Title:

The effectiveness of pain science education on caregiver and children's knowledge, beliefs, attitudes and behaviors– a systematic review and meta-analysis.

Short running title: Caregiver pain science education: a systematic review

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Abstract

Pain science education can be used as part of treatment and prevention for chronic pain in children. We assessed the effectiveness of pain science education on knowledge, beliefs, attitudes, and behaviors in children and the people that care for children. We set a minimum criterion for education to address pain biology knowledge. We included studies aimed at both the treatment and prevention of chronic pain. We conducted searches using five databases. We assessed the risk of bias using the Cochrane Risk of Bias 2 tool. Data were pooled using a random-effects meta-analysis or assessed using a narrative synthesis. The certainty of evidence was assessed using the GRADE. We screened 14505 records and included seven studies involving 351 caregivers and 1285 children. Four studies were included in meta-analyses. We found low certainty evidence that PSE has a large beneficial effect on caregiver knowledge and beliefs compared to alternative education (SMD=1.14 (95%CI: 0.88 to 1.42; I^2=0%). We found no change to functional disability in children with chronic pain after PSE (MD=0.73 (95%CI: -0.81 to 2.27; I=0%). Narrative syntheses showed low certainty for improved knowledge and beliefs in children with preventative and treatment effects. Overall, there is limited evidence. This, along with high risk of bias significantly contributed to the (mainly) low certainty of findings. The effect of learning pain science for both preventative and treatment effects in children, carers and the child/carer dyad remain mostly unknown. This review was prospectively registered with PROSPERO (CRD42022344382) on 22 July 2022. This review was prospectively registered with PROSPERO (CRD42022344382) on 22 July 2022.

Perspective

This review examines the effect of pain science education (PSE) on pain-related knowledge, beliefs, attitudes, and behaviors in children and the people that care for children (0-18). The findings contribute to knowledge about pain treatments and health promotion for caregivers of children with and without chronic pain. Clear recommendations for improving the quality of evidence in future studies are outlined.

Keywords

Pediatric pain; pain science education; chronic pain; parents; teachers.

INTRODUCTION

Chronic pain (i.e. pain lasting longer than 3 months) is an experience that involves biological, psychological and social influences, and can develop because of ongoing stress to these factors[1]. While the exact prevalence in children is unclear, it is common, with the medium prevalence in community samples being 11 to 38 percent[2,3]. Chronic pain in children and adolescents can negatively impact many aspects of life including sleep, movement, interpersonal relationships, school functioning and educational attainment[4-678,]. Chronic pain can persist into adulthood and is associated with reduced health outcomes including ongoing functional disability, poor vocational functioning, psychiatric morbidity, increased risk of opioid use and reduced quality of life[9-11].

Social influences on children's pain may include emotional and behavioral responding from parents and family, teachers, coaches, and peers. Parent and family factors (e.g. parental responses to child pain) have been shown to have a direct association with their child's functioning[12,13]. Furthermore, child pain memories can also be influenced by parental responses to their pain, which in turn can affect future pain experiences[14]. Children experience pain-related stigma at school, which is increased by a lack of pain knowledge and understanding from their teachers[15,16]. Teachers may not appreciate the complexity of pain and question the reality of a student's pain[17,18]. It is unknown whether education about the science of pain might influence primary or secondary caregiver knowledge, understanding and responses to children's pain experiences.

Recommended treatments for chronic pain should align with the biopsychosocial framework and are often centered around functional improvement[19,20]. As such, pain science education (PSE) is a first line intervention that aims to provide a common language to communicate the

biopsychosocial nature and complexity of pain[21]. Additionally, it is proposed that PSE promotes healthy attitudes and beliefs about pain which may drive behavioral responses to symptoms[22]. It is unknown whether understanding pain in childhood might influence the trajectory of health and prevent the onset of chronic pain and disability in adulthood. While the effect of PSE has been systematically reviewed in adults, it has not been reviewed in caregivers and/or their children[23-25]. Therefore, in this systematic review, we aim to assess the effectiveness of PSE compared to any control intervention (e.g., alternative or no education) on caregiver and children's knowledge, beliefs, attitudes and behaviors.

METHODS

Design

For this systematic review of randomized controlled trials, we used the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) and the Synthesis without meta-analysis (SWiM) reporting guidelines[26,27].

Eligibility criteria

We included randomized controlled trials conducted in clinical (e.g. hospitals, outpatient departments), community (e.g. schools) and laboratory settings. We only included full-text articles (i.e. not conference abstracts), and studies published in English, German and Dutch (as we were limited by the capacity of skills within our research team).

To be included in the review, the study population included children (0-18) with or without any pain and/or adult caregivers (e.g. parents, grandparents, teachers, teacher-aides, support workers and respite workers) working in a non-health professional role for any length of time (e.g. 1 hour of babysitting through to a full-time teacher). These caregivers were caring for

children (0-18 years) with any pain conditions, including acute and chronic pain, as well as healthy children.

Included interventions were required to meet our minimum criteria for PSE which was to include information addressing the biological processes that underpin pain (e.g. to explain the body and mind link through the nervous system during a pain experience). We defined these minimum inclusions to separate *pain science education*, which targets reconceptualization of pain and related processes, from *psychoeducation* (e.g. relationship of sleep and stress with pain) or education that solely addressed *pain management* or *assessment* (e.g. post-operative pain management and vaccination pain management). Example interventions include PSE; Pain neuroscience education (PNE); Biopsychosocial pain education; Explain Pain (EP) and Therapeutic Neuroscience Education (TNE). To capture studies with all interventions aimed at the reconceptualization of pain, we did not restrict interventions based on dose or delivery. While we recognize the benefits of combining pain science education with other therapeutic interventions for the treatment of chronic pain (e.g. exercise and cognitive behavioral therapy), to assess the effectiveness of pain science education only, we included studies where pain science education could be isolated as an intervention.

Control interventions included education not targeting concept of pain, placebo/sham education, usual care, or no intervention.

We included caregiver and child reported outcomes for pain knowledge (e.g. scores from a neurophysiology of pain questionnaire), pain beliefs (e.g. questions related to beliefs about whether pain and tissue damage are directly related), pain attitudes (e.g. pain catastrophizing)

and behaviors related to pain management (e.g. child-related functional disability, medication use, school absence).

Search strategy

We conducted searches via Medline (Ovid), CINAHL (EBSCO), PsycINFO (EBSCO), AMED (Ovid) and Embase (Ovid) databases from inception to May 2023. The research team generated the search terms in collaboration with an information specialist from the University of Technology Sydney. Search terms included terms relating to children and their caregivers (e.g. child, adolescent, parent, teacher); pain (e.g. chronic and acute pain); education (e.g. therapeutic education); and study design (randomized controlled trial or controlled clinical trial). We used the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity-maximizing version (2008 revision)[28]. Search strategies were adapted for the relevant databases (Supplementary material 1).

Study selection

We uploaded the results of the database searches to Covidence (http://covidence.org), a web-based application that allows for screening and recording decisions regarding eligibility of studies. Three independent review authors (RF, MA, PS) screened titles and abstracts so that each reference was screened twice. Full-text screening was completed independently by two review authors (RF, JN). Conflicts relating to inclusion were resolved between the reviewers. A third review author (JP) was consulted for agreement on the final included studies. We contacted authors when we were unsure if studies met inclusion criteria, particularly in relation to pain science education content. We used forward and backward citation tracking of included studies to identify additional papers.

Data extraction

Three review authors (RF, JN, MA) independently extracted study data using a standardized form in Excel (version 2020). The form was trialed and revised as required.

Study characteristics, such as study design and setting, and baseline characteristics, such as the presence of chronic pain or not, location of pain and pain intensity, were extracted. Characteristics of the intervention and control conditions were also extracted, such as the mode of delivery (e.g. video); duration of the education sessions (e.g. 15 mins); the format (e.g. individual or group); and key content/curriculum. We reviewed intervention content in the supplementary materials of included papers when this was not reported in sufficient detail. Outcomes were extracted for caregivers and children, then sorted into one of the four categories of pain-related knowledge (e.g. pain neurophysiology questionnaire scores), beliefs (e.g. self-report agreement to pain beliefs), attitudes (e.g. pain catastrophizing) and behaviors (e.g. school attendance). We extracted the effect of the intervention on these outcomes (e.g. mean (standard deviation) and/or effect size and variance) at all post-intervention and follow-up time points (e.g. 1 month and 6 months). We contacted study authors when these data were not reported. If more than one publication related to a single trial, we only extracted data once.

Risk of Bias Assessment

Two review authors (RF and JP) independently assessed risk of bias for each outcome at each timepoint, using the Cochrane Collaboration's Tool for Assessing Risk of Bias 2 (RoB2)[29]. The RoB2 assesses bias in five distinct domains: 1) bias arising from the randomization process; 2) bias due to deviations from the intended interventions; 3) bias due to missing

outcome data; 4) bias in measurement of the outcome; 5) bias in selection of the reported result. Within each domain, assessors answer one or more signaling questions which lead to judgements of 'low risk of bias', 'some concerns', or 'high risk of bias', which in turn lead to an overall risk-of-bias judgment. Disagreement about rating was resolved by consensus and, and if still unresolved, by consultation with a third review author (AV).

Analysis

We grouped studies based on the population (i.e. caregivers and children) and cohort (e.g., the presence of chronic pain or not) and analyzed the outcomes of knowledge, beliefs, attitudes, and behaviors for both.

For continuous outcomes, we calculated between-group mean differences (MD) and 95% confidence intervals (95% CI) for the post-intervention and last available follow-up data in each study. When studies used different outcome measure instruments, we calculated standardized mean differences (SMD) and 95% CI where possible. An effect size (SMD) was considered negligible when <0.2; small when ≥0.2 to 0.49; medium between 0.5 to 0.8 and large >0.8[30].

We pooled the results when multiple studies with adequate clinical study homogeneity (e.g. similar populations, cohorts and outcomes) provided data. We explored clinical heterogeneity by comparing the studies according to potential effect modifiers, such as mean age of children; outcomes (i.e., knowledge and beliefs, attitudes, and behaviors); and methods/tools used for measuring outcomes (e.g., behaviors measured with functional disability inventory (FDI)[31] or self-reported medication use). To account for developmental differences in how children may learn from PSE (and how their caregivers might be involved), we separated the

analysis for some outcomes with children aged < thirteen years, and ≥ thirteen years. We chose this age as it represents the transition between primary and secondary schooling in most countries, which also represents a change in educational context (from foundational skills to more specialized knowledge and critical thinking) and teaching methods (e.g., more scaffolded teaching to methods where students take responsibility for their own learning)[32,33]. We assessed each analysis separately with consideration to how the outcomes and their measures might be influenced by the learning context to decide if separation into age groups should be considered. Where we deemed that outcome measures were appropriate to combine age groups for analysis, we have provided explanations (e.g., The FDI has been assessed to have high reliability and good validity in children aged 8-17 years with chronic pain[34] and behaviors assessed in this measure are less influenced by learning contexts).

We used random effects models and Review Manager Web statistical software for forest plots and the meta-analyses (RevMan Web 2022). Where data was not available, we synthesized narratively. We developed bubble plots to visually convey findings including the populations studied, risk of bias and study size, and we used tables to illustrate the direction of effect and certainty of evidence.

Assessment of the certainty of the findings

We assessed the certainty/quality of evidence using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE)[36]. As all studies were randomized controlled trials, the certainty/quality of evidence was considered high if at least two studies were included. This could be downgraded to moderate, low or very low certainty/quality based on the following criteria: 1) Limitations in design: we downgraded one level if the overall risk of bias for the outcome being assessed was high in greater than 25% of studies; 2)

Inconsistency: we downgraded one level if the statistical heterogeneity (I^2 value) was high, meaning > 75%; 3) Indirectness: we downgraded one level if the included studies only reported on a subsample of our population in question (e.g., only report on children with chronic pain or children with intellectual impairment) that could not be generalized to the whole sample or synthesized separately, or if PSE interventions were sufficiently different in their delivery; 4) Imprecision: we downgraded if a descriptive synthesis was performed, if the total number of participants was less than 400, or if the majority of studies were not adequately powered (e.g. if a number of studies were pilot studies). 5) Publication bias: we assessed publication bias when 10 or more studies were included in a pooled analysis. When GRADE assessment is performed for single studies of less than 400 participants (i.e., not pooled for analysis) they will start at low certainty due to imprecision and inconsistency and can further be downgraded.

Deviations from protocol

We deviated from the original protocol and performed meta-analysis in less than 5 studies for two analyses. In these instances, review authors agreed on the benefits of providing a more specific estimate of the effect of PSE. In addition, one study provided a range of effect estimates due to imputation calculations to account for missing data. For this study we used their most conservative estimate.

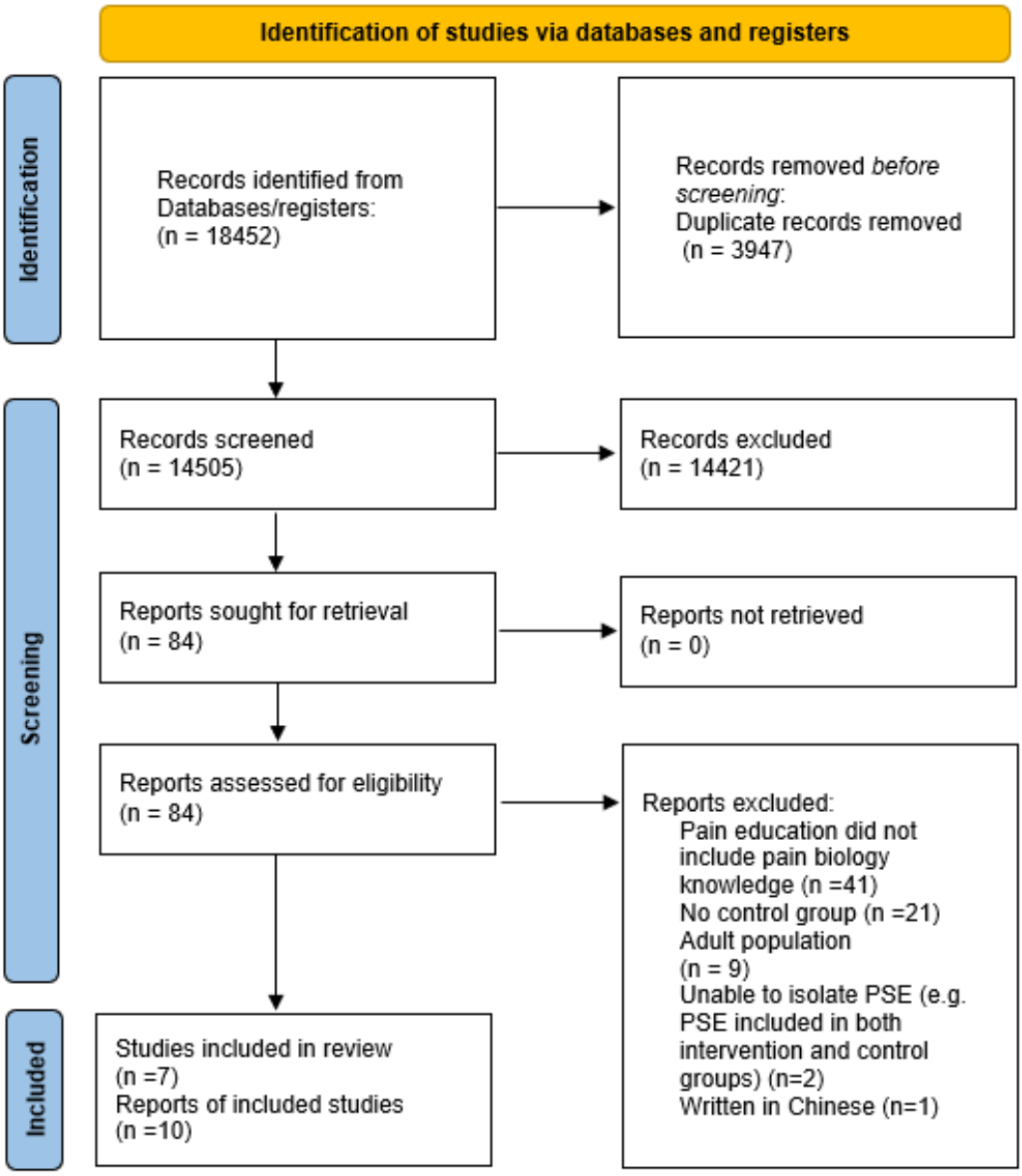
RESULTS

Search Results

The search yielded 18,452 records (see Figure 1). An additional 5 papers were identified through searching reference lists. After duplicates were removed, we screened 14,505 titles and abstracts. This resulted in 84 full-text publications to screen, with a final 10 meeting our

inclusion criteria presenting seven studies. Three authors were contacted to resolve queries about inclusion criteria, study design and to provide additional data. All three authors provided sufficient information to resolve queries. Three of the included studies each had 2 publications/reports included ([37,38] and[39,40] and [41,42]). In this manuscript we refer to the most recent publication if we refer to the whole study. If we refer to a portion of the study, we refer to the relevant publication. Data were extracted from all 10 publications/reports as each reported on separate outcomes.

Figure 1. PRISMA diagram summarizing search results.



Description of included studies

All studies were randomized controlled trials, with four studies being cluster randomized trials in schools or pediatric respite centers[38,40,43,44].

Four studies included caregivers[38,42,45,46], and five included children[40,42-44,46]. Two studies involved children with chronic pain[44,46] and the remaining three involved healthy populations (which may have had a proportion of children experiencing chronic pain)[40,42,43] (Table 1). Three studies were conducted in schools[40,43,44]; one in a respite center [38]; one in a laboratory[42]; one in a hospital[46]; and one in a university[45]. Although five studies assessed children's outcomes, study design and purpose varied, meaning that caregivers attended PSE with children in only two of these[42,46] One study presented outcome data from both children and caregivers[42]. One study assessed outcomes from caregivers and used parent proxy measures to assess children's outcomes[46].

Demographic characteristics of participants varied. No studies reported participant gender. Two studies conducted using chronic pain cohorts recruited varying ages of 9 years[46] and 16 years[44]; both were predominantly female, and predominantly Caucasian[46] (one did not report race or ethnicity[44]). Three studies recruiting from community samples, recruited similar aged children (12.3 years[40], 11.4 years[43] and 12 years[41]), with one of these recruiting 100% Flemish children[41], and the remaining two not reporting race or ethnicity[40,43]. The two studies involving only adult caregivers (and no children) involved adults that worked with children or had experience working with children aged 0-18 years. These caregivers were predominantly white/European (90%[45]; 83%[37]).

PSE interventions varied in dose and delivery. The dose ranged from a 10-minute video to multiple one-on-one education sessions delivered by a health professional. Similarly, studies varied in their method and mode of teaching the content (e.g. use of metaphors and games to illustrate complex ideas; use of audio-visual material; interactive discussion; lecture style presentation). For example, one study assessed whether a 10-minute video was sufficient to change pain knowledge and pain-related behaviors in school children[43]. Another study explored the same outcomes using a 30-minute PSE lecture presentation using metaphors and

illustrations from a health professional with the addition of a 10 minute booster video at 2 months[40]. Of the two studies that solely involved caregivers (i.e. education was not delivered to children), PSE involved up to three and a half hours of lecture style presentations and interactive case-based learning[38,45]. Comparator interventions varied across studies. The two studies that involved chronic pain populations evaluated additional PSE with either exercise[44] or hypnotherapy[46] to exercise or hypnotherapy alone. All other studies compared PSE to usual care/usual classes (at school)[43], no intervention[42], or an alternative education (such as sports injury management)[38,40,45].

A variety of outcome measures were used to assess knowledge, beliefs, attitudes and behaviors in caregivers and children. We used the same classification of these constructs as reported by individual studies, where available. Outcomes for knowledge and beliefs often overlapped in the same assessment tool. Review authors (RF, JP and LH) categorized outcomes based on consensus into 1) combined knowledge and beliefs; 2) attitudes 3) behaviors.

We summarized the characteristics of outcome measures used, to assist in comparison between studies and assessment of risk of bias (Supplementary 2). Results for calculated between group mean differences (MD 95%CI) are presented in Supplementary 3.

Table 1. Summary of study characteristics.

Study (first author, year) characteristics	Interventions (number of participants	Outcomes and instruments used					
		Caregiver			Child		
		Knowledge and beliefs	Attitudes	Behaviors	Knowledge and beliefs	Attitudes	Behaviors
CHRONIC PAIN POPULATION (n=2 studies)							
Andias, 2022 Portugal Cluster RCT Schools (2) M age = 16y	Intervention: PSE+ exercise. 8 sessions 30-45 mins each – including approx. 2.5 hours total PSE (F2F or WhatsApp. Mixed Group and individual delivery). n=60 Control: exercise only across 8 sessions. n=58	-	-	-	NPQ (0-12)	PCS TSK CSES	FDI BaSIQs
Pas, 2020 Belgium RCT Clinic/ Hospital M age = 9y	Intervention: n=14; 1 session of PSE (45 mins F2F individual delivery) and 1 session of hypnosis. n=14 Usual care/control: n=14; 2 sessions of hypnosis. n=14	-	FOPQ-P PCS-P		-	-	FDI-P
POPULATION-BASED (n=3 studies)							
Louw, 2019/ 2020* USA Cluster RCT Schools (8) M age =12.3y	Intervention: 30-minute presentation (group) with 32 slides. Presenters were trained PT or OT scored >90% NPQ. n=221 Control: 30-minute sports injury lecture taken from school curriculum. (Delivered by clinicians). n=198 PNE Boost Intervention: received the PNE lecture plus 10-minute booster video at 2 months and 4 months during class. (group). n=250. *	-	-	-	NPQ (0-12) Pain beliefs (researcher developed)	FABQ-PA	RDS: Researcher developed survey *

Study (first author, year) characteristics	Interventions (number of participants	Outcomes and instruments used					
		Caregiver			Child		
		Knowledge and beliefs	Attitudes	Behaviors	Knowledge and beliefs	Attitudes	Behaviors
Kisling, 2021 Germany Cluster RCT Schools (4) M age= 11.4y	Intervention: 10-minute video plus QR code to rewatch (unlimited). Delivered by teacher to class group). n=219 Control: no video (usual classes). n=162	-	-	-	PKQ-CH	-	PPCI-r PPDI SA MU
Rheel, 2021/2022** Belgium RCT Lab M age = 12y	Intervention: 15 min video based on PNE4Kids tested content. n=44 Control: no video. n=45	-	-	**Coded parent verbalizing*	Learner-specific questionnaire (PNE4Kids)	CFS PCS-C (modified)	**Coded child verbalization
CAREGIVER-ONLY (n=2 studies)							
Genik, 2017 Canada RCT University	Intervention: 45-minute pain education presentation delivered by researchers and clinicians. n=41 Control: 45 min presentation on visual supports. n=36	QUPID-C PPKAQ-R	-	-	-	-	-
Genik,, 2021a/2021b *** Canada Cluster RCT Respite centers (14)	Intervention: 3-3.5 hours PowerPoint and case studies (delivered in groups). n=65 Control: 3-3.75-hour presentation about family-centered care approach to improving care to children with IDD. 'F words to childhood disability'. n=92	QUPID-CR	-	PAMSQ; Responses to vignettes, Focus groups***	-	-	-

Abbreviations: n=total number of participants. NPQ[47] (0-12) = Revised neurophysiology of pain questionnaire 12-point scale[47]. FABQ-PA: Fear avoidance Beliefs Questionnaire – physical activity subscale[48]. PCS=pain catastrophizing scale[49]. TSK= Tampa Scale of Kinesiophobia[50]. CSES= child self-efficacy scale[51]. FDI: Functional Disability Inventory[34]; BaSIQs: Basic scale on insomnia and

quality of sleep[52] PKQ-CH (0-20) = Pain Knowledge Questionnaire for Children[53]. PPCI-r = pediatric pain coping inventory subscale (pain passive coping)[54]. PPDI= Pediatric pain disability index[55]. SA= pain related school absence. MU=Pain related medication use. RDS=researcher developed survey of behaviors (Measuring participation in school, physical education class, recess and sport; health care utilization and medication use). FOPQ-P=Fear of pain questionnaire-parent report[56]. PCS-P=Pain catastrophizing scale – parent[57]. FDI-P= functional disability inventory – parent report (proxy)[31,34]. CFS=children's fear scale[58]. QUPID-C= Questionnaire for Understanding Pain in Individuals with Intellectual Disabilities – Caregiver Report[45]. PPKAQ-R= Pediatric Pain Knowledge and Attitudes Questionnaire Revised (Adapted)[45]. QUPID-CR=Questionnaire for Understanding Pain in Individuals with Intellectual Disabilities – caregiver version Revised[38]. PAMSQ= Pain Assessment and Management Strategies Questionnaire[38]. .# other ethnicities identified in the study were: Aboriginal/first Nations/Metis (3); black/African/Caribbean (4), Persian (1), south Asian (3), southeast Asian (2) and west Asian (1).

*Louw 2019, and Louw 2020 are based on the same population with outcomes reported across different timepoints. In addition, Louw 2020 presented a third arm (PNE boost) that was not presented in the 2019 publication. Additional outcomes related to the 2020 publication are marked with asterisk.
**Rheel 2021 and Rheel, 2022 are based on the same population with outcomes reported separately across two studies (i.e. knowledge and beliefs part 1; Behaviors part 2). Outcomes marked with asterisk are relevant to the 2022 paper.
***Genik, 2021a and Genik, 2021b are based on the same population with outcomes reported separately across two publications. Outcomes marked with asterisk are relevant to the 2021b publication.

Risk of bias

We assessed 37 outcomes across the 7 studies at post-intervention and (if available) follow-up timepoints (Table 2 and Supplementary 4). All children's knowledge outcomes were high risk of bias because the assessment tools used have not been validated in children. We summarized all the outcome measures and their modifications to support our risk of bias assessment (Supplementary 2). Most studies did not pre-register a statistical analysis plan, leading to some concerns across each outcome in that study.

Table 2. Risk of bias assessments for each outcome

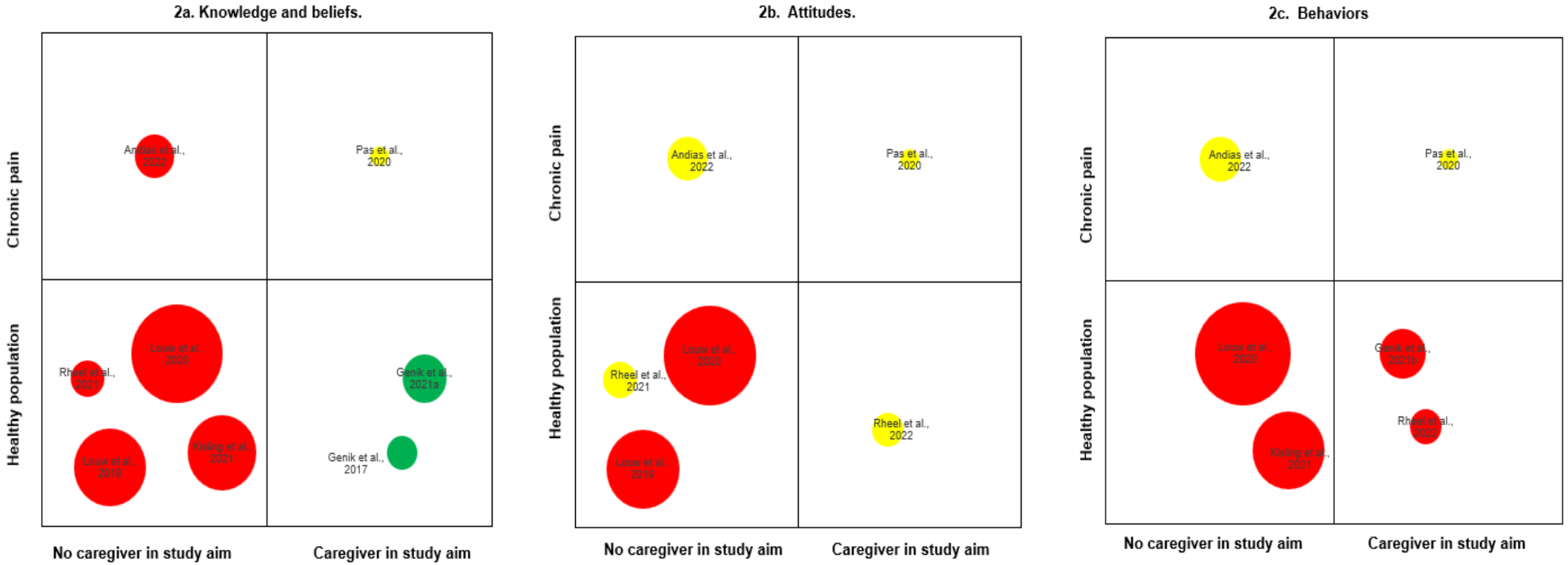
Study	Outcome (outcome measure)	Randomisation process	Cluster trial part b*	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Non-cluster studies								
Genik 2017	Carer understanding (QUPID-C)	+		+	+	+	+	+
	Carer knowledge (Adapted PPKAQ-R)	+		+	+	+	+	+
Pas 2020	Caregiver function (FDI-P)	+		+	+	+	-	-
	Caregiver beliefs (PCS-P)	+		+	+	+	-	-
Rheel 2021	Child fear (CFS)	+		+	+	+	-	-
	Child catastrophising (PCS-C)	+		+	+	+	-	-
	Child knowledge (8 questions)	+		+	+	!	-	!
Rheel 2022	Parent/Child verbalisations	+		-	!	-	-	!
Cluster studies								
Andias 2022	Child knowledge (Adapted rNPQ-12)	+	+	+	+	!	-	!
	Child function (FDI)	+	+	+	+	+	-	-
	Child catastrophising (PCS)	+	+	+	+	+	-	-
	Child kinesiophobia (TSK)	+	+	+	+	+	-	-
	Child insomnia (BaSIQS)	+	+	+	+	+	-	-
	Child self-efficacy (CSES)	+	+	+	+	+	-	-
Genik 2021a	Carer knowledge and beliefs (QUPID-CR)	+	+	+	+	+	+	+
Genik 2021b	Carer strategies (PAMSQ)	+	+	+	!	!	!	!
Kisling 2021	Child knowledge (PKQ-CH)	-	+	+	-	!	-	!
	Child passive coping (PPCI-r)	-	+	+	-	+	-	-
	Child disability (PPDI)	-	+	+	-	+	-	-
	Child school absence (number of days)	-	+	+	-	!	-	!
	Child medications (number of days in past 4 weeks)	-	+	+	-	!	-	!
Louw 2019	Child fear avoidance (Adapted FABQ-PA)	+	+	-	-	!	-	!
	Child knowledge (Adapted rNPQ)	+	+	-	-	!	-	!
	Child beliefs Q1 Pain is normal	+	+	-	-	!	-	!
	Child beliefs Q2 Pain means something is wrong	+	+	-	-	!	-	!
	Child beliefs Q3. Pain always means you have to stop	+	+	-	-	!	-	!
	Child beliefs Q4. You can control how much pain you feel	+	+	-	-	!	-	!
	Child beliefs Q5. Your brain decides if you feel pain	+	+	-	-	!	-	!
Louw 2020	Child knowledge (Adapted rNPQ)	+	+	-	-	!	-	!
	Child beliefs (Adapted FABQ-PA)	+	+	-	-	!	-	!
	Child school absence (days)	+	+	-	-	!	-	!
	Child physical education absence (days)	+	+	-	-	!	-	!
	Child recess absence (days)	+	+	-	-	!	-	!
	Child sport absence (days)	+	+	-	-	!	-	!
	Child doctor visit for pain (times)	+	+	-	-	!	-	!
	Child rehabilitation visit for pain (times)	+	+	-	-	!	-	!
	Child pain medication (yes/no)	+	+	-	-	!	-	!

Key: '!' denotes high risk of bias; '- 'denotes some concerns; '+' denotes low risk of bias. We assessed follow-up timepoints, but they had the same risk of bias scores, so we have not presented these in the table. *The ROB 2 tool for cluster trials involves a part (a) and a part (b) for randomization.

Categorization of existing studies

Figure 2 shows a bubble plot of the included publications that assessed outcomes, sorted by pain status, risk of bias, and whether the study involved children, caregivers or both. Panel A presents knowledge and beliefs; Panel B presents attitudes and Panel C presents behaviors. More studies have been conducted in healthy children with a preventative focus (e.g., in school settings), and these have not involved caregivers (parents or teachers)..

Figure 2. Bubble plot of the included publications, arranged according to oucomes.



Outcomes are arranged according to sample size with larger circles denoting larger samples. Outcomes are color-coded according to overall risk of bias with red indicating high risk, yellow indicating some concerns, and green indicating low risk. Outcomes are positioned across the x axis according to whether or not they included caregivers in their study aims and on the y axis according to their pain status. *Genik 2021a and 2021b have overlapping sample populations. Rheel 2021 and 2022 have overlapping samples. Louw 2019 and Louw 2020 have overlapping samples. They are represented separately to incorporate the differences in reported outcomes, study aims and risk of bias for each outcome.

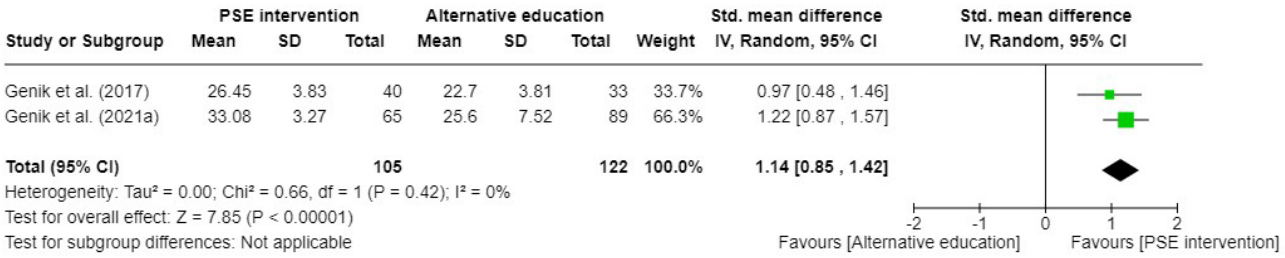
Effectiveness of PSE:

Knowledge and beliefs of caregivers

Two studies (227 participants) both of low risk of bias, evaluated PSE compared to alternative education interventions[37,45]. Both studies assessed caregiver's knowledge and beliefs using different versions of a questionnaire for understanding pain in individuals with intellectual disabilities (QUPID-C (0-35) and QUPID-CR (0-39)). One study did not pool their five different imputed data sets and provided a range of mean differences (MD) and standard deviations (SD) for the five data sets separately[37]. We used the most conservative estimates of one of these imputed datasets for our meta-analysis. The pooled effect of PSE on caregivers compared to alternative education is SMD=1.14 (95%CI: 0.88 to 1.42) (I^2=0%) (Figure 3).

We found low certainty evidence (downgraded for indirectness as this sample only provides evidence on a sub-sample of caregivers caring for children with intellectual disability; and imprecision) for a large effect of PSE on caregiver knowledge and beliefs compared to alternative education (Table 3).

Figure 3. Forest plot and pooled estimate for the effect of PSE compared to control on caregiver pain-related knowledge and beliefs.



Caregiver attitudes

Caregiver attitudes were assessed in a single study (n=28) with some risk of bias concerns, targeting pain management in a cohort of children with functional abdominal pain. They compared PSE combined with hypnotherapy to hypnotherapy alone[46]. They used the pain catastrophizing scale – parent (PCS-P), which measures catastrophizing of a parent regarding their child's pain. There was no difference between groups (MD = -2.63 (-10.13 to 4.86)). We conclude there is very low certainty (single study, further downgraded for limitations in design) for no differences to caregiver attitudes for additional PSE combined with hypnotherapy (Table 3).

Caregiver behaviors

Two studies (n=227), both with high risk of bias, evaluated PSE compared to alternate education or no education. One study, targeted to understanding preventative effects, assessed behaviors in caregivers such as parental responses to pain (through verbalizations)[42] and another study assessed pain assessment and management strategies used by caregivers working in respite care[38]. We were unable to pool the data due to lack of data and clinical heterogeneity (difference in study purpose and different control groups).

In the single study assessing parent verbalizing behaviors, we found a 9% (95%CI: 1% to 18%) difference in the proportion of parent pain-attending verbalizations in the PSE group compared to the group who did not receive PSE. We conclude there is very low certainty (single study, downgraded for limitations in design) for a very small benefit from PSE compared to no treatment[42].

The other study described that they found 'no significant changes' between caregiver pain assessment and management strategies after PSE compared to alternate education[38].

Table 3. Summary of findings for the effect of PSE compared to control on caregiver's pain related outcomes

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control	**Risk with PSE**				
Caregiver knowledge	-	SMD **1.14 SD higher** (0.85 higher to 1.42 higher)		227 (2 RCTs)	⨁⨁◯◯ Low[c,d]	PSE likely results in a large increase in caregiver knowledge.
Caregiver attitudes	One pilot study assessed a parent's pain catastrophising regarding their child's pain. MD (95%CI) -2.63 (-10.13 to 4.86).			28 (1 RCT)	⨁◯◯◯ Very low[a,e]	The evidence is very uncertain about the effect of PSE on caregiver attitudes.
Caregiver behaviours	One study assessed caregiver behaviours (i.e., parental response to pain) and showed a small beneficial difference in verbalizations.		9% (1% to 18%)	89 (1 RCT)	⨁◯◯◯ Very low[a,e]	The evidence is very uncertain about the effect of PSE on caregiver behaviours.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations
a. Downgraded one level for limitations in design.
b. Downgraded one level for inconsistency.
c. Downgraded for indirectness.
d. Downgraded for imprecision.
e. Small single study.

Knowledge and beliefs in children

Four studies (n=1257) assessed the effectiveness of PSE compared to control (usual classes, alternate education and exercise alone) on children's knowledge and beliefs[40,41,43,44] (Table 4). We were unable to pool these results due to lack of data in two studies (no point estimates

and measures of variability)[41,43], and clinical heterogeneity (age of children; healthy children vs. children with chronic pain).

Three studies targeted to preventative PSE, assessed 1139 school children aged 11-12 years. [40,41,43]. Two of these studies did not provide data, but concluded that PSE improved knowledge and beliefs compared to usual classes[43] or no education[41]. The third study, with high RoB, showed an increase in knowledge and beliefs in their education group (PNE) and the group who received an additional 10 minute video booster at 2 and 4 months (PNE boost group) compared to an alternative education at post intervention (MD=2.2; 95% CI 1.8 to 2.6)[39]. They also showed an increase in knowledge and beliefs at 6 months, but only in the PNE boost group (MD= 0.62; 95% CI 0.18 to 1.06)[40]. From this study, we conclude very low certainty evidence (single study; further downgraded for limitations in design) for improved knowledge after PNE and additionally after 6 months if provided with booster sessions.

One study of high risk of bias compared PSE + exercise to exercise alone in 118 older adolescents (15-17 years) with chronic idiopathic neck pain post intervention and at 6 months follow-up using the revised neurophysiology of pain questionnaire (NPQ; score range 0-12)[44]. We found a difference between groups of MD=3.09 (95% CI: 2.28 to 3.9) post-intervention and MD=2.85 (95% CI: 1.88 to 3.82) at 6 months follow-up. We conclude very low certainty evidence (single study, further downgraded for limitations in design) for a large beneficial effect of additional PSE on exercise post intervention and at 6 months follow-up in older adolescents with chronic idiopathic neck pain.

Table 4. Summary of evidence for the effects of PSE compared to control on children's pain-related knowledge and beliefs.

Study	Sample size (n)	Risk of Bias	Outcome measure (score range)	Knowledge change	GRADE*
Andias, 2022	118	🔴	NPQ (0-12)	Improved	⊕◯◯◯ Very low
Kisling, 2021	381	🔴	PKQ-CH (0-20)	Improved	
Louw, 2019/2020	669	🔴	NPQ (0-12)	Improved	⊕◯◯◯ Very low
Rheel 2021	89	🔴	PNE4Kids questionnaire (0-32)	Improved	

Risk of bias is indicated by color, with red indicating high risk, yellow indicating some concerns and green indicating low risk. The magnitude of effect could not be determined, so the direction of effect for knowledge change is provided. *As these were all single studies, we only performed GRADE assessments if we were able to calculate results (Kisling, 2021 and Rheel, 2021 did not provide data).

Children's attitudes

Three studies (n=876) evaluated the effect of (additional) PSE compared to no education/usual classes, alternate education or exercise alone)[40,41,44] (Table 5). All studies assessed a range of children's attitudes about pain (e.g. fear of pain, catastrophizing, kinesiophobia, self-efficacy) using different assessment tools (e.g. pain catastrophizing scale for children (PCS-C); and fear avoidance beliefs questionnaire- physical activity subscale (FABQ-PA) and the child fear scale (CFS)). We were unable to pool the data due to clinical heterogeneity (mean age of children, differences in pain state, differences in study purpose, and various control interventions) and lack of data[41].

Two studies (n=758) involved children under 13 years without chronic pain[40,41]. One study of high risk of bias assessed pain-related attitude scores using the FABQ-PA (score range 0-24; lower scores represent improved attitudes) at post intervention and at 6 months after receiving PSE at school. We found a difference in pain-related attitude scores at post intervention compared to the control group who received alternative education (MD=-3.3 (95%CI=-4.28 to -2.32))[39]; and no differences at 6 months follow-up in the group who

received PSE compared to the group that received alternative education (MD=0 (95%CI: -0.1 to 0.1)) or the group that received a booster 10 minute education video at 2 and 4 months (PNE boost group) compared to the group that received alternative education (MD=0.02 (95%CI: -0.07 to 0.011)[40]. We conclude very low certainty evidence (single study; further downgraded for limitations in design) for a small difference in pain-related attitudes after PSE compared to the alternative education, but these were not maintained at 6 months. The other study did not provide data but reported 'no group by time effects' in the PSE group compared to the control group who received no education[41].

One study involving 118 older children (mean age 16 years), with some risk of bias concerns compared PSE + exercise to exercise alone for adolescents with chronic idiopathic neck pain[44]. We found very low certainty evidence (single study; further downgraded for indirectness as this study only provides evidence for sub-sample of adolescents with neck pain) for no difference in effect between both groups for pain catastrophizing or kinesiophobia immediately after the intervention and at 6 months follow-up[44] (Mean differences provided in Supplementary 3).

Table 5. Summary of evidence for the effect of PSE compared to control on children's pain-related attitudes.

Study	Sample size (n)	Risk of Bias	Outcome measure (score range)	Pain-related attitude change	GRADE*
Andias, 2022	118	🟡	PCS (0-52)	Nill	⊕◯◯◯ Very low
		🟡	TSK (13-52)	Nill	
Louw, 2019/2020	669	🔴	FABQ-PA (0-24)	Improved	⊕◯◯◯ Very low
Rheel, 2021	89	🟡	CFS (0-4)	Nill	
		🟡	PCS-C (0-10)	NIll	

Risk of bias is indicated by color, with red indicating high risk, yellow indicating some concerns and green indicating low risk. The magnitude of effect could not be determined for all studies, so we have provided the direction of effect as reported by the study. *As these were all single studies, we only performed GRADE assessments if we were able to calculate results (Rheel, 2021 did not provide data).

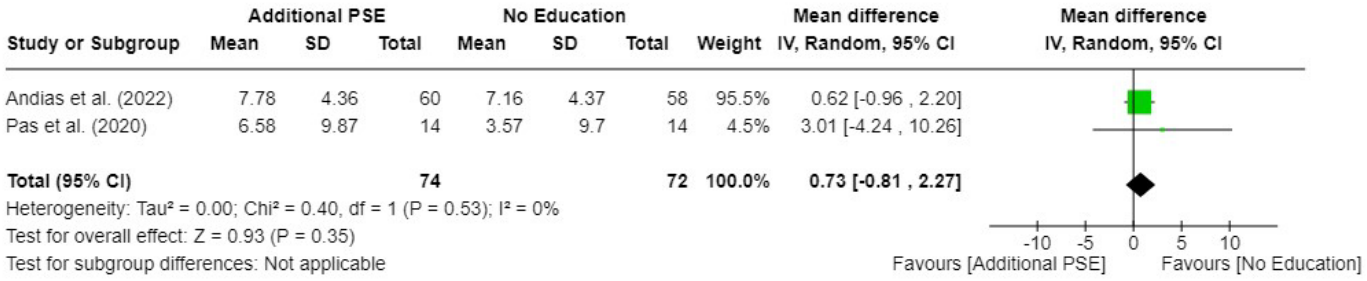
Children's Behaviors

Four studies (n=1196) assessed the effectiveness of (additional) PSE on children's behaviors, and used a variety of comparisons including no education, alternative education, exercise alone or hypnotherapy alone [40,43,44,46]. Two studies assessed children with chronic pain and two assessed school children. These studies assessed a variety of children's behaviors: child or parent-reported functional disability[43,44,46]; pain coping[43]; school attendance[40,43]; participation in sport, recess and physical education[40]; health practitioner visits[40]; and medication use[40,43].

Two studies of some risk of bias concerns (n=146) assessed the behavior of children with chronic pain after receiving PSE using the functional disability inventory and parent proxy (FDI and FDI-P)[44,46], where higher scores indicate greater disability, with a total possible score of 60 points. Both studies compared additional PSE to either exercise or hypnotherapy

alone. Although there was clinical heterogeneity related to the differences in mean age, we nevertheless pooled the results because we deemed the FDI appropriately accounted for development in this population, and has good psychometric properties (test-retest reliability child report, .74; parent-report, .64; internal consistency reliability ranging from .86 to .91)[34].

Figure 4. Forest plot and pooled estimate for the effect of PSE compared to no education on children's functional disability*.



*Functional disability is measured using the functional disability inventory (FDI) and parent proxy (FDI-P). Higher scores indicate greater disability out of a total possible score of 60 points.

Pooled results showed no differences between the groups: MD = 0.73 points (95%CI: -0.81 to 2.27). We therefore conclude there is low certainty evidence (downgraded for indirectness and imprecision) for no difference in functional disability of additional PSE compared to exercise or hypnotherapy alone (Figure 4; Table 6).

Table 6. Summary of findings for PSE compared to control for children's functional disability

Patient or population: Interventions relating to managing children's pain
Setting: clinical or community
Intervention: Additional PSE
Comparison: exercise or hypnotherapy alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control	**Risk with PSE**				
Children's functional disability assessed with: FDI or FDI-P Scale from: 0 to 60		MD **0.73 points higher** (0.81 lower to 2.27 higher)	-	146 (2 RCTs)	⨁⨁◯◯ Low[a,b]	There is limited evidence and low certainty that PSE results in no difference in children's functional disability.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations
a. Downgraded one level for imprecision.
b. Downgrade one level due to indirectness

For other children's behaviors we could not pool the data due to clinical heterogeneity (differences in control interventions). Two studies (n=1050) aimed at pain prevention with high risk of bias for behavioral outcomes, assessed the effect of PSE compared to either usual classes or alternative education on school attendance, participation in sport, recess and physical activity classes, and health practitioner visits[40,43]. One study concluded 'no difference' for any behavioral outcomes after PSE compared to the group that received usual classes[43]. In addition, the other study also showed no differences between groups for PSE or PSE boost groups compared to alternative education for school attendance; participation in sport, recess and physical activity classes; and health practitioner visits[40] (Calculated mean differences are provided in Supplementary 3).

These studies also evaluated medication use in the months after PSE. One study reported no group by time differences between the PSE and usual care for medication use in the previous 4 weeks[43]. Another study reported the proportion of students using medication for pain in the previous 6 months after PSE (with a booster session at 2 and 4 months) and found a small difference of 12.5% in favor of the PSE group[40]. Medication use included any medication used for pain relief purposes.

We conclude very low certainty evidence (single studies; further downgraded for limitations in design) for little no difference to children's behaviors (Table 7).

Table 7. Summary of evidence for the effect of PSE compared to control on children's pain-related behaviors.

Study	Sample size (n)	Risk of Bias	Outcome assessed	Pain-related behavior change	GRADE*
Louw, 2020	669	🔴	School attendance	No change	⊕◯◯◯ Very low
		🔴	Participation in sport	No change	
		🔴	Participation recess	No change	
		🔴	PE class	No change	
		🔴	Healthcare visits	No change	
		🔴	Medication use	Small improvement	
Kisling, 2021	381	🔴	School attendance	No change	
		🔴	Medication use	No change	

Risk of bias is indicated by color, with red indicating high risk, yellow indicating some concerns and green indicating low risk. The magnitude of effect could not be determined for all studies and all outcomes, so the direction of effect is provided. *As these were all single studies, we only performed GRADE assessments if we were able to calculate results (Kisling, 2021 did not provide data).

DISCUSSION

Interest in the use of PSE for the treatment and prevention of pediatric chronic pain has been growing in recent years. This systematic review and meta-analyses present results for caregiver and children's outcomes relating to knowledge, beliefs, attitudes, and behaviors. We found few randomized controlled trials, and the oldest included study was conducted in 2017,

highlighting this field of research is relatively new. High risk of bias and clinical heterogeneity (e.g., diversity in PSE interventions) reduce the certainty of the evidence, meaning that results must be interpreted with caution. Imprecision due to low participant numbers also contributes to the reduced certainty for some outcomes and highlights the need for more research to improve the certainty of the evidence. We found low certainty evidence that PSE has a large beneficial effect on caregiver knowledge and beliefs compared to control in interventions targeted to pain prevention and management for children. Similarly, PSE positively influences children's knowledge and beliefs in both healthy and chronic pain samples, but the evidence is of low certainty. We found low certainty evidence for no difference to children's functional disability in chronic pain samples, and the effect of PSE on carer and children's attitudes and additional pain-related behaviors (such as school attendance and carer pain management strategies), remains unclear with only low certainty evidence available. Overall, we observed that existing evidence did not always account for childhood development (e.g. selection of outcome measures was not validated in children) and this contributes to the low certainty of the evidence.

The hypothesized effects of PSE are understudied and remain unclear. Our findings are consistent with a recent overview of systematic reviews related to neuroscience education and chronic pain which found scarce quality evidence for adolescent or pediatric chronic pain[59]. Most articles had serious limitations due to methodological flaws such as the use of non-validated outcome measures (e.g. the use of the NPQ in children) or behavioral retrospective self-report measures that would likely not be sensitive to plausible intervention effects in children (e.g. child retrospective self-reported medication use over the previous 6 months). If outcome measures are not sensitive enough, they may not capture potential changes

associated with interventions[60]. Our review supports the development of core outcome sets to improve the quality of future research interventions.

Developmental sensitivity is a key factor that not only applies to outcome measures, but to all aspects of research that involves children. A condition of childhood is that caregivers make decisions about children's care, and they respond to children, thereby influencing children's learning. Thus, it makes sense that interventions, such as PSE delivered to children, would be guided by how caregivers might interact with the learning, or respond to behaviors in children associated with the learning, in a developmentally sensitive way. This is true whether interventions are targeted to pain treatment or pain prevention. A recent before-and-after study assessed children and their parents' pain beliefs and recommended assessing both parent and child outcomes when designing targeted PSE for children with chronic pain and their families[61]. Another before-and-after study conducted with healthy children and their parents, found parental knowledge of pain and child fear of pain improved after PSE[62]. Only two of the studies in our review included caregivers when PSE was delivered to children[42,46], and only one assessed child and caregiver behaviors associated with this learning[42]. In this study, caregiver knowledge or beliefs were not assessed, so little is known about what cognitive processes may have occurred alongside behaviors such as talking about pain with their child. More research is needed to understand the complexity of caregiver outcomes alongside the caregiver/child relationship when learning about pain.

Recent findings suggest that PSE can improve attitudes and behaviors in healthcare professionals[63]. We found very low certainty evidence for these findings in caregivers and children. However, we did observe that studies developed interventions with consideration of contextual factors that may support learning processes, and these factors may in turn improve

attitudes and behaviors. This is illustrated by the use of booster sessions[40], interactive case studies[37,38] and opportunities for questions and applying knowledge during exercise activities[44]. The inclusion of these elements in PSE design and delivery in our included studies supports a developing understanding in the field that pain conceptualization/ reconceptualization is a complex and dynamic process that involves learning[64].

Limitations

Our systematic review has some limitations. First, we did not include studies where PSE could not be isolated from other interventions. This limits our findings, particularly for clinical studies involving chronic pain, because the recommended treatment for chronic pain includes PSE *as part of* multidisciplinary treatment[21]. Therefore, it is potentially challenging to ethically study the effects of PSE in isolation in chronic pain populations. Exploring the clinical course of outcomes following interventions that combine PSE (e.g., combined with cognitive behavioral therapy; exercise or as part of cognitive functional therapy) may provide insight into how PSE can be best integrated into therapeutic approaches. Second, we excluded studies that used more instructional pain management approaches (even if they were obviously informed by a biopsychosocial approach), because they did not meet our criteria addressing pain biology knowledge. This resulted in studies relevant to chronic pain or the prevention of chronic pain dominating our findings, with minimal representation of studies for acute pain (such as needle pain). Including 'bio-psychosocially informed' pain education interventions (rather than the stricter criteria we applied here) may have broadened our findings particularly related to how and when caregiver involvement is best incorporated. Third, we did not assess or compare the details of the interventions (e.g. mode, delivery, dose etc.). This limits our ability in this review to comment on how these factors may influence effectiveness. Fourth, we could not provide a comprehensive overview of studies published in

languages outside of our team's capability to interpret (e.g. we noted one study in our included full-text articles published in Mandarin). Lastly, no studies reported on gender and the included study samples were predominantly white/European (if reported), meaning that caution is warranted when interpreting the results.

Clinical and public health implications

This review shows low certainty evidence that PSE delivered to carers can positively influence their pain-related knowledge and beliefs, with a similarly large effect on children, albeit very low certainty evidence. While theoretically PSE could be beneficial for carer and children's attitudes and behaviors, we did not find high-quality evidence to support this. We did not find any RCTs that assessed both carer and child pain-related knowledge and beliefs outcomes simultaneously, and only one study that assessed both child and carer behaviors[42] . This limits our understanding of how caregivers and children interact when learning about pain, and any potential associated behavior change that may occur when learning about pain simultaneously and/or together. Future research involving PSE with child/caregiver dyads with study designs that consider the dynamic and complex social interactions involved in pain expression and responding, could begin to address this gap.

Our review highlights increasing interest in the potential to prevent or reduce the development of chronic pain and disability in children and adolescents, by enhancing their pain-related health literacy. However, the long-term effects of PSE on health outcomes are unclear, and further research is needed.

Future research

This systematic review is timely given the recent increase in pediatric pain PSE trials. Future research should consider the social influence of caregivers on children's

conceptualization/reconceptualization of pain. Selecting developmentally sensitive, previously validated outcome measures is also important to reduce the risk of bias and improve the quality of evidence. To aid understanding, we have summarized the outcome measures used in included studies (Supplementary 2). Future research could investigate the psychometric properties of outcome measures to guide clinical application, future study design, and aid the development of core outcome sets.

Conceptualization/reconceptualization of pain is a learning process that is dynamic and relational[64,65]. Future research should strive to deliver and assess interventions that incorporate this dynamic process of learning over longer periods of time. Additionally, consideration of classroom learning theory, such as Bandura's social learning theory[66] and Vygotsky's sociocultural theory[67,68], could guide PSE interventions and the assessment of outcomes in a developmentally sensitive way, whether the PSE interventions be designed for treatment or prevention.

CONCLUSIONS

Research involving PSE and children has increased in recent years. Despite this, the effectiveness of PSE delivered to children and their carers remains understudied. There is low certainty evidence that PSE has a large beneficial effect on caregiver knowledge and beliefs, with very low certainty evidence for similar effects on children. The available evidence regarding the effect of PSE on the attitudes and behaviors of both caregivers and children is limited and of low and very low certainty. Further research is needed.

Figure Legend

Figure 1. PRISMA diagram summarizing search results.

Figure 2**.** Bubble chart of the 10 included publications, arranged according to outcomes.

Figure 3. Forest plot and pooled estimate for the effect of PSE on caregiver knowledge compared to control.

Figure 4. Forest plot and pooled estimate for the effect of PSE on children's functional disability.

Table Legend

Table 1. Summary of study characteristics.

Table 2. Risk of bias assessments for each outcome.

Table 3. Summary of findings for the effect of PSE compared to control on caregiver's pain-related knowledge and beliefs, attitudes and behaviors.

Table 4. Summary of evidence for the effect of PSE compared to control on children's pain-related knowledge and beliefs.

Table 5. Summary of evidence for the effect of PSE compared to control on children's pain-related attitudes.

Table 6. Summary of findings for the effect of PSE compared to control on children's functional disability.

Table 7. Summary of evidence for the effect of PSE compared to control on children's pain-related behaviors.

Supplementary Material

Supplementary 1. Search strategy.

Supplementary 2. Summary of outcome measures used to assess knowledge, beliefs, attitudes and behaviors in included studies.

Supplementary 3. Table of calculated and extracted results for between group differences at post intervention and all available follow-up timepoints.

Supplementary 4. Risk of Bias assessments.

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