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# Prognostic factors of chronic postsurgical pain in children and adolescents: a systematic review and meta-analysis

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## ABSTRACT

**Background** Approximately 28% of children and adolescents undergoing major surgery develop chronic postsurgical pain (CPSP; pain persisting>3 months). A previous review attempted to investigate biopsychosocial prognostic factors for pediatric CPSP; however, due to lack of data, no meta-analytic techniques were employed. Since that review, numerous studies have investigated risk/protective factors that fall within an Interpersonal Fear Avoidance Model for CPSP, thus warranting a reinvestigation of prognostic factors.

**Objective** This systematic review and meta-analysis aimed to examine prognostic factors, measurement tools applied, and their effect on the development of CPSP.

**Evidence review** Prospective, observational studies examining prognostic factors of pediatric CPSP using validated self-report measures were included. 4884 unique publications were screened and 15 met inclusion criteria.

**Findings** The pooled effect size for the association between presurgical child pain intensity and the presence of child CPSP was significant, OR=0.540 (95% CI=0.184 to 0.894). Child anxiety, child pain-related anxiety, and parent pain catastrophizing were not significant prognostic factors for child CPSP. Using Grading of Recommendations, Assessment, Development, and Evaluation, the certainty in prognostic estimates was moderate. Risk of bias using Quality in Prognostic Study tool ranged from low to moderate.

**Conclusions** Presurgical pain was the only presurgical risk factor at the meta-analytic level that significantly predicted pediatric CPSP, highlighting the importance of prioritizing pain management throughout the perioperative experience, starting before surgery. Depressive symptoms and sleep disturbance were the two potential risk/protective factors that were unable to be assessed due to insufficient data or use of an unvalidated measure indicating a critical need for future research.

**PROSPERO registration number** CRD42022306340.

## INTRODUCTION

Approximately 20% of children and adolescents develop chronic postsurgical pain (CPSP) following major surgery.[1] The International Classification of Diseases (ICD-11) recently defined CPSP as pain that: develops or increases in intensity after a surgical procedure; is localized to the surgical field or projected to a referred area; persists beyond the healing process (ie, >3 months); and other causes of pain are excluded.[2 3] ICD-11 also specifies that pain intensity, pain-related distress (eg, anxiety and depression), and functional interference are overarching elements of pain severity.[3]

Since the prior systematic review of risk factors for CPSP in 2017, there has been a substantial increase in the number of prospective, longitudinal studies exploring prognostic factors for pediatric CPSP, thus warranting an updated examination of these risk factors. Given (1) the high prevalence of CPSP and the lack of guidance on how to address CPSP, (2) a recent priority setting partnership with patients identifying prevention of CPSP as the number one top priority for pediatric pain research,[4] and (3) the recent launch of an new NIH funding program, HEAL KIDS, which aims to address chronic pediatric pain, including its prevention of pain, it is critical to conduct an updated review.

A predominant model in the literature to describe the development of pediatric chronic pain is the Interpersonal Fear Avoidance Model (IFAM).[5] This model originated from the cognitive–behavioral fear avoidance model of chronic pain, which purported that pain may be perceived as a threat and that pain-related fears dominate thought processes when pain is not confronted.[6–8] More recently, the diathesis-stress model was combined with the IFAM to explain the vulnerabilities of children and caregivers to fear avoidance in the context of CPSP.[9] These models provide a framework for examining various biopsychosocial factors (eg, genetics, sleep disturbances, pain-related anxiety, anxiety sensitivity, pain) deemed significant in independent studies for the development of CPSP. Rabbitts *et al*[1] attempted to investigate such prognostic factors for pediatric CPSP within a meta-regression analysis; however, due to a lack of data, no meta-analytic techniques were employed.

The aim of this systematic review and meta-analysis was to examine, summarize, and synthesize previously included articles from the original 2017 review with newly published studies reporting preoperative prognostic factors for pediatric CPSP. This would provide a more accurate depiction of which prognostic factors are significant at a multivariate level as well as a meta-analytic level.

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## METHODS

The study protocol was registered in the international prospective register of systematic reviews, PROSPERO, on March 3, 2022, (CRD42022306340). There were no protocol deviations in this review.

### Eligibility criteria

Studies were evaluated according to a hierarchical exclusion criteria that used the Population, Intervention/Exposure, Comparison, Outcomes and Study (PICOS) framework.[10] Specifically, the *population* of interest was children 6–18 years old. The cut-off age of 6 years old was chosen as the lower age range for pediatric self-report scales validated for postoperative pain assessment.[11] Studies with participants outside of the eligible age range were considered if the majority of the population were within the age range, or if the data presented was stratified by age and could be extracted according to the eligible age range. Children must have received surgery with general or regional anesthetic (*intervention*), excluding diagnostic, non-invasive, cancer or dental procedures. Children with cancer or neurological disabilities were excluded due to potential confounding variables with pain experience and recovery. We considered a variety of prospective study designs, including case series, case–control, and cohort studies. Single case reports, retrospective, randomized intervention, qualitative, non-human, and cell studies were excluded. Studies with less than 10 participants were also excluded. Studies must have employed a longitudinal design to report on presurgery risk factors associated with pain between 3 and 12 months after surgery (*outcome*) and postoperative pain outcomes between 3 and 12 months after surgery (*comparison* was those who developed CPSP to those who did not) with a validated pain measure. Risk factors included, but were not limited to (1) age and sex, (2) medical (baseline pain severity and location), (3) psychosocial risk (eg, presurgery child anxiety, child pain catastrophizing, child depression, child sleep patterns, parent anxiety, and parent pain catastrophizing), (4) resiliency (eg, self-efficacy), and (5) clinical (eg, surgery type and length, hospital length of stay). Published, peer-reviewed articles written in English were considered for inclusion (*studies*). We excluded non-English studies as we did not have resources to translate foreign languages. Dissertations, abstracts only, guidelines/consensus, protocols, and reviews were excluded.

### Information sources, search strategy, and selection process

Searches of the Ovid MEDLINE, EMBASE, and PsycINFO databases were conducted from the time of the previous Rabbitts *et al*.[1] review search (January 2016) to April 20, 2023. Peer-reviewed articles that matched the predefined search criteria were identified. All identified articles were imported to the Joanna Briggs Institute's System for the Unified Management, Assessment, and Review of Information software for screening. Two reviewers (VW, GG, SDF, BNR, and JR) independently screened titles and abstracts according to the PICOS hierarchical exclusion criteria. The full texts of suitable abstracts were retrieved and assessed for eligibility by two independent reviewers (VW and SDF). The full texts included in the published 2017 systematic review were also retrieved and reassessed for eligibility by two independent reviewers (VW and BNR) according to the more stringent eligibility criteria applied in this updated systematic review and meta-analysis. Conflicts during the screening process were resolved by consensus through discussion involving a third reviewer (KAB). Full-text articles which passed the eligibility assessment were re-evaluated by a third reviewer (JR) for additional criteria, such as use of duplicate samples.

### Study risk-of-bias (RoB) assessment

RoB was assessed for each included article by two independent reviewers (SDF and CSP) using the QUality In Prognosis Studies (QUIPS) tool.[12] Each study was assessed in the four domains of study participation, study attrition, outcome measurement, and study confounding, as part of the companion systematic review reporting prevalence of CPSP. In addition, each included article was assessed for two additional domains, including prognostic factor measurement, and statistical analysis and reporting of prognostic factors. The articles received a rating of a "low", "moderate", or "high" RoB for each QUIPS category, resulting in six total ratings for each article. The criteria used to determine RoB was standardized across all articles, and the assessment was specifically focused around prognostic factors and outcomes of relevance to this study. An article scored a low RoB if all criteria for one QUIPS category were met, a moderate RoB if only some criteria were met, and a high RoB if there were significant shortcomings in a specific QUIPS category (eg, low participation rate, high attrition, confounding factors not considered, inappropriate data analysis). A participation rate of less than 20% was considered low,[13] and attrition of more than 30% was considered high.[14] After both independent reviewers completed the RoB ratings for each article, discrepancies were discussed and resolved. Rating RoB for each included article allows readers to understand how likely an article is to demonstrate bias.

### Data collection process and data items

Data presented in the included articles was collected by one reviewer (VW or GB) manually, and checked by another reviewer (BNR). The data extracted were pain outcome(s) 3–12 months after surgery, preoperative time point, comparisons of interest (ie, analysis conducted to confirm whether the investigated preoperative factors can predict pain at follow-up and presentation of those findings), measures used to assess preoperative prognostic factors, description of those factors, type of factor (ie, child/adolescent or caregiver factors), analysis used to conduct investigation (ie, univariate or multivariate analysis) as well as the significance level chosen by the authors and the computed p value. Data on all investigated preoperative biopsychosocial and medical factors with the potential to predict pain at follow-up was extracted.

### Effect measures and synthesis methods

When a study examined more than one relevant risk factor, effect sizes were examined in separate meta-analyses. When there were overlapping samples or analyses (eg, variable assessed in multiple studies[15 16]), the analysis with the larger sample size, more relevant to the current research question, or most similar to other analyses was included. Effect sizes adjusted for relevant covariates were selected over unadjusted effect sizes. When available, child-reported data for child risk factors and outcomes and parent-reported data for parent risk factors were used.

### Statistical analysis

Random effects meta-analyses were conducted in Comprehensive Meta-Analysis Software V.3.0 (BioStat) when there were sufficient data (three or more studies). Random effects meta-analyses were chosen given the differences in types of surgeries, and therefore the model could account for heterogeneity. To estimate ORs and 95% CIs for the association between risk



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factors (ie, child general anxiety, child pain-related anxiety, child depression, child pain intensity, child functional impairment, parent anxiety, parent pain catastrophizing) and the presence of child CPSP (ie, pain present for three or more months after surgery), all ORs with CIs and event rates from studies were collected and pooled. Analyses were performed per risk factor. Heterogeneity of the effect sizes was assessed with the $I^2$ index. (ie, $I^2$ was considered significant when ≥50%). Publication bias was examined through inspection of funnel plots and the Egger test (significance=$p<0.10$).

### Certainty assessment

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach,[17] which is applied to a body of non-intervention research and similar to other meta-analyses of prognosis, was used to assess the quality of the evidence base for each meta-analysis.[18] Limitations in the quality of included studies were assessed with specific items from the NIH Quality Assessment Tools that aligned with key criteria in the *GRADE Handbook*.[19] The analysis was conducted by two independent assessors (VW and BNR), and any conflicts between reviewers were resolved through discussion with a third assessor (JR). Inconsistency in estimates was based on variance in estimates, degree of overlap of confidence intervals, and statistical significance of heterogeneity statistics. Indirectness of outcome measurement was based on the use of child-reported outcomes. Publication bias was determined from the funnel plots and Egger tests. Imprecision of results was determined from the overall sample size (based on power calculations with $\alpha=0.05$ and $\beta=0.80$) and range of the confidence intervals of the estimates. Ratings on the five domains for each analysis were decided through consensus of two coders.

## RESULTS

### Study selection

The 3 updated database searches yielded 4871 unique total records. After automated removal duplicates in Covidence, 3460 records were identified for the selection process. After title and abstract screening, 185 articles were retrieved and assessed for full-text review, 13 of which were included from the original 2017 publication. On initial full-text review from the updated search and the original n=13 articles, 31 articles met inclusion criteria. However, of these articles, 16 were then removed for the following reasons after further assessment: cohort described in multiple articles (n=12), article already identified in initial review search (n=2), indirect effect on chronic pain outcomes (n=1), and age range out of bounds (n=1).

In total, 15 studies were included in this review update, including 2 studies from the original 2017 publication. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram, depicting the selection process, is shown in figure 1.

### Study characteristics

Study characteristics are presented in table 1. The articles that met the eligibility criteria studied 32–291 participants at baseline. The age range of the participants included children from 6 to 18 years, with 39.9%–86.1% were women. The effects of spine/spinal surgery were studied in most articles (66.7% of the included articles), while the remaining articles focused on a combination of surgical procedures (33.3% of the included articles).

### RoB in studies

Ratings across the QUIPS categories leaned toward the low-to-moderate RoB range (figure 2A,B). The QUIPS category in which the articles collectively performed the best was prognostic factor measurement, followed closely by study participation, outcome measurement, and study confounding. For prognostic factor measurement, 10 articles (66.6% of the included articles) received a low RoB rating and 4 articles (26.6% of the included articles) received a moderate RoB rating (figure 2A,B). Articles received a moderate RoB if some, but not all, tools to measure prognostic factors were valid and reliable. For the other three QUIPS categories mentioned above, patterns of most frequent errors were observed: First, for study participation, the most common reasons articles received a moderate RoB rating were due to (a) poor details delineating inclusion/exclusion criteria, (b) missing the number of participants who were approached versus started the study, and (c) missing the recruitment time frame. Second, for outcome measurement, the most common reasons articles received a moderate RoB rating were due to a failure to state how surveys and/or where surveys were delivered (eg, via email, on paper, at home, in-clinic). Third, for study confounding, the most common reason articles received a moderate RoB rating was due to failure to control for confounding factors (eg, through study design or in analyses).

The QUIPS categories in which included articles performed the most poorly were study attrition and statistical analysis and reporting. For example, in the QUIPS category study attrition, four articles (26.6% of the included articles) received a high RoB rating and seven articles (46.6% of the included articles) received a moderate RoB rating (figure 2A,B). The most common reasons articles received a moderate or high RoB rating for this QUIPS category were due to (1) poor details explaining reasons for dropouts, (2) failing to compare completers versus non-completers, (3) a low ratio of completer to non-completers, and/or (4) an unacceptably high rate of participant attrition.

### Prognostic factors summarized

Prognostic factors at the multivariate level were grouped into child (ie, youth aged 6–18 years) or caregiver categories. Within the child category, pain intensity (n=7), pain-related anxiety (ie, pain catastrophizing and pain anxiety; n=6), general anxiety (n=1), mood (n=2), psychological flexibility (n=1), surgical duration (n=2), age (n=7), and pain self-efficacy (n=1) were assessed. All, but age, were found to be significant in at least one included paper with pain intensity being the significant often (n=4) followed by pain-related anxiety (n=2). Within the caregiver category, general anxiety (n=1) and pain catastrophizing (n=3) were examined at the multivariate level and both were significant.

#### Prognostic meta-regression analyses

Meta-analytic results for prognostic factors associated with the presence of child CPSP are displayed in figure 3. Prognostic factors for which there was sufficient data are reported below. There were insufficient data to conduct meta-analytics on factors including child depression, child functional impairment, parent anxiety, child sleep, surgical duration or child sex.

#### Child pain intensity

The pooled effect size for the association between child pain intensity and the presence of child CPSP from four studies was significant, OR=0.540 (95% CI 0.184 to 0.894).[20–23] There was some evidence of significant between-study heterogeneity of



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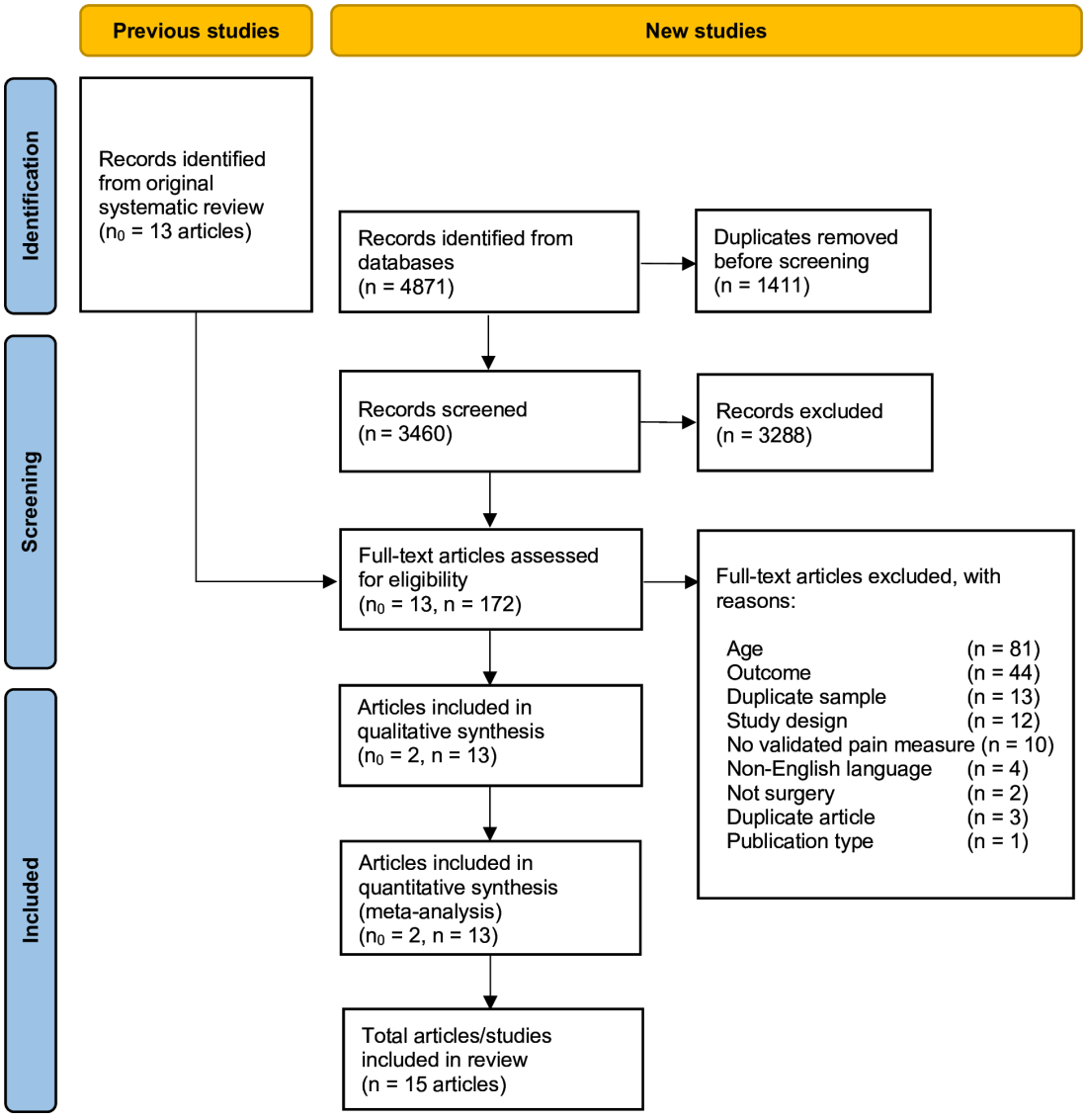


**Figure 1** Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram showing the selection of articles from the initial literature searches through to the final inclusion in this systematic review and meta-analysis.

effect sizes ($I^2$=58.62). This indicates that preoperative pain is a significant, but small, risk factor for child CPSP (ie, the higher the pain intensity a child experiences prior to surgery, the more likely they are to develop CPSP).

### Child general anxiety

The pooled effect size for the association between child general anxiety and the presence of child CPSP from three studies (Rosenbloom *et al*[15]; Bailey et al 2021; Rabbitts et al 2020) was not significant, OR=0.004 (95% CI −0.021 to 0.030). This indicates that preoperative child general anxiety is not identified as a significant risk factor for child CPSP.

### Child pain-related anxiety

The pooled effect size for the association between child pain-related anxiety (ie, pain catastrophizing and pain anxiety) and the presence of child CPSP from four studies (Rosenbloom *et al*[15]; Bailey et al 2021; Rabbitts et al 2015; Rabbitts et al 2020) was not significant, OR=−0.006 (95% CI −0.032 to 0.019). This indicates that preoperative child pain-related anxiety is not a significant risk factor for child CPSP in the present analysis.

### Parent pain catastrophizing

The pooled effect size for the association between parent pain catastrophizing and the presence of child CPSP from three studies (Bailey et al 2021; Rabbitts et al 2020; Rabbitts et al 2015) was not significant, OR=0.015 (95% CI −0.066 to 0.0960). This indicates that preoperative parent pain catastrophizing is not identified as a significant risk factor for child CPSP.

## Certainty assessment

Ratings of the quality of the evidence across the GRADE criteria for each estimate that was analyzed for the association between prognostic factors and the presence of child CPSP are displayed in table 2. Overall, confidence in these estimates were reduced due to limitations in the quality of the studies across all analyses (eg, study attrition, statistical



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**Table 1** Characteristics of the 15 articles included in this systematic review

| Study | Baseline (n) | Mean age, years* (range) | Sex: female (n)/male (n) (% female) | Race/ethnicity† | Surgery type | Follow-up (n) | % lost to follow-up |
|---|---|---|---|---|---|---|---|
| Bailey *et al*[37] | 220 | 14.6 (10–20) | 189/31 (86.0%)‡ | NR | Posterior scoliosis correction | 148 (3 months), 155 (6 months), 138 (12 months) | 30%–37% |
| Batoz *et al*[22] | 291 | 12.04 (6–18) | 116/175 (39.9%)‡ | NR | Elective surgery (62% orthopedics) | 258 (3 months) | 13% |
| Beeckman *et al* [38] | 100 | 15.19 (12–18) | 77/23 (77.0%) | White 99%, Asian 1% | Posterior spinal fusion surgery | 88 (6 months) | 12% |
| Chidambaran *et al*[21] | 144 | 14.44 (10–18)§ | 106/38 (73.4%)‡ | Caucasian 84.9%, no other race/ethnicity data described | Posterior spine fusion surgery | 127 (2–3 months), 110 (10–12 months) | 12%–24% |
| Connelly *et al*[39] | 50 | 14.5 (11–17) | 41/9 (82%)‡ | Caucasian 87%, African American 13% | Posterior spinal fusion surgery | 44 (3 months), 40 (6 months) | 12%–20% |
| Julien-Marsollier *et al*[40] | 36 | 15 (NR) | 31/5 (86.1%) | NR | Posterior fixation spinal surgery | 36 (12 months) | 0% |
| Narayanasamy *et al*[41]¶ | 144 | 14.88 (12.06–17.75) | 93/51 (64.81%)‡ | Caucasian 81%, African-American 12%, other 7%, non-Hispanic 96%** | Posterior spine fusion surgery | 105 (6 months), 71 (12 months) | 38% |
| Perry *et al*[42] | 36 | 14 (10–17)§ | 27/9 (75.0%) | White 58.3%, black 11.1%, Asian 5.6%, other/missing 25% | Corrective spinal fusion surgery | 36 (4–6 months) | 0% |
| Rabbitts *et al*[23] | 60 | 14.7 (10–18) | 40/20 (66.7%) | White 83.4%, African-American 3.3%, Asian 3.3%, other/not reported 10% | Major spine or chest wall surgery | 54 (4 months), 46 (12 months) | 28% |
| Rabbitts, Palermo *et al*[20] | 119 | 14.9 (10.0–18.9) | 75/44 (63%) | White 78.2%, African American 4.2%, Asian 3.4%, other/not reported 14.3% | Major musculoskeletal surgery | 114 (4 months) | 11% |
| Rosenbloom *et al*[15] | 265 | 14.1 (8–18) | 155/110 (58.5%) | Caucasian 65.95%, African Canadian 6.03%, South Asian 5.60%, East Asian 4.35%, African Caribbean 1.72%, Hispanic 1.72%, Aboriginal 1.29%, other 11.64% | Orthopedic surgery or general surgery (50% scoliosis surgery and 36% osteotomy). | 214 (6 months), 225 (12 months) | 15%–19% |
| Rosenbloom *et al*[16]¶ | 79 | 14.56 (9–18) | 46/33 (58.2%) | NR | Orthopedic or general surgery | 79 (12 months) | 0% |
| Sieberg *et al*[43] | 32 | 13.9 (10–17) | 25/7 (78.1%) | White 87.5%, black 9.375%, Asian 3.125% | Spinal fusion surgery | 27 (4–6 months) | 16% |
| Siemer *et al*[44] | 95 | NR (10–17)§ | 74/21 (78%)‡ | NR | Spinal fusion surgery | 76 (12mo) | 20% |
| Voepel-Lewis *et al*[45] | 95 | NR (10–17) | 72/23 (76%) | NR | Posterior spine fusion surgery | 76 (12 mo) | 20% |

*Reported as mean (range) or median (IQR), with one exception.
†Race/ethnicity were reported as originally reported in the study.
‡Number derived from percentage.
§Did not explicitly state range, but stated 'aged (range)' in Methods section (eg, as an inclusion criterion).
¶Study characteristics presented for the sample completing follow-up assessments (in contrast to baseline presented for the other studies).
**Race is only reported for All chronic postsurgical pain patients (n=109).

analysis, and reporting) and inconsistency. There were no concerns with indirectness, imprecision, or publication bias.

## DISCUSSION

The results from this systematic review and meta-analysis reveal that most included studies report at least one significant preoperative prognostic factor for pediatric CPSP. Individual studies found child pain intensity, pain-related anxiety (ie, pain catastrophizing and pain anxiety), general anxiety, mood, psychological flexibility, and surgical duration to be significant, as well as caregiver general anxiety and pain catastrophizing. However, at the meta-regression level, only pain intensity prior to surgery was found to be significant (OR=0.540 (95% CI .184 to 0.894)) which was based on a minority of included studies (n=4; 27%) that provided sufficient data for meta-analysis. This finding is similar to the adult literature of prognostic factors for CPSP, where presurgery pain intensity predicts CPSP.[24 25] Unlike the adult literature, commonly studied prognostic factors, such as pain-related anxiety (ie, pain catastrophizing and pain anxiety), general anxiety, and caregiver pain catastrophizing, were not significant in their respective meta-regression analyses. This could indicate, like the IFAM theorizes, that the relationship between variables in the development of pediatric CPSP is not linearly related, with the exception of pain intensity. It could also indicate that the studies included in the



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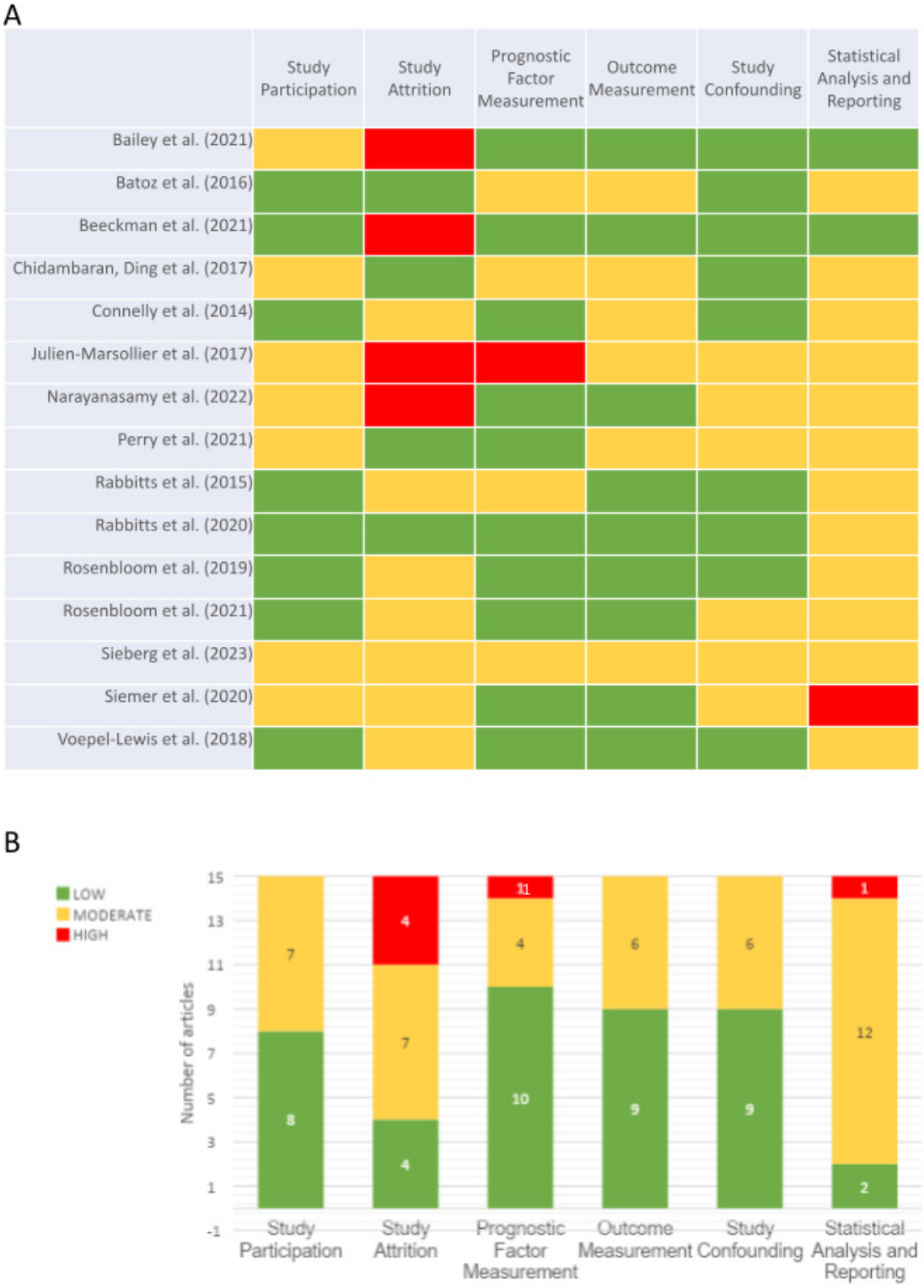


**Figure 2** Quality assessment of the 15 included articles using the QUality In Prognosis Studies (QUIPS) tool to reveal potential risk of bias (RoB) for factors of relevance to this study. (A) Overview of the RoB assessments (ratings of low, moderate, or high RoB) for each included article, covering the six QUIPS categories namely study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting. (B) Number of articles with low, moderate, and/or high RoB for each QUIPS category.

meta-analyses were underpowered, and there were mixed findings in terms of effect sizes and direction in the individual studies. Confidence in the current estimates, as assessed by GRADE, were reduced due to limitations in the included studies. For example, mostly all the studies did not have adequate statistics reporting or information on study attrition.

Of particular note, sex and gender were not included in any multivariate analyses for risk/protective factors for CPSP in included studies. This could be because they were not significant at the univariate level or for another reason (eg, underpowered for more variables in the model; unbalanced sex distribution due to surgery type, that is, spinal fusion predominantly performed in females).



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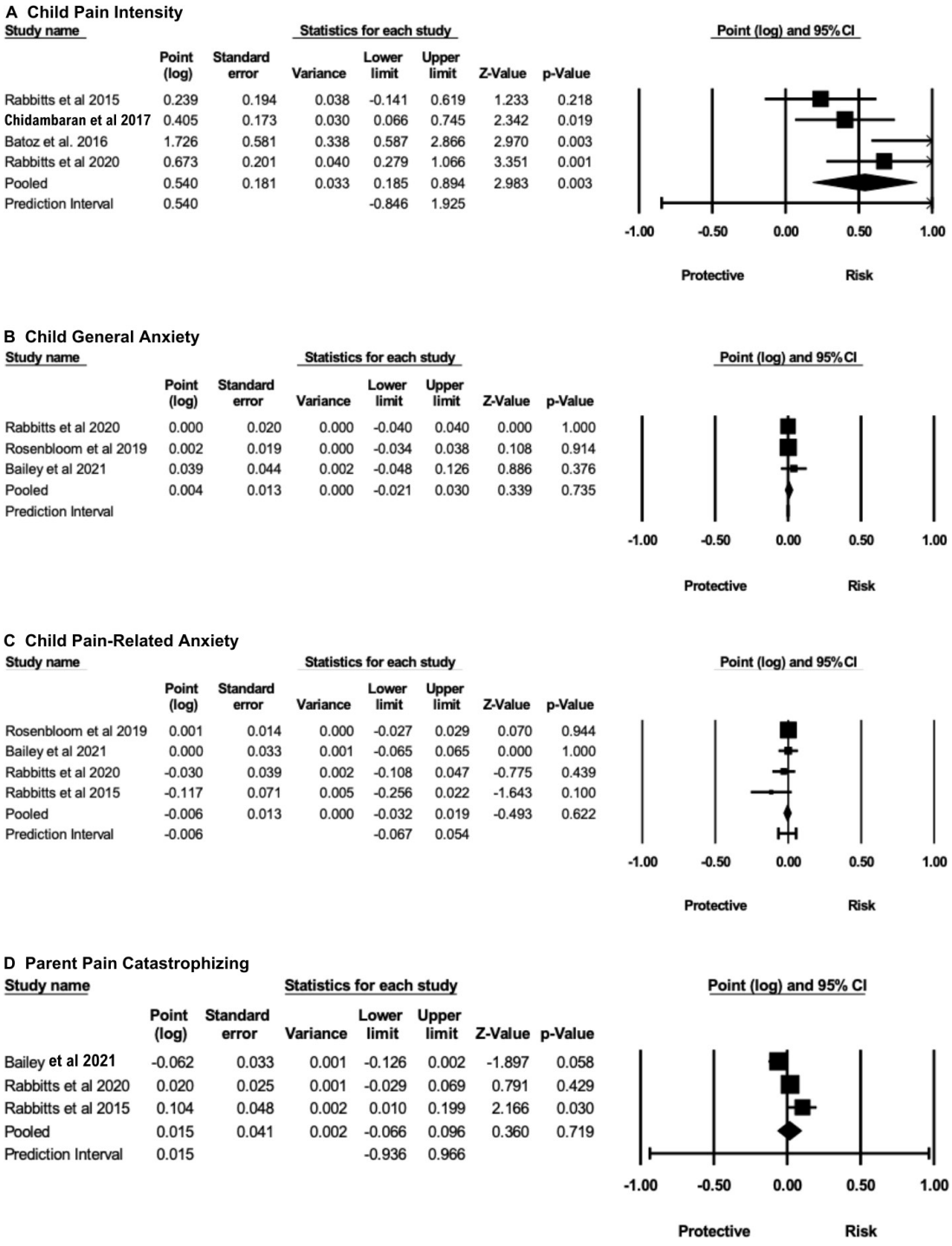


**Figure 3** Meta-analytic results from prognostic factors with three or more studies evaluating their effect.

Sex and gender have complex interactions with pain.[26] Differences in pain coping strategies are observed between girls and boys,[27] and girls are disproportionately affected by risks factors for chronic pain (eg, emotional distress), and gender biases exist in pain care.[28] However, there is limited research on sex and gender influences on CPSP. Currently, the rates of major surgery and the development of CPSP are similar for boys and girls.[1] Future studies should include sex and gender in their analyses, as they may be important moderators of CPSP outcomes. Studies examining whether sex differences exist in CPSP and that probe potential mechanisms may provide insights into why more females experience pediatric chronic pain.

Studies identified in this review focused on anxiety and catastrophizing, and other potentially important factors (depressive symptoms, sleep disturbance) have had limited attention. Focus primarily on anxiety as a risk factor for pediatric CPSP has stemmed from adult research showing these as most important; however, the IFAM, adapted for pediatrics, CPSP highlights that other factors that may be most important in children. Nevertheless, due to insufficient data, we were unable to include predictors in a meta-analysis, such as sleep disturbances and depressive symptoms. A recent umbrella review of adult prognostic factors for CPSP found that factors, such as mood, are significant predictors of adult



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**Table 2** Quality of evidence examined through the GRADE criteria for each estimate.

| Prognostic factor (studies (n)) | Limitations | Inconsistency | Indirectness | Imprecision | Publication bias | Pooled risk factor (95% CI) | Patients (n) | GRADE assessment |
|---|---|---|---|---|---|---|---|---|
| Child general anxiety (n=3) | Some limitations | Low heterogeneity ($I^2$=0%) | No serious indirectness | No serious imprecision | Undetected | OR=0.004 (95% CI −0.02, 0.03) | 604 | Moderate |
| Child pain-related anxiety (n=4) | Some limitations | High heterogeneity ($I^2$=2.85%) | No serious indirectness | No serious imprecision | Undetected | OR=−0.006 (95% CI −0.03, 0.02) | 664 | Moderate |
| Child pain intensity (n=4) | No serious limitations | Moderate significant heterogeneity ($I^2$=58.62%) | No serious indirectness | No serious imprecision | Undetected | OR=0.540 (95% CI 0.184, 0.894) | 614 | Moderate |
| Parent pain catastrophizing (n=3) | No serious limitations | Statistical Significance of high heterogeneity ($I^2$=77.28%) | No serious indirectness | Some imprecision | Undetected | OR=0.014 (95% CI −0.07, 0.01) | 399 | Moderate |

GRADE, Grading of Recommendations, Assessment, Development, and Evaluation.

CPSP.[29] In pediatrics, one study found that both disturbed sleep and depressed mood were significant at predicting acute and CPSP, whereas anxiety was not.[20] More research on variables outside of anxiety is critically needed to identify the most important targets of intervention for youth having surgery.

The results from this review highlight areas for clinical intervention and future research. Clinically, our findings highlight the importance of prioritizing pain management throughout the perioperative experience beginning in the preoperative period for all patients. It is critical to assess preoperative pain intensity, and at a minimum provide pain management education and develop a pain plan for patients with significant preoperative pain.[30] Unfortunately, this still reportedly occurs in a minority of instances.[31] Pain management during the acute postsurgical pain is critical. Although outside the scope of this review, acute postsurgical pain is a predictor for CPSP in adults,[29] and limited pediatric studies[20 21] indicate it is likely also a critical window for pediatric surgical care to optimize treatment and prevent transition from acute to CPSP.[32] Preventing the development of chronic pain, including CPSP, is a top priority of youth and their parents.[4 31 33]

Multidisciplinary pain services are being developed across the world with the aim of preventing the onset of pediatric chronic pain.[34] Services, such a pediatric Transitional Pain Services (pTPS), include coordination of multiple disciplines that act toward treating presurgical, acute and subacute pain so that the pain does not become chronic, and providing earlier transition to chronic pain services when needed.[34 35] These services target the biopsychosocial nature of pain, which are reflective of the prognostic factors identified in this review. Few children and adolescents are prescribed preoperative opioids for pain management[15]; however, it is important to consider safe and effective use of opioids for pain management in this population during the acute postoperative phase, as such following established guidelines is essential.[30 36] Currently, there is no validated way of identifying youth at high risk of CPSP for appropriate referral to such services. Thus, this review provides researchers with a summary of the current state of the literature in terms of tested prognostic factors that have been evaluated prior to surgery and prior to the onset of CPSP. Namely, it is clear that those assessing children for surgery (eg, nurses, surgeons, anesthesiologists) can assess for presurgical pain intensity as a risk factor for CPSP. This provides guidance about referral pathway pTPS as well as treatment options.[36] Clearly, further research comprehensively examining biopsychosocial factors in acute to chronic pain transition is critically needed to identify prognostic factors and mechanisms of pediatric CPSP. In the meantime, we continue to rely on broader pain research that indicate that child and parent psychosocial factors are integral in pain experience, to guide prevention and treatment efforts.

### Limitations

This review has a comprehensive search strategy, which allowed for an evaluation of numerous biopsychosocial prognostic factors for CPSP. Only prospective, longitudinal studies were included in this review allowing for presurgical (ie, risk/ protective factors that are present prior to the onset of CPSP) to be evaluated. Limitations include: the correlational nature of the results, limiting causal inferences; the low to moderate quality of some included studies, which increases RoB and reduces confidence in the current estimates; and, additionally, the low number of studies in some analyses, which limits the robustness of results. Further, the search yielded primarily studies within the adolescent age range and with a subset of surgeries (eg, spinal fusion) by a small number of authors, which limits the results to adolescents. Future studies should consider recruitment strategies to include younger children, more varied surgeries, and research conducted across the world.

## CONCLUSIONS

With moderate certainty, we found that presurgical pain intensity is a risk factor for pediatric CPSP, highlighting the importance of prioritizing pain management throughout the perioperative experience, starting before surgery. Psychological factors, such as child general and pain-related anxiety and caregiver pain catastrophizing, were not significant in predicting CPSP when measured presurgically. However, potentially important factors such as sex, sleep, and mood were not able to be included due to insufficient studies. Further research is needed to increase the quality and quantity of evidence, as well as understand the complex interplay between psychological variables in the development of pediatric CPSP.

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