not well addressed by other evidence, including a focus on prevention (prophylaxis) and management of acute pain flares. Only one review focused on interventions in the emergency department. This is of great relevance given the high frequency with which children with chronic pain seek care in the emergency setting, its high economic cost, the use of opioids to treat acute pain, and the potential for interdisciplinary care to reduce utilization of emergency care. Other reviews largely addressed interventions in outpatient or community clinics or within tertiary care centers.

With regards to intervention impact, all reviews addressed the PedIMMPACT recommended outcome of pain intensity, with fewer reporting on outcomes related to physical (disability, mobility), emotional (anxiety, depression), and role functioning (school attendance) or quality of life. Fewer still reported outcomes of treatment satisfaction or adverse events, with very little about sleep or economic factors. This reflects a neglect of outcomes identified as relevant by patients, family members, and treating health care providers, such as self-efficacy, participation in meaningful activities, social roles and relationships, vocational planning, concentration, acceptance, and resilience. Although almost half of reviews addressed emotional functioning, many excluded children with co-occurring primary mental health disorders. Thus, these reviews effectively omitted a large proportion of children with chronic pain with mental health concerns and decreased the relevance of available evidence to the identified patient-oriented priority about how co-occurring chronic pain and mental health can be effectively addressed. Given that the estimated annual incremental costs of treating an individual with chronic pain are CA $1742 per person, costing billions to society overall, there is a clear need to better demonstrate the economic benefit of evidence-based interventions to guide policymakers and decision makers. Though this review focused on previously recommended key outcome categories for clinical trials of interventions for pediatric chronic pain, we note that this approach is likely to miss all outcomes included in the systematic reviews, clinical practice guidelines, or the original studies they include. Other than physical and psychological interventions, less than 10% of included reviews addressed any of the other top ten patient-oriented priorities. The movement toward patient engagement and partnership in health research offers a great opportunity to lessen the divide between existing intervention studies and outcomes and that of patient priorities.

Figure 4. Summary of evidence for top ten patient-oriented research priorities in pediatric chronic pain.
Effectiveness-implementation hybrid research designs are gaining traction to enhance public health impact through efficient, feasible, sustainable, and widespread adoption of studied treatments.13,92,93

Limitations

Several limitations warrant mention in considering the above presented evidence. First, this review and evidence and gap map included published systematic reviews and clinical practice guidelines only. A comprehensive review of all original intervention studies in pediatric chronic pain would be a phenomenal undertaking and beyond the scope and resources available. However, it is possible, if not likely, that additional original studies exist with relevance to identified patient-oriented research priorities that are not captured here (see interventions to educate teachers94 and health care providers95 about pediatric chronic pain, for example). This suggests that the current review overlooks areas or priorities where systematic reviews have not yet been conducted and/or in research areas less likely to rely on randomized controlled trials or other traditional treatment study designs. The patient-oriented priorities with minimal systematic review evidence shown here would likely benefit from quality systematic reviews of original studies.

Conclusions

This systematic review reveals the great amount of contemporary evidence synthesis that has been conducted to identify effective multimodal interventions for pediatric chronic pain to date. Creation of an evidence and gap map identifies the availability of sufficient quality evidence to guide the development of evidence-informed policies and additional practice guidelines, most notably regarding psychological and pharmacological interventions to improve children’s pain and quality of life and across physical, emotional, and role functioning domains. Despite this success, the numerous obvious evidence gaps in the top patient-oriented research priorities and treatment outcomes in pediatric chronic pain should be noted by health research funders and researchers to guide prioritization of funds, as well as study aims and design.

Acknowledgments

The authors express sincere gratitude to other Partnering For Pain team members, including Dr. Krista Baerg, Dr. Fiona Campbell, Dr. Jill Chorney, Katherine Dib, Mary Anne Dib, Esther Fleurimond, Dr. Paula Forgeron, Isabel Jordan, Dr. Christine Lamontagne, Justina Marianayagam, Kimberly Nelson, Dr. Melanie Noel, Dolores Pahtayken, Dr. Patricia Poulin, and Adam Val Bonzil.

Disclosure statement

Kathryn A. Birnie does not have any conflicts of interest. Carley Ouellette does not have any conflicts of interest. Tamara Do Amaral does not have any conflicts of interest. Jennifer N. Stinson does not have any conflicts of interest.

Funding

This work was supported by an EMPOWER Award from the Ontario Strategy for Patient-Oriented Research (SPOR) SUPPORT Unit. As required by the funder, a policy brief describing the entirety of the Partnering For Pain project, including the priority-setting partnership,7 and aspects of this evidence and gap map will be developed and made available on the project website: www.partneringforpain.com.

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