A comprehensive categorical and bibliometric analysis of published research articles on pediatric pain from 1975-2010

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SUMMARY

Using categorical and bibliometric meta-trend analysis methods, this article provides a comprehensive overview of published peer-reviewed research articles on pediatric pain from 1975-2010.

ABSTRACT

The field of pediatric pain research began in the mid-1970's and has undergone significant growth and development in recent years as evidenced by the variety of books, conferences, and journals on the topic as well as the number of disciplines engaged in work in this area. Using categorical and bibliometric meta-trend analysis, the current study offers a synthesis of research on pediatric pain published between 1975 and 2010 in peer-reviewed journals. Abstracts from 4256 articles, retrieved from Web of Science, were coded across four categories: article type, article topic, type and age of participants, and pain stimulus. The affiliation of the first author and number of citations were also gathered. The results suggest a significant increase in the number of publications over the time period investigated, with 96% of the included articles published since 1990 and most research being multi-authored publications in pain-focused journals. First authors were most often from the United States, and affiliated with a medical department. The majority of studies were original research articles; the most frequent topics were pain characterization (39.86%), pain intervention (37.49%), and pain assessment (25.00%). Clinical samples were most frequent, with participants most often characterized as children (6-12 years) or adolescents (13-18 years) experiencing chronic or acute pain. The findings provide a comprehensive overview of contributions in the field of pediatric pain research over 35 years and offers recommendations for future research in the area.

1. INTRODUCTION

The field of pain research has made tremendous advances over the last 30 years. A recent comprehensive categorical and bibliometric meta-trend analysis of original research articles published in the journal *PAIN* between 1975-2007 highlighted developments in pain research over time [23]. This review documented a shift in topic area (from human intervention to animal behavior pharmacology) and experimental methods (from thermal to mechanical stimuli). Although 30% of the included studies evaluated the efficacy of interventions, most of the highly cited papers documented new animal models [e.g., 4,15] or the development of measures (e.g., McGill Pain Questionnaire [22] with 2400 citations).

Pediatric pain is a robust research area that began in the 1970's [20]. Early studies comparing adult and child pain management revealed significant undermedication of children, fuelled by a belief that children (especially infants) did not feel pain, or that anesthetics were too risky to be used in surgery for this population [5,10,28]. Research by Anand and colleagues (1987) revealed a substantial stress response as well as higher mortality and morbidity rates in children undergoing surgery without anesthetics, and these findings created public appreciation for the importance of optimal pain management in children [2]. Public awareness was further intensified by the story in the late '80s of Jeffrey Lawson, an infant who died from complications following surgery without proper anesthesia, whose mother Jill spoke out about this experience in a Washington Post article [27]. These events catalyzed public interest and research in pediatric pain [20].

Prior reviews of the state of the field of pediatric pain research have shown a significant increase in published journal articles on pediatric pain over time, especially in neonates [3,13]. The field has also been advanced by publication of key textbooks (e.g., Oxford Textbook of Paediatric Pain (2013)), international meetings (e.g., International Symposium on Pediatric Pain (http://childpain.org/ispp.shtml), International Forum on Pediatric Pain (http://pediatric-

pain.ca/ifpp)), the initiation of the International Association for the Study of Pain's Special Interest Group on Pain in Childhood (IASP; http://childpain.org), and international training programs (e.g., Pain in Child Health (PICH); http://paininchildhealth.dal.ca [33]). As a consequence of its rapid growth and multidisciplinary nature, pediatric pain literature is scattered across disciplines and journals, making it challenging to develop a comprehensive overview of the current evidence [26]. For instance, secondary analyses on data gathered by Mogil and colleagues [23] revealed that 5% of the published articles in *PAIN* involve children. An in-depth, systematic analysis of the current state of the science of pediatric pain research and its evolution over time is warranted.

The present study used similar methodology to Mogil and colleagues (2009) [23]. Bibliometric analysis, a set of methods to quantitatively analyze scientific literature in order to document the impact and trends within a field, was used to provide a quantitative overview of research on pediatric pain published in peer-reviewed journals between 1975-2010. In addition, geographical and disciplinary distribution of authors are reported, as well as categorization of topic and sample characteristics (i.e., age of participants, type of pain experience) over time.

2. METHOD

2.1 Bibliometric data acquisition

A four-step approach was followed to select the final set of articles on pediatric pain, published in peer-reviewed journals between 1975 and 2010, to be included in this categorical and bibliometric meta-trend analysis. Similar to Mogil and colleagues (2009) we chose 1975 as a starting point, as this marks the inception of the leading journal *PAIN* [23]. The end year 2010 was chosen as it represents the end of a decade, allowing us to use evenly distributed five-year blocks to present the data. Due to pediatric pain research being published in a wide range of journals, and our interest in not only original research articles but also reviews, theoretical articles and clinical guidelines, we did not limit our analyses to empirical research

published in the journal *PAIN*. We expanded our journal source to include any journal publishing any type of article on pediatric pain. Given the breadth of our search approach and the range of expected publication sources, we limited our data extraction to abstracts only and not the full text of the selected articles. Pilot testing data extraction from the abstracts demonstrated that the majority of the information could be identified from consulting the abstract only.

In the first step, the ISI Web of Science database™ was used as the main database to conduct our search. The ISI Web of Science™ database was chosen over other existing databases as it covers more scientific disciplines (vs. PubMed which is focused on medicine and biomedical science), a broader range of dates of publications (vs. SCOPUS which is limited to articles published after 1995), a large spread of countries (i.e., 46 different languages represented) and provides a detailed citation analyses [11]. A title-search was conducted in ISI Web of Science™, requiring the presence of at least one developmental and one pain-related keyword in the article title. The keywords for this search were selected in consultation with a librarian specializing in systematic reviews. Specifically, the developmental keywords used were based on recommendations by Leclercq and colleagues (2013) for selection of comprehensive and highly sensitive pediatric search terms [19]. To obtain an inclusive list of pain terms, the pain-related keywords were based on two recent and comprehensive (i.e., not focusing on one specific type of pain) reviews on pain [9,26]. See Appendix A part 1 for the exact keywords used within the search. This first step, conducted in January 2013, resulted in a total of 7667 articles.

For the second step, two authors (L.C. and K.E.B.) independently screened the titles to check eligibility for inclusion and to screen for duplicates. All decisions were compared and any disagreements were resolved with consensus. Duplicates and articles that, based on their title, met one of the exclusion criteria (e.g., dissertations, case studies, conference abstracts,

books; see Table 1 for full list) were excluded (*N* = 1916 or 24.99%), resulting in a sample of 5751 articles that were retained for the next step. Primary reasons for exclusion at this stage were: the title of the article revealed that the articles were case studies (*N* = 770 or 40.19%), articles that had been identified in the search based on unrelated words captured by truncated search terms (e.g., the search term pain* revealing abstracts about "paint") or misspellings (*N* = 363 or 18.95%) or articles solely focusing on adult samples (*N* = 289 or 15.08%). If eligibility for inclusion was unclear based on the title alone, the article was retained and checked for eligibility during the fourth step.

In the third step, for reasons of feasibility only the abstracts of the 5751 articles that had been retained for inclusion were retrieved from a scientific database. If the abstract was not available in Web of Science™, PubMed was searched for the availability of an abstract, as PubMed constitutes an important and easy to access resource to retrieve biomedical scientific information [11]. Google Scholar was not used as a source because evidence indicates this database could be less trustworthy due to occasional inadequacies and less control over the access of the covered content [11]. If an abstract could not be located on either Web of Science™ or PubMED, only the article title was retained for the next step (i.e., coding). A total of 55 duplicates, which were not captured during the title screening were removed at this time, resulting in 5696 articles selected for the fourth step (i.e., abstract coding).

In the final and fourth step, all abstracts were equally divided between 11 coders in a random method and coded using the coding system described below. In this step, each coder screened their allocated abstracts for inclusion using the in- and exclusion criteria (see Table 1). A total of 1440 abstracts were excluded during this phase, with main reasons being: no abstract available (*N* = 1048 or 72.78%), case study (*N* = 145 or 10.07%), use of an adult sample only (*N* = 106 or 7.36%), or pain was not of primary interest (*N* = 66 or 4.58%). Therefore, the data presented in the subsequent analyses is based on the final number of coded

and included abstracts, N = 4256. Figure 1 provides an overview of the article selection process.

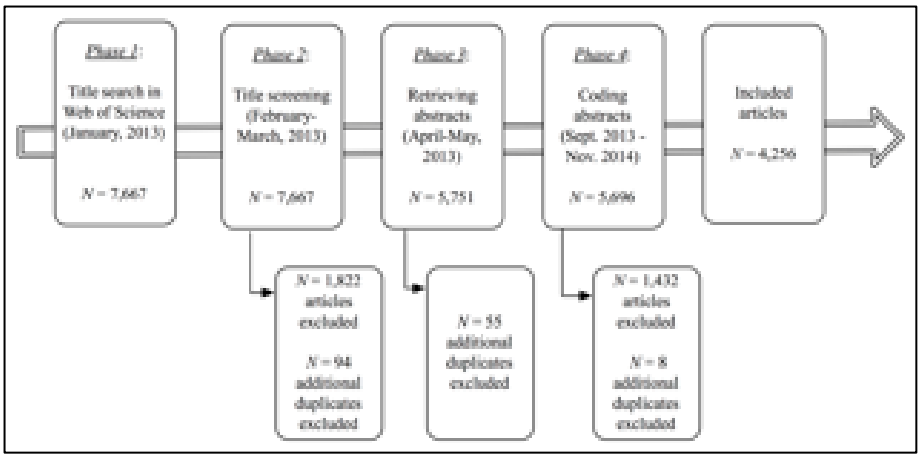

Figure 1: Overview of article selection process.

Table 1. Overview of inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
peer-reviewed articles	dissertations
original research articles or clinical guidelines or reviews or theoretical papers	commentaries
articles in which pediatric pain was of primary interest	(news)letters
English abstract available	case studies
article investigating or referring to pain in children between 0 and 18 years, including studies where adults, such as parents, teachers, or health professionals, were reporting on pain-related issues in children between 0 and 18 years	conference abstracts
	book chapters and book reviews
	articles with misspellings in the title (e.g., “pianist” instead of “pianist”) and articles that were not related to pain, but were captured by the truncated search term ‘pain*’, e.g., articles about paint
	articles discussing emotional (rather than physical) pain
	articles about medical conditions that did not include or discuss any pain-related outcomes

2.2 Coding strategy

The abstracts of the included articles were coded using a modified version of the coding system developed by Mogil and colleagues (2009) [23]. Specifically, our coding system included the following categories: 1) type of article (i.e., research article; narrative or systematic review; theoretical article; guidelines), 2) topic of article (e.g., article focuses on pain assessment, pain intervention, characterization of pain, development of a model or factors that influence the pain experience; see Appendix A part 2 for more details), 3) age and type of participants (i.e., healthy vs. clinical sample, further description provided below), and 4) pain stimulus (e.g., experimentally induced pain such as cold pressor task or mechanical pain threshold, acute pain, chronic pain or disease-related pain; see Appendix A part 3 for more details). With respect to the type of participants, a distinction was made between healthy samples with no diagnosed pain-related medical condition (e.g., school children, community sample, healthy animals) and clinical samples (e.g., post-operative sample, recurrent abdominal pain sample, hospitalized samples such as neonatal or pediatric intensive care units, emergency departments). In addition, it was indicated whether the subjects were animals or children and whether the sample also included parents, teachers and/or health professionals. The categories used to code the age of the participants were based on the definition of the MeSH terms used by Medline and included the following categories: premature (born <37 weeks of gestation), newborn (0-30 days), infant (1-23 months), preschool (2-5 years), child (6-12 years), adolescent (13-18 years) and adult (>18 years). A category 'child NOS' was added to indicate that the article represented children, but the age range could not be deduced from the abstract. In addition, to code age characteristic in animal studies the following age guidelines were used: premature (rat of 0-6 days), newborn (rat of 7-13 days), child animal (rat of 14-20 days), adolescent (rat of 21-63 days) and adult (>63 days) [21]. In accordance with the coding strategy by Mogil and colleagues (2009) at least one code in each category was required, but multiple codes were allowed (e.g., an article including both a clinical and healthy sample would receive

two codes for the category ‘sample type’: one for clinical sample and one for healthy sample) [23].

The adjusted coding system was piloted by all co-authors and adapted accordingly. After pilot testing the coding system, all 11 coders (i.e., all co-authors) independently coded their allocated articles. To ensure interrater reliability, a random selection of 10% of each coders’ articles were coded by the primary author (L.C.). Abstracts on which the primary and reliability coder disagreed on were checked by a third, independent coder. Intraclass correlation coefficients indicated a good to excellent interrater reliability of the coders with a mean value of .83 (range .70 – 1.00) [18].

In addition to the above-mentioned categories the country, state/province/region, and discipline (e.g., medical science, nursing, psychology, pharmacology, physiotherapy, dentistry) of the first author was retrieved if available from the abstract. Lastly, the citation score (i.e., the number of citations since publication) for each included abstract was obtained on December 1, 2014.

2.3 Analyses

For each category code (e.g., original research article, review article, pain assessment, pain intervention, healthy sample, acute pain, chronic pain) a percentage score was calculated per 5 years (1975 - 1980; 1981 - 1985; 1986 - 1990; 1991 - 1995; 1996 - 2000; 2001 - 2005; 2006 - 2010) by dividing the total frequency of the specific category code for the 5-year period by the total number of publications in that respective 5-year period [23]. An important note with respect to the percentages is that due to the possibility of an article qualifying for more than one code of a particular category (e.g., article reports both on pain assessment and intervention), the sum of the percentages within a given category could exceed 100%. These percentage scores were used in linear regression analyses, with the time period as the independent variable and each respective categories as the dependent variables, to investigate whether the percentage significantly increased or decreased over time.

3. RESULTS

3.1 Full dataset

The excel file of the full dataset (encompassing both the included and excluded articles from step 4, each in a different file) can be found as Supplemental Digital Content. In this dataset, each included article appears as a row entry. The articles are ranked chronologically from 1975 until 2010, and for each included article the dataset contains from left to right: identifying information (year, authors, title and journal); citation score, and all category codes (where 1 = present and 0 = absent). At the end of each 5-year period, a row is inserted providing the totals for the respective 5-year period (see Supplemental Digital Content 1). For the excluded articles, only the identifying information is provided (see Supplemental Digital Content 2). This data file is available for readers to use for further analyses.

3.2 Bibliometric information and trends

As shown in Figure 2, the results indicated a significant, steep increase ($\beta = .95$, $p < .01$) in the number of publications from a total of 41 included in our search between 1975 and 1980 to a total of 1630 in the last 5-year period (2006 - 2010). Table 2a provides an overview of the top 20 articles with respect to their total citation score, while Table 2b provides an overview of the top 20 included articles with respect to their relative citation score (i.e., taking into account the number of years since publication). Articles reporting on pain assessment (35% for raw and 25% for relative citations ranking), effectiveness of various pain treatments

Table 2a. Top 20 articles based on total citation score

Rank	Year	Authors	Title	Journal
1	1988	Sorge et al.	Flunarizine in Prophylaxis of Childhood Migraine - a Double-Blind, Placebo-Controlled, Crossover Study	Cephalalgia
2	1997	Taddio et al.	Effect of neonatal circumcision on pain response during subsequent routine vaccination	Lancet
3	1990	Bieri et al.	The Faces Pain Scale for the Self-Assessment of the Severity of Pain Experienced by Children - Development, Initial Validation, and Preliminary Investigation for Ratio Scale Properties	Pain
4	1987	Grunau & Craig	Pain Expression in Neonates - Facial Action and Cry	Pain
5	2000	Perquin et al.	Pain in children and adolescents: a common experience	Pain
6	1994	Abu-Arefeh & Russell	Prevalence of headache and migraine in schoolchildren	BMJ
7	1996	Stevens et al.	Premature infant pain profile: Development and initial validation	Clinical Journal of Pain
8	1997	Merkel et al.	The FLACC: a behavioral scale for scoring postoperative pain in young children	Pediatric Nursing
9	2001	Anand et al. (International Evidence-Based Group for Neonatal Pain)	Consensus statement for the prevention and management of pain in the newborn	Archives of Pediatrics & Adolescent Medicine
10	1989	Linet et al.	An epidemiologic study of headache among adolescents and young adults	JAMA
11	1993	Lawrence et al.	The development of a tool to assess neonatal pain	Neonatal Network
12	1987	Varni et al.	The Varni Thompson Pediatric Pain Questionnaire .1. Chronic Musculoskeletal Pain in Juvenile Rheumatoid-Arthritis	Pain

13	1996	Hyams et al.	Abdominal pain and irritable bowel syndrome in adolescents: A community-based study	Journal of Pediatrics
14	1993	Craig,K.D et al.	Pain in the Preterm Neonate - Behavioral and Physiological Indexes	Pain
15	2001	Hagan et al. (Am Acad Pediatrics; Amer Pain Soc)	The assessment and management of acute pain in infants, children, and adolescents	Pediatrics
16	1995	Taddio et al.	Effect of Neonatal Circumcision on Pain Responses during Vaccination in Boys	Lancet
17	2003	Simons et al.	Do we still hurt newborn babies? - A prospective study of procedural pain and analgesia in neonates	Archives of Pediatrics & Adolescent Medicine
18	1996	Burton et al.	The natural history of low back in adolescents	Spine
19	1996	McGrath et al.	A new analogue scale for assessing children's pain: An initial validation study	Pain
20	2006	Stinson et al.	Systematic review of the psychometric properties, interpretability and feasibility of self-report pain intensity measures for use in clinical trials in children and adolescents	Pain

Table 2b. Top 20 articles based on relative citation score (i.e., taking into account the number of years since publication)

Rank	Year	Authors	Title	Journal
1	2000	Perquin et al.	Pain in children and adolescents: a common experience	Pain
2	1997	Taddio et al.	Effect of neonatal circumcision on pain response during subsequent routine vaccination	Lancet
3	2008	Carbajal et al.	Epidemiology and treatment of painful procedures in neonates in intensive care units	Journal of the American Medical Association
4	2006	Stinson et al.	Systematic review of the psychometric properties, interpretability and feasibility of self-report pain intensity measures for use in clinical trials in children and adolescents	Pain
5	2008	McGrath et al.	Core outcome domains and measures for pediatric acute and chronic/recurrent pain clinical trials: PedIMMPACT recommendations	Journal of Pain
6	1988	Sorge et al.	Flunarizine in Prophylaxis of Childhood Migraine - a Double-Blind, Placebo-Controlled, Crossover Study	Cephalalgia
7	2001	Anand et al. (International Evidence-Based Group for Neonatal Pain)	Consensus statement for the prevention and management of pain in the newborn	Archives of Pediatrics & Adolescent Medicine
8	2007	von Baeyer et al.	Systematic review of observational (behavioral) measures of pain for children and adolescents aged 3 to 18 years	Pain
9	2010	Palermo et al.	Randomized controlled trials of psychological therapies for management of chronic pain in children and adolescents: An updated meta-analytic review	Pain
10	1994	Abu-Arefeh et al.	Prevalence of headache and migraine in schoolchildren	BMJ
11	2009	von Baeyer et al.	Three new datasets supporting use of the Numerical Rating Scale (NRS-11) for children's self-reports of pain intensity	Pain

12	2003	Simons et al.	Do we still hurt newborn babies? - A prospective study of procedural pain and analgesia in neonates	Archives of Pediatrics & Adolescent Medicine
13	1996	Stevens, et al.	Premature infant pain profile: Development and initial validation	Clininical Journal of Pain
14	1997	Merkel et al..	The FLACC: a behavioral scale for scoring postoperative pain in young children	Pediatric Nursing
15	2006	Bartocci et al.	Pain activates cortical areas in the preterm newborn brain	Pain
16	2005	Roth-Isigkeit et al.	Pain among children and adolescents: Restrictions in daily living and triggering factors	Pediatrics
17	1990	Bieri et al.	The Faces Pain Scale for the Self-Assessment of the Severity of Pain Experienced by Children - Development, Initial Validation, and Preliminary Investigation for Ratio Scale Properties	Pain
18	2010	Slater et al.	Oral sucrose as an analgesic drug for procedural pain in newborn infants: a randomised controlled trial	Lancet
19	2001	Hagan et al. (Am Acad Pediatrics; Amer Pain Soc)	The assessment and management of acute pain in infants, children, and adolescents	Pediatrics
20	2004	Lewis et al. (American Academy of Neurology Quality Standards Subcommittee)	Practice parameter: pharmacological treatment of migraine headache in children and adolescents: report of the American Academy of Neurology Quality Standards Subcommittee and the Practice Committee of the Child Neurology Society	Neurology

(30% for raw and 40% for relative citations ranking), and the epidemiology of pain (25% for raw and 20% for relative citations ranking) are prominent within both lists.

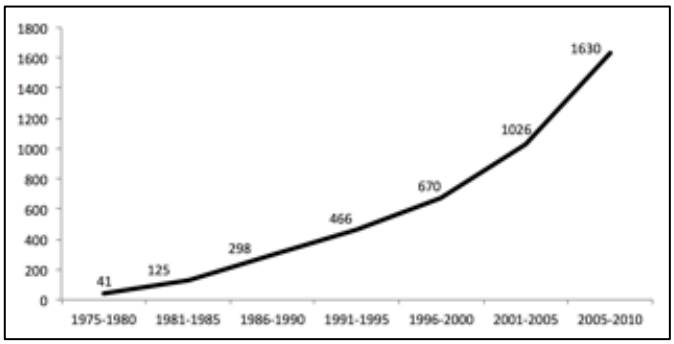

Figure 2: Overview of the growth in published articles on pediatric pain between 1975 -2010.

Included articles were published in a total of 904 different peer-reviewed journals, with pain-focused, rather than pediatric-focused, journals (i.e., *PAIN*, *Headache* and *Cephalalgia*) marking the three journals with the highest number of published articles. To account for the different inception dates of each journal, the final ranking of journals was calculated based on the total number of included articles published in the journal divided by the numbers of years since 1975 that the journal has been available. For example, a total of 147 articles on pediatric pain published in *Cephalalgia* between 1975 and 2010 were included in the search. *Cephalalgia* was however only established in 1981. Therefore, the total amount of included articles from *Cephalalgia* (N = 147) was divided by 29 (= 2010 - 1981), resulting in a proportion score of 5.07 included articles on pediatric pain per year on average. An overview of the top 20 journals according to the relative amount of articles on pediatric pain, included in our search, each journal has published can be found in Table 3.

With respect to the number of authors per article, Figure 3 indicates that for all 5-year time periods, the majority of the articles were collaborations between multiple ($\geq$ 2) authors. This tendency grew stronger over the years with linear regression analyses indicating a significant increase over the years in the percentage of articles with multiple authors (β = .94, $p < .01$), while a decrease in the percentage of single authored articles was observed (β =

-.94, $p < .01$). A small number of included articles were published anonymously ($N = 11$; 0.03%).

Table 3. Top 20 journals based on proportion of published articles since inception or since 1975 (if inception of journal was before 1975)

Journal	**# Articles**[a]	**Proportion of articles since inception**
Pain	202	5.77
Headache	187	5.34
Cephalalgia	147	5.07
European Journal of Pain	52	4.00
Pediatrics	130	3.71
Pediatric Anesthesia	67	3.53
Clinical Journal of Pain	88	3.38
Journal of Pediatrica Psychology	91	2.68
Acta Paediatrica	79	2.26
Journal of Pain and Symptom Management	51	2.12
Journal of Pain	39	2.05
Journal of Pediatric Nursing	43	1.79
Pediatric Emergency Care	37	1.48
Pediatric Clinics of North America	51	1.46
Journal of Pediatrics	44	1.26
Spine	40	1.18
Journal of Pediatric Gastroenterology & Nutrition	32	1.14
Pediatric Nursing	37	1.06
Archives of Disease in Childhood	34	0.97
Developmental Medicine & Child Neurology	33	0.94

[a]number of articles on pediatric pain for which an abstract was available online via a scientific database and included in the current search

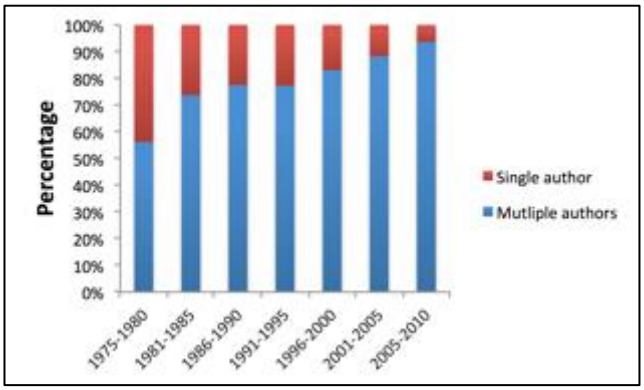

Figure 3: Trends in the percentage of single versus multiple authored articles per 5 years.

Based on the country of the first author, the majority of the included articles originated in the USA (*N* = 1620), followed by Canada (*N* = 466) and the United Kingdom (*N* = 316). An overview of all the countries and their ranking according to number of published articles is illustrated within a world map (see Figure 4).

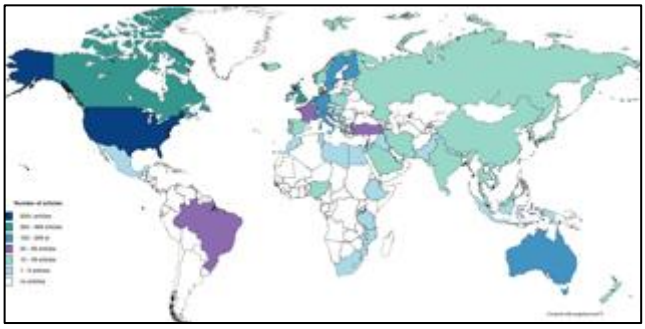

Figure 4: World map of total country output based on the country of the first author.

The majority of included articles were published by a first author based in a medical department (e.g., pediatrics, psychiatry, neuroscience, sports medicine, critical care medicine), but this showed a significant decline over the years (β = -.78, p < .05, from 56.10% in 1975 - 1980 to 39.94% in 2006-2010). Multidisciplinary departments (e.g., developmental & behavioral science, department of public health, institute of health sciences, center for pain services) represented the second most frequent discipline or department, with a stable representation over the years around 14% (β = .48, *ns*). With the exception of physiotherapy and anesthesia, all other departments had a fairly stable representation. Physiotherapy (β = .92, p < .01, from 0% in 1975 - 1980 to 2.02% in 2006 - 2010) and anesthesia (β = .83, p <

.05, from 0% in 1975 - 1980 to 7.67% in 2006 - 2010) showed an increasing representation over time (see Figure 5 for more details). Importantly, for a number of included articles there was no information available on the affiliation of the first author (N = 345 or 8. 11% in total).

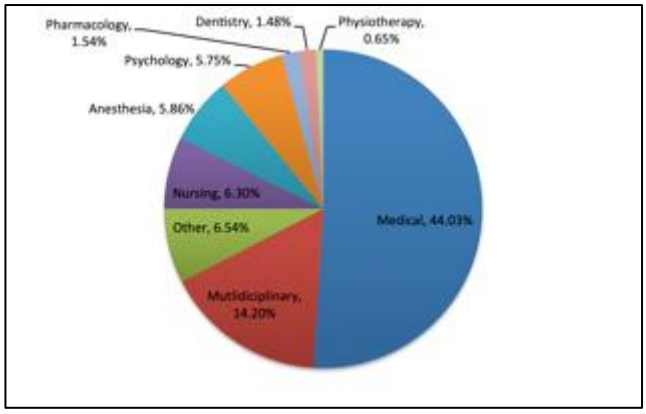

Figure 5: Average percentage of first author's discipline between 1975 -2010.

3.3 Domain coding

3.3.1 Type of article

Original research articles showed a clear dominant representation in all time periods, accounting for 70-80% of all included articles from 1975 - 2010 (β = .49, *ns*). While both theoretical articles and clinical guidelines had an equally low representation (between 1 to 5% over all time periods), review articles showed a steady representation between 15% and 23% between 1975 and 2010 (β = -.59, *ns*; see Figure 6 for the average representation from 1975 -

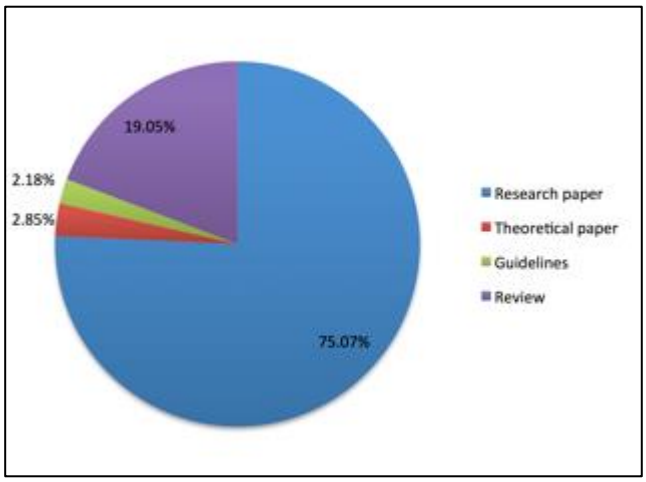

Figure 6: Average percentage of each article type between 1975 - 2010.

2010). Of those reviews, the majority consisted of narrative reviews (≥87% of all reviews in any given 5-year time period). Although systematic reviews represented only a small portion of all review articles, an increasing trend was observed in the percentage of systematic reviews published over time (β = .74, p = .060).

3.3.2 Topic of article

As depicted in Figure 7, the most popular topics in the included articles throughout the years were pain intervention (representation from 1975 - 2010 between 24.39 - 44.63%), pain characterization (representation from 1975 - 2010 between 30.20 - 56.10%), and pain assessment (representation from 1975 - 2010 between 18.90 - 34.15%), with articles on pain intervention dominating the literature since 1986. All content categories, with the exception of articles on model development and procedural factors, showed a stable representation throughout the years (all β < .67, *ns*). Model development (β = .84, p < .05; from 0.00% in 1975 - 1980 to 7.91% in 2006 - 2010) and procedural factors (β = .81, p < .05; from 0.00% in 1975 - 1980 to 3.13% in 2006 - 2010) showed a significant increase in representations throughout the years.

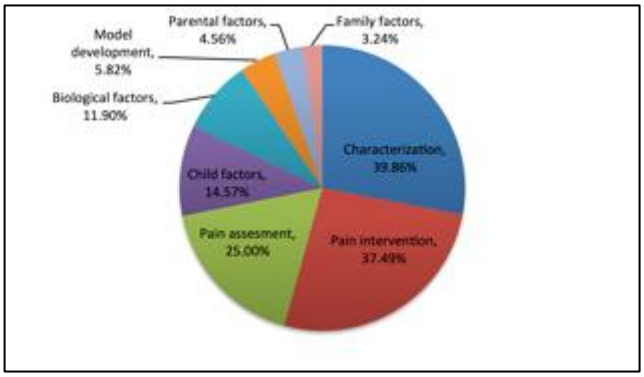

Figure 7: Average percentage of the article topics between 1975 - 2010

3.3.3 Type and age of participants

With respect to the type of samples, clinical samples (e.g., post-operative sample, children with inflammatory bowel disease, children reporting to emergency services or

hospitalized in pediatric intensive care units) showed a clear dominance since the start, although a steady, significant decrease was observed over time (β = -.90, p < .01; from 82.93% in 1975- 1980 to 66.87% in 2006 - 2010). Articles including healthy samples showed a significant increase over time (β = .87, p < .05, from 12.20% in 1975 - 1980 to 25.21% in 2006 - 2010), although they still only represented 25% of all published and included articles in the last 5-year period (2006 - 2010; see Figure 8). Only a small, but significantly increasing portion of the included articles were animal studies (β = .78, p < .05; from 00.00% in 1975-1980 to 1.72% in 2006 - 2010).

Until 1995, the majority of the included articles (from 73.17% between 1975 - 1980 to 50.00% between 1991 - 1995) did not report any detail on the participants' age in the abstract. The practice of not reporting any information on age within the abstract showed a significant decline over the years (β = -.99, p < .001). When age is indicated, children (between 6 and 12 years of age) and adolescents (between 13 and 18 years of age) were the most frequently represented age ranges, with both also showing a significant increase in representation over the years (β = .97, p < .001 for children, from 14.63% in 1975-1980 to 34.29% in 2006 - 2010, and β = .92, p < .01 for adolescents, from 9.76% in 1975- 1980 to 40.55% in 2006 - 2010). With the exception of a significant increase in studies involving a premature age range (β = .82, p < .05 from 2.44% in 1975 - 1980 to 5.40% in 2006 - 2010) and a trend for an increase in studies involving newborns (β = .73, p = .058 from 4.88% in 1975 - 1980 to 8.28% in 2006 - 2010), all other age groups (infants, preschoolers and child animals) had a steady representation throughout the years (all β < .68, *ns*, see Figure 9).

With respect to the inclusion of relevant others (i.e., parents, teachers, and/or health care professionals), on average, few of the included articles in our search involved or solely focused on parents (10.29%), health care professionals (9.29%), or teachers (0.29%). At their peak, parents were included in 14.04% of the articles (in the period 2001 - 2005) and health professionals in 14.38% (in the period 1991 - 1995). Despite this low representation of

articles on the social context of pediatric pain or the use of multiple informants within our search, a significant trend was observed of articles increasingly including parents over time (β = .76, p < .05; from 9.76% in 1975 - 1980 to 13.25% in 2006 - 2010).

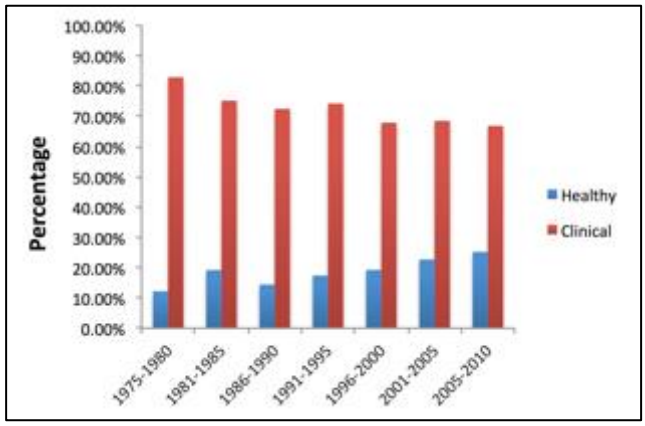

Figure 8: Trends in the percentage of usage of a healthy/population-based or clinical sample per 5 years.

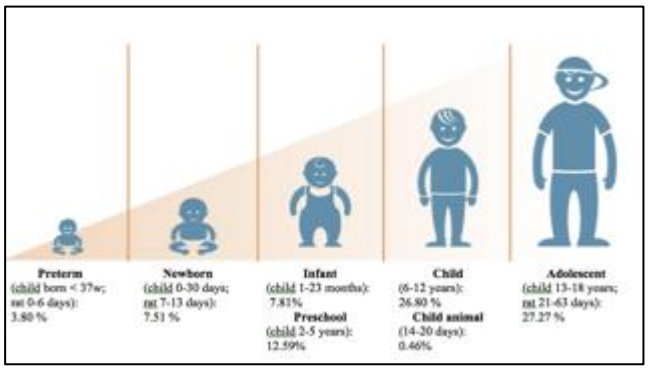

Figure 9: Average percentage on articles for each child developmental stage. Picture adapted from Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH, HHS. http://www.nichd.nih.gov.

3.3.4 Pain stimulus characteristics

Articles investigating chronic or acute pain experiences in children showed a clear dominance, relative to articles on disease-related pain and experimentally-induced pain. The largest proportion of articles reported on chronic pain until 1991, after which, the largest proportion of included articles focused on acute pain. However, between 2006 and 2010 both chronic and acute pain had an equally high representation of about 32% of all included articles. Overall, articles on acute pain showed a significant increase throughout the years (β = .88, p < .05; from 21.95% in 1975 - 1980 to 31.84% in 2006 – 2010; See Figure 10 for more

details). A closer examination of the specific types of acute pain experiences studied (see Figure 11) indicated that, although between 1975 -1980 no articles on procedural pain were found and included in our search, the study of procedural pain significantly increased over the years (β = .83, p < .05, from 0.00% in 1975 - 1980 to 54.14% in 2006 - 2010) becoming more frequent than articles reporting on surgical pain.

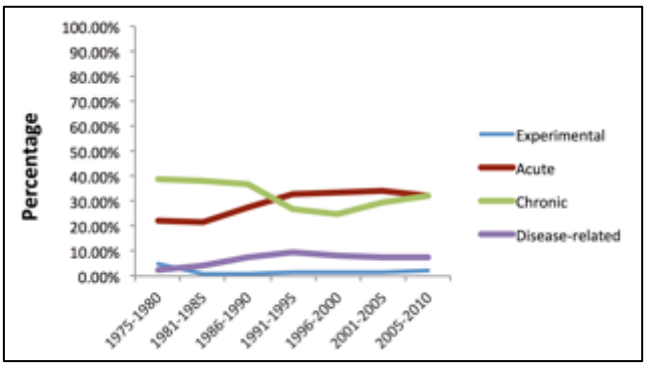

Figure 10: Trends in the percentage of pain characteristics per 5 years.

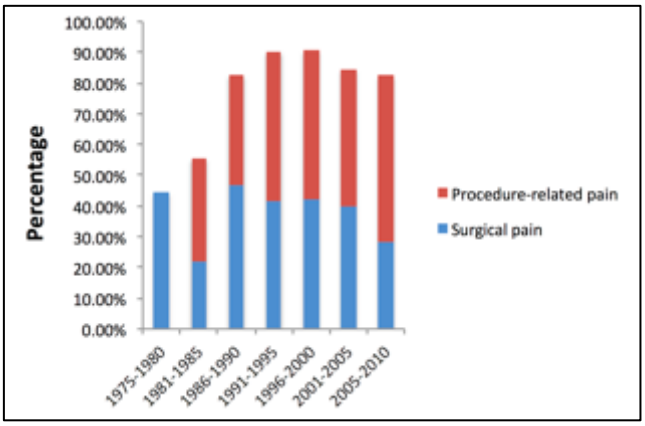

Figure 11: Trends in the percentage of surgical versus procedural pain per 5 years.

With respect to the experimental designs used in animal studies, thermal pain induction was most frequently used (average representation between 1981 – 2010 of 59.62%), followed by mechanical pain paradigms (average representation between 1981 – 2010 of 41.57%; see Figure 12 for more details). Only the use of experimentally induced inflammation showed a change over time, with a significant increase observed (β = .82, p < .05) from 0.00% in 1981 -1985 (the first time period including animal studies) to 67.86% in 2005-2010 animal studies using this pain model.

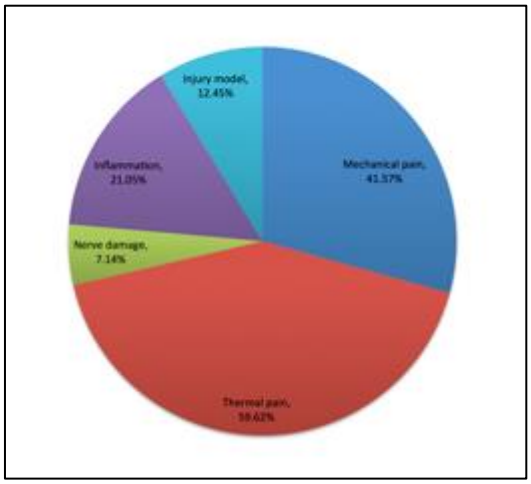

Figure 12: Average percentage of experimental designs used in animal studies between 1981 - 2010.

4. Discussion

The results of this categorical and bibliometric meta-trend analysis provide a comprehensive overview of the development of the scientific literature in pediatric pain over 35 years following the inception of the field. In accordance with the observed increase of research on pain in general [23], our findings revealed a continued increase of pediatric pain literature since 1975. This growth was especially notable since 1990, which coincided with a shift in focus from chronic pain to acute pain. This shift to acute pain research is in contrast with the adult pain literature where a growing focus on chronic or disease-related pain seems apparent [23,24]. It is possible that this shift reflects increased awareness about the problem of procedural pain in children, which has been the focus of recent clinical practice guidelines and other knowledge translation work [30]. Furthermore, the focus on acute pain in childhood might also be prevalent due to growing acknowledgment of the possible role of early life pain experiences in the development of chronic pain or altered pain processing [29]. Similar to earlier reviews [3,13], our findings show a continued increase in research on neonatal pain over time. This likely reflects the increased survival and need for care of preterm neonates and associated ubiquitous procedural pain exposure.

The most popular research topics identified were pain characterization, intervention, and assessment, which is also reflected in the top most cited articles mainly consisting of

studies on pain assessment, randomized-controlled intervention trials, and epidemiological studies. Although mostly in line with trends observed within the larger field of pain [23], notable differences were observed for articles on pain characterization, with a substantially larger representation within pediatric pain, and pain anatomy/physiology, which was considerably less represented within pediatric pain literature [23]. These differences might reflect the position of pediatric pain as a relatively new, emerging field within the larger pain field therefore prioritizing a better understanding or characterization of pediatric pain experiences. Additionally, this finding reflects the mostly clinical orientation of pediatric pain research, but the relative lack of basic science exploring biomedical mechanisms specific to pediatric pain experiences. This orientation might also be partially explained by ethical challenges involved in applying methodologies to investigate underlying pain mechanisms (e.g., imaging, experimental pain induction) within a vulnerable sample of children [6]. Further supporting this clinical focus is the observed increase in systematic reviews. This may be a result of the Cochrane Collaboration established in 1993, which includes the Pain and Palliative Care group promoting systematic reviews on interventions for acute and chronic pain across the lifespan to advance evidence-based pain management.

Consequently, similar to the strategic pain research agenda for the 21st century, outlined by Gereau and colleagues (2014), the field of pediatric pain could benefit from a more strategic approach to identify future research directions. The findings from this review can be first step in this direction. For instance, our finding of a small number of animal studies or research studies utilizing experimental pain paradigms in children supports the need for increased bidirectional, translational research between clinical and basic science, which could further our understanding by investigating similar research questions with different methodologies [12]. For example, animal studies could have the particular potential to shed more light on the impact and continuity of pediatric pain into adulthood. This need to promote collaborative activities between research and clinical settings has also been identified as an

important future direction within the field of pediatric psychology [7]. However, not all areas for which a relative low representation was identified might require increased research efforts. For example, despite a low representation of research in infants and preschoolers, the identified distribution of research attention across age groups maps well onto established pain prevalence rates throughout development [25]. Nonetheless, one could argue that more efforts are needed to understand how pain responses and pain management are shaped early on in development and how this impacts later pain sensitivity. Consequently, further initiatives (e.g., panel discussions with field experts and patients) are needed to further develop a strategic research agenda for the field and establishing research priority areas. Given the importance of public awareness and advocacy within the history of pediatric pain, continuing, or even increasing, our efforts to involve and make the public aware of pediatric pain as a major health problem will be crucial for the success of this strategic agenda [7,12].

Our findings with respect to the bibliometric indicators are largely consistent with the indicators for general pain research [23,26], with *PAIN* identified as the top ranked journal publishing most pediatric pain research, followed by the journals *Headache*, *Cephalalgia*, *European Journal of Pain and Pediatrics*. This ranking indicates that pediatric pain researchers focus on reaching a broader pain-related audience rather than a pediatric-focused audience. Furthermore, two of the top ranked journals are specifically focused on headache (i.e., *Headache* and *Cephalalgia*), thereby endorsing previous findings of headache being the pediatric pain condition receiving most attention [8,17]. Further in alignment with the larger pain field is the dominance of the USA within pediatric pain literature. However, a striking difference is the relative contribution of Canada to the field of pediatric pain, which ranked second in our review compared to third or fourth [23,26] for contributions to general pain literature. This finding reflects previous findings [31] and training efforts (e.g., initiating the international training program PICH) by Canada to increase capacity for pediatric pain research by publishing more articles on pediatric pain than expected using average world

publication rates as a guidance [31].

The main strengths of the current review are the breadth in both the scope of the search and content analyses of the included articles. Our search was not limited to one journal, which contributes to the richness of the gathered data, and the results confirm the large spread of the available evidence (across 904 different journals). Additionally, bibliometric analyses are often limited to providing quantitative indicators on the development of a field in terms of number of publications, citation scores and geographical spread. The current review went beyond the sole reliance on these indicators and conducted a rigorous analysis of the available abstracts to reveal more in depth qualitative trends on the content of the published research. Due to the vast amount of data gathered, it is beyond the scope of this review to provide an in-depth discussion of all the trends. The analyses described above represent a fraction of the possibilities and readers interested in specific trends and evolutions are encouraged to take advantage of the supplementary data files.

Notwithstanding the rigorous approach, some limitations need to be carefully considered. The review only included articles for which an English abstract was available via an online database. Although most journals use English as the main language and provide an abstract free of charge, this restriction might have induced a language and publication bias. For example, the need for an abstract to be eligible for the coding process resulted in a moderate number of exclusions and in some key articles not being included in the final selection [e.g., 1,32]. The exclusion of non-English abstracts and use of the USA-based Web of Science™ as the main database could also have influenced our results regarding country representations. Furthermore, for reasons of feasibility, only the abstract, not the full text, was coded. Pilot testing of the coding scheme revealed that most relevant information could be identified from the abstract. Only with respect to the age characteristics was it noted that a large percentage of articles did not provide sufficient details on the age of their sample within the abstract. Although this practice significantly decreased over the years, in the last time

period (2006-2010) still over a third of articles did not clarify the specific age of their sample. The new Consolidated Standards of Reporting Trials for Children (CONSORT-C) and Standard Protocol Items for Randomized Trials for Children (SPIRIT-C) to standardize reporting on pediatric clinical trials also identified the need for clearer reporting of age characteristics and might further facilitate this positive trend. Lastly, a librarian with expertise in systematic reviews and previous bibliometric analyses on pain [26] were consulted to define our search terms. Despite this careful selection of search terms the breadth of the topic area precluded inclusion of every possible relevant term. Consequently, this strategy might not have captured original seminal papers [e.g., 2] due to the absence of definitive terms that distinguish the emerging field of pediatric pain at that time.

Despite these limitations, this extensive review provides a comprehensive overview of the topics within pediatric pain literature over 35 years. The findings illustrate a considerable growth in pediatric pain literature, particularly noticeable for neonatal pain and systematic reviews. Content analyses revealed a primarily clinical orientation within pediatric pain research focused on pain characteristics, management and assessment within children and adolescents experiencing acute or chronic pain. Findings lay the groundwork for future pediatric pain research and additional growth in the area.

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FIGURE LEGEND

Figure 1: Overview of article selection process.

Figure 2: Overview of the growth in published articles on pediatric pain between 1975 -2010.

Figure 3: Trends in the percentage of single versus multiple authored articles per 5 years.

Figure 4: World map of total country output based on the country of the first author.

Figure 5: Average percentage of first author's discipline between 1975 -2010.

Figure 6: Average percentage of each article type between 1975 - 2010.

Figure 7: Average percentage of the article topics between 1975 - 2010.

Figure 8: Trends in the percentage of usage of a healthy/population-based or clinical sample per 5 years.

Figure 9: Average percentage on articles for each child developmental stage. Picture adapted from Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH, HHS. http://www.nichd.nih.gov.

Figure 10: Trends in the percentage of pain characteristics per 5 years.

Figure 11: Trends in the percentage of surgical versus procedural pain per 5 years.

Figure 12: Average percentage of experimental designs used in animal studies between 1981 - 2010.

DIGITAL CONTENT LIST

Supplemental Digital Content 1: Excel dataset containing the included articles.

Supplemental Digital Content 2: Excel dataset containing the excluded articles.

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Appendix A
Search and coding strategy

Part 1. Search terms Web of Science.

Developmental Terms	**Pain Terms**
Infant OR infan OR newborn OR newborn* OR new-born* OR baby OR baby* OR babies OR neonat* OR perinat* OR postnat* OR child OR child* OR schoolchild* OR schoolchild OR school child OR school child* OR kid OR kids OR toddler* OR adolescent OR adoles* OR teen* OR boy* OR girl* OR minors OR minors* OR underag* OR juvenil* OR youth* OR kindergar* OR puberty OR puber* OR pubescen* OR prepubescen* OR prepuberty* OR pediatrics OR pediatric* OR paediatric* OR peadiatric* OR schools OR nursery school* OR preschool* OR pre school* OR primary school* OR secondary school* OR elementary school* OR elementary school OR high school* OR highschool* OR school age OR schoolage OR school age* OR schoolage* OR infancy OR schools, nursery OR infant, newborn*	*pain* or headache* or "head ache*" or head-ache* or migraine* or cephalalgi* or "stomach ache*" or "tummy ache*" or "abdominal ache*" or "belly ache*" or earache* or ear-ache* or toothache* or tooth-ache* or odontalgi* or dysmenorrh* or neuralgi* or cervicodyn* or analg*or nocicept* or hyperalg*or hypoalg*or fibromyalg*or radiculalg*or colic or sciatic* or arthralg* or causalg* or eudyn* or maldyn* or brachialg*or ophthalmodyn* or cephalalg* or otalg**

Part 2. Overview and explanation of topic categories.

Code	Definition
Pain assessment	Articles focusing on pain evaluation or a diagnostic test for pain. Examples are articles describing the efficacy, side-effects, cost-effectiveness, utility of a diagnostic test. Includes also articles in non-clinical subjects designed to explain the mechanism of action of the diagnostic test. Also includes outcome studies and articles reporting on the training, experimental ethics or healthcare policy
Pain intervention	Articles focusing on an intervention for pain (e.g., surgical, energetic, pharmacological, psychological, physical/behavioral). Examples are articles on the efficacy, side-effects, cost-effectiveness, utility for an intervention for pain. Includes also articles in non-clinical subjects designed to explain the mechanism of action of the intervention. Also includes outcome studies and articles reporting on clinical pain management, training, experimental ethics or healthcare policy/usage.
Pain characterization/ epidemiology	Articles describing or characterizing a pain syndrome or phenomenon in terms of its incidence, prevalence or impact, features or symptoms, classification, predictive or risk factors, or effects on other variables. This also includes epidemiological articles and articles describing pain behaviors or symptoms in general, not in the context of pain assessment or investigation of a modulatory effect on pain behavior.
Model development	Articles presenting, refining, translating, characterizing and/or evaluating the validity, reliability or usefulness of a model, scale, questionnaire, dependent measure, paradigm or technique.
Procedural factors	Articles reporting on the modulatory effect of procedural factors of a painful procedure (e.g., the impact of length of a procedure on the pain experience, which immunization to give first)
Biological factors	Articles reporting on the modulatory effect of biological factors, organismic factors or molecules on pain, as well as articles reporting on where pain processing or modulation occurs. Also includes articles reporting on physiological processes related to pain.
Child factors	Articles reporting on the modulatory effect of a child-related factor on pain (e.g., age, sex)
Parental factors	Articles reporting on the modulatory effect of a parent-related factor on pain or the impact of pain on parental functioning (e.g., impact of parental catastrophic thinking, impact on parental functioning, emotional well-being)
Family factors	Articles reporting on the modulatory effect of a family-related factor on pain or the impact of pain on family functioning (e.g., family functioning, siblings, relationship between parent-child).

Overview and explanation of pain stimulus categories.

Code	Definition
Experimental pain	Experimental induced pain was used or review/theoretical articles relates to experimental pain. For animal studies only, the specific type of experimental pain paradigm used was coded: - Mechanical: mechanical force (dynamic or static pressure, distention, or vibration) was applied or elicited by an action of the subject. For example, withdrawal threshold to vonFrey filaments. - Thermal: heat or cold stimuli were applied. For example latency to withdraw from a heat source. - Nerve damage: traumatic (surgical) or chemical nerve damage was applied. For example nerve axotomy or compression. - Inflammation: a noxious stimulus was applied that is a known inflammatory substance or a manipulation known to release chemical algogens was used (Algogens include carrageenan, Freund's adjuvant (into the hindpaw or knee), hypo/hypertonic saline). - Injury models: an animal model of a specific human clinical pain state was used (e.g., amputation, fracture, burn, laparotomy, polyarthritis models (including Freund's adjuvant into the tail)).
Acute pain	Samples of children currently experiencing acute pain (e.g., acute abdominal pain, immunization, blood draw, post-operative pain) or review/theoretical paper relates to acute pain. This also includes research articles and reviews on samples in healthy children in which no pain was induced, but children had to reflect on acute pain experiences (e.g., healthy sample of children used to validate a pain-related questionnaire). If the article reviews or investigates acute pain, then the type of acute pain was coded: • Surgical pain: pain related to surgery or operation (e.g., post-surgical pain) • Procedural pain: pain related to a medical procedure (e.g., immunization pain, lumbar punctures, pain due to dental procedure)
Chronic pain	Samples of children diagnosed with a chronic, persistent or recurrent pain condition or review/theoretical paper relates to a chronic pain condition (e.g., dysmenorrhea, chronic abdominal pain, migraines).
Disease-related pain	Samples of children currently experiencing pain related to a disease (e.g., cancer-related pain, pain due to sickle cell disease, arthritis) or review/theoretical paper relates to pain related to a disease.