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Establishing consensus on biopsychosocial factors associated with pediatric chronic pain: A modified Delphi study

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ABSTRACT

A variety of factors are associated with the development and maintenance of chronic pain in children. Identifying modifiable factors associated with pediatric chronic pain is important to use them as target outcomes in the development and evaluation of interventions for the prevention and management of chronic pain. This study aimed to reach expert consensus on factors associated with pediatric chronic pain and their modifiability and population-level effect. Pediatric pain experts were questioned using a web-based two-round modified Delphi method. Two rounds of questions with Likert scaling were used to identify influencing factors (Round 1) and to reach consensus on each factor (Round 2) in terms of: 1) strength of association with chronic pain in children; 2) modifiability; and 3) population-level effect. An inductive approach was used to derive categories (ranging from 'very low' to 'very high') and subcategories (ranging from 'low' to 'high'). In total, 48 experts from 14 different countries completed Round 1, and 31 completed Round 2. A list of 47 factors was considered to be associated with pediatric chronic pain. Four factors (physical activity (PA), sedentary behavior (SB), pain-related school absence, and pain concept/knowledge of the child) were considered highly modifiable and three factors having a high population-level effect (PA, SB, and the child's depressive or negative emotional feelings). Expert consensus was established about modifiable and population-level factors associated with pediatric chronic pain through this web-based modified Delphi study, guiding target outcomes for its prevention and management.

Perspective: This article presents the results of a modified Delphi study with pediatric pain experts to gain consensus on factors associated with pediatric chronic pain. Relationship strength, modifiability, and population-level effect of associated factors were rated to identify areas of research priority and interventions aiming to reduce the development and maintenance of chronic pain in children.

Introduction

Chronic pain (i.e., pain in ≥ 1 anatomic region persisting or recurring for >3 months¹) in children is an increasingly recognized clinical problem with alarmingly high and rising prevalence rates.^{2,3} Worldwide 20.8 % of children and adolescents experience chronic pain, with > 5 % of these children experiencing moderate to severe chronic pain.³⁻⁷

Children may experience chronic pain related to injuries or underlying diseases, or, pain can be primary in nature (e.g., fibromyalgia), sometimes without any specific identifiable cause or disease (e.g., functional abdominal pain).^{1,8,9} Chronic pain can deleteriously impact the lives of children and their family, and has been associated with a range of negative consequences, including impaired physical and psychosocial functioning, reduced school attendance, poorer reading levels, increased

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healthcare utilization, and decreased overall quality of life.^{10–12} Moreover, it increases the risk of chronic pain across the lifespan^{13–16} and may even reduce life expectancy.^{17,18} Also children's families can experience significant physical and psychosocial sequelae due to the child's pain,¹⁹ such as anxiety and depressive symptoms,²⁰ and financial burden due to (in)direct medical costs associated with their child's pain condition.²¹

A variety of factors are associated with chronic pain in youth, including demographic (e.g., sex and age,⁵ socio-economic status²²), physical (e.g., sedentary behavior (SB),²³ physical activity (PA),²⁴ insomnia²⁵), and psychosocial (e.g., family history of chronic pain,²² symptoms of depression and generalized anxiety,²⁶ lower school satisfaction and perceived school performance²⁶) factors. For children undergoing surgery, presurgical pain intensity, anxiety, pain coping efficacy, depressive symptoms, sleep quality, and parental pain catastrophizing have been identified as significant predictors of post-surgical chronic pain development in children.^{27,28} Another study indicated that early childhood adversity, such as being bullied or abused, and family conflict may be risk factors for chronic pain in adolescence.²⁹ Being the child of a parent with chronic pain increases the risk of developing chronic pain as well.³⁰ Despite the number of studies exploring factors associated with the development or maintenance of chronic pain in childhood, many factors remain underexplored (e.g., endocrine disruptors, pubertal maturation, parenting style) and existing studies have investigated the biopsychosocial nature of pain from different perspectives (e.g., theoretical models, clinical observations). This results in heterogeneous and sometimes low-quality studies making it difficult to draw conclusions, resulting in an incomprehensive perspective on the onset or maintenance of chronic pain in children.

The Delphi method is a time and cost-effective structured process of collecting and distilling knowledge from a panel of experts by means of questionnaires interspersed with controlled opinion feedback.³¹ Delphi studies employ multiple iterations of questionnaires and feedback to develop a consensus of opinion that concerns a particular problem or topic. Moreover, Delphi studies allow access to a diverse group of experts, including researchers and clinicians from various disciplines in the field of study (in this case: pediatric pain), removing geographical limitations imposed by other research techniques.³² The aim of this web-based modified Delphi study was to identify and reach expert consensus on factors associated with pediatric chronic pain. Relationship strength with chronic pain in children, modifiability (i.e., the extent to which it is possible to change the influence of the factor in a healthful direction) and population-level effect (i.e., the expected impact or reach of the factor on chronic pain in children, taking into account both the strength of association between the factor and chronic pain as well as prevalence of exposure to that factor in children) of associated factors were rated to identify areas of research priority and interventions aiming to reduce chronic pain onset as well as the transition from acute to chronic pain in children.

Methods

Ethics and study design

Ethics approval was obtained from the Ethics Committee of the University Hospital Brussels/Vrije Universiteit Brussel on May 10th, 2023 (B.U.N. 1432023000075). A modified web-based two-round Delphi methodology was used to gather consensus on factors associated with pediatric chronic pain and their modifiability and population-level effect. Given the active role of the research team in generating consensus, and the pre-selection of factors for the Round 1 survey, the study methodology is described as a modified Delphi methodology.³² The use of a modified web-based Delphi methodology allows for anonymity, limits time burden on participants and allows for the inclusion of a wider geographical area to capture opinions and experiences of pediatric pain experts. The methodology of this study was based on

principles used to develop the DONE Framework by Stok et al.,³³ and principles used in the Delphi study by Mutsaers et al.³⁴ The study was completed between June and August 2023 in compliance with the principles of the Declaration of Helsinki, the principles of Good Clinical Practice and in accordance with all applicable regulatory requirements.

Expert recruitment

Purposive sampling was used to invite potential experts who met the inclusion criteria. The research team selected three (inter)national organizations that are well-known for their expertise in the study and practice of pain and pain relief: 1) the Pain in Motion International Research Consortium (PiM) (www.paininmotion.be), 2) the Special Interest Group (SIG) Pain in Childhood from the International Association for the Study of Pain (IASP) (www.iasp-pain.org/group/pain-in-childhood), and 3) the Belgian Pediatric Pain Association (BePPA) (www.belgianpainsociety.org/sig-1/beppa). Other inclusion criteria were: 1) being a researcher and/or clinician (e.g., medical doctor, physiotherapist, psychologist, nurse) with expertise in the field of pediatric pain, and 2) having sufficient proficiency of the English language. With a homogeneous group a minimum sample size of 10 has been supported in the Delphi literature.³⁵ Due to experts belonging to the same field and pediatric pain being a niche within the field of pediatrics, a pragmatic approach was used to recruit experts. Experts were first invited to participate by the research team via email and a call on social media (LinkedIn, Twitter). Through the call on social media, interested experts could reach out to the research team via email, after which they received the same invitation email if eligible for study participation. This email included an information letter with detailed information about the study and eligibility criteria, as well as the link to Round 1 of the survey. Completion of the questionnaire constituted implied consent. Privacy and confidentiality were maintained by anonymizing the questionnaires, and no responses were linked to an individual email address. However, at the end of Round 1, experts were asked their permission to contact them via email to participate in Round 2, where, if given consent, their email address was requested. To link responses from Round 1 to responses of Round 2, experts were asked to enter a personal code (XX-XX-XX) at the start of each survey, consisting of the following instructions: last 2 digits year of birth – mother's initials (first letter first name followed by first letter last name) – father's birth month.

Focus and procedure of the modified Delphi study

The focus of this modified Delphi study was to query expert opinion regarding factors associated with the development or maintenance of pediatric chronic pain and their modifiability and population-level effect. Because conflated concepts such as predictor, risk factor, determinant, mediator, and moderator are being used interchangeably, the term 'factor associated with' was chosen to be able to capture all aforementioned concepts. During Round 1, a list of 50 potential factors associated with the development or maintenance of chronic pain was presented. The list of factors was based on clinical expertise from the research team and a non-systematic scientific literature search in PubMed/MEDLINE to examine the existing evidence supporting the following topics: determinants, risk factors, predictors, prognostic factors, or influencing factors of chronic pain in children from 0–18 years old (e.g.,^{5,15,23,36–38}). Experts were asked to rate each of the factors in terms of *strength of association* with pediatric chronic pain. Experts also had the option to select 'Not my expertise' for items for which they felt they did not have the appropriate expertise. Comment boxes enabled open-ended responses to gather expert feedback on the proposed factors and ask for additional factors that might have been overlooked when creating the initial list of factors.

Experts who completed Round 1 and provided consent to be invited for Round 2, received the link to Round 2 as well as a summary report of Round 1. In Round 2, experts were asked to score each factor that

proceeded from Round 1 (i.e., assessed as associated (to a large extent) with the development or maintenance of chronic pediatric pain) in terms of *modifiability* (the extent to which it is possible to change the influence of the factor in a healthful direction) and *population-level effect* (the expected impact or reach of the factor on chronic pain in children, taking into account both the strength of association between the factor and chronic pain as well as prevalence of exposure to that factor in children). Experts again had the option to select 'Not my expertise' for items for which they felt they did not have the appropriate expertise and comment boxes enabled open-ended responses to gather expert feedback on the proposed factors and ask for additional factors that might have been overlooked when creating the initial list of factors. For both Round 1 and Round 2, experts had 3 weeks to complete the survey and received two reminders (one after week 1 and one after week 2). A summary report of Round 2 and the overall findings was sent to all experts, including experts who only completed Round 1, in January 2024. Experts were invited to review the summary report and send any additional remarks via email. At the end of Round 2, all experts were asked for their approval to be acknowledged in the final publication of the study. The other experts chose to remain anonymous.

Data collection and analysis

Surveys were distributed and data were collected via Qualtrics®, using an anonymous link assuring that the responses were not identifiable and no identifying information was collected. Before distribution to the experts, the surveys were pilot tested by three members of the research team to remove typos and estimate the time experts would need to complete each survey. Socio-demographic data were questioned at the beginning of each survey, including age, sex, primary affiliation, country of work, professional role (e.g., researcher, medical doctor, physiotherapist), and highest degree. Descriptive characteristics of the expert panel were described using means and standard deviations for continuous data and frequencies and percentages for categorical data. Differences between experts from Round 1 and Round 2 were analyzed using independent t-tests for continuous normal distributed variables and Pearson Chi-square test for categorical data. The distribution of continuous data within each group was assessed by histograms, QQ-plots, and the Shapiro-Wilk test. Likert type scales allowed experts to assess the strength of association with pediatric chronic pain (Round 1), modifiability (Round 2), and population-level effect (Round 2) of each factor. Likert scales are commonly used in Delphi rounds and allow for data to be analyzed using rating techniques. Statistical analysis was performed with the statistical software IBM SPSS Statistics 29 (SPSS IBM, New York City, NY).

Strength of association (Round 1)

Strength of association with pediatric chronic pain was assessed by the experts using a 5-point Likert type scale, ranging from 1 ('not associated with chronic pain in children') to 5 ('associated to a large extent with chronic pain in children'). Likert scores of 1 to 2 were categorized as a low score (item is not considered to be associated with chronic pain in children), a score of 3 as moderate (item should be discussed), and scores of 4 to 5 as a high score (item is highly associated with chronic pain in children). An item that was ranked as low (score 1–2) by more than 2/3rd of the experts, and had no feedback indicative for rewording of the item, was deemed to meet consensus and removed from Round 2. Any item that was ranked as high (score 4–5) by more than 2/3rd of the experts, and had no feedback indicative for rewording of the item, was deemed to meet consensus and entered Round 2. In case the majority of experts ranked the factor as moderate (score 3) or no consensus could be reached based on the 2/3rd rule, the research team discussed the factor again based on the experts' scores and feedback, available evidence, and research/clinical experience, and made the final decision to include or exclude the factor for round 2. Additionally, the research team discussed the experts' suggestions for the wording of

factors and additional factors. The consensus meeting of the research team took place on July 5, 2023.

Modifiability and population-level effect (Round 2)

In Round 2, experts assessed each of the factors that either proceeded from Round 1 or that were additionally suggested by the experts in Round 1 and agreed upon to add to the list by the research team, in terms of modifiability and population-level effect. Factors that were additionally added to the list based on feedback from Round 1 were first assessed in terms of strength of association, using the same 5-point Likert type scale and methodology as used in Round 1. Each factor was assessed in terms of modifiability using a 5-point Likert type scale ranging from 1 ('not modifiable') to 5 ('very modifiable'), and population-level effect using a 3-point Likert type scale ranging from 1 ('low population-level effect') to 3 ('high population-level effect'). For these outcomes, we looked at the mean scores to decide on the final category: modifiability categorized as low (1.00–2.49), moderate (2.50–3.49), or high (3.50–5.00); population-level effect categorized as low (1.00–1.49), moderate (1.50–2.49), or high (2.50–3.00). The research team held an online consensus meeting on September 11th, 2023, to discuss factors for which consensus in terms of strength of association could not be reached based on the experts' scores, to discuss the experts' comments, and to discuss the results of the assessments of the factors' modifiability and population-level effect.

Results

The process of this modified Delphi study is summarized in Fig. 1.

Participating experts

A total of 325 members of PiM, IASP SIG Pain in Childhood, and BePPA were invited to the Delphi study. At the time the study was conducted, PiM counted 100 members, IASP SIG Pain in Childhood counted 137 members, and BePPA counted 89 members. Since some experts are members of several of the aforementioned groups, the number of unique potential experts was 295. Forty-eight experts from 14 different countries with expertise in pain in children completed Round 1 (16.3 % response rate), of which 31 also completed Round 2 (64.6 % retention rate). Experts consisted of physiotherapists, psychologists, medical doctors, researchers, combinations of the aforementioned professions, nurses, a speech language pathologist, and a health innovation specialist. The majority of experts were female (64.6 %) and the mean age was 48.0 (± 12.4) years. No differences were found between the expert panel in Round 1 and Round 2, respectively. Expert characteristics are summarized in Table 1.

Round 1

After Round 1, consensus was reached by the experts on 26 out of 50 factors. All 26 factors were scored as highly associated with chronic pain in children. For the remaining 24 factors, consensus could not be reached based on the scores of the experts, and required discussion by the research team. Taking into account the expert scores and feedback on these factors and building upon research and clinical experience, the research team decided to exclude 14 factors from the list as they were considered poorly associated with chronic pain in children. The remaining 10 factors were evaluated as highly associated with chronic pain in children, and were included in Round 2. From these 10 factors, 7 factors (diet, depression, parental mental health, parental anxiety, number of pain sites, pain mechanisms, history of surgery) were reworded, and some additional explanation to 3 factors (pain-related school absence, diet, family functioning) was added, based on the experts' suggestions. One factor (negative emotional symptoms) was combined with the factor 'depression' into 'Depressive or negative emotional feelings of the child'. For all factors in Round 2, it was explicitly defined whether the factor was referring to the child or to

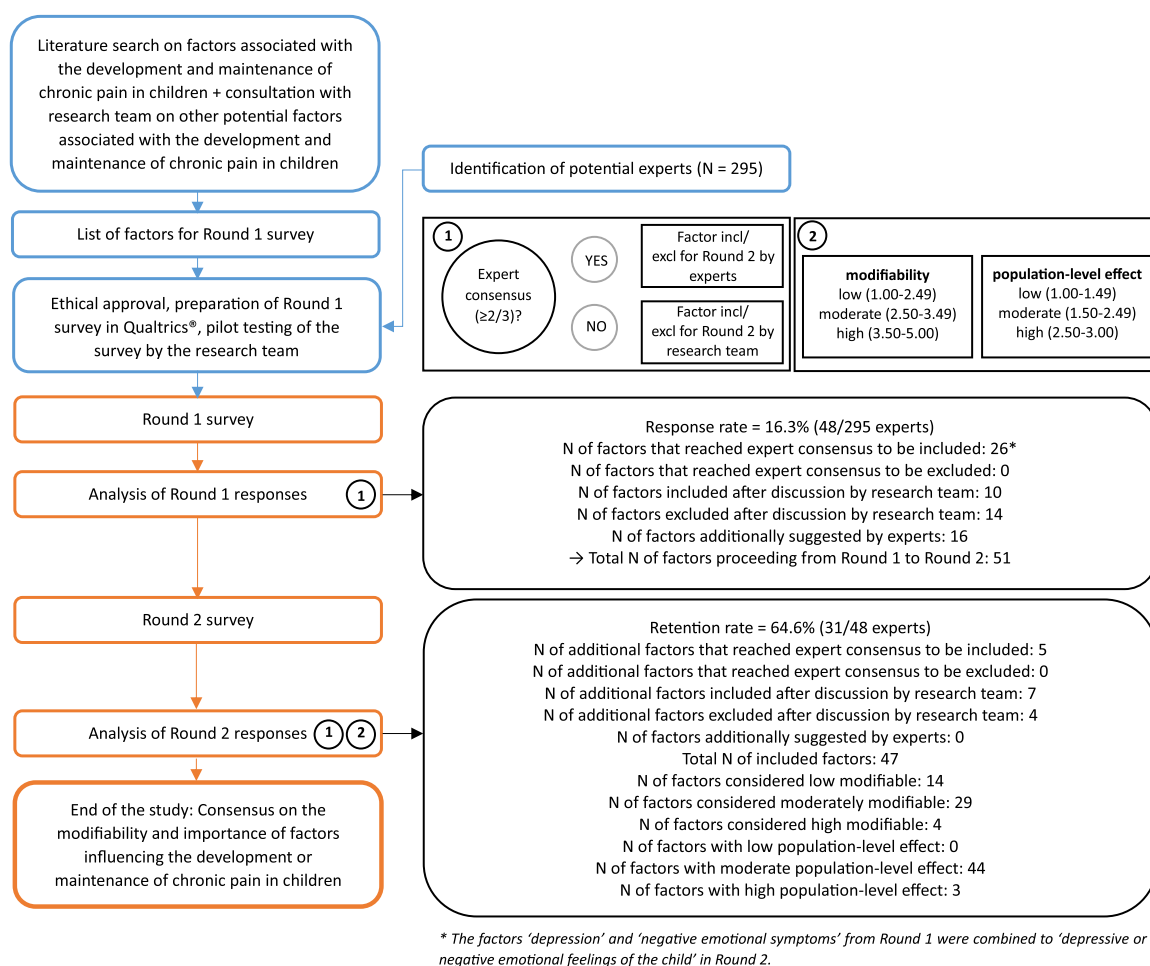


Fig. 1. Overview of the modified Delphi study process.

others (e.g., parents). The reason for this adjustment was that, despite the fact that the Round 1 instructions clearly stated 'Each of the following factors are child characteristics, unless indicated otherwise (e.g., parents).', it became clear from some of the experts' comments that for some of the factors (e.g., alcohol consumption) they were unsure whether the factor referred to children or to their parents/family. Thorough review of the experts' feedback and suggestions resulted in 16 factors that were additionally added to the list, resulting in a total of 51 factors to be presented to the experts in Round 2.

Round 2

From the 16 additional factors, expert consensus was reached for 5 factors ((behavioral) responses of the parent(s) to the child's pain, pain catastrophizing of the parent(s), relationship of the child with peers, previous psychological or emotional trauma of the child, (chronic) medical diagnoses of the child) and these were all considered highly associated with chronic pain in children. The remaining 11 additional factors were discussed by the research team, taking into account the expert scores and feedback on these factors and building upon research and clinical experience. This discussion resulted in 7 factors considered as highly associated (relationship of the child with healthcare providers, developmental disorders of the child, health literacy of the child, access to healthcare of the child, experiences of racism and stigma of the child, parenting style of the parent(s), multisensory sensitivity of the child) and 4 factors considered as poorly associated (endocrine disruptors/hormonally active agents, pubertal maturation of the child, early parentification of the child, weather factors) with chronic pain in children.

Finally, Round 2 resulted in a list of 47 factors associated with the development or maintenance of pediatric chronic pain. Of these 47 factors, 4 (pain-related school absence, PA, SB, and pain concept/knowledge of the child) were considered highly modifiable, 29 were considered moderately modifiable, and 14 were considered lowly modifiable. Three factors were considered having a high population-level effect (PA, SB, and depressive or negative emotional feelings of the child), while all other factors were considered having a moderate population-level effect. An overview of the decision process for all factors through the modified Delphi process is presented in Table 2. Average scores across factors on relationship strength, modifiability, and population-level effect are visualized in Fig. 2. Factors in the top-right corner that have larger circles, i.e., physical activity and sedentary behavior, can be considered the most important factors as these factors score high on all three rating domains. A complete overview of the results of the modified Delphi study process for Round 1 and 2 is summarized in Appendix 1 and 2, respectively (see Supplementary Files).

Discussion

This modified Delphi study identified 47 factors associated with pediatric chronic pain. These factors are in line with previous Delphi efforts in the field of pediatric chronic pain.³⁶⁻³⁸ The most recent work by Palermo et al.³⁸ identified mandatory (pain severity, pain interference, overall well-being, adverse events) and optional (emotional functioning, physical functioning, sleep) domains to assess in pediatric chronic pain clinical trials, all of which were covered in the current

Table 1

Characteristics of the expert panel.

Characteristics	Round 1 (n = 48)	Round 2 (n = 31)	Between-group difference p-value
Age ^a	M (SD) 48.0 (12.4) n (%)	46.2 (13.6)	.557
Sex ^b			
Male	16 (33.3)	12 (38.7)	.885
Female	31 (64.6)	19 (61.3)	
Prefer not to say	1 (2.1)	0 (0.0)	
Continent of work space ^b			
Europe	30 (62.5)	20 (64.5)	.981
North-America	7 (14.6)	5 (16.1)	
South-America	3 (6.3)	2 (6.5)	
Asia	3 (6.3)	2 (6.5)	
Oceania	5 (10.4)	2 (6.5)	
Country of work space ^b			
Belgium	18 (37.5)	11 (35.5)	1.00
The Netherlands	3 (6.3)	1 (3.2)	
Belgium/The Netherlands	1 (2.1)	1 (3.2)	
United States of America	6 (12.5)	5 (16.1)	
United Kingdom	5 (10.4)	4 (12.9)	
Australia	4 (8.3)	2 (6.5)	
France	2 (4.2)	2 (6.5)	
Brazil	2 (4.2)	1 (3.2)	
Canada	1 (2.1)	0 (0.0)	
New Zealand	1 (2.1)	0 (0.0)	
Uruguay	1 (2.1)	1 (3.2)	
Spain	1 (2.1)	1 (3.2)	
India Singapore	1 (2.1)	1 (3.2)	
Taiwan	1 (2.1)	1 (3.2)	
	1 (2.1)	0 (0.0)	
Professional role ^b			
Researcher	8 (16.7)	6 (19.4)	.997
Physiotherapist	4 (8.3)	2 (6.5)	
Medical doctor	11 (22.9)	6 (19.4)	
Psychologist	3 (6.3)	2 (6.5)	
Researcher/	7 (14.6)	6 (19.4)	
physiotherapist	7 (14.6)	4 (12.9)	
Researcher/medical	3 (6.3)	1 (3.2)	
doctor	1 (2.1)	0 (0.0)	
Researcher/psychologist	2 (4.2)	2 (6.5)	
Researcher/	1 (2.1)	1 (3.2)	
physiotherapist/	1 (2.1)	1 (3.2)	
psychologist			
Nurse			
Speech language			
pathologist			
Health innovation			
specialist			
Highest degree ^b			
Bachelor of Science	2 (4.2)	1 (3.2)	.977
Master of Science	17 (35.4)	11 (35.5)	
PhD	29 (60.4)	19 (61.3)	

The distribution of the continuous data within each group were assessed by histograms, QQ-plots, and the Shapiro-Wilk test.

M = mean; SD, standard deviation; n = count; % = percentage.

^a Continuous data that were normally distributed and subsequent group differences were analyzed using the independent samples t-test;

^b Categorical data were analyzed by performing the Pearson Chi-square test.

study. The main added value of this study was to assess modifiability and population-level effect of the factors to identify areas of research priority and interventions aiming to reduce chronic pain onset and maintenance in children. The expert panel rated 4 factors (PA, SB, pain-related school absence, pain concept/knowledge of the child) as highly modifiable and 3 (PA, SB, depressive or negative emotional feelings of the child) as having high population-level effect.

PA and SB were rated as highly modifiability with high population-level effect. PA is well-known to provide multiple health-related benefits.³⁹ However, 81 % of adolescents are physically inactive (not complying with PA guidelines³⁹), with differences across sex, regions, and countries.⁴⁰ Physical inactivity is even more present in children with chronic pain.^{24,41} Children recognize pain as an obstacle to be physically

active, which can result in school absenteeism and overall poor health in adulthood.^{42,43} Increasing PA can be part of successful multimodal chronic pain management in children.⁴⁴ From a preventive perspective, both extremes of PA levels (very low and very high levels) can be a risk factor for the development of chronic pain in children,^{45,46} yet regular PA is considered preventive for the development of chronic pain.⁴⁷

Worldwide, excessive SB is widespread among children⁴⁸ and emerging evidence points to its negative health effects.⁴⁹ A sedentary lifestyle has been identified as a risk factor for low back and neck pain in children.^{23,50} However, a recent umbrella review found no or insufficient evidence for an association of screen time (one of the most prominent SBs) with pain.⁵¹ Despite the importance and modifiability of SB according to our experts, the association of SB with chronic pain and the importance of targeting SB in chronic pain management in children remains unclear.

Pain-related school absence and pain concept/knowledge were identified as highly modifiable factors with moderate population-level effect. A recent meta-analysis⁵² indicated that children with chronic pain (5–18y) were absent for 22.0 % of school days within a 60-day period. A study in 8641 children (6–17y), including 30.3 % reporting pain over the preceding 12 months,⁵³ showed that having pain was associated with higher rates of chronic school absenteeism (missing >15 schooldays during the past 12 months). Such school disengagement can have harmful effects on children's educational, emotional, and social development, and overall school functioning.^{54,55} When unaddressed, school disengagement can even lead to school failure,⁵⁴ impacting developmental, social, emotional, and financial outcomes for these children and their families.^{7,54} Since 20.8 % of children experience chronic pain,⁶ these findings call for early targeted interventions to improve school attendance. One feasibility study investigated the effects of a group intervention targeting school functioning in children with chronic pain (12–17y),⁵⁵ providing little evidence for this approach. Potential modification of pain-related school absence may lie in the role of parents, since parental pain catastrophizing and protective responses to their child's pain, suggested as additional factors for Round 2, each independently predict child school attendance rates and overall school impairment.⁵⁶ This points to the value of intervening with parents to help children successfully engage and succeed in school despite pain.

An essential part of coping with pain is related to the knowledge one has about it.^{57–59} Unfortunately, several misconceptions and conceptual gaps about pain are pervasive in society.^{60,61} For example, a popular belief is that pain is always a consequence of and proportional to tissue damage,⁶² while contemporary pain science taught us that pain experiences are determined by a wide range of biopsychosocial factors (e.g., cognitions, genetics, parental responses).⁶³ Maladaptive pain beliefs can result in higher levels of fear-avoidance and pain catastrophizing, which can contribute to chronic pain development.^{64–66} Contemporary pain science also taught us how to improve children's misconceptions and gaps about pain, more specifically, by providing pain science education (PSE) as part of multidisciplinary pain management.⁶⁷ PSE is a conceptual change strategy facilitating one's understanding of the biopsychosocial mechanisms of pain.^{63,68} Evidence in children in clinical and non-clinical settings shows that PSE results in improved outcomes, such as improved pain knowledge^{69–71} and beliefs,^{59,72,73} and less pain catastrophizing,⁷⁴ pain-related fear,⁷⁵ functional disability,⁷⁵ and fear of PA.⁷² One promising study showed beneficial effects of PSE on 11–13 year-old children's school attendance,⁵⁸ indicating that this might be an effective approach to improve school functioning in children with chronic pain.

Depressive or negative emotional feelings of the child was rated as having a high population-level effect, with moderate modifiability. Pain is an unpleasant sensory and emotional experience,⁷⁶ which can affect children's mood when chronic or severe enough. Depressive symptoms and chronic pain in children co-occur at high rates, exceeding those found among non-chronic pain populations.^{77–79} Key mutually maintaining factors are neurobiological, intrapersonal (sleep disturbances,

Table 2
Summary of results of the modified Delphi study.

Round 1 factors	Round 1 expert consensus strength of association (low/ 'moderate/should be discussed'/high)	Round 1 decision research team (include/exclude in Round 2)	Adjusted factors Round 2	Round 2 expert consensus modifiability (low/moderate/high)	Round 2 expert consensus population-level effect (low/moderate/high)
Sex	Moderate/should be discussed	Include	Sex of the child	Low	Moderate
Age	High	Include	Age of the child	Low	Moderate
Socio-economic status	Moderate/should be discussed	Include	Socio-economic status of the family (based on a combination of occupational, economic, and educational criteria)	Moderate	Moderate
Geographical background	Moderate/should be discussed	Exclude	/	/	/
Cultural background	Moderate/should be discussed	Include	Cultural background of the child	Low	Moderate
Employment status of the parents	Moderate/should be discussed	Exclude	/	/	/
Occupation of the parents	Moderate/should be discussed	Exclude	/	/	/
History of abuse or interpersonal violence	High	Include	History of abuse or interpersonal violence of the child	Low	Moderate
School satisfaction	High	Include	School satisfaction of the child	Moderate	Moderate
Perceived school performance	High	Include	Perceived school performance of the child	Moderate	Moderate
Pain-related school absence	High	Include	Pain-related school absence of the child (i.e., child stays home from school because of pain, either acute or chronic)	High	Moderate
Smoking	Moderate/should be discussed	Exclude	/	/	/
Sleep quality	High	Include	Sleep quality of the child	Moderate	Moderate
Diet	Moderate/should be discussed	Include	Dietary aspects (incl. diet, nutrition and eating behavior) of the child	Moderate	Moderate
Alcohol intake	Moderate/should be discussed	Exclude	/	/	/
Physical activity	High	Include	Physical activity of the child	High	High
Sedentary behavior	High	Include	Sedentary behavior of the child	High	High
Stress	High	Include	Stress of the child	Moderate	Moderate
Anxiety	High	Include	Anxiety of the child	Moderate	Moderate
Depression	High	Include	Depressive or negative emotional feelings of the child*	Moderate	High
Self-esteem (i.e., confidence in one's own worth or abilities)	High	Include	Self-esteem (i.e., confidence in one's own worth or abilities) of the child	Moderate	Moderate
Negative emotional symptoms	High	Include*	/	/	/
Personality	Moderate/should be discussed	Exclude	/	/	/
Perfectionism	Moderate/should be discussed	Include	Perfectionism of the child	Moderate	Moderate
Self-efficacy (i.e., own belief in one's capacity to act in the ways necessary to reach specific goals)	High	Include	Self-efficacy (i.e., own belief in one's capacity to act in the ways necessary to reach specific goals) of the child	Moderate	Moderate
Parental mental health	High	Include	Mental health of the parent(s)	Moderate	Moderate
Family functioning	High	Include	Family functioning (i.e., frequency of normal family routines, effectiveness of family communication and problem solving, family cohesiveness, and how well family members get along)	Moderate	Moderate
Parental anxiety	High	Include	Anxiety of the parent(s)	Moderate	Moderate
Sexual orientation	Moderate/should be discussed	Exclude	/	/	/
Catastrophizing beliefs about pain (i.e., tendency to describe a pain experience in more exaggerated terms than the average person, to ruminate on it more, and/or to feel more helpless about the experience)	High	Include	Catastrophizing beliefs about pain (i.e., tendency to describe a pain experience in more exaggerated terms than the average person, to ruminate on it more, and/or to feel more helpless about the experience) of the child	Moderate	Moderate
Fear avoidance (i.e., avoidance of movements or activities based on the fear of increased pain or re-injury)	High	Include	Fear avoidance (i.e., avoidance of movements or activities based on the fear of increased pain or re-injury) of the child	Moderate	Moderate

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Table 2 (continued)

Pain concept/knowledge	High	Include	Pain concept/knowledge of the child	High	Moderate
Pain intensity	High	Include	Pain intensity of the child	Moderate	Moderate
Number of pain sites	High	Include	Number of pain locations of the child	Moderate	Moderate
Pain location(s)	Moderate/should be discussed	Include	Pain location(s) of the child	Low	Moderate
Duration of pain episodes	High	Include	Duration of pain episodes of the child	Moderate	Moderate
Frequency of pain episodes	High	Include	Frequency of pain episodes of the child	Moderate	Moderate
Pain mechanisms (i.e., nociceptive, neuropathic, neuroplastic)	Moderate/should be discussed	Include	Pain mechanisms (i.e., nociceptive, neuropathic, nociplastic) of the child	Low	Moderate
Parents/family with chronic pain	High	Include	Parents/family with chronic pain	Low	Moderate
Previous (chronic) pain	High	Include	Previous (chronic) pain of the child	Low	Moderate
Joint hypermobility	Moderate/should be discussed	Exclude	/	/	/
Preterm birth	Moderate/should be discussed	Exclude	/	/	/
Low birth weight	Moderate/should be discussed	Exclude	/	/	/
Cognitive function	Moderate/should be discussed	Exclude	/	/	/
Overweight and obesity of the child	Moderate/should be discussed	Include	Overweight and obesity of the child	Moderate	Moderate
Health status	Moderate/should be discussed	Include	Health status (i.e., one's general wellness, considering the presence of biological and physiological dysfunction, functional impairment, mental well-being, and physical illness) of the child	Moderate	Moderate
Baseline disability	Moderate/should be discussed	Exclude	/	/	/
History of surgery	Moderate/should be discussed	Include	Previous medical trauma (PICU/NICU admission, surgery ...) of the child	Low	Moderate
Exposure to non-concordant pharmacotherapies	Moderate/should be discussed	Exclude	/	/	/
Diagnostic imaging	Moderate/should be discussed	Exclude	/	/	/
Round 2 additional factors	Round 2 expert consensus strength of association (low/ 'moderate/should be discussed'/high)	Round 2 decision research team	/	Round 2 expert consensus modifiability (low/moderate/high)	Round 2 expert consensus population-level effect (low/moderate/high)
(Behavioral) responses to pain of the parent(s)	High	Include	/	Moderate	Moderate
Pain catastrophizing (i.e., tendency to describe a pain experience in more exaggerated terms than the average person, to ruminate on it more, and/or to feel more helpless about the experience) of the parent(s)	High	Include	/	Moderate	Moderate
Endocrine disruptors/hormonally active agents (e.g., found in certain cleaning products, cosmetics, food and beverage packaging, toys, carpet, and pesticides)	Moderate/should be discussed	Exclude	/	/	/
Relationships of the child with peers	High	Include	/	Moderate	Moderate
Relationship of the child with healthcare providers	Moderate/should be discussed	Include	/	Moderate	Moderate
Developmental disorders (e.g., autism spectrum disorder (ASS), attention-deficit/hyperactivity disorder (ADHD), developmental coordination disorder (DCD), ...) of the child	Moderate/should be discussed	Include	/	Low	Moderate
Health literacy (i.e., one's knowledge, motivation and competencies to	Moderate/should be discussed	Include	/	Moderate	Moderate

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Table 2 (continued)

access, understand, appraise, and apply health information in order to make judgments and take decisions in everyday life concerning healthcare, disease prevention and health promotion to maintain or improve quality of life during the life course) of the child					
Access to healthcare (i.e., the ease with which health services are reached in terms of physical access (geographical distribution), costs, time, and availability of qualified personnel) of the child	Moderate/should be discussed	Include	/	Moderate	Moderate
Previous psychological or emotional trauma (e.g., bullying, divorce, family conflict, abuse, separation, war experience, ...) of the child	High	Include	/	Low	Moderate
(Chronic) medical diagnoses (e.g., rheumatoid arthritis, kidney disease, cancer, ...) of the child	High	Include	/	Low	Moderate
Pubertal maturation (i.e., process of physical changes through which a child's body matures into an adult body capable of sexual reproduction) of the child	Moderate/should be discussed	Exclude	/	/	/
Experiences of racism and stigma (i.e., negative feelings that people have about particular circumstances or characteristics that somebody may have) of the child	Moderate/should be discussed	Include	/	Low	Moderate
Parenting style of the parent(s) (i.e., authoritarian, authoritative, permissive, uninvolved)	Moderate/should be discussed	Include	/	Moderate	Moderate
Early parentification (i.e., when a child is forced to take on the role of an adult early in life) of the child	Moderate/should be discussed	Exclude	/	/	/
Multisensory sensitivity (i.e., heightened sensitivity to multiple senses, such as bright lights, noises, strong perfumes, or clothing tags) of the child	Moderate/should be discussed	Include	/	Low	Moderate
Weather factors (e.g., temperature, humidity, atmospheric pressure, ...)	Moderate/should be discussed	Exclude	/	/	/

*The factors 'depression' and 'negative emotional symptoms' from Round 1 were combined to 'depressive or negative emotional feelings of the child' in Round 2. Low, moderate, and high levels of strength of association/modifiability/population-level effect are indicated in red, orange, or green font, respectively.

emotion regulation), and interpersonal (parental mental health, genes) factors.⁸⁰ In terms of modifiability, a Cochrane review⁸¹ found no beneficial effect of psychological interventions (relaxation therapy, biofeedback) on depressive symptoms in children with chronic headache or mixed chronic pain. However, mindfulness-based interventions showed to reduce symptoms of anxiety and depression, and improvements in overall quality of life.⁸² Additionally, PA interventions may be used to reduce depressive symptoms in children, with greater improvements observed in children > 13 years and with a mental illness and/or depression diagnosis.⁸³ Although in children, the recommended PA modalities (frequency, duration, supervision) need further investigation, mindfulness-based and PA interventions show promise to improve depressive symptoms in children with chronic pain. PA thus seems to be an important direct and indirect factor in the development or maintenance of chronic pain in children.

Strengths and limitations

Online modified Delphi processes have the ability to engage experts with diverse perspectives, despite geographic or transportation barriers.⁸⁴ This was clear in our expert panel, consisting of international pediatric pain experts from 5 different continents and 14 different countries. Additionally, intermediate (after Round 1) and final (after Round 2) detailed feedback was provided to the experts. Controlled feedback is a means by which information from the group is passed between panelists so that individual judgments may be modified or refined.⁸⁵ Knowing that this study ensured anonymity, iteration, and group consensus, the study entailed the vital elements of Delphi methodology.³²

Some limitations need to be acknowledged as well. Only 48 of 295 contacted experts participated in Round 1 (16.3 % response rate), and

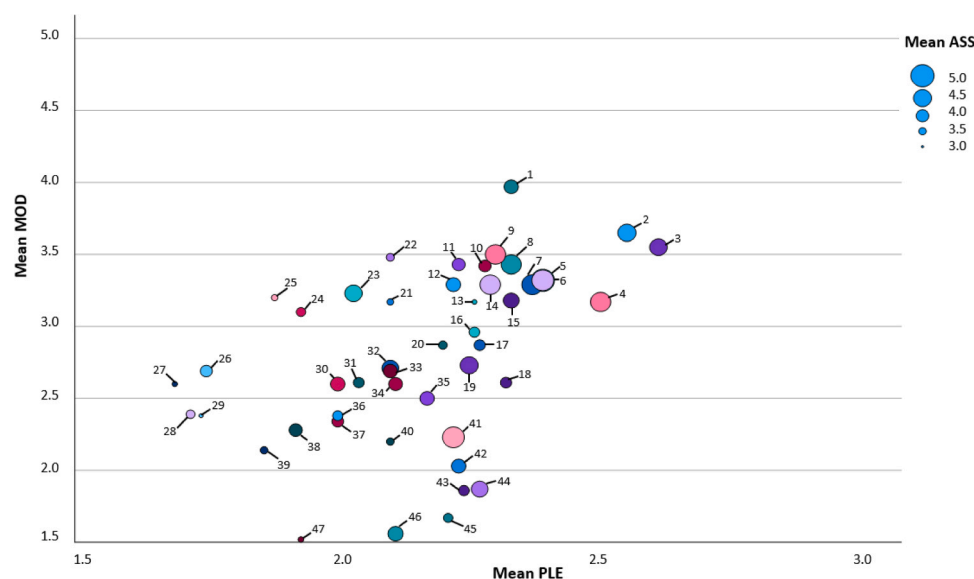


Fig. 2. Average scores across factors on strength of association, modifiability, and population-level effect. Factors in the top-right corner that have larger circles can be considered potentially important factors as these factors score high on all three rating domains. ASS = strength of association [3.0–5.0]; MOD = modifiability [0.0–5.0]; PLE = population-level effect [0.0–3.0]; 1 = pain concept/knowledge; 2 = sedentary behavior; 3 = physical activity; 4 = depressive or negative emotional feelings; 5 = anxiety; 6 = stress; 7 = sleep quality; 8 = fear-avoidance; 9 = ain-related school absence; 10 = self-efficacy; 11 = school satisfaction; 12 = (behavioral) responses to pain (parents); 13 = overweight and obesity; 14 = catastrophizing beliefs about pain; 15 = pain catastrophizing (parents); 16 = access to healthcare; 17 = pain intensity; 18 = socio-economic status (family); 19 = family functioning (family); 20 = health status; 21 = health literacy; 22 = dietary aspects; 23 = self-esteem; 24 = perceived school performance; 25 = relationship with healthcare providers; 26 = perfectionism; 27 = parenting style (parents); 28 = pain location(s); 29 = experiences of racism and stigma; 30 = duration of pain episodes; 31 = relationships with peers; 32 = anxiety (parents); 33 = frequency of pain episodes; 34 = number of pain location(s); 35 = mental health (parents); 36 = multisensory sensitivity; 37 = (chronic) medical diagnoses; 38 = pain mechanisms; 39 = developmental disorders; 40 = cultural background; 41 = history of abuse or interpersonal violence; 42 = previous psychological or emotional trauma; 43 = age; 44 = parents/family with chronic pain; 45 = sex; 46 = previous (chronic) pain; 47 = previous medical trauma. *Note:* All factors are child factors unless mentioned otherwise between brackets (parents or family).

31 of 48 experts also participated in Round 2 (64.6 % retention rate). The time to complete the survey in each round may have been a barrier for busy clinicians or researchers, although each survey was constructed to be completed in less than 20 min. Additionally, the study took place during summer, which might have contributed to the low response rate. Although there is no consensus in the literature on the optimal number of Delphi participants, 31 experts completing both survey rounds, can still be considered a relatively large panel size.³¹ Secondly, there was an uneven representation of different professions among the expert panel. However, this variety of professions might be considered a strength as well, and because of the fine balance between clinicians, researchers, and experts combining research and clinical work, the odds of results being skewed due to this imbalance in professions seems limited. Skewness statistics were not performed since they hold little value to prove normality in Likert-type scales. Thirdly, although being international organizations, the core group of two of the targeted pain organizations (i.e., BePPA and Pain in Motion) is based in Belgium, which was visible in the number of Belgian experts. Other countries were less represented, and no African experts participated. Involving additional experts with different geographical and clinical backgrounds would have increased the external validity of this study. The identification of additional factors (with regard to ethnic minorities, for whom context and influencing factors may be very different in other geographical areas), as well as procuring additional ratings of the proposed factors might have been different.

The most important limitation is that the direction of the association with chronic pain in children might have been insufficiently clear. For example, chronic pain might develop or maintain due to low sleep quality, however, sleep quality might be impacted by experiencing chronic pain as well. Early studies propose a bi-directional relationship between pain and sleep, such that sleep deficiency and pain reciprocally

maintain symptoms over time.⁸⁶ Another challenge was the potential interrelationships between the factors, as indicated by some of the experts. Having a clear picture on these interrelationships is necessary in order to identify the moderators and mediators that modulate the direct impact of factors on chronic pain in children.

Implications and future directions

Given the high and raising prevalence rates of pediatric chronic pain,^{2,3} it is key to identify modifiable population-level effect factors that are associated with the development and maintenance of chronic pain in children. Our expert panel rated PA, SB, pain-related school absence, pain concept/knowledge, and depressive or negative emotional feelings of the child as being highly modifiable and/or having a high population-level effect, making these factors priority for future research and interventions aiming to reduce chronic pain onset and maintenance. A future step could be to establish Directed Acyclic Graphs (DAGs) together with the expert panel,⁸⁷ which may yield valuable insights about the interrelationships between the identified factors, detailing the manner in which each type of variable can be used to inform novel developments in research and clinical practice.

Conclusions

This modified Delphi process with pediatric pain experts identified a list of 47 factors considered to be associated with the development or maintenance of pediatric chronic pain. PA, SB, pain-related school absence, pain concept/knowledge, and depressive or negative emotional feelings of the child might be key to consider as target outcomes for the prevention and management of chronic pain in children.

Declaration of Competing Interest

The authors have no conflicts of interest to declare. Kelly Ickmans and Emma Rheel developed a pain science education board game for children (PNE4Kids), but the royalties are collected by Vrije Universiteit Brussel, Brussels, Belgium.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.jpain.2024.104703](https://doi.org/10.1016/j.jpain.2024.104703).

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