Review Paper

Factors that Alleviate and Exacerbate Chronic Pain in Children and Adolescents: A Systematic Review

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ABSTRACT

Background: Pediatric chronic pain is a complex, multidimensional phenomenon with profound implications for children's and adolescents' biopsychosocial development. Despite its high prevalence and clinical significance, the underlying mechanisms remain insufficiently characterized. Accumulating evidence suggests that chronic pain in youth results from the dynamic interplay between biological vulnerabilities, psychological distress, and adverse social conditions. However, prior research has often isolated these domains rather than investigating their integrated effects.

Objectives: This systematic review aimed to synthesize current empirical findings regarding the biological, psychological, and social determinants of chronic pain in individuals aged 5–18 years. A particular focus was placed on identifying exacerbating and alleviating factors, such as maladaptive emotional responses or resilience mechanisms, to inform the development of holistic and developmentally attuned interventions.

Methods: We performed a systematic review adhering to preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2020 guidelines. Multiple databases (Google Scholar, PubMed, Scopus, Web of Science, EMBASE, and PsycINFO) were searched for studies from 2010 to 2024 involving children and adolescents (aged 5–18 years) with chronic pain. Eligible studies were evaluated using the STROBE checklist.

Results: Thirty-eight studies met the inclusion criteria. The findings indicated that among the biological factors, female gender, dysfunction in pain inhibitory systems, obesity and systemic inflammation, functional alterations in the mesolimbic dopaminergic pathway, neuroplasticity changes, and increased age and maturation of neural systems play a role in pediatric chronic pain. Among psychological factors, psychological distress, pain catastrophizing, difficulties in emotion regulation, low resilience, and receiving physical and psychological treatments were identified as contributing factors. Furthermore, among social factors, adverse family conditions, educational environment and peer relationships, and low socioeconomic status were found to influence chronic pain in children and adolescents.

Conclusions: A multifactorial approach is essential to understanding chronic pain in children and adolescents. Integrating biological vulnerabilities, social contexts, and individual psychological coping mechanisms, particularly pain acceptance and adaptive strategies, can inform holistic and personalized treatment planning.

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Introduction

Chronic pain is a prevalent and complex issue that, with its unclear etiology and poor response to treatment, presents significant challenges for clinicians and has substantial impacts on an individual's quality of life and social costs [1]. In children and adolescents, chronic pain refers to pain that persists for more than three months and, unlike acute pain, does not serve a protective function but instead becomes a persistent condition that affects various aspects of life, including education, social relationships, and mental health [2].

The prevalence of chronic pain in both adults and children is alarmingly high [3, 4], imposing significant economic burdens on healthcare systems [5]. However, a comprehensive and accurate classification for chronic pain is still underdeveloped [6]. Although previous systematic reviews have explored various aspects of chronic pain, gaps remain in understanding the intricate interplay between biological, psychological, and social factors. Recent findings highlight newly identified contributors to pain persistence, necessitating an updated review to integrate these insights [7].

Chronic pain among youth involves not only medical concerns but also carries considerable consequences on their societal and financial circumstances [8]. Even with continued interventions, a full recovery remains out of reach for a considerable number of sufferers [9].

When pain transitions into a chronic state, it no longer serves as a protective alert and causes both bodily and emotional complications [10]. Adolescents, in particular, encounter distinct challenges due to developmental transitions, heightened academic demands, and evolving social interactions, all of which can contribute to the persistence and severity of chronic pain [11]. Research indicates that this condition can reduce academic performance, increase drug dependence, and result in school absenteeism and decreased physical activity [4, 12]. Additionally, studies show that children with chronic pain are at a significantly higher risk of developing depression, anxiety, and cognitive impairments compared to their peers [13, 14].

Given the widespread changes in children's and adolescents' lifestyles due to technological advancements and the pervasive presence of social networks, chronic pain is expected to become one of the major health challenges of the future [15]. Many factors contribute to chronic pain in children and adolescents. For instance, psychological distress, such as anxiety, can amplify the perception of pain, whereas strong familial support can serve as an exacerbating factor, helping children and adolescents cope more effectively [16, 17]. In order to comprehensively grasp this issue, adopting a model that incorporates biological, psychological, and social dynamics is crucial.

Among these, psychological factors play a crucial role in the experience of pain and the response to treatment. Although physiotherapy efforts have grown, the psychological domain of this problem in the pediatric population has remained relatively neglected [18].

The purpose of this systematic review was to address this deficiency by examining biological, psychological, and social influences to form a more integrated view of chronic pain in younger individuals [11]. Many past studies have mainly concentrated on distinct therapeutic strategies or singular aspects of chronic pain rather than considering a multidimensional perspective. Nonetheless, it is vital to develop a complete framework that includes the interactive roles of biological, psychological, and social dimensions for effective pain care [17].

Newer reviews emphasize the importance of revising population-based data concerning youth chronic pain. The prevalence of chronic pain varies significantly across different demographic groups, and emerging research suggests that socioeconomic and cultural influences play a pivotal role in shaping pain experiences. This review will incorporate the latest findings to enhance the accuracy and depth of understanding regarding chronic pain in children and adolescents [7].

Furthermore, earlier systematic reviews often limited their scope to particular treatments or isolated elements of chronic pain, such as pharmacological or physical interventions. Yet, a holistic model addressing the mutual impact of biological, psychological, and social domains remains essential for adequately managing chronic pain in children and adolescents [17].

This systematic review was designed to overcome these limitations by combining findings related to biological, psychological, and social elements, offering a unified understanding of pain in children and adolescents [11]. Previous reviews have focused on specific treatments or types of pain, but there have been fewer comprehensive reviews that simultaneously examine biological, psychological, and social exacerbating and moderating factors in children with chronic pain. This study aimed to address this gap in the knowledge base.

This review aimed to synthesize these data points to identify the main biological, psychological, and social variables that either worsen or ease chronic pain. Appreciating these multidimensional factors is key to enhancing support measures and optimizing therapeutic strategies for children and adolescent patients.

Methods

This systematic review aimed at identifying and synthesizing studies that explored the alleviating and exacerbating factors of chronic pain in children and adolescents (5 to 18 years).

A comprehensive search was conducted using specialized keywords across multiple English-language databases, including PubMed, Scopus, Web of Science, EMBASE, and PsycINFO, and the Google Scholar search engine, covering publications from January 2010 to November 2024. The final search was conducted in November 2024 to ensure the inclusion of the most recent and relevant studies.

Study authors were not approached for further data collection or identification of unpublished work. The search strategy was developed using Boolean operators (AND/OR) to combine relevant keywords, including ("pediatric chronic pain" OR "adolescent chronic pain" OR "persistent pain") AND ("psychological factors" OR "family functioning" OR "parental distress") AND ("pain management" OR "biopsychosocial factors") AND ("systematic review" OR "Risk and protective factors"). In PubMed, searches were conducted without restrictions on study type but were limited to English-language publications between January 2010 and November 2024. The inclusion criteria required studies to focus on children and adolescents aged 5 to 18 years diagnosed with chronic pain lasting more than three months, specifically examining psychological, social, or family-related influences. Eligible studies employed empirical research methods using cross-sectional or longitudinal designs and were published in reputable, peer-reviewed scientific journals in English.

The exclusion criteria eliminated theoretical papers, case studies, and qualitative research, along with studies addressing acute pain or specific medical conditions, such as cancer. Non-English publications were excluded to maintain consistency in data analysis. These criteria were designed to enhance sample homogeneity, ensure a clear focus on psychosocial dimensions rather than medical conditions, and improve the generalizability of findings. While the PICOS framework was not explicitly implemented, its fundamental components, population, exposure, outcome, and study design were implicitly considered.

The researchers screened titles and abstracts for relevance. Disagreements were resolved through discussion or consultation with a third researcher. The STROBE checklist was applied to evaluate study quality; each article received a score from 0 to 18, with those under 9 designated as low-quality. Following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart (Figure 1), duplicate articles were removed before two independent reviewers examined the full texts of potentially eligible studies based on predefined inclusion and exclusion criteria. As this review did not involve a meta-analysis, a narrative synthesis approach was applied.

Data extraction was carried out by one researcher using a pre-designed data extraction form, followed by verification by a second researcher to ensure accuracy. Extracted information included study characteristics (authors, year, country, and design), participant details (sample size, age, gender, and type of chronic pain), assessed biological, psychological, social, and family-related variables associated with pain, measurement tools used, and key findings regarding the relationship between these variables and chronic pain. The review assumed consistency in the definition of chronic pain across included articles, as pain lasting over three months, and no follow-up contact was made with study authors to verify or add to the data.

Risk of bias was assessed at the study level using the standardized Joanna Briggs Institute (JBI) checklist for quantitative studies, which evaluates factors, such as study design, clarity of inclusion/exclusion criteria, adequacy of data collection methods, and control of confounding variables. Two researchers independently assessed study quality, resolving disagreements through discussion. The findings from the bias assessment were considered in the narrative synthesis, though no statistical weighting was applied, as this review did not include a meta-analysis. Given that most studies were observational, STROBE was used to ensure the adequacy of scientific reporting, methodological legitimacy, and reliability of findings.

Results

In this review, 38 articles on chronic pain in children and adolescents were classified according to the biopsychosocial model. The biological aspect (9 articles), the psychological aspect (13 articles), and the social aspect (9 articles) were reviewed, and 9 articles were a combination of factors. Overall, the studies emphasized biological, psychological and social factors, and the results highlight the importance of a multidimensional approach to the treatment of chronic pain in children. Overall, the strength of evidence was moderate to high for psychological and social domains, while for biological factors, the evidence strength was moderate.

The findings from the reviewed articles on the alleviating and exacerbating factors in chronic pain among children and adolescents are presented in Table 1.

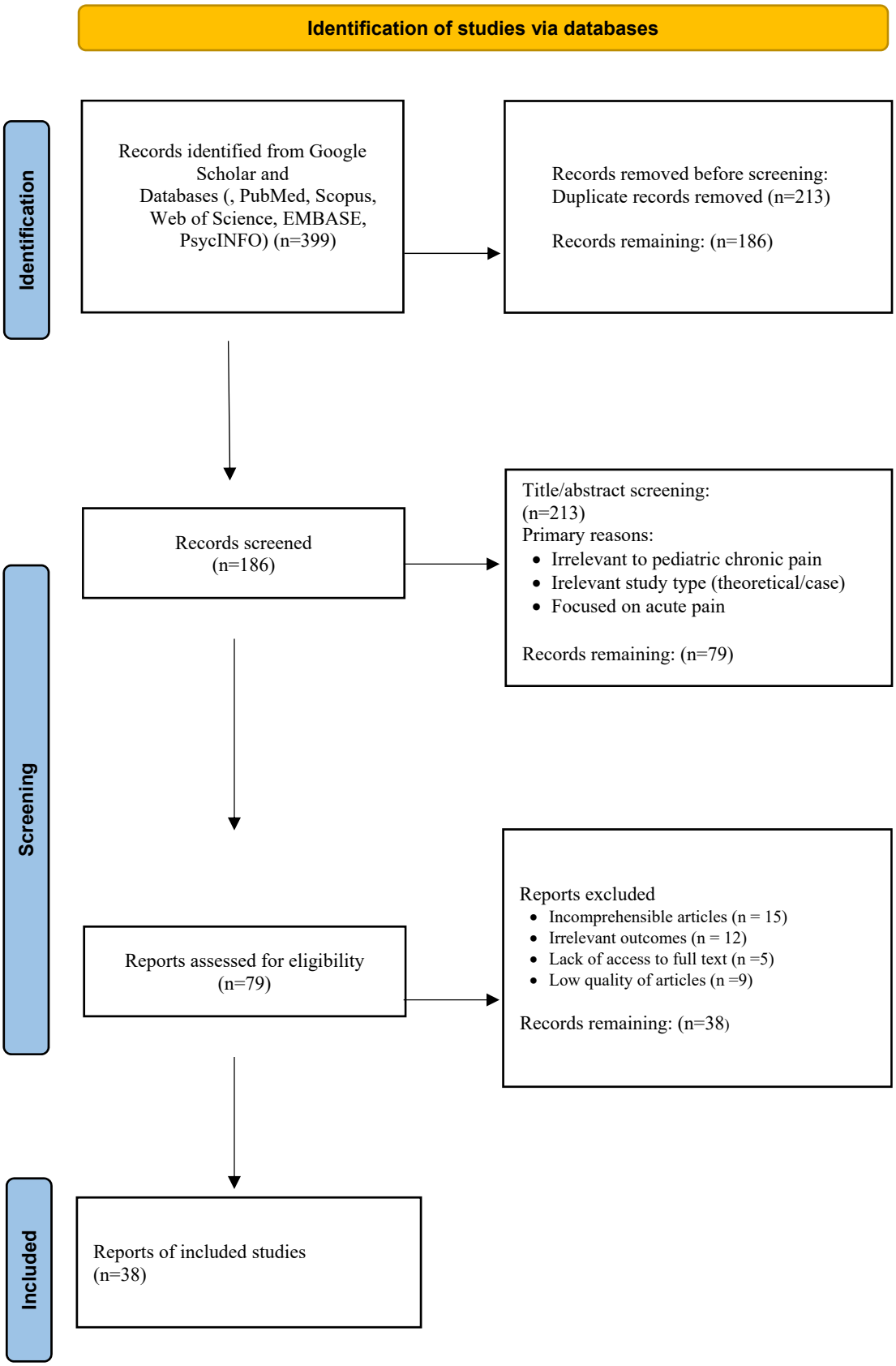

Figure 1. PRISMA diagram

Table 1. Summary of studies on chronic pain in children and adolescents

Row	Author(s), Year	Title	Age Range	Methodology	Instrument	PICOS/Additional Info	Risk of Bias	Main Findings
1	Chen et al. 2024 [19]	Social determinants of health and youth chronic pain. Complementary therapies in clinical practice	5–18 years	National survey	Caregiver-reported	P: 5–18-year-old US children I: Social/economic exposures C: None O: Chronic pain prevalence S: Cross-sectional	Moderate	Parental unemployment, low school engagement, poor school safety, limited access to quality healthcare, frequent hospital visits, alternative care use, bullying victimization, adverse childhood experiences, and poor amenity conditions were linked to a higher likelihood of chronic pain.
2	Pavlova et al. 2024 [20]	Early childhood risk factors for later onset of pediatric chronic pain: A multimethod longitudinal study	8–11 years	Longitudinal	Standardized questionnaires	P: 8–11-year-old children I: Early pain, maternal pain C: Boys vs girls O: Pain frequency & interference S: Prospective cohort	Low	Gastrointestinal problems, emergency department visits, recurrent pain and headaches, and female gender were linked to increased chronic pain risk; maternal chronic pain at age 8 predicted more pain frequency and interference at age 11, while boys reported lower interference.
3	Vandeleur et al. 2024 [21]	Association of neighborhood characteristics and chronic pain in children and adolescents in the United States	6–17 years	Cross-sectional	Parental questionnaires	P: 6–17-year-old US children I: Neighborhood adversity C: Adjusted sociodemographics O: Pain prevalence S: Observational	Moderate	Children living in unsupportive, unsafe neighborhoods—with unsafe schools, fewer amenities, and more adverse elements—had significantly higher rates of chronic pain (P<0.0001); after adjustment, an adjusted prevalence ratio of 1.7 (95% CI, 1.5%, 1.9%) was observed.
4	Wolock et al. 2025 [22]	Systematic review of social functioning and peer relationships in adolescents with chronic pain	10-18 years	Systematic Review	Meta-analysis	P: 10-18 year-old adolescents w/ chronic pain I: Peer difficulties (loneliness, social anxiety, withdrawal, victimization) C: Healthy peers (where available) O: Social connectedness, peer victimization, loneliness, social withdrawal S: Systematic review	Moderate	Adolescents with chronic pain frequently showed loneliness, social anxiety, withdrawal, and peer victimization, underscoring reduced social connectedness and the need for longitudinal research.
5	Ross et al. 2018 [23]	Social risk and resilience factors in adolescent chronic pain: Examining the role of parents and peers	13–18 years	Correlational	Health outcomes registry	P: Adolescents 13–18 years old adolescents I: Parenting style, peer support C: None O: Adaptive vs maladaptive coping S: Cross-sectional	Low	Effective parenting and high-quality peer relationships play a crucial role in supporting adaptive responses in adolescents with chronic pain.
6	Palermo et al. 2024 [24]	Family and parent influences on pediatric chronic pain: A developmental perspective	5–18 years	Systematic Review	Investigator-developed	P: 5–18-year-old children with pain I: Family functioning C: Not specified O: Developmental pain modulation S: Narrative review	Moderate	Developmental processes may shape children's pain experiences; parental emotions, behaviors (e.g. overprotectiveness), and heightened distress are significant influences.

Row	Author(s), Year	Title	Age Range	Methodology	Instrument	PICOS/Additional Info	Risk of Bias	Main Findings
7	Lewandowski et al. 2010 [25]	Systematic review of family functioning in families of children and adolescents with chronic pain	6–18 years	Meta-analysis	Questionnaires	P: Families of 6–18-year-old children I: Dysfunctional family units C: NA O: Pain disability link S: Meta-review	Moderate	Poorer family functioning was associated with greater child disability in chronic pain, although its direct association with pain was less consistent.
8	Donnelly et al. 2020 [26]	Parent cognitive, behavioural, and affective factors and their relation to child pain and functioning in pediatric chronic pain: A systematic review and meta-analysis	5–18 years	Meta-analysis	PRISMA	P: 5–18 y I: Parental catastrophizing, support C: None O: School & pain functioning S: Meta-review	Moderate	Higher parental supportive behavior was linked to poorer academic functioning, with modest associations between parental pain catastrophizing, increased child disability, and elevated parental depression/anxiety.
9	Poppert Cordts et al. 2019 [27]	The (parental) whole is greater than the sum of its parts: A multifactorial model of parent factors in pediatric chronic pain	5–18 years	Not specified	Not specified	P: Children I: Parental chronic pain C: Not described O: Adjustment impairment S: Theoretical model	High	The conceptual model was largely supported, except for parental responses to child pain; findings advocate for including parental chronic pain status and their physical/psychological functioning in assessments.
10	Haraldstad et al. 2017 [28]	Health-related quality of life and pain in children and adolescents: A school survey	8–18 years	Analytical study	KID-SCREEN-52, Lubeck	P: 8–18 y (n=1099) I: Physical activity, HRQoL C: Gender O: Pain coping, participation S: Cross-sectional	Low	60% of participants reported chronic pain (with 76% of girls aged 16–18 reporting pain); higher quality of life and physical activity were linked to better pain coping and treatment engagement.
11	Groenewald et al. 2020 [29]	Adverse childhood experiences and chronic pain among children and adolescents in the United States	6–17 years	Multivariate Logistic	Lübeck questionnaire	P: 6–17 y I: Adverse childhood experiences C: None O: Pain intensity S: Epidemiological	Moderate	Approximately 8.49% of children suffered from chronic pain; low family income, poorer mental health, and female gender were associated with greater pain intensity and prevalence.
12	Calvo-Muñoz et al. 2013 [30]	Physical therapy treatments for low back pain in children and adolescents: A meta-analysis	7–14 years	Meta-analysis	Self-report & clinical	P: 7–14 y I: psychological skills and education C: Gender O: Pain relief S: Meta-analysis	Low	Physiotherapy treatments that incorporated psychological skills and education were more effective; girls were generally more receptive to treatment than boys.
13	Forgeron et al. 2010 [31]	Social functioning and peer relationships in children and adolescents with chronic pain: A systematic review	5–18 years	Systematic review	Self-report	P: 5–18 y I: Peer support C: Healthy peers O: Social functioning S: Review	Low	Poor social relationships and having fewer friends were linked to higher levels of chronic pain and depression, exacerbating the condition.

Row	Author(s), Year	Title	Age Range	Methodology	Instrument	PICOS/Additional Info	Risk of Bias	Main Findings
14	Roth-Isigkeit et al. 2005 [32]	Risk factors for back pain in children and adolescents	6–14 years	Systematic review	Clinical reports	P: 6–14 y I: Lifestyle, posture, screen time C: Not defined O: Pain onset S: Review	Moderate	Multiple factors—including physical activity, posture, lifestyle, screen time, age, gender, depression, anxiety, and overall mental health—were identified as contributors to the onset and exacerbation of chronic pain.
15	Simons, 2016 [33]	Fear of pain in children and adolescents with neuropathic pain and complex regional pain syndrome	7–16 years	Correlational	Beck + Lübeck	P: 7–16 y I: Pain-related fear C: None O: Anxiety, depression S: Observational	Moderate	Higher levels of pain-related fear were associated with increased depression and anxiety and with a reduced likelihood of seeking medical or psychological help.
16	Stahlschmidt et al. 2020 [34]	Posttraumatic stress disorder in children and adolescents with chronic pain	8–17 years	Correlational	Checklist	P: 8–17 y I: PTSD symptoms C: Trauma exposure O: Pain persistence S: Observational	Moderate	Between 2% and 18% of participants met criteria for PTSD; those with more traumatic experiences reported a variety of chronic pain types and suboptimal treatment outcomes.
17	Miller et al. 2016 [35]	Perceived injustice is associated with pain and functional outcomes in children and adolescents with chronic pain: A preliminary examination	10–15 years	Correlational	IEQ	P: 10–15 y I: Injustice, anxiety C: SES O: Pain severity S: Observational	High	Increased pain catastrophizing, emotional non-acceptance, anxiety, pain-related stress, and lower socioeconomic status were associated with greater chronic pain severity.
18	Wager et al. 2020 [36]	Prevalence and associated psychosocial and health factors of chronic pain in adolescents: Differences by sex and age	10–18 years	Regression Models	Standard survey	P: 10–18 y I: Anxiety, support C: Sex O: Coping, severity S: Large survey	Moderate	Chronic pain was reported by 30% of participants (with a higher prevalence among girls); depression, anxiety, school absenteeism, and poorer quality of life and sleep were common, while social support and physical activity positively influenced outcomes.
19	Palermo et al. 2020 [37]	A digital health psychological intervention (Web-MAP mobile) for children and adolescents with chronic pain: Results of a hybrid effectiveness-implementation stepped-wedge cluster randomized trial	7–16 years	Quasi-experimental	Digital tools	P: 7–16 y I: Online therapy C: Gender O: Pain & distress S: Quasi-experimental	Low	The treatment group reported lower pain intensity and reduced psychological distress; adolescent girls showed greater treatment acceptance and maintained positive outcomes at follow-up.
20	Simons et al. 2012 [38]	Anxiety and functional disability in a large sample of children and adolescents with chronic pain	6–12 years	Retrospective	Files review	P: 6–12 y I: Anxiety subtypes C: None O: Pain levels S: Correlational	Moderate	Clinical anxiety was found in 11%, social anxiety in 14%, and somatic anxiety in 27% of participants; difficulties in regulating anxiety were associated with higher levels of chronic pain.

Row	Author(s), Year	Title	Age Range	Methodology	Instrument	PICOS/Additional Info	Risk of Bias	Main Findings
21	Mei et al. 2019 [39]	The relationship between the psychological stress of adolescents in school and the prevalence of chronic low back pain: A cross-sectional study in China	18 years	Cross-sectional	SCL-90	P: 18-year-old students I: Stress, academics C: Gender O: Chronic back pain S: Survey	Moderate	Chronic back pain was highly prevalent; adolescents with higher levels of depression, anxiety, stress, and aggression experienced more severe chronic back pain.
22	Pascali et al. 2019 [40]	Cognitive, emotional, and behavioral profile in children and adolescents with chronic pain associated with rheumatic diseases: A case-control study	6–18 years	Case-control	VAS, CBCL	P: 6–18 y I: Depression, attention issues C: Healthy group O: Pain outcomes S: Observational	Moderate	Compared to healthy controls, children and adolescents with chronic pain exhibited higher levels of depression and more problems with attention, memory, concentration, and behavior; they also showed lower physical activity, poorer social connections, and reduced vitality.
23	Fisher et al. 2018 [41]	Psychological therapies for the management of chronic and recurrent pain in children and adolescents	7–16 years	Meta-analysis	RCTs	P: 7–16 y I: CBT, ACT C: Waitlist O: Long-term pain relief S: Meta-analysis	Low	A wide range of psychological interventions for abdominal pain, back pain, musculoskeletal pain, headaches, and multiple pain conditions demonstrated long-term efficacy; cognitive-behavioral therapy, chronic pain management, and acceptance and commitment therapy were among the most effective.
24	Knook et al. 2011 [42]	Psychiatric disorders in children and adolescents presenting with unexplained chronic pain: What is the prevalence and clinical relevancy?	8–17 years	Observational	DISC-P	P: 8–17 y I: Psychopathology C: None O: Pain impact S: Cross-sectional	Moderate	21% of participants were found to have psychiatric disorders, with anxiety (18%) being most common; greater psychiatric severity was associated with increased chronic pain and poorer treatment response.
25	Noel et al. 2016 [43]	Chronic pain in adolescence and internalizing mental health disorders: A nationally representative study	7–16 years	Survey	Beck inventories	P: 7–16 y I: Anxiety, depression C: Gender O: Emotional distress S: Survey	Moderate	Adolescents with chronic pain showed higher rates of emotional disturbances, depression, and anxiety; additionally, girls experienced chronic pain for a longer duration compared to boys.
26	Tegethoff et al. 2015 [44]	Comorbidity of mental disorders and chronic pain: Chronology of onset in adolescents of a national representative cohort	13–18 years	Observational	WHO-DI	P: 13–18 y I: Chronic pain types C: None O: Psychiatric comorbidity S: Observational	Moderate	Approximately 9.25% of participants reported long-term chronic pain, with back pain, abdominal pain, and headaches being most common; all chronic pain types were linked to psychological disorders, a trend more pronounced in girls.
27	Cousins et al. 2015 [45]	Topical review: Resilience resources and mechanisms in pediatric chronic pain.	6–12 years	Systematic Review	Ecological model	P: 6–12 y I: Resilience traits C: None O: Coping & outcomes S: Review	Low	Unique individual and socio-environmental resilience resources and mechanisms in chronic pain were identified, which promote adaptive coping strategies.

Row	Author(s), Year	Title	Age Range	Methodology	Instrument	PICOS/Additional Info	Risk of Bias	Main Findings
28	Young et al. [46]	Pediatric chronic pain, resilience, and psychiatric comorbidity in Canada: A retrospective, comparative analysis	7–17 years	Retrospective analysis	Epidemiologic data	P: 7–17 y I: Resilience, sex, SES C: None O: Psychiatric symptoms S: Comparative	Low	Greater positive social behavior and resilience were associated with fewer psychiatric symptoms; female gender, family history, and lower socioeconomic status were linked to chronic pain.
29	Koechlin et al. [47]	The role of emotion regulation in chronic pain: A systematic literature review	7–17 years	Meta-analysis	Review of emotion regulation (ER)	P: 7–17 y I: ER strategies C: None O: Pain onset/persistence S: Review	Low	Maladaptive response-focused ER was linked to chronic pain, while antecedent-focused strategies were less directly associated; maladaptive response-focused regulation may be a key risk factor in the onset and persistence of chronic pain.
30	Caes et al. [48]	The cyclical relation between chronic pain, executive functioning, emotional regulation, and self-management	7–17 years	Observational	COPES model	P: 7–17 y I: Executive function C: None O: Disability S: Observational	Moderate	Relative immaturity of executive functions during adolescence negatively affected self-management abilities, increasing pain-related disability and perpetuating chronic pain.
31	Griggs et al. [49]	The role of hope for adolescents with a chronic illness: An integrative review	7–17 years	Meta-analysis	PRISMA	P: 7–17 y I: Hope levels C: None O: Symptom control S: Meta-analysis	Low	Higher levels of hope enabled adolescents to identify multiple pathways toward goal attainment, view setbacks as challenges, and better manage psychological symptoms.
32	Champion et al. [50]	Familial and genetic influences on the common pediatric primary pain disorders: A twin family study	6–18 years	Correlational	Twin study	P: 6–18 y I: Family/genetics C: Twins O: Pain disorders S: Genetic study	Moderate	Shared genetic and familial environmental factors play a major role in the occurrence of primary pain disorders (e.g. migraine, functional abdominal pain), with high concordance in monozygotic twins reinforcing the genetic contribution.
33	Hainsworth et al. 2021 [51]	Circulating inflammatory biomarkers in adolescents: Evidence of interactions between chronic pain and obesity.	13–17 years	Cross-sectional	IL-6, CRP	P: 13–17 y I: Obesity, inflammation C: None O: Pain intensity S: Biological	Moderate	Adolescents with both obesity and chronic pain showed higher levels of systemic inflammation, suggesting a synergistic effect in eliciting an elevated inflammatory response.
34	Vinall et al. 2016 [52]	Mental health comorbidities in pediatric chronic pain: A narrative review of epidemiology, models, neurobiological mechanisms, and treatment	5–18 years	Narrative review	Review articles	P: 5–18 y I: Anxiety, depression C: None O: Psychological burden S: Narrative review	Moderate	There is significant comorbidity between chronic pain and psychological disorders such as anxiety and depression; biopsychosocial models have been used to explain these interactions.
35	Serafini et al. 2020 [53]	The mesolimbic dopamine system in chronic pain and associated affective comorbidities.	15–18 years	Neurobiological review	Review	P: 15–18 y I: Mesolimbic function C: None O: Motivation, comorbidities S: Neurobiological	Moderate	Functional alterations in the mesolimbic dopamine pathway may result in reduced motivation and increased affective disorders among individuals with chronic pain.

Row	Author(s), Year	Title	Age Range	Meth-odology	Instrument	PICOS/Additional Info	Risk of Bias	Main Findings
36	Liossi et al. 2024 [54]	A system-atic review and meta-analysis of conditioned pain modulation in children and young people with chronic pain	6–18 years	Meta-analysis	CPM tests	P: 6–18 y I: CPM function C: Healthy youth O: Inhibition im-pairment S: Meta-analysis	Low	Children with chronic pain exhibited impaired pain inhibitory system function, which may contribute to pain persistence.
37	Lepping et al. 2024 [55]	Pediatric neural changes to physical and emotional pain after intensive interdisciplinary pain treatment: A pilot study	10–17 years	Pilot Study	fMRI, scales	P: 10–17 y I: Interdisciplinary treatment C: Pre/post O: Neural activity S: Pilot	Moder-ate	Following intensive interdisciplinary treatment, significant changes in brain activity related to physical and emotional pain were observed—specifically, decreased amygdala activity and increased prefrontal cortex activity indicated im-proved emotion regulation and pain processing.

Abbreviations: P: Population; I: Intervention; C: Comparison; O: Outcomes; S: Study.

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Biological factors

A review of studies shows that biological factors play an important role in chronic pain in children and adolescents. In this regard, several studies have shown that girls are at a higher risk of developing chronic pain. Specifically, research shows that 76% of girls aged 16–18 experience chronic pain [20, 28, 29, 32, 37].

Additionally, dysfunction in endogenous pain inhibitory systems [54], obesity, and systemic inflammation [51] have been identified as contributing factors. Findings also suggest that functional alterations in the mesolimbic dopaminergic pathway [53] play a role in exacerbating chronic pain. Among biological factors, neuroplasticity changes [55], aging, and neural system maturation [48] have been recognized as influencing self-regulation of pain.

Psychological factors

Findings from this systematic review indicate that, based on the biopsychosocial model, psychological factors are recognized as both alleviating and exacerbating chronic pain [33].

Among psychological factors, psychological distress, including depression, anxiety, and stress [32-37, 39, 41, 50], and pain catastrophizing [26, 33, 35] play a significant role in the onset and persistence of chronic pain. Difficulty with emotion regulation has been highlighted as a critical factor in sustaining chronic pain over time. Psychological factors can act as both alleviating and exacerbating elements depending on how they are regulated or expressed. Other cognitive factors, such as excessive attention to pain [40] and cognitive biases, have been identified as exacerbating factors that influence pain perception.

Additionally, findings suggest that among psychological modulators of chronic pain, resilience, including traits, such as hope [43-45, 23, 49], and access to physical treatments like physiotherapy [30], as well as psychological therapies, such as acceptance and commitment therapy (ACT), cognitive behavioral therapy (CBT), and pain management programs [37, 41], can significantly support children and adolescents with chronic pain. These approaches enable them to maintain meaningful participation in daily activities despite pain.

Social factors

Findings from the reviewed studies indicate that various social factors contribute to either the exacerbation or moderation of chronic pain in children and adolescents. Among the most significant exacerbating social factors, family-related factors, such as poor family functioning and inappropriate parenting styles (e.g. excessive parental overprotection) [23-26], as well as parental psychological distress and a history of chronic pain [24, 26, 27, 46], have been identified.

School-related contributors, like reduced attendance [19], unsafe environments [19, 21], repeated absences [37], and weak peer relationships [23, 31, 46], have been consistently linked to increased rates of chronic

pain. Additionally, from a socioeconomic perspective, documented studies have shown that factors, such as parental unemployment [19], low household income [29], and residence in disadvantaged neighborhoods [21] are correlated with increased prevalence and severity of chronic pain.

Discussion

This study was conducted with the aim of examining exacerbating and moderating factors influencing chronic pain in children and adolescents, with a particular emphasis on the biopsychosocial framework. According to this model, psychological factors play a crucial role in modulating and intensifying chronic pain in pediatric populations. In this context, findings highlight the critical role of psychological distress, including depression, anxiety, and stress, in both the initiation and persistence of chronic pain conditions. These affective disorders are linked to increased pain intensity, reduced coping capacity, and lower levels of physical activity, ultimately leading to greater disability, social withdrawal, and functional impairment. These findings are consistent with growing evidence emphasizing that psychological distress and pain symptoms mutually reinforce one another in pediatric populations [32-37, 39, 40, 52].

Among cognitive-affective mechanisms, pain catastrophizing has emerged as a key exacerbating factor. Consistent with previous studies [26, 33, 35], higher levels of catastrophizing were found to be associated with greater pain intensity, increased disability, heightened fear of movement, and diminished quality of life. Catastrophizing perpetuates a maladaptive cycle, wherein negative expectations regarding pain amplify both the sensory and emotional components of pain perception and reinforce avoidance behaviors and social withdrawal [35]. One study noted a weaker link between parental catastrophizing and disability in children, possibly reflecting the influence of factors like parenting style [26].

Emotion regulation difficulties were also identified as critical factors contributing to the persistence of chronic pain. Maladaptive strategies, such as rumination, experiential avoidance, and emotional suppression, were associated with greater disability and poorer psychological outcomes [35, 47]. Conversely, adaptive emotion regulation strategies, including cognitive reappraisal and emotional acceptance, showed a positive correlation with improved functionality and resilience. These results support theoretical models that position emotion regulation at the core of chronic pain maintenance during youth [47].

Among psychological factors, resilience was identified as a significant protective factor, enabling children and adolescents to maintain meaningful engagement in daily activities despite persistent pain. Higher resilience levels were linked to lower anxiety, depression, and stress, as well as more active coping strategies [45, 23, 49].

Optimism, a central component of resilience, may help buffer the negative effects of chronic pain by supporting adaptive emotion regulation and encouraging future-oriented positivity [41].

However, not all studies reported uniform protective effects. Ross et al. found that resilience may only exert its protective benefits in the presence of supportive peer relationships [23], emphasizing the importance of social factors, such as school and peer environments, in shaping resilience outcomes.

Findings further underscore that integrating psychosocial interventions alongside physical treatments may substantially improve patient outcomes. Physical therapies, including physiotherapy [30], and psychological interventions, such as ACT, CBT, and comprehensive pain management programs, have demonstrated potential in fostering acceptance, psychological flexibility, and adaptation [37, 41]. The primary goal of these treatments is to break the negative cognitive-emotional loop and enhance function, highlighting the value of a multimodal strategy in treating pediatric chronic pain.

Individual differences, including age and gender, significantly influence vulnerability to chronic pain. Compared to boys, girls tend to exhibit lower resilience, heightened anxiety, and increased pain severity [56]. Such insights reinforce the importance of customizing psychological support to enhance coping capacity among children and adolescents with chronic pain. Interventions focusing on cognitive training, emotion regulation strategies, and resilience enhancement should be integral components of pain management programs for pediatric populations.

This systematic review also examined the role of social determinants in the amplification and mitigation of chronic pain in children and adolescents. Findings suggest that the social environment exerts a profound influence on the individual's experience of chronic pain, consistent with the biopsychosocial framework. This model conceptualizes chronic pain as not only biological but also socially shaped, involving variables, like family dynamics, school pressures, friendships, and economic

context. The family unit, as a primary social structure, plays a pivotal role in both the development and management of chronic pain in children. This perspective is supported by several studies [23-27], indicating that overprotective or neglectful parenting is tied to more severe pain and poorer adaptability in children [23–26]. These parenting behaviors may reinforce helplessness and dependency, thereby obstructing the development of effective coping strategies. Additionally, parental psychological distress or a history of chronic pain may indirectly exacerbate pain intensity in children by instilling negative pain-related expectations and fostering maladaptive coping responses [23, 24, 26, 27].

The educational environment also constitutes a critical social domain. School disengagement, poor attendance, and unsafe academic settings have all been associated with increased rates of pediatric chronic pain [19, 21, 37]. Likewise, problematic peer dynamics can act as stress triggers, intensifying both pain symptoms and emotional distress in young individuals [23, 31, 57].

Socioeconomic status also exerts a significant influence on chronic pain experiences. Evidence indicates that children living in underprivileged households marked by parental joblessness or low income are more likely to suffer from frequent and intense chronic pain episodes [19, 29, 21]. Mechanisms such as persistent stress, limited access to medical care, and weaker coping skills may explain this socioeconomic link to chronic pain [58, 59]. While socioeconomic status may not directly dictate pain severity, it can shape outcomes by affecting healthcare access and treatment equity [60].

Finally, findings highlight the biological underpinnings of chronic pain, including gender disparities, dysfunctions in endogenous pain inhibition systems, neuroplasticity modifications, neural maturation, obesity-related systemic inflammation, and genetic/epigenetic influences.

One of the most notable biological observations is the elevated risk of chronic pain in girls aged 16–18, with prevalence reaching 76% according to cited studies. Possible explanations for this gender difference include hormonal variability, neural distinctions, and multifactorial biopsychosocial influences [20, 28]. Overall, these insights underscore the need for developmentally tailored biopsychosocial treatment approaches to effectively address chronic pain in children and adolescents.

Conclusion

Chronic pain in children and adolescents is a complex, multifaceted phenomenon shaped by the intricate interplay of biological, psychological, and social determinants. Genetic predispositions, female sex, dysfunction in endogenous pain-inhibitory systems, obesity-related systemic inflammation, alterations in the mesolimbic dopaminergic circuitry, neuroplasticity changes, as well as advancing age and neural maturation may heighten pain sensitivity. At the same time, psychological components, such as emotional distress, catastrophic thinking, difficulties in regulating emotions, levels of resilience, and availability of multidisciplinary interventions, strongly shape both how pain is perceived and how well individuals function.

In addition to personal traits, the social context, including problematic family environments, school-related obstacles, peer interactions, and economic background, plays a crucial role in shaping how children and adolescents experience chronic pain. Findings from this systematic review emphasize the biopsychosocial model as a pivotal framework in understanding chronic pain etiology.

Collectively, the findings underscore the necessity of creating age-appropriate, integrated biopsychosocial approaches that respond comprehensively to the specific needs of children and adolescents. It is essential that future research emphasize long-term and interventional designs to clarify causal relationships and evaluate the effectiveness of evidence-based, multidisciplinary treatments grounded in the biopsychosocial perspective.

Study limitations

Many of the included studies employed cross-sectional designs, which restrict conclusions about causality. There was heterogeneity in measurement tools and definitions across studies, making synthesis and comparison more complex. Additionally, only English-language, peer-reviewed studies were included. This review has several limitations that should be considered when interpreting the findings, potentially introducing language and publication bias. Although study-level risk of bias was assessed using a standardized checklist, bias at the outcome level was not consistently evaluated. Moreover, the exclusion of grey literature and unpublished data might have limited the comprehensiveness of the review.

To overcome these limitations, future studies are recommended to adopt longitudinal or experimental designs to explore causal relationships between biopsychosocial factors and chronic pain. The development of culturally relevant frameworks tailored to non-Western populations and the use of standardized international tools can enhance the comparability of studies. Additionally, integrating physiological data (such as inflammatory markers) with psychosocial factors and focusing on specific subgroups (e.g. adolescents with comorbid disorders) may provide a deeper understanding of the underlying mechanisms and support the design of personalized interventions. These approaches could pave the way for the development of more comprehensive strategies in managing chronic pain in children and adolescents.

Ethical Considerations

Compliance with ethical guidelines

This article is a systematic review with no human or animal sample.

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Authors contributions

All authors contributed equally to the conception and design of the study, data collection and analysis, interception of the results and drafting of the manuscript. Each author approved the final version of the manuscript for submission.

Conflicts of interest

The authors declared no conflict of interest.

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