CHRONIC PAIN: AN EPIDEMIOLOGICAL ANALYSIS OF THE PREVALENCE, IMPACT, AND TRENDS IN CHILDREN AND ADOLESCENTS

Josep Roman Juan

Josep Roman Juan

Chronic Pain: An Epidemiological Analysis of the Prevalence, Impact, and Trends in Children and Adolescents

DOCTORAL THESIS

Department of Psychology

UNIVERSITAT ROVIRA i VIRGILI

Tarragona, 2024

UNIVERSITAT ROVIRA I VIRGILI
CHRONIC PAIN: AN EPIDEMIOLOGICAL ANALYSIS OF THE PREVALENCE, IMPACT, AND TRENDS IN CHILDREN AND ADOLESCENTS
Josep Roman Juan

Josep Roman Juan

Chronic Pain: An Epidemiological Analysis of the Prevalence, Impact, and Trends in Children and Adolescents

DOCTORAL THESIS

Supervised by Dr. Jordi Miró

Department of Psychology

UNIVERSITAT ROVIRA i VIRGILI

Tarragona, 2024

UNIVERSITAT ROVIRA I VIRGILI
CHRONIC PAIN: AN EPIDEMIOLOGICAL ANALYSIS OF THE PREVALENCE, IMPACT, AND TRENDS IN CHILDREN AND ADOLESCENTS
Josep Roman Juan

UNIVERSITAT ROVIRA I VIRGILI
DEPARTAMENT DE PSICOLOGIA

Carretera de Valls, s/n
43007 Tarragona
Tel. +34 977 55 80 75
Fax +34 977 55 80 88

I STATE that the Present Dissertation: “Chronic Pain: An Epidemiological Analysis of the Prevalence, Impact, and Trends in Children and Adolescents”, presented by Josep Roman Juan, for the award of the degree of Doctor of Philosophy, has been carried out under my supervision at the Department of Psychology of this university.

24 May 2024, Tarragona

Dr. Jordi Miró Martínez

UNIVERSITAT ROVIRA I VIRGILI
CHRONIC PAIN: AN EPIDEMIOLOGICAL ANALYSIS OF THE PREVALENCE, IMPACT, AND TRENDS IN CHILDREN AND ADOLESCENTS
Josep Roman Juan

Acknowledgments

I would like to express my deepest gratitude to all those who have supported and guided me throughout this journey.

First and foremost, I am profoundly grateful to my thesis director, Dr. Jordi Miró, for entrusting me with the opportunity to work in his esteemed research group. His unwavering support, belief in my abilities, and invaluable guidance have been instrumental in shaping this dissertation. I am indebted to him for his dedication and encouragement at every step of the way.

Neus, I extend a heartfelt gratitude to you for your unconditional support during these four years. You've lifted me up when I fell, encouraged me to continue when it seemed I couldn't, patiently endured all my frustrations, and celebrated all the successes. For this and much more, thank you.

I extend my heartfelt appreciation to my esteemed colleagues in the ALGOS group. Eli, for her unwavering support during one of the most challenging periods of my doctoral studies - the pandemic - when I felt most lonely and lost, she was there to hold me. Rubén, Pere, and Jessica, for infusing laughter and joy into the often-intense journey of doctoral research. Ester, Elena, Helena, Jesús, Ariadna, and Lorena, whose collaboration and insights have enriched my research experience immeasurably.

I am deeply grateful to Dr. Mark P. Jensen for his invaluable contributions to my academic journey. His mentorship and guidance have been instrumental in shaping my understanding of research methodologies

and approaches. I am indebted to him for his generosity in sharing knowledge and expertise, which have undoubtedly enriched the quality of my research.

Special gratitude is reserved for Dr. Pere Joan Ferrando, whose stimulating conversations on data and statistics have been both enlightening and enriching. His insights have not only deepened my understanding of the subject matter but have also inspired further exploration and inquiry.

I am also grateful for the contributions of the undergraduate and graduate students who have supported the EPIDOL project from which my thesis is based, with special mention to Paula, Ester, Núria, and Èrika. Their dedication to the project and assistance with data collection and analysis have been invaluable.

A profound thank you is due to the children and adolescents who generously participated in the studies. Their willingness to contribute to research has played a pivotal role in advancing our understanding of chronic pain in young populations, and their resilience is truly inspiring.

To my family, friends, and loved ones, who have been my unwavering source of strength and support despite the geographical distance, I extend my deepest gratitude. Your love, encouragement, and belief in me have sustained me through the challenges and triumphs of this journey.

To the Ministry of Science and Innovation for granting me the FPI scholarship (PRE2019-089283), the PICH, the Department of Psychology of the URV, and the IASP for their funding to attend conferences.

In closing, I want to express my heartfelt gratitude to each and every individual who has contributed to my personal and academic growth. Your support, encouragement, and guidance have been invaluable, and I am profoundly grateful for your presence in my life.

Thank you all, from the bottom of my heart!

Index

Abstract

Chronic pain is a prevalent condition in children and adolescents, standing as the primary cause of disability across the lifespan and imposing significant burdens on healthcare systems. Research indicates that chronic pain among youth has increased in recent decades, highlighting the need for a comprehensive evaluation of the issues surrounding chronic pain in this population, including strategies for an accurate assessment, prevention, and intervention.

This doctoral dissertation addresses these challenges focusing on the prevalence of chronic pain in children and adolescents, including high-impact chronic pain, while also identifying potential biopsychosocial factors contributing to its increase. Furthermore, this dissertation aims to improve the assessment of children and adolescents with chronic pain by adapting and validating a questionnaire to grade chronic pain severity. Lastly, this dissertation provides new and important data on several biopsychosocial factors that are significantly associated with physical and emotional function, the use of medication, and sleep in this population.

The main findings of this dissertation are summarized in the following pages, with detailed information provided in the included articles. The main conclusions are:

Abstract

- Chronic pain prevalence among children and adolescents is very high and increasing.
- Community-based interventions targeting modifiable factors related to early menarche, sedentarism, obesity, sleep disturbance, and psychological symptoms may help prevent the increase in chronic pain among adolescents.
- The Pediatric version of the Graded Chronic Pain Scale-Revised is a valid instrument to grade the severity of chronic pain in children and adolescents.
- Addressing fatigue in children with chronic pain may prevent sleep disturbance and reduce daily pain impact.
- Addressing pain catastrophizing in children and adolescents with chronic pain using pain-related medication can reduce the risk of medication misuse and related adverse effects.
- Addressing sleep disturbance in children and adolescents with chronic pain who have experienced adverse childhood events may prevent the worsening of emotional function.

1. Introduction

This doctoral dissertation represents the culmination of four years of research conducted at the Unit for the Study and Treatment of Pain - ALGOS and the Chair in Pediatric Pain, Universitat Rovira i Virgili, under the guidance of Dr. Jordi Miró, and with the invaluable support of my colleagues at the ALGOS group.

The dissertation is organized into three main parts. The first part presents foundational concepts of pain, distinguishing between acute and chronic pain, and introducing the concept of high-impact chronic pain to better identify individuals significantly affected by chronic pain. Subsequently, it presents data on the concerning prevalence and temporal trends of chronic pain in children and adolescents, particularly in Europe.

Following this, the biopsychosocial model of chronic pain is introduced, emphasizing childhood vulnerabilities that influence its development. The core outcome domains of chronic pain are then described, along with recommended measures for their assessment. Additionally, the introduction addresses the management of chronic pain in children and adolescents from a biopsychosocial perspective.

The introduction concludes by highlighting the crucial role of epidemiological research in advancing our understanding of chronic pain, including its prevalence across various age and sociodemographic groups, and in determining the factors contributing to its increase over time. Furthermore, it highlights the utility of epidemiological studies in developing

assessment tools and providing practical information for the treatment of children and adolescents with chronic pain.

The second section of the dissertation delineates the six objectives and an overview of the methods used, describing the selection of participants, procedures, and measurement tools. Subsequently, the section presents the results of the nine studies included in the dissertation.

The third section includes a comprehensive discussion synthesizes the findings of the studies and offers insights into potential avenues for future research. The dissertation concludes with a succinct summary of the key findings.

1.1. Pain, acute pain, chronic pain, and high-impact chronic pain

1.1.1. Pain

The International Association for the Study of Pain (IASP) defined *pain* in 1979 as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (IASP, 1979). This definition remained in use for over four decades and gained a widespread acceptance among health care professionals and researchers. It was also endorsed by various professional, governmental, and nongovernmental organizations, including the World Health Organization (WHO). However, advancements in pain research prompted a reevaluation of the definition. Consequently, the IASP recently revisited the terminology, opting to replace phrases that relied

solely on a person's ability to articulate the experience to qualify as pain. The updated definition now states that pain is: “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage” (Raja et al., 2020).

Having pain, albeit unpleasant, is normal and could even be adaptive; for example, when a child accidentally touches a hot stove, the immediate sensation of pain prompts her or him to quickly retract her or his hand, thereby preventing further injury. In this way, pain acts as a protective mechanism, facilitating the avoidance of dangerous situations and promoting safety. On the other hand, the continuous absence of any pain at all is profoundly abnormal and appears only as congenital nociceptor deficiency or dysfunction. This situation is far from adaptive, notably leading to major clinical problems associated with the absence of defensive responding and learning, and with a severe shortening of life expectancy (Drissi et al., 2020; E. T. Walters & Williams, 2019; Weisman et al., 2019).

Pain can be categorized through various parameters such as location, quality, intensity, duration, or presentation (IASP, 1994; Miró, 2010). Within the scope of this doctoral dissertation, the duration of pain is of paramount importance, given that duration can indicate whether one’s pain serves as adaptive or not. When describing duration, pain is classified as either acute or chronic. The terms "acute" and "chronic" denote specific time frames; simply put, “acute" refers to short-lived issues whereas "chronic" indicates long-term conditions.

1.1.2. Acute Pain

According to the IASP, acute pain is a transient response to a noxious stimulus or injury, typically associated with tissue damage (IASP, 2022). It serves an adaptive function by signaling potential harm to the system. Acute pain is inherently time-limited, dissipating as the threat resolves and the damaged tissue heals (Carr & Goudas, 1999).

Acute pain typically may last up to 3 months and encompasses anything from brief muscular discomfort to postoperative pain (Johansen et al., 2012; Werner & Kongsgaard, 2014). It is a common and expected part of daily life from childhood to adulthood, and most everyday acute pain does not require clinical intervention. In adults, for example, a European study involving 8506 patients, 70% of adults reported experiencing pain at least once a month, such as headaches, menstrual pains, or muscle aches (Vowles, 2014). In youths, an observational study of everyday pain in 3- to 7-year-olds reported an incident rate of 0.33 per hour per child (Noel et al., 2018). In addition, acute pain can also occur deliberately as part of a social process (e.g., body adornment, contact sport, or ritual), suggesting normalized and common experiences of pain across cultures and societies.

1.1.3. Chronic pain

Pain that persists beyond the expected period of healing, is known as “chronic pain” (IASP, 1994; Treede et al., 2019). Unlike acute pain that serves the important function of signaling harm to the body's integrity, chronic pain is in itself a disease with poor prognosis, featuring peripheral and central sensitization to pain signals (Siddall & Cousins, 2004; Tracey &

Bushnell, 2009). Temporally speaking, according to the IASP, chronic pain is any pain that persists beyond three months (Smith et al., 2019). This definition of chronic pain was recently included in the *International Classification of Diseases* (ICD-11), which classifies chronic pain into seven distinct groups: chronic primary pain, chronic cancer pain, chronic posttraumatic and postsurgical pain, chronic neuropathic pain, chronic headache and orofacial pain, chronic visceral pain, and chronic musculoskeletal pain (Treede et al., 2015, 2019).

Historically, chronic pain was considered to start at 6 months post-onset for adults and 3 months post-onset for children. However, although agreed upon by the international pain research community, the temporal-centered definition of chronic pain has some limitations (Dzau & Pizzo, 2014; Von Korff & Dunn, 2008). For example, as with acute pain, 3 months is an absolute cutoff and does not account for life stage. For example, 3 months for a 6-month-old is 50% of his or her life but 0.4% of the life of a 60-year-old. Similarly, this definition of chronic pain would be inapplicable to describe the experience of a child of 2 months who has experienced pain from birth, even though having lived their life in pain is expected to be clinically meaningful (Emre Ilhan et al., 2022). After discussing the problem of definitions that rely on duration has been discussed (Von Korff & Dunn, 2008), 3 months post-onset of pain is now thought to be more clinically relevant for adults and children alike, and it serves as the dividing boundary that differentiates chronic from acute pain.

The inclusion of pain frequency (e.g., daily, once or twice a week) in the definition of chronic pain has been suggested as a potential solution to better identify individuals with chronic pain, including treatment responders (Deyo et al., 2014; Herman et al., 2023). Furthermore, beyond temporal considerations, the current definition of chronic pain fails to capture the multidimensional nature of chronic pain, including activity limitations and participation restrictions (Dunn et al., 2008; Mackey, 2016; Von Korff, 2011; Von Korff et al., 2016), which are classifications recognized by the World Health Organization (World Health Organization, 2007).

1.1.4. High-impact chronic pain

In response to the criticisms around the current definition of chronic pain, particularly when capturing activity limitations and participation restrictions, the concept of high-impact chronic pain has emerged as a means to identify individuals experiencing significant life disability due to chronic pain (Von Korff et al., 2016). This concept also enables better delineation of individuals who contribute to the substantial economic costs associated with chronic pain (Von Korff et al., 2016), thereby facilitating strategic economic planning. Multiple definitions of high-impact chronic pain have been used in different studies. For example, several studies mainly conducted with the general adult population in the United States defined high-impact chronic pain as either pain present most days or every day in the past three months with significant limitations in one or more activities (Pitcher et al., 2019), or chronic pain that limited life or work activities on most days or every day during the past 6 months (Dahlhamer et al., 2018).

Individuals with high impact chronic pain have been shown to have significantly higher levels of disability, anxiety, depression, fatigue, and cognitive dysfunction than those with chronic pain that is not of high-impact (Pitcher et al., 2019).

1.2. Chronic pain in children and adolescents: a public health problem

Chronic pain is also a widespread problem among children and adolescents worldwide. A recent systematic review that included studies from 71 different countries reported that 1 in 5 children and adolescents have chronic pain, although prevalence rates vary depending on the assessment methods and definitions of chronic pain used (Chambers et al., 2024). Further, the prevalence of chronic pain varies across demographic groups, with girls reporting higher rates compared to boys (Chambers et al., 2024). Additionally, some demographic groups such as immigrant children and adolescents may also exhibit higher prevalence rates of chronic pain (Alfven, 1993; Luntamo et al., 2012). Nevertheless, the high prevalence of pediatric chronic pain inherently poses a significant burden on society. The ongoing medical care required by children and adolescents with chronic pain, including the use of pain medications (Huguet & Miró, 2008; Könning, Rosenthal, Friese, et al., 2021), significantly contributes to economic strain of healthcare systems (Groenewald et al., 2014; Groenewald & Palermo, 2015; Kitschen et al., 2024; Tumin et al., 2018). For instance, in the United States alone, the economic costs of pediatric chronic pain averages US$1339 per patient, and result in nationwide costs of US$19.5 billion

annually (Groenewald et al., 2014), which is likely to increase when pain associated with long-term conditions is also considered.

Available data from both clinical and community samples suggest that pain conditions in childhood persist into adulthood in more than 50% of the cases (Horst et al., 2014; Kashikar-Zuck et al., 2014, 2019; Larsson et al., 2018; Stanford et al., 2008; Walker et al., 2010). Moreover, in many chronic health conditions (e.g., sickle cell disease, chronic pancreatitis) pain becomes more severe at the adult stage (Dampier et al., 2017). Affecting between one-fifth and one-half of the general population (Breivik et al., 2006; Fayaz et al., 2016), chronic pain poses a significant global health challenge (James et al., 2018) and ranks as the leading cause of disability worldwide (Rice et al., 2016).

1.2.1. Prevalence and trends of chronic pain in children and adolescents in Europe

The prevalence of chronic pain in children and adolescents is high in Europe (Haraldstad et al., 2011; Huguet & Miró, 2008; Perquin et al., 2000; Roth-Isigkeit et al., 2005; Vervoort et al., 2014; Wager et al., 2020; Walters et al., 2018). For example, a recent cross-national study showed that up to 40% of European youths experience some form of pain weekly over a period of 6 months (Gobina et al., 2019). Moreover, the prevalence of pediatric chronic pain in Europe has also witnessed a notable increase over the past decade. A number of studies from different European countries have documented this trend, highlighting a rise in various chronic pain conditions (Anttila et al., 2006; Bandell-Hoekstra et al., 2001; Hakala

et al., 2002; Laurell et al., 2004; Luntamo et al., 2012). Particularly significant is Roy and colleagues' recent study (2022) where pooled data from 33 primarily European countries revealed a 3.3% increase in the prevalence of chronic back pain among adolescents over a span of 14 years, with 22% of adolescents experiencing chronic back pain in 2014. This worrying trend highlights the need for urgent attention and concerted efforts from healthcare providers, policymakers, and researchers to address the multifaceted impact of pediatric chronic pain on individuals and society as a whole, and to determine the factors contributing to its increase.

1.3. Developmental Models of Chronic Pain: The biopsychosocial model

One of the prevailing conceptual frameworks for understanding chronic pain is the biopsychosocial model of pain (Gatchel et al., 2007; Turk et al., 2011), which has been applied to pediatric pain (Liossi & Howard, 2016). According to this model, the experience of chronic pain is the result from the interaction of biological (e.g., nociceptive information is encoded by the central nervous system), psychological (e.g., how nociception is understood) and social factors (e.g., socioeconomic status). Extending beyond its original formulation, researchers have adapted this model to highlight developmental considerations, including pediatric-specific and lifespan perspectives. (Palermo et al., 2014; Rosenbloom et al., 2017; Walco et al., 2016). Recently, Palermo (2020) proposed a model delineating childhood biopsychosocial vulnerabilities that influence both the development of chronic pain in children and adolescents and long-term

outcomes into adulthood. These vulnerabilities include emotional, health behavior, social and familial, and neurobiological factors. A summary of vulnerabilities and therefore potential actionable targets follow.

1.3.1. Emotional vulnerabilities

In Palermo's model regarding the biopsychosocial factors involved in the development of chronic pain in children and adult outcomes, emotional vulnerabilities play a pivotal role. These vulnerabilities encompass various factors, including pain coping abilities, threat appraisal, anxiety and depressive symptoms, and other psychiatric conditions. Prospective studies indicate that early emotional concerns, such as anxiety and depression, often precede the chronification of pain in childhood (Jones et al., 2003; Stanford et al., 2008). Additionally, emotional vulnerabilities frequently co-occur with chronic pain in children and adolescents, exacerbating pain experiences and contributing to long-term adverse outcomes in adulthood (Holley et al., 2016; Mano et al., 2019; Soltani et al., 2019). For instance, individuals exhibiting high levels of emotional distress during adolescence tend to experience more severe pain symptoms and are at greater risk of developing comorbid conditions, such as functional gastrointestinal disorders and comorbid anxiety or depressive disorders, in adulthood (Walker et al., 2012).

1.3.2. Health behavior vulnerabilities

Health behavior vulnerabilities that arise during childhood and adolescence, such as sleep problems, lack of physical activity, and

nutritional factors (Christoph et al., 2019; Rovio et al., 2018; Zhang et al., 2017), are identified as potential contributors to the development and maintenance of chronic pain in childhood and adolescence. For example, research suggests that sleep problems during childhood may predict the development of chronic pain in adolescence (Incledon et al., 2016). While there is limited data on the full range of health behavior vulnerabilities predicting the onset of childhood pain, current research primarily focuses on concurrent associations between childhood chronic pain and various health behaviors. For instance, children with chronic pain often experience declines in physical activity and struggle to engage in vigorous activities (Swain et al., 2016; Wilson & Palermo, 2012).

1.3.3. Social and Family-related Vulnerabilities

The model underscores the importance of social and family vulnerabilities in shaping childhood chronic pain experiences and long-term outcomes. These vulnerabilities encompass various aspects, including the child's relational skills, autonomy, parenting behaviors, parental psychological distress, family functioning, and socioeconomic context. Research has primarily examined how parent pain status and socioeconomic indicators are associated with the onset of pain in childhood (Fryer et al., 2017; Stone & Wilson, 2016). Findings suggest that having one or both parents with chronic pain increases the child's risk of developing chronic pain in a dose-response fashion (Higgins et al., 2015; Moore et al., 2020). Moreover, specific parent and family factors, such as protective behaviors and parental distress, are associated with increased pain and

disability in children with chronic pain (Claar et al., 2008; Liossi & Howard, 2016; Palermo et al., 2014). Family and peer relationships are also significantly impacted by chronic pain experiences (Cservenka et al., 2015; Solé et al., 2023). Furthermore, social vulnerabilities during childhood predict future adult health outcomes, with socioeconomic conditions and housing quality in childhood linked to adult onset of chronic pain (Muthuri et al., 2018).

1.3.4. Neurobiological Vulnerabilities

In exploring neurobiological vulnerabilities associated with chronic pain, a crucial focus lies on understanding the structural and functional brain circuitries involved in pain, emotion, stress, and behavior, particularly considering the role of neuroplasticity across developmental stages from neonatal to young adulthood. Studies investigating pain heritability offer insights into potential neural correlates linked to the risk of chronic pain development. For instance, a pilot fMRI study revealed altered brain activity in adolescents with a parent experiencing chronic pain, suggesting an early emergence of a phenotype associated with chronic pain conditions before significant pain symptom onset (Cservenka et al., 2015). Notably, these adolescents exhibited reduced brain activity in visual processing and affective brain regions like the amygdala, along with differences in frontoparietal regions, reminiscent of findings in adults and youth with chronic pain (Cservenka et al., 2015). Additionally, research on youth with existing chronic pain demonstrates structural changes, including widespread gray-matter atrophy across various brain regions involved in

motor, affective, motivational, emotional, cognitive, memory, and fear-related functions (Simons et al., 2014). Functional connectivity changes in neural networks and amygdala-based covariance have also been observed. However, the direct linkage of specific childhood neurobiological vulnerabilities to future adult outcomes remains uncertain.

Although Palermo's model does not include cognitive factors, research has demonstrated that cognitive vulnerabilities such as pain catastrophizing or pain threat appraisal play a significant role in chronic pain in children and adolescents (Fisher et al., 2018) These cognitive vulnerabilities have been suggested to amplify or maintain pain in childhood and to predict poor long-term outcomes. For example, higher levels of pain catastrophizing - an exaggerated negative mindset towards pain, characterized by feelings of helplessness, excessive focus on pain sensations, and pessimistic thoughts about the ability to control pain (Sullivan et al., 2001) - have been associated with poorer outcomes in children and adolescents with chronic pain including higher pain intensity and disability, and emotional function (Miller et al., 2018).

1.4. Core domains of chronic pain in children and adolescents

Determining the presence or absence of chronic pain in children and adolescents is just the first step to addressing this public health problem. To improve care, the use of appropriate psychometrically-sound pain-related outcome measures is essential, as well as accurate assessment of these outcomes (Laures et al., 2019).

Introduction

In 2006, a pediatric working group of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (PedIMMPACT) conducted a Delphi poll, reaching consensus and identifying eight core outcome domains to consider in the treatment of children and adolescents with chronic pain: pain intensity, physical function, symptoms/adverse events, global satisfaction with treatment, emotional function, role function, sleep, and economic factors (McGrath et al., 2008). These PedIMMPACT recommendations have been available to guide outcomes measurement in clinical registries and trials (e.g., Bhandari et al., 2016; Palermo et al., 2016). However, some concerns about the uptake of these recommendations over the past 12 years arose. For example, in a systematic review of reporting practices in 107 randomized controlled trials of pediatric chronic pain interventions (Connolly et al., 2019), nearly all trials included pain intensity as an outcome domain. However, fewer than 35% included outcomes in any other recommended domain, suggesting insufficient use of this core outcome set (Connolly et al., 2019; Fillingim et al., 2016).

In light of these concerns, in 2021, a working group headed by Palermo developed a new set of key outcome domains that incorporated scientific innovations in outcome measurement and include patients' perspectives (Palermo et al., 2021). This set of domains includes three mandatory domains (i.e., pain severity, pain interference with daily living, and adverse events) and four optional domains (i.e., overall well-being, emotional function, physical function, and sleep; Palermo et al., 2021). Furthermore, this working group also developed a list of the patient-

reported measures recommended to assess each domain, considering their clinical utility and measurement properties (Palermo et al., 2024). These mandatory and optional domains along with the recommended patient-reported questionnaires are briefly described below.

1.4.1. Mandatory domains

1.4.1.1. Pain Severity

Epidemiological research has shown that up to 13% of children and adolescents experience severe chronic pain (Vervoort et al., 2014) and that most patients receiving medical intervention for their chronic pain have moderate to severe chronic pain (Wager et al., 2013).

The current standard instrument to assess the severity of chronic pain is the Graded Chronic Pain Scale (GCPS). This system was developed by Von Korff et al. in 1992 for use in adults (Von Korff et al., 1992) and has been subsequently adapted for use in children and adolescents either in epidemiological (Huguet & Miró, 2008; Könning, Rosenthal, Brown, et al., 2021; Vervoort et al., 2014) and clinical studies (Wager et al., 2013). This system classifies the severity of chronic pain into different grades which vary from 0 “no chronic pain” to 4 “severe, disabling chronic pain.” In the original version for adults, pain severity is calculated based on an algorithm including the patient’s rating of pain intensity, disability days (i.e., days being kept from usual activities due to pain), and pain-related disability (i.e., interference of daily activities and work due to pain). In versions adapted for children and adolescents (Huguet & Miró, 2008; Könning, Rosenthal, Brown, et al., 2021; Wager et al., 2013), absence from school is considered

instead of workdays missed, and pain-related disability is assessed using scales such as the Functional Disability Inventory (FDI; Walker & Greene, 1991).

However, Palermo and colleagues (Palermo et al., 2024) determined that the GCPS was minimally validated in pediatric populations and recommended using the Numerical Rating Scale (NRS), which is a well-established and commonly used questionnaire for the assessment of pain intensity in children and adolescents (Castarlenas et al., 2017). With this measure, patients are asked to rate their pain intensity using a number from 0 to 10 where 0 means no pain and 10 very much pain. However, assessing chronic pain severity extends beyond quantifying pain intensity; it also involves considering factors such as the frequency of pain occurrences (Palermo et al., 2021).

Recognizing limitations in the original instrument's adaptation to evolving definitions of chronic pain and high-impact chronic pain (Dahlhamer et al., 2018; Deyo et al., 2014; Pitcher et al., 2019; Von Korff et al., 2016), and the need for shorter pain metrics to reduce patient burden, Von Korff and colleagues developed a revised, shorter version of the instrument in 2020 (Von Korff et al., 2020). This revised version of the GCPS (i.e., GPCS-R) uses five items to grade the severity chronic pain into four grades: "chronic pain absent" (grade 0), "mild chronic pain" (grade 1), "bothersome chronic pain" (grade 2), and "high-impact chronic pain" (grade 3) and has shown to be valid (Von Korff et al., 2020), hence lays the groundwork for a new, comprehensive tool for assessing chronic pain severity in youth.

1.4.1.2. Pain Interference

Chronic pain can significantly disrupt the lives of children and adolescents. For example, children and adolescents with chronic pain report higher levels of physical disability than their healthy counterparts (Huguet & Miró, 2008). This impairment extends to various domains of their daily function, including their ability to attend school regularly (Groenewald et al., 2020; Vervoort et al., 2014) and their participation in extracurricular social, physical, and athletic activities (Palermo, 2000; Swain et al., 2016), among others.

Assessing pain interference often involves utilizing various measures tailored to capture its multidimensional nature. The Child Activity Limitations Interview (CALI-9; Holley et al., 2018) has been recommended to evaluate pain interference in pediatric pain patients. Other measures that have proved good psychometric properties include the 8-item PROMIS Pediatric Pain Interference (Varni et al., 2010), which has been widely used in clinical and community samples (e.g., Noel et al., 2018; Solé et al., 2022).

1.4.1.3. Adverse events: Side Effects

Adverse events refer to undesirable symptoms or reactions resulting from treatment, including pharmacological treatment. These events include a spectrum of manifestations, ranging from mild discomfort to more severe complications, contingent upon the specific intervention and individual patient characteristics. Examples of such adverse events include gastrointestinal disturbances like stomach upset or vomiting, sensations of fatigue, dizziness, headaches, skin irritations, and alterations in mood or

cognitive function. In the most severe cases, adverse events can even result in death (Palermo et al., 2021).

Despite the importance of assessing adverse events, the committee faced a challenge in identifying a suitable self-reported measure for this domain and concluded that there is a lack of self-report tools to assess adverse events comprehensively in children and adolescents with chronic pain (Palermo et al., 2024).

1.4.2. Optional domains

1.4.2.1. Overall Well Being

The pervasive influence of pain interference on the daily lives of children and adolescents with chronic pain profoundly diminishes their overall quality of life and well-being. One of the firsts studies that comprehensively assessed the multidimensional concept of quality of life of children and adolescents with chronic pain, showed significant deficits across psychological, social, functional, and physical domains in this population (Hunfeld et al., 2001). Subsequent studies supported these findings (Gold et al., 2009; Huguet & Miró, 2008), highlighting the enduring challenges faced by children and adolescents individuals afflicted with chronic pain.

The committee recommended the Patient Global Impression of Change (PGIC; Dworkin et al., 2005; Guy, 1976) as the preferred instrument for evaluating overall well-being in pediatric pain patients. Unlike other measures such as the PedQL Generic Core (Varni et al., 2001) or the PROMIS Pediatric Global Health (Forrest et al., 2014), which were found to

overlap with other domains, PGIC offers a single-item patient rating of overall treatment improvement.

1.4.2.2. Emotional Function: Anxiety and depressive symptoms

Children and adolescents with chronic pain often experience mental health comorbidities. For example, studies have consistently shown that children and adolescents with chronic pain experience anxiety and depressive symptoms at significantly higher rates than those without chronic pain (Blaauw et al., 2015; Bromberg et al., 2017; Soltani et al., 2023; Tegethoff et al., 2015). Moreover, the prognosis for children and adolescents with both pain and mental health problems/disorders is poorer than that of youth who experience either condition alone (Sinclair et al., 2016).

The recommended patient-reported measures to evaluate emotional function based on the available evidence include the 10-item Children's Depression Inventory–Short Version (CDI-S; Kashikar-Zuck et al., 2011) and those derived from the Pediatric Patient-Reported Outcomes Measurement Information System (PROMIS): the PROMIS Pediatric Depression 8a, PROMIS Pediatric Anxiety 8a (Irwin et al., 2010). The CDI-S assesses depressive symptoms within the past two weeks, while the PROMIS instruments evaluate depressive and anxiety symptoms over the past 7 days. All of these instruments have shown good psychometric properties (Allgaier et al., 2012; Caqueo-Urízar et al., 2014; Li et al., 2023).

1.4.2.3. Physical function

Children and adolescents with chronic pain often face challenges in physical function, including their ability to engage in daily activities, school participation, and maintain overall physical well-being (Groenewald, Tham, et al., 2020; Swain et al., 2016; Vervoort et al., 2014).

Although not considered the best option by the committee, the Bath Adolescent Pain Questionnaire—Physical Functioning Scale (Eccleston et al., 2005) was the instrument recommended for evaluating overall well-being in pediatric pain patients (9 committee members voted for the PROMIS physical activity as the best option, while just 3 voted for the Bath questionnaire as the top option). Other measures that have proved good psychometric properties include the 8-item PROMIS Pediatric Mobility (Varni et al., 2014), which has been widely used for research and clinical studies (e.g., Richardson et al., 2020).

1.4.2.4. Sleep disturbance

Sleep disturbances, including difficulties with falling asleep, staying asleep, or experiencing non-restorative sleep, are highly prevalent among children and adolescents with chronic pain, with more than 50% experiencing such disturbances (Long et al., 2008; Palermo et al., 2011; Palermo & Kiska, 2005).

The recommended patient-reported measures to evaluate sleep disturbance based on the available evidence include the Adolescent Sleep Wake Scale-Short Form (ASWS-SF; Sufrinko et al., 2015). The ASWS-SF has 10 items that assess sleep patterns, including 3 subscales (i.e., Falling

Asleep and Reinitiating Sleep, Returning to Wakefulness, and Going to Bed), and has shown sufficient internal consistency and good known-groups validity (Essner et al., 2015; Sufrinko et al., 2015). Other measures that have proved good psychometric properties include the 8-item PROMIS Pediatric Sleep Disturbance (Forrest et al., 2018), which has been widely used in clinical and community samples (e.g., Jacobson et al., 2013; Solé et al., 2022).

1.5. Management of chronic pain in children and adolescents

Many children and adolescents with chronic pain seek care for their pain, with up to 70% of them consulting healthcare providers (Könning, Rosenthal, Friese, et al., 2021). Timely intervention is crucial due to the potential persistence and exacerbation of chronic pain (Grimby-Ekman et al., 2018; Sillanpää & Saarinen, 2017; Stanford et al., 2008). Moreover, giving the intricate interplay of biological, psychological, and social determinants of chronic pain (Liossi & Howard, 2016; Rajapakse et al., 2014), effective treatment typically requires an interdisciplinary approach (Hechler et al., 2015; Miró et al., 2017). However, despite this need, there is limited availability of specialized pediatric pain programs (De La Vega & Palermo, 2024), resulting in waiting lists averaging almost 200 days from time of first referral to the new patient's appointment (Palermo et al., 2019). This delay often leads to patient deterioration, including escalating pain, depression, and decreased health-related quality of life (Collett et al., 2010).

1.5.1. The biopsychosocial approach to treatment

These interventions ideally encompass a broad spectrum of modalities, including pain education, physical, psychological, and pharmacological therapies (Dilini Rajapakse et al., 2014; Miró et al., 2017).

Pain education: Central to this paradigm is pain education, aimed at bridging the gap between scientific insights into chronic pain and the subjective experiences of afflicted children. Whether through educational materials or interactive sessions, the primary objective is to dispel misconceptions and empower children with a nuanced understanding of pain mechanisms (Koechlin et al., 2020).

Physical therapy: Concurrently, physical interventions such as physiotherapy, massage therapy, and innovative modalities like Transcutaneous Electrical Nerve Stimulation and mirror box therapy assume prominence for their rehabilitative potential and capacity to counteract sedentary lifestyles (Dilini Rajapakse et al., 2014; Lynch-Jordan et al., 2014). A recent meta-analysis assessing the effectiveness of physical therapy in alleviating pain and related outcomes revealed that physical activity can lead to a moderate reduction in pain intensity and functional disability post-treatment. However, uncertainties persist regarding the long-term sustainability of these benefits. Conversely, physical therapies did not show significant improvements in overall well-being and quality of life, emotional function, or sleep. Furthermore, insufficient data exist regarding adverse events associated with these therapies (Fisher et al., 2022).

Psychological therapy: Psychological interventions for children and adolescents with chronic pain have been developed with a focus on the self-management of pain and related disability (Palermo, 2012). In addition, psychological therapies are also available for parents of children and adolescents with chronic pain, and play a pivotal role in supporting pediatric chronic pain management. Psychological therapies targeted at parents of children and adolescents with chronic pain include cognitive-behavioral therapy, family therapy, motivational interviewing, multisystemic therapy, and problem-solving therapy.

Several Cochrane Reviews confirm the effectiveness of psychological therapies either for both children and adolescents with chronic pain and their parents (Eccleston et al., 2016; Law et al., 2019). Psychological interventions for pediatric chronic pain may include relaxation, hypnosis, coping skills training, biofeedback, and cognitive behavioral therapy, and have been proven to be effective in reducing pain intensity and disability (Eccleston et al., 2016; Fisher et al., 2022). Similarly to physical therapy, studies on psychological therapies did not reveal significant improvements in overall well-being and quality of life, emotional function, or sleep for children and adolescents with chronic pain, and it is unclear whether they are associated with adverse events associated with these therapies (Fisher et al., 2022). Psychological therapy may improve parenting behavior (problem-solving therapy and cognitive-behavioral therapy) and may also have beneficial effects on parent mental health (e.g., Problem-solving therapy; Law et al., 2019).

Pharmacological therapy: Pharmacological interventions are typically the first line of approach in pain management, involving the use of analgesics, non-steroidal anti-inflammatory drugs, opioids, anticonvulsants, and antidepressants. However, the effectiveness of pain medications for pediatric chronic pain has not been consistently demonstrated (Eccleston et al., 2019), although certain medications such as anticonvulsants have shown efficacy in reducing pain intensity (Fisher et al., 2022). Conversely, they have not demonstrated effectiveness in improving emotional function, and there is insufficient data to support their impact on functional disability, quality of life, and sleep disturbance (Fisher et al., 2022). Moreover, adverse effects associated with the use of pain medications include appendicitis, suicidal ideation, cholelithiasis, and major depression (Fisher et al., 2022) with their long-term safety remaining unclear (Cooper et al., 2017; Eccleston et al., 2017). Therefore, adequate and appropriate use of pain medications in children and adolescents with chronic pain is of utmost importance. Despite the lack of evidence, analgesics are regularly prescribed to children and adolescents with chronic pain (Walco et al., 2017), highlighting a significant gap in translating research to clinical practice and patient care.

1.6. The Need for Epidemiological Research

Despite the high (and growing) prevalence of chronic pain in children and adolescents, it continues to be largely unrecognized, understudied, and undertreated (Eccleston et al., 2021). Epidemiological research plays a crucial role in advancing our understanding of pediatric

chronic pain (Croft et al., 2010). By investigating its prevalence across different age and sociodemographic groups we gain insights into the developmental trajectories of chronic pain (Jones & Botello, 2010) and can tailor interventions and healthcare policies to address the specific needs of vulnerable populations (e.g., females, immigrants). Furthermore, by identifying the factors contributing to its observed increase over time (Roy et al., 2022), tailored healthcare policies aimed at preventing chronic pain at a community level can be designed and implemented.

Epidemiological research may also serve as an avenue for developing new tools to measure pain-related outcomes (e.g., pain severity), thereby improving the assessment of pain and related domains in pediatric chronic pain patients. Additionally, it can offer valuable and practical insights for improving current chronic pain management programs by identifying factors associated with the worsening of the condition (e.g., pain interference). Finally, data from epidemiological studies can also be used to help prevent negative or side effects associated to treatment.

2. Objectives

The primary aim of this doctoral dissertation was to improve our understanding of chronic pain, including high-impact chronic pain, among children and adolescents, with a specific focus on its prevalence, sociodemographic distribution, and impact. Additionally, the dissertation seeks to identify key biopsychosocial factors contributing to the rising prevalence of chronic pain in adolescents.

Furthermore, this doctoral dissertation aimed to enhance the assessment of chronic pain in children and adolescents by adapting and validating a new measure for assessing chronic pain severity. Finally, it aimed to provide practical knowledge for the treatment of pediatric chronic pain by examining the influence of several biopsychosocial factors on the impact of chronic pain, the potential misuse of pain medication that could lead to adverse events, the emotional functioning, and sleep of children and adolescents with chronic pain. The specific objectives, as related to the different studies involved, were as follows:

2.1. Objective 1

To study the prevalence of chronic pain and high-impact chronic pain, as well as its correlates and distribution across different sociodemographic characteristics, including sex, age, and immigration background. This investigation is reported in Studies I and II.

2.2. Objective 2

To study whether increases in (1) early menarche, (2) sedentary screen-based behaviors and obesity, and (3) sleep disturbances and psychological distress observed among European adolescents contributed to the increase in the prevalence of chronic back pain over time in this population. This is addressed in Studies III-V.

2.3. Objective 3

To translate, adapt, and study the concurrent validity of the revised version of the Graded Chronic Pain Scale for its use with pediatric samples (P-GCPS-R). This study is reported in Study VI.

2.4. Objective 4

To determine if fatigue underlies the co-occurrence and mutual maintenance of sleep disturbance and pain intensity and pain interference over time in children and adolescents with chronic pain. This research is described in Study VII.

2.5. Objective 5

To examine the association between psychological factors and pain medication use in adolescents with chronic pain. This study is shown in Study VIII.

2.6. Objective 6

To examine the influence of adverse childhood events (ACEs) on emotional function in children and adolescents with chronic pain. This research is shown in Study IX.

3. Methods

This doctoral dissertation comprises nine studies. Six of these studies (Studies I - II and Studies VI - IX) used data from the EPIDOL project and three studies (Studies II - V) used data from The Health Behaviour in School-aged Children (HBSC) study. The methods of each of the studies are only briefly described in this section as they are described in detail in each of the articles included in this dissertation.

3.1. Participants

Studies I - II (Miró et al., 2023; Roman-Juan, Sánchez-Rodríguez et al., 2024) and Studies VI – IX (Roman-Juan, Ceniza-Bordallo et al., 2024; Roman-Juan, Solé, et al., 2023a, 2023b; Roman-Juan, Sánchez-Rodríguez, et al., 2023), were conducted with a convenience sample of children and adolescents participating in the EPIDOL project, a longitudinal epidemiological study of pain in children and adolescents conducted by the Chair in Pediatric Pain URV-FG and directed by Dr. Jordi Miró, the director of this Doctoral dissertation. Data for studies III - V (Roman-Juan et al., 2022; Roman-Juan, Jensen, et al., 2023; Roman-Juan, Jensen, et al., 2024) were extracted from 801,648 children and adolescents participating in the HBSC study, a collaborative cross-sectional study facilitated by the World Health Organization.

3.2. Procedure and measures

The EPIDOL project underwent participant recruitment and follow-ups once between 2018 and 2020 (pre-COVID) and once between 2022 and 2023 (post-COVID) of children and adolescents schools located in the Camp de Tarragona, a region in the South East of Catalonia, Spain. Participants were asked to provide sociodemographic information and respond to a paper-and-pencil survey with questions about pain-related characteristics and function. A more detailed explanation of the EPIDOL project, the procedures implemented, and the measures recorded can be found in the papers included in this dissertation (Miró et al., 2023; Roman-Juan, Solé, et al., 2023a, 2023b; Roman-Juan, Sánchez-Rodríguez, et al., 2023; Roman-Juan, Ceniza-Bordallo et al., 2024; Roman-Juan, Sánchez-Rodríguez et al., 2024;).

The HBSC study is a repeated cross-sectional study that initiated in 1983-1984 and collects data every 4 years from independent, nationally representative samples of 11-, 13-, and 15-year-old school-aged children, using multi-stage stratified random cluster sampling, with school classes or schools as the sampling unit. Study participation is voluntary and anonymous. Data collection is conducted through standardized self-administered questionnaires with questions about health-related behaviors in classroom settings. A more detailed explanation of the HBSC study and the measures used can be found in the papers included in this dissertation (Roman-Juan et al., 2022; Roman-Juan, Jensen, et al., 2023; Roman-Juan, Jensen et al., 2024).

4. Results

In this section, the nine studies included in the dissertation are presented as published in the journals when possible. Studies III and VII are still under review.

- Study I. Miró, J., Roman-Juan, J., Sánchez-Rodríguez, E., Solé, E., Castarlenas, E., & Jensen, M. P. (2023). Chronic pain and high impact chronic pain in children and adolescents: a cross-sectional study. *The Journal of Pain*, *24*(5), 812-823.
- Study II. Roman-Juan, J., Sánchez-Rodríguez, E., Solé, E., Castarlenas, E., Jensen, M. P., & Miró, J. (2024). Immigration background as a risk factor of chronic pain and high-impact chronic pain in children and adolescents living in Spain: differences as a function of age. *PAIN*, *165*(6), 1372-1379.
- Study III. Roman-Juan, J., Jensen, M. P., & Miró, J. (2024) The increase in early menarche is associated with the increase of chronic back pain in female adolescents: The HBSC study 2002-2014. *Clinical Journal of Pain* (under review).
- Study IV. Roman-Juan, J., Roy, R., Jensen, M. P., & Miró, J. (2022). The explanatory role of sedentary screen time and obesity in the increase of chronic back pain amongst European adolescents: The HBSC study 2002–2014. *European Journal of Pain*, *26*(8), 1781-1789.

- Study V. Roman-Juan, J., Jensen, M. P., & Miró, J. (2024). Increases in Sleep Difficulties and Psychological Symptoms are Associated with the Increase of Chronic Back Pain in Adolescents: The HBSC Study 2002 to 2018. *The Journal of Pain*, *25*(2), 407-417.
- Study VI. Roman-Juan, J., Solé, E., Sánchez-Rodríguez, E., Castarlenas, E., Jensen, M. P., & Miró, J. (2023b). Validation of the pediatric version of the Graded Chronic Pain Scale Revised in school-aged children and adolescents. *PAIN*, *164*(11), 2606-2614.
- Study VII. Roman-Juan, J., Ceniza-Bordallo, G., Sánchez-Rodríguez, E., Jensen, M. P., & Miró, J. (2024). Fatigue, sleep disturbance, and pain interference in children and adolescents with chronic pain: a longitudinal study. *PAIN* (under review).
- Study VIII. Roman-Juan, J., Sánchez-Rodríguez, E., Solé, E., Castarlenas, E., Jensen, M. P., & Miró, J. (2023). Psychological factors and pain medication use in adolescents with chronic pain. *Pain Medicine*, *24*(10), 1183-1188.
- Study IX. Roman-Juan, J., Solé, E., Sánchez-Rodríguez, E., Castarlenas, E., Jensen, M. P., & Miró, J. (2023a). Adverse childhood events and chronic pain in adolescents: the role of sleep disturbance. *Journal of pediatric psychology*, *48*(11), 931-939

4.1. Study I

Chronic pain and high impact chronic pain in children and adolescents: a cross-sectional study.

USASP
US ASSOCIATION FOR THE STUDY OF PAIN

PUBLISHED BY
ELSEVIER

The Journal of Pain, Vol 24, No 5 (May), 2023: pp 812–823
Available online at www.jpain.org and www.sciencedirect.com

Chronic Pain and High Impact Chronic Pain in Children and Adolescents: A Cross-Sectional Study

Jordi Miró,[*,†] Josep Roman-Juan,[*,†] Elisabet Sánchez-Rodríguez,[*,†] Ester Solé,[*,†] Elena Castarlenas,[*,†] and Mark P. Jensen[‡]

[*]*Universitat Rovira i Virgili,* [†]*Department of Psychology, URV, Institut d'Investigació Sanitària Pere Virgili, Universitat Rovira i Virgili, Catalonia, Spain,* [‡]*Department of Rehabilitation Medicine, University of Washington, Seattle, Washington*

Abstract: **The aims of this study were to: 1) estimate the prevalence of chronic pain (CP) and high impact chronic pain (HICP) in a community sample of children and adolescents; and 2) compare groups (those without CP, those with CP but no HICP, and those with HICP) with respect to demographic variables, pain variables, and physical, psychological, and school-related function. One thousand one hundred and fifteen children and adolescents participated (56% girls; age: $\bar{x}$ = 11.67; SD = 2.47; range = 8–18 years). The prevalence of CP and HICP was 46% and 5%, respectively, and was higher in girls and increased with age. Participants with HICP reported greater pain intensity and higher pain frequency than those with CP but no HICP. In addition, participants with HICP reported lower mobility, greater fatigue, worst sleep quality, more anxiety and depression symptoms, worst cognitive function, missing more school days, and worse perceived school performance. HICP is a prevalent condition in children and adolescents and is associated with many negative consequences. Stakeholders must be aware of this and ensure that treatment programs are available to reduce the individual and societal impact of HICP in young individuals.**

Perspective: ***This article provides information on CP and HICP prevalence and impact in children and adolescents. By better understanding the nature and score of these conditions, we will be able to develop more effective early interventions to help this population and thereby reduce their long-term negative impact.***

Key words: *High impact chronic pain, adolescents, epidemiology, sex, prevalence.*

Chronic pain (ie, pain lasting 3 or more months[39,48]; is a common problem among children and adolescents,[19] with negative consequences to the individual,[15,23,24] the family,[49] and society.[13] Recent studies have noted the rise in the prevalence of chronic pain over the past few decades. For example, Roy and colleagues[41] reported an overall increase of 3% from 2001 to 2014 in the prevalence of chronic back pain among adolescents, using data from the Health Behavior in School-Aged Children study.[4]

Epidemiology research is key to understanding chronic pain.[3] Understanding its prevalence in different age groups helps to better appreciate developmental trajectories,[18] and epidemiological research identifying the determinants of chronic pain can inform the development of more effective interventions and improve management.[25] A number of studies have identified factors that are associated with chronic pain in children,

Received July 6, 2022; Revised December 16, 2022; Accepted December 16, 2022.
Funding Sources: Financial support for this activity was provided, in part, by grants from the Spanish Ministry of Economy, Industry and Competitiveness (RTI2018-09870-B-I00; RED2018-102546-T; PRE2019-089283), the Spanish Ministry of Science and Innovation (MCIN/AEI/10.13039/501100011033; PID2020-113869RA-I00; PID2020-114146RJ-I00)), the European Regional Development Fund (ERDF), the Government of Catalonia (AGAUR; 2017SGR-1321), and Universitat Rovira i Virgili (PFR program). JM's work is supported by Fundación Grünenthal and ICREA-Acadèmia.
Disclosures: The authors declare no financial or other relationships that might lead to a conflict of interest related to this study.
Address reprint requests to Jordi Miró, PhD, Departament de Psicologia, Universitat Rovira i Virgili, Carretera de Valls, s/n, 43007 Tarragona, Spain. E-mail: jordi.miro@urv.cat
1526-5900/$36.00

https://doi.org/10.1016/j.jpain.2022.12.007

including demographic (eg, female sex[17];), physical (eg, pain extension[12];), psychosocial (eg, anxiety[20,21];), and school-related factors (eg, school performance[20]).

Most epidemiology studies, however, report findings as if the population of children with chronic pain was homogenous. However, this is a heterogeneous group, and individual differences may explain the extent and impact of chronic pain.[12,28] For example, treatment outcomes have been shown to be associated to individual differences.[53] In addition, prior studies have mostly defined chronic pain by its duration only (eg, as being present for more than 3 months; cf.[15]) or used a combination of duration and frequency (eg,[12]). However, chronic pain does not affect individuals equally, and these definitions of "chronic pain" do not take into consideration its impact.[37]

The concept of high impact chronic pain (HICP) has been proposed to better identify individuals with significant levels of life interference due to chronic pain.[8] Moreover, individuals with HICP account for the largest share of the economic costs of chronic pain.[55] There has been a call to study HICP in specific populations, including children.[55] However, to the best of our knowledge, no study has yet examined the prevalence and correlates of HICP in children and adolescents. Determining the prevalence of chronic pain in general and HICP in particular in children and adolescents can help define the special needs of these populations, and therefore inform decisions regarding resource allocation. In addition, most epidemiology studies with youth are conducted with adolescents. Research that includes younger children is also needed to apply a lifespan developmental perspective to the study and treatment of young individuals with chronic pain.[57]

Given these considerations, the objectives of the current research were to: 1) estimate the prevalence of chronic pain and HICP in a community sample of both younger children and adolescents; and 2) compare the subsamples within the study – specifically participants who do not have chronic pain, those who have chronic pain that is not high impact (No HICP), and who have HICP – with respect to demographic, pain, and physical, psychological, and school-related function variables. Based on the prior studies conducted with adult samples,[37] we hypothesized that: 1) participants with No HICP would report worse functioning in all domains compared to participants who do not have CP, and 2) participants with HICP would report worse function in all domains compared to participants who have chronic pain that is not high impact.

Methods

Procedure

This is a cross-sectional analysis of data from the EPIDOL Project (which is a longitudinal epidemiological study of pain in children and adolescents conducted in the South East of Catalonia, Spain). Data for this study were collected before the lockdown due to COVID-19. The ethics committee of the Universitat Rovira i Virgili approved the study (*Institut d'Investigació Sanitària Pere Virgili; ref.: 136/2018)*. Current analysis, reported in this article, used baseline data from the EPIDOL project only.

Eleven schools were approached to participate; one did not accept the invitation, reporting that the staff did not have the time to participate. Schools were randomly selected from all (nonspecial) schools in the region. Study data were collected from children and adolescents attending 4 primary schools, 3 secondary schools, and 3 schools which both education levels in Reus, Catalonia (Spain).

Following the acceptance of study participation by the school boards, all parents of children aged from 8 to 18 attending these schools (N = 3,167) were mailed a letter describing the project and asking them to provide consent for their children to participate. Thirty-six percent of these parents agreed (N = 1,142), and 35 percent of the children (N = 1115) provided data and were included in the analyses for this study. The children of these parents were then asked to respond to a paper-and-pencil survey during the school day, following instructions provided by research staff. Of the total school children included in the study, 12% (N = 136) did not finish the questionnaire or skipped questions.

In order to participate, both the students and their parents had to provide their assent and consent, respectively. Participating students received a gym sack and a calendar for their participation (approximate value = €3 each). In an effort to enroll as many interested participants as possible, we scheduled additional assessment sessions for those that were absent at the first time of data collection.

Measures

Demographic Information

The children who participated were asked to provide information regarding their sex, age, and school grade.

Pain Characteristics: Pain Location, Pain Extent, Frequency, and Intensity

The participants were asked to provide information about the characteristics of any significant pain problem(s) they had experienced in the last 3 months, including the pain(s)' location(s), frequency, and intensity. We used a pain site checklist to assess *pain location*. It included 11 specific locations (ie, head, neck, chest, shoulders, back, arms, hands, bottom/hips, belly/pelvis, legs, and feet) and an "other" category. This pain site checklist has been used in previous studies.[6,26,27] *Pain extent* was computed by summing all of the locations with pain (possible range, 0–12). *Pain frequency* for each pain problem was assessed using a 5-point Likert scale (1 = "Every day," 2 = "More than once a week," 3 = "Once a week," 4 = "Once or twice times per month," 5 = "Once in the last 3 months"). Finally, children reported the usual (average) *pain intensity* in the

last 7 days for each pain location, using a 0 to 10 Numerical Rating Scale (NRS-11) where 0 = "No pain" and 10 = "Very much pain." The NRS-11 has been shown to provide reliable and valid scores when used with children as young as 6 years old.[1]

On the basis of current definitions[39] and previous epidemiology studies,[17,20,42,56,60] we defined chronic pain as a pain that has lasted for at least 3 months and that was present at least once a week during this 3-month period. Using this definition in the current study allowed us to be able to compare the results with other highly cited studies (eg,[20]). For descriptive purposes, one primary pain location was chosen for each participant with chronic pain for purposes of describing pain frequency and intensity. For those participants with pain in only one site, their chronic pain location was defined as the pain problem at this site. For those reporting chronic pain at more than one site, the primary pain location was defined as that location associated with the highest reported average pain intensity. Following Wager and colleagues' procedures,[56] when participants reported the same pain intensity at more than one site (n = 46 in the current study), or participants neglected to rate pain intensity at all of the pain sites indicated (n = 68 in the current study), the participant's primary pain location was defined as that location they indicated which had the highest prevalence in the sample as a whole (ie, based on the following order list of pain locations: headache, back pain, leg pain, feet pain, belly/pelvis pain, neck pain, shoulder pain, arm pain, "other" pain, chest pain, hand pain and abdominal pain and bottom/hips, respectively; for example, if a participant rated leg pain and chest pain as having the same pain intensity, that participant's primary pain was defined as being leg pain, because leg pain is more common than chest pain in the sample as a whole).

Pain-Related Interference

We used the Spanish version of the 8-item Pediatric Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference scale v2.0 (PROMIS-PI[51];) to assess pain interference. With the PROMIS-PI, respondents are asked to rate how often pain has interfered with 4 activities during the last 7 days using a 5-point Likert scale (1= "Never," 2="Almost never," 3="Sometimes," 4="Often," and 5="Almost always"). Sample items include "It was hard for me to walk one block I had pain" and "It was hard for me to pay attention when I had pain." In order to obtain pain interference scores, the participants' ratings for each item were summed and this total sum was transformed to a T-score. Higher scores reflect higher pain interference. The pediatric form of the PROMIS-PI has been shown to provide valid and reliable data of pain interference in children and adolescents.[50] In this sample, the Cronbach's alpha was good (α = .86).

Based on the participants' reports of having chronic pain or not, as well as their level of pain interference for those who did have chronic pain, we classified the sample into 3 groups: 1) those without chronic pain (No CP); 2) those with chronic pain but not with HICP (No HICP); and (3) those with HICP. The definition of HICP that was used in this study is based on the one published by von Korff and colleagues, which defines HICP as pain limiting life or work activities most or every day in the previous 3 months.[54] The labels given to PROMIS Pain Interference Scale score ranges are as follows: 0 to 49.9 = "pain interference within normal limits"; 50 to 54.9 = "mild pain interference"; 55 to 64.9 = "moderate pain interference"; and 65 to 100 = "severe pain interference".[32] In this study, participants were classified as having HICP if they had both CP and a PROMIS Pain Interference Scale T-score $\geq$ 65 (ie, $\geq$1.5 SD units). Those with CP with PROMIS-PI scales <65 were classified as being into the No HICP group. Those without CP were put into the No CP group.

Physical Function

Participants were asked to respond to measures assessing mobility, fatigue, and sleep quality. We used the Spanish version of the 4-item physical function-mobility from the Pediatric-25 Profile Form v.2 (PROMIS-PF-M[50,9];) to assess mobility. With this scale, respondents are asked to indicate how able they were to perform 4 activities during the last 7 days using a 5-point Likert scale (1 = "Not able to do," 2 = "With a lot of trouble," 3 = "With some trouble," 4 = "With a little trouble," and 5 = "With no trouble"). Sample items include "I could do sports and exercise that other kids my age could do" and "I could walk up stairs without holding on to anything." Responses were summed and transformed to T-scores. Higher scores reflect being better able to be mobile. Evidence supports the reliability and validity of the pediatric form of the PROMIS-PF-M in children and adolescents.[50] In the current sample, the Cronbach's alpha was acceptable (α = .79).

We used the Spanish version of the 4-item fatigue short form from the PROMIS Pediatric-25 Profile Form v.2 (PROMIS-F[50];) to assess fatigue. With the PROMIS-F, respondents are asked to rate how often they experience each fatigue response in the last 7 days using a 5-point Likert scale (1 = "Never," 2 = "Almost never," 3 = "Sometimes," 4 = "Often," and 5 = "Almost always"). Sample items include "Being tired made it hard for me to keep up with my schoolwork" and "I was too tired to enjoy the things I like to do." In order to obtain fatigue scores, responses were summed and transformed to T-scores. Higher scores in the PROMIS-F reflect greater fatigue. Previous research supports the reliability and validity of the PROMIS-F items provide for assessing fatigue in children and adolescents.[38] In this sample, the Cronbach's alpha was borderline acceptable (α = .68).

We used the Spanish version of 5 sleep disturbance items of the item Bank v1.0 of the PROMIS[38]) to assess sleep quality. The PROMIS Sleep Disturbance scale (PROMIS-SD) contains items that assess a variety of sleep quality indicators, and scores from this scale have been shown to provide valid and reliable information about sleep quality when used with young individuals.[11,14]

With this scale, respondents are asked to indicate the frequency with which they experienced each sleep problem indicator during the last 7 days using a 5-point Likert scale (1 = "Never," 2 = "Almost never," 3 = "Sometimes," 4 = "Often," and 5 = "Almost always"). Sample items include "My sleep was refreshing" and "I had a problem with my sleep." In order to obtain sleep disturbance scores, responses were summed and transformed to T-scores. Higher scores in the PROMIS-SD reflect greater sleep disturbance. The internal consistency of the measure in the current sample was good (α = .80).

Psychological Function

Participants were asked to respond to measures of cognitive function, anxiety, and depressive symptoms. We used the Spanish version of the 7-item PROMIS pediatric cognitive function short form v1.0 (PROMIS-CF[9,50];) to assess cognitive function. With this scale, respondents are asked to indicate how often they had experienced problems with 7 different cognitive function domains during the last 4 weeks using a 5-point Likert scale (1 = "All the time," 2 = "Most of the time," 3 = "Some of the time," 4 = "A little of the time," and 5 = "None of the time"). Sample items include "I have to read things several times to understand them" and "I have trouble keeping track of what I am doing if I get interrupted." In order to obtain cognitive function scores, the participants' responses were summed and transformed to T-scores. Higher scores reflect better cognitive function. Research supports the reliability and validity of the scores of the pediatric form of the PROMIS-CF.[50] In this sample, the Cronbach's alpha was good (α = .83).

Anxiety was assessed using the Spanish version of the anxiety subscale of the PROMIS Pediatric-25 Profile Form v2.0.[50] With the PROMIS-A, respondents are asked to rate the frequency with which they experienced 4 anxiety symptoms in the last 7 days using a 5-point Likert scale (1 = "Never," 2 = "Almost never," 3 = "Sometimes," 4 = "Often," and 5 = "Almost always"). Sample items include "I felt something awful might happen" and "I felt nervous." Responses to the PROMIS-A items were summed and transformed to T-scores. Higher scores reflect more frequent anxiety symptoms. The Pediatric-25 Profile Form scales have been shown to be able to report reliable and valid scores of anxiety symptoms.[38] In this sample, the Cronbach's alpha indicated good internal consistency (α = .85).

Depressive symptom severity was assessed using the Spanish version of the Depressive Symptoms subscale of the PROMIS Pediatric-25 Profile Form v2.0 (PROMIS-DS[50];). With this measure, respondents are asked to rate the frequency with which they experienced 4 depressive symptoms in the last 7 days using a 5-point Likert scale (1 = "Never," 2 = "Almost never," 3 = "Sometimes," 4 = "Often," and 5 = "Almost always"). Sample items include "I felt everything in my life went wrong" and "It was hard for me to have fun." In order to obtain PROMIS-DS scores, the participants' responses were summed and transformed to T-scores. Higher scores reflect greater depressive symptoms. The Pediatric-25 Profile Form scales have been shown to be able to report reliable and valid scores depressive symptoms.[38] In this sample, the Cronbach's alpha for the PROMIS-DS was good (α = .83).

School Function

Participants were asked to respond to 2 different and independent questions related to 1) the number of missed days due to pain in the previous 3 months, and 2) perceived school performance relative to other classmates. In response to the question about the number of missed days due to pain, participants were asked to report: 1) the total number of full/complete days missed, and 2) total number of partial/non-complete days missed in the past 3 months. The sum of both scores was the score used in the analysis. In relation to *perceived school performance*, participants were asked to respond to the following question "Compared to the majority of your classmates, what is your academic performance like?" using a 5-point Likert scale (1 = "Much worse," 2 = "Worse," 3 = "Equal," 4 = "Better," and 5 = "Much better"). The responses to each question were examined separately in the data analyses.

Data Analyses

We first computed percentages, means, and standard deviations of the sociodemographic and study variables to describe the sample. Chi-Square tests and t-tests were conducted to compare sex and age differences on pain locations respectively for the whole sample. Next, we computed the number and rates of individuals in each of the 3 study groups (No CP, No HICP, and HICP) in the sample. We then compared the three study groups (ie, No CP, No HICP, and HICP) with respect to demographic and physical-, psychological-, social-, and school-related characteristics. For continuous variables (ie, age, physical function-mobility, fatigue, sleep disturbance, cognitive function, anxiety, depression, and pain-related school absence), we used Univariate Analyses of Variance (ANOVA); for nominal variables (ie, sex), we used Chi-Square tests; and for ordinal variables (ie, perceived school performance), we used Kruskal-Wallis tests. Bonferroni-adjusted post hoc tests were conducted to identify differences between the study groups. We then compared the CP and the HICP groups with respect to pain-related characteristics. For continuous variables (ie, pain intensity and pain extension), we used univariate t-tests; for nominal variables (ie, pain location), we used Chi-Square tests; and for ordinal variables (ie, pain frequency), we used Kruskal-Wallis tests. Pairwise deletion was used to handle missing values.

Effect sizes were reported using the *Cramér's V* (interpretation depending on degrees of freedom according to Cohen)[2] for the Chi-Square tests; the partial η^2 (Cohen, 1988) for ANOVAs (small effect: η^2_p = 0.01, medium effect: η^2_p = 0.06; large effect: η^2_p = 0.14); the ε^2 (small effect: ε^2 = 0.01, medium effect: ε^2 = 0.06; large effect: ε^2 = 0.14) [47] for the Kruskal-Wallis tests; and the

Cohen's *d* (small effect: *d* = 0.2; medium effect: *d* = 0.6; large effect: *d* = 0.8)[2] for univariate t-tests. A 2-tailed significance level of $P < .05$ was defined as statistically significant. Data analyses were conducted using SPSS version 28.01 (IBM, Armonk, NY, USA), and STATA 14 (Stata Corp., Texas, USA).

Results

Sample Characteristics

Table 1 provides a summary of the characteristics of the participants. The sample included a higher number of girls (n = 630; 56%) than boys (n = 485; 44%). The mean age of the participants was 11.67 years (SD = 2.47; range = 8–18). This sample was a healthy sample for the most part (only 27% reported having an illness in the previous 3 months).

Most of the participants (89%; see Table 2) reported having experienced pain in the past three months of responding to the survey, and 57% of these reported that they missed school due to pain problems (mean number of full days missed = 3.54, SD = 3.57; mean number of partial days missed = 2.52, SD = 2.56). Also, a substantial subset of participants reported having

Table 1. Descriptive Statistics for Demographic, Physical, Psychosocial, and School-Related Characteristics of Participating Children and Adolescents (n = 1,115)

Variable (Range	*N*	*%*	*Mean*	*SD*
Sex				
Female	630	56		
Male	485	44		
Age* (8–18)	1,114		11.67	2.47
Physical function				
Mobility† (20–80)	1,076		48.49	9.04
Fatigue‡ (20–80)	1,071		49.88	10.93
Sleep quality§ (20–80)	1,065		49.64	9.45
Psychological function				
Cognitive function# (20–80)	1,057		48.75	7.59
Anxiety‡ (20–80)	1,071		52.49	11.46
Depression‖ (20–80)	1,075		51.02	10.79
Perceived School performance‡‡				
Much worse	29	3		
Worse	102	9		
Equal	471	42		
Better	326	29		
Much better	122	11		

Note: Range for age is actual range in the sample, whereas Ranges for the measures represent possible ranges for each variable. Pain intensity reports average pain intensity. The numbers in "n" vary among variables due to the number of missing information in each case
*n = 1,114 (missing = 1).
†n = 1,076 (missing = 39).
‡n = 1,071 (missing = 44).
§n = 1,065 (missing = 50).
#n = 1,057 (missing = 58).
‖n = 1,075 (missing = 40).
¶n = 853 (missing = 136).
**n = 882 (missing = 107).
††n = 881 (missing = 108).
‡‡n = 1,050 (missing = 65).

Table 2. Descriptive Statistics for Pain-Related Characteristics of Participating Children and Adolescents (n = 1,115)

Variable (Range)	*N*	*%*	*Mean*	*SD*
Pain prevalence				
Pain in the past 3 months*	989	89		
Pain location				
Head	593	53		
Neck	288	26		
Chest	141	13		
Shoulders	186	17		
Back	358	32		
Arms	169	15		
Hands	151	14		
Bottom/Hips	87	8		
Belly/Pelvis	402	36		
Legs	358	32		
Feet	295	26		
Other	102	9		
Pain extent (0–12)			2.80	2.24
0	126	11		
1	225	20		
2	257	23		
3	167	15		
≥4	340	30		
Chronic pain (≥weekly pain for ≥3 months)	510	46		
Chronic pain location				
Head‡	201	18		
Neck§	102	9		
Chest#	43	4		
Shoulders‖	83	7		
Back¶	180	16		
Arms#	48	4		
Hands**	42	4		
Bottom/hips#	23	2		
Belly/Pelvis††	106	10		
Legs‡‡	122	11		
Feet§§	113	10		
Other##	46	4		
Chronic pain extent (0-12)			1.03	1.49
0†	605	54		
1	221	20		
2	129	12		
3	82	7		
≥4	78	7		
Pain-related school absence‖‖ (n = 989)				
No absence	288	29		
Absence	565	57		
Full days¶¶	464	47	3.54	3.57
Partial days***	426	43	2.51	2.56
Chronic pain characteristics (n = 510)				
Most intense chronic pain location				
Head	132	26		
Neck	22	4		
Chest	14	3		
Shoulders	23	5		
Back	90	18		
Arms	14	3		
Hands	7	1		
Bottom/hips	3	1		
Belly/Pelvis	59	12		
Legs	65	13		

(*continued on next page*)

Table 2. Continued

Variable (Range)	*N*	*%*	*Mean*	*SD*
Feet	56	11		
Other	25	5		
Pain frequency				
Once a week	130	25		
More than once a week	233	46		
Every day	147	29		
Pain intensity-Average in the past 7 days††† (0-10)	442		6.06	2.37
Pain interference‡‡‡ (20-80)	483		53.58	9.04

*Forty-seven participants reported pain but did not report the frequency and/or duration, thus could not be determined if the pain was or not chronic.
†Includes the 47 participants that reported pain in the previous 3 months but did not provide additional information to classify the pain as chronic. The numbers in "n" vary among variables due to the number of missing information in each case.
‡n = 1,094 (missing = 21).
§n = 1,100 (missing = 15).
#n = 1,109 (missing = 6).
‖n = 1,108 (missing = 7).
¶n = 1,098 (missing = 17).
**n = 1,003 (missing = 12).
††n = 1,095 (missing = 20).
‡‡n = 1,099 (missing = 16).
§§n = 1,096 (missing = 19).
##n = 1,110 (missing = 5).
‖‖n = 853 (missing = 136).
¶¶n = 882 (missing = 107).
***n = 881 (missing = 108).
†††n = 442 (missing = 68).
‡‡‡n = 483 (missing = 27).

experienced pain (any type of pain, including chronic pain) in the past 3 months at more than one site (n = 764; 68%). The most frequent locations were the head (53%), the belly/pelvis (36%), the back and legs with the same percentage (32%); less common pain locations were the chest (13%) and the bottom/hips (8%). Girls reported pain in the head, neck, chest, back, bottom/hips, and belly/pelvis more frequently than boys. Boys reported pain in the legs more frequently than girls (see Supplementary Table 1).

The analyses indicated that there were age differences with respect to pain locations, such that participants who reported pain in the head, neck, chest, shoulders, back, arms, hands, bottom/hips, belly/pelvis, legs, and feet were significantly older than those that did not report pain in those locations (see Supplementary Table 2). The sample had fewer children (n = 247; 22%) than adolescents (n = 868; 78%; the World Health Organization defines adolescence as the phase of life that goes from 10 to 19 years old, see https://www.who.int/health-topics/adolescent-health#tab=tab_1). Sixty-four percent of children (n = 159) did not report chronic pain, 19% (n = 48) reported no HICP, and 3% (n = 7) reported HICP. With respect to the adolescent subsample, 46% (n = 399) did not report chronic pain, 44% (n = 383) reported no HICP, and 5% (n = 45) reported HICP. Given the very small sample size of children with HICP (n = 7) compared to the sample size of adolescents with HICP (n = 45), we compared the prevalence of chronic pain status (ie, No CP, No HICP, and HICP) in the sample as a whole, collapsed across age group.

Prevalence of Chronic Pain

Regardless of the impact, the prevalence of chronic pain (ie, pain that lasted for at least three months and was present at least once a week) in any location was

Table 3. Pain-related Characteristics of Participants in the High Impact Chronic Pain (HICP) Group Compared With Participants in the Chronic Pain that is not High Impact (No HICP)Group

	No HICP (N = 431)			*HICP (N = 52)*				
CP Characteristics	*N*	*% Within Subsample*	*M (SD)*	*N*	*% Within Subsample*	*M (SD)*	*CP vs HICP*	*P (Effect Size)*
Most intense chronic pain location	431			52			$X^2_{(11)} = 9.93$	.536 (0.14)
Head		26			31			
Neck		4			4			
Chest		2			8			
Shoulders		4			6			
Back		18			15			
Arms		3			0			
Hands		2			0			
Bottom/hips		1			0			
Belly/Pelvis		11			12			
Legs		13			10			
Feet		11			13			
Other		5			2			
Pain extent	431		2.12 (1.44)	52		2.52 (1.70)	$t_{(481)} = -1.82$	.069 (-0.26)
Pain Frequency	431			52			$X^2_{(1)} = 10.59$	.001 (0.02)
Once a week		27			10			
More than once a week		46			46			
Every day		27			44			
Pain Intensity	366*		5.82 (2.35)	49†		7.39 (2.08)	$t_{(413)} = -4.43$	<.001 (-0.67)

Note: The numbers in "n" vary among variables due to the number of missing information in each case
*n = 366 (missing = 65).
†n = 46 (missing = 6).

high (n = 510; 46%). The head was the most common location, experienced by 18% of the sample, followed by the back (16%) and the legs (11%), whereas the arms (4%), chest (4%), hands (4%), and bottom/hips (2%) were the less frequently locations reported.

High Impact Chronic Pain

With the definition of HICP used in this study, the prevalence of HICP in the sample was 5%. The prevalence of HICP was higher for girls than for boys (8% vs 2%, $X^2_{(1)} = 19.76$, $P < .001$) and participants with HICP were significantly older than those without HICP (mean = 12.46, SD = 2.75 vs mean = 11.70, SD = 2.45, $t_{(1,038)} = 2.16$, $P = .031$).

The locations of reported HICP were diverse. However, the most frequent locations were the head (31%), back (15%), and lower extremities (legs: 15%; feet: 14%). There were no significant differences in locations between girls and boys but there were differences related to age. In this sample, participants reporting pain in the head were older (mean = 13.56 years, SD = 2.73 vs mean = 11.59 years, SD = 2.49, $T_{(50)} = 2.73$, $P = .009$) and participants reporting pain in the feet were younger (mean = 10.87 years, SD = 1.86 vs mean = 13.16 years, SD = 2.81, $t_{(50)} = -2.97$, $P = .004$). Pain extent (ie, the number of locations with chronic pain) was 2.52 (SD = 1.70) and most participants (n = 32; 62%) reported multi-site chronic pain. However, there were no differences in pain extent between participants in the HICP and No HICP group (see Table 3).

Participants in the HICP group reported greater pain intensity (mean = 7.39; SD = 2.08) and a higher pain frequency (eg, almost half of them reported experiencing pain every day), than those in the No HICP group (see Table 3). In addition, participants in the HICP group reported worse physical function (ie, lower mobility, greater fatigue, and worst sleep quality), and psychological function (ie, more anxiety and depression symptoms, and worst cognitive function) than those in the No CP group (see Table 4). The data also showed significant differences in relation to school-related characteristics; that is, those with HICP reported missing more school days and worse perceived school performance than those in the No CP and the No HICP groups. Participants in the HICP group also reported worse perceived school performance than those in the No CP group, although no differences were found between the HICP and No HICP groups (see Table 4).

Discussion

The aims of this study were to estimate the prevalence of CP and HICP in a community sample of children and adolescents, and compare individuals in the 3 groups (ie, No CP, No HICP, and HICP) with respect to their demographic, pain, and physical, psychological, and school-related function. Four key findings emerged. First, the prevalence of CP in this community sample of children and adolescents was high (46%), in line with findings reported in other studies of children like this sample.[12,52] However, in this study the prevalence of CP was higher than the one found in a study that we conducted 15 years ago in the same region with a similar sample of participants (37%[17];). There are a number of potential explanations for these differences, which are not mutually exclusive. First, although the samples were for the most part similar, there is a slight age-related difference between the samples (ie, the current sample had a larger age range: 8–18 years old, whereas in the previous study the age range was 8 to 16 years old, and research has shown that chronic pain prevalence increases with age.[44] In addition, the two samples might be different in other ways that we could not evaluate here. Second, we used different procedures for data collection for the two studies. In our previous study (ie,[17]) the information was collected using individual interviews. In the current study, we used a written survey. A recent meta-analysis[43] showed that collecting data with an interview method is associated to lower CP prevalence rates than data collected via questionnaires. It is also possible that the differences in prevalence rates found between the 2 studies might be associated with an actual increase in the rates of CP over time. Such a possibility would be consistent with recent findings[41] showing an increase in the prevalence of chronic back pain among adolescents in a study with samples from 33 countries and/or regions. Studies using children and adolescents from additional populations are needed to confirm whether the prevalence of CP in children is increasing in Spain and other locations. Moreover, research to study the factors responsible for such increases, if they are present, is also warranted.[40] Particularly, research should seek to identify the modifiable factors that may be responsible for the increase in CP prevalence, as such findings could inform the development of strategies that could reduce the prevalence of CP. Research has shown that as pain becomes chronic, it becomes increasingly difficult to treat, and CP has long-term effects on children and adolescents. For example, in a study with a cohort of pediatric patients with functional abdominal pain that was followed for 15 years, the data showed that 35% of the patients continued to experience abdominal pain into adulthood, and showed an increased risk for depression and anxiety.[58] Thus, it is important to implement effective treatment as soon as possible to help improve life course trajectories for these individuals.

A second key finding is that the prevalence of HICP was also found to be high, relative to the prevalence found in other studies. The 5% rate we found here is higher, for example, than the 1% to 2% prevalence reported in estimations of children in the highest level of chronic pain-related disability reported in previous studies, including a study conducted with a sample with similar characteristics and from the same region,[17,20] but similar to other studies with samples of children (see[44]). The same potential explanations for the differences found between studies apply. Nevertheless, the findings suggest that not only might CP be increasing in frequency, but the most severe cases may also be growing. If this were a

Table 4. Demographic, Physical, Psychological, and School-Related Characteristics of Participants in the High Impact Chronic Pain (HICP) Group Compared with Participants in the Chronic Pain (CP) and the Chronic Pain that is not High Impact (No HICP) Groups (n = 1,041)

	No CP (N = 558; 54%)			*No HICP (N = 431; 41%)*			*HICP (N = 52; 5%)*					
Characteristics	*N*	*% Within Subsample*	*M (SD)*	*N*	*% Within Subsample*	*M (SD)*	*N*	*% Within Subsample*	*M (SD)*	*Chi Square Test*	*P (Effect Size)*	*Post Hoc Comparisons**
Demographics												
Sex										$X^2_{(2)} = 29.46$	<.001 (0.17)	
Female	284	49		262	61		45	87				No CP < No HICP < HICP
Male	274	51		169	39		7	13				No CP > No HICP > HICP
										One-way ANOVA	*P* (effect size)	Post Hoc Comparisons
Age in years	557†		11.03 (2.27)	431		12.57 (2.41)	52		12.46 (2.75)	$F_{(2,1037)} = 54.92$	<.001 (0.09)	No CP < No HICP, HICP
Physical function												
Mobility	537‡		49.06 (9.08)	423§		48.63 (8.44)	51#		41.90 (10.60)	$F_{(2,1008)} = 15.13$	<.001 (0.03)	No CP, No HICP > HICP
Fatigue	531‖		47.26 (10.73)	425¶		51.37 (9.97)	52		63.27 (9.63)	$F_{(2,1002)} = 64.72$	<.001 (0.11)	No CP < No HICP < HICP
Sleep quality	529**		47.78 (9.15)	423§		50.93 (8.99)	52		58.57 (10.26)	$F_{(2,1001)} = 39.92$	<.001 (0.07)	No CP < No HICP < HICP
Psychological function												
Cognitive function	524††		50.17 (7.20)	422‡‡		47.90 (7.34)	52		42.56 (7.76)	$F_{(2,995)} = 31.54$	<.001 (0.06)	No CP > No HICP > HICP
Anxiety	532§§		49.61 (10.42)	424##		54.53 (11.03)	51#		65.56 (12.27)	$F_{(2,1004)} = 64.05$	<.001 (0.11)	No CP < No HICP < HICP
Depressive symptom severity	532§§		47.78 (9.28)	427‖‖		53.54 (10.71)	52		63.61 (11.56)	$F_{(2,1008)} = 82.15$	<.001 (0.14)	No CP < No HICP < HICP
School function												
Number of days of pain-related school absence	369¶¶		2.33 (3.65)	383***		3.08 (3.95)	46		6.09 (7.53)	$F_{(2,944)} = 20.63$	<.001 (0.04)	No CP < No HICP < HICP
										Kruskal Wallis test	*P* (effect size)	Post Hoc Comparisons*
Perceived school performance	517†††			418§§§			50###			$X^2_{(2)} = 10.42$	.005 (0.01)	
Much worse		1			4			10				No CP < No HICP, HICP
Worse		6			11			17				No CP < No HICP, HICP
Equal		44			40			40				n.s.
Better		30			30			19				n.s.
Much better		11			11			10				n.s.

*shows the order of groups in each comparison; The numbers in "n" vary among variables due to the number of missing information in each case.
†n = 557 (missing = 1).
‡n = 537 (missing = 21).
§n = 423 (missing = 8).
#n = 51 (missing = 1).
‖n = 531 (missing = 7).
¶n = 425 (missing = 6).
**n = 529 (missing = 29).
††n = 524 (missing = 34).
‡‡n = 422 (missing = 9).
§§n = 532 (missing = 26).
##n = 424 (missing = 7).
‖‖n = 427 (missing = 4).
¶¶n = 369 (missing = 63).
***n = 383 (missing = 48).
†††n = 46 (missing = 6).
‡‡‡n = 517 (missing = 41).
§§§n = 418 (missing = 13).
###n = 50 (missing = 2).

reliable finding, it would mean, a call to action to address and reduce the individual and societal impact of No HICP and HICP in children and adolescents should be issued. A regional or national chronic pain strategy would require the participation of all stakeholders and the inclusion of different actions, including but not limited to increasing the number of specialized treatment programs,[31] improving the training of primary healthcare professionals,[30] and taking advantage of the digital tools (eg, mobile applications) which have already shown that can facilitate access to health care (eg,[7,22]).

A third key finding from this study is that there were differences in HICP related to sex and age, in that HICP prevalence was higher in girls than boys, and that the age of those with HICP was significantly higher than in those with CP. Furthermore, in this study, 60% of the participants with HICP reported chronic pain in at least 2 sites, and 25% reporting 4 or more sites. This finding is consistent with research showing that multisite pain is more prevalent than single site pain in individuals with CP regardless of the impact.[16,35,36,46]

Epidemiology studies have also shown that being female is a risk factor for a large variety of CP conditions.[44] Research should study the factors that are associated with the higher prevalence of CP among girls. It has not yet been determined if there are CP treatments that may be better suited for girls and women than for boys and men. However, there is an evidence of different practices and treatments used with women and men. For example, a study with adults, found that female patients were more likely to receive a larger variety of pain treatments than male patients, including both contraindicated and recommended polypharmacy.[34]

The fourth key study finding – perhaps not surprising – is that participants with HICP were severely impacted in all studied domains. Specifically, participants with HICP reported higher levels of physical (ie, fatigue and sleep disturbance), psychological (ie, greater symptoms of anxiety and depression, and worst cognitive function), and school (ie, were less able to attend school due to pain) dysfunction than those with no CP and No HICP. There is mounting evidence showing the deteriorating effects of CP on young individuals' general health and well–being,[45] which may negatively influence their physical, psychological, and social development. This finding has also practical implications. Importantly, that treatments for children and adolescents with CP should be multidisciplinary,[59] and address the whole person rather than to the CP problem alone. Different treatments have been shown to help improve young individuals with CP.[10,29,33] However, one of the limitations in relation to treatment for this population has been the tendency to treat all individuals with CP with essentially the same treatment program. As noted previously, research has shown that individuals with CP are not equal. Therefore, those individuals should be treated differently, based on their characteristics and needs.

The study has a number of limitations that should be considered when interpreting the findings. First, this was a cross-sectional study. Therefore, it precludes any conclusions regarding causative factors, including those that may impact the development of HICP. Longitudinal studies to determine what factors might be associated with both the development and resolution of CP in this population is warranted. Second, the data for this study were collected from a convenience sample of children and adolescents and only 36% of parents approached consented to have their children participate. Also, although we put a great deal of effort to locate students whose parents agreed they could participate in the study, but who were not present the day of the data collection at school, we were not able to locate them all. That said, if this did bias the sample, it would seem likely that the prevalence of HICP could be even higher than estimated here, as individuals with HICP are the ones that are more severely affected in their function and tend to miss school more days. Similarly, characteristics of the parents (eg, education, general health) that have been found to be associated to CP, are an additional source of potential bias, which could have affected (self-)selection into the study. Measures of these potential biasing factors should be included in future studies. In addition, although the definition of CP used for this study has been successfully used in previous studies (eg,[17]), it is not the only classification system that could be used. Some studies in adults, for example, use a more conservative threshold for CP (eg, CP defined as pain that is present most day or every day; eg,[5]). Researchers should carefully consider which definition to use, and base their decision on the aims of the study, recognizing that the definition will ultimately impact the rates of CP found in any one sample. Moreover, although we used validated measures they covered different time spans. We cannot be certain if and how these differences have impacted the findings. This potential problem is very common in the pain research literature (see[20]). Therefore, it would be recommendable that researchers seek to use measures that cover the same time periods whenever possible. Finally, we were not able to compare children and adolescents groups with respect to HICP because of the small number of individuals who met criteria for HICP in the children group (n = 7). Future studies with larger sample sizes are needed.

Despite these limitations, this study provides new valuable information that improves our understanding of the prevalence of chronic pain and HICP in children and adolescents, as well as of the associations between chronic pain and children's physical, psychological, and school-related function. These findings can now be used by stakeholders interested in improving the quality of life of this population, as it provides important information about the overall need of this population of children who bear a great burden of pain. By understanding the factors that are associated with these conditions, researchers and clinicians will be able to develop more effective early interventions to help better this population.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jpain.2022.12.007.

REFERENCES

1. Castarlenas E, Jensen MP, Von Baeyer CL, Miró J: Psychometric properties of the numerical rating scale to assess self-reported pain intensity in children and adolescents. Clin J Pain 33:376-383, 2017

2. Cohen J: Statistical Power Analysis for the Behavioral Sciences, 2nd ed. Hillsdale, NJ, Lawrence Erlbaum Associates, 1988

3. Croft P, Blyth F, Van Der Windt D: Chronic Pain Epidemiology: From Aetiology to Public Health. Oxford, England, Oxford University Press, 2010

4. Currie C, Nic Gabhainn S, Godeau E: The Health Behaviour in School-aged Children: WHO Collaborative Cross-National (HBSC) study: origins, concept, history and development 1982-2008. Int J Public Health Switzerland 54(Suppl 2):131-139, 2009

5. Dahlhamer J, Lucas J, Zelaya C, Nahin R, Mackey S, DeBar L, Kerns R, Von Korff M, Porter L, Helmick C: Prevalence of chronic pain and high-impact chronic pain among adults - United States, 2016. MMWR Morb Mortal Wkly Rep 67:1001-1006, 2018

6. de la Vega R, Racine M, Sánchez-Rodríguez E, Tomé-Pires C, Castarlenas E, Jensen MP, Miró J: Pain extent, pain intensity, and sleep quality in adolescents and young adults. Pain Med 17:1971-1977, 2016

7. de la Vega R, Roset R, Galan S, Miró J: Fibroline: A mobile app for improving the quality of life of young people with fibromyalgia. J Health Psychol 23:67-78, 2016

8. Department of Health and Human Services USG: National Pain Strategy: A comprehensive population health strategy for pain. [Internet]. Available at: https://iprcc.nih.gov/docs/HHSNational_Pain_Strategy.pdf. Accessed March 15, 2022.

9. DeWitt EM, Stucky BD, Thissen D, Irwin DE, Langer M, Varni JW, Lai J-S, Yeatts KB, Dewalt DA: Construction of the eight-item patient-reported outcomes measurement information system pediatric physical function scales: built using item response theory. J Clin Epidemiol 64:794-804, 2011

10. Eccleston C, Palermo TM, Williams AC de C, Lewandowski Holley A, Morley S, Fisher E, Law E: Psychological therapies for the management of chronic and recurrent pain in children and adolescents. Cochrane Database Syst Rev: CD003968, 2014. https://doi.org/10.1002/14651858.CD003968.pub4

11. Forrest CB, Meltzer LJ, Marcus CL, de la Motte A, Kratchman A, Buysse DJ, Pilkonis PA, Becker BD, Bevans KB: Development and validation of the PROMIS Pediatric Sleep Disturbance and Sleep-Related Impairment item banks. Sleep 41, 2018

12. Gobina I, Villberg J, Välimaa R, Tynjälä J, Whitehead R, Cosma A, Brooks F, Cavallo F, Ng K, de Matos MG, Villerusa A: Prevalence of self-reported chronic pain among adolescents: Evidence from 42 countries and regions. Eur J Pain 23:316-326, 2019

13. Groenewald CB, Essner BS, Wright D, Fesinmeyer MD, Palermo TM: The economic costs of chronic pain among a cohort of treatment-seeking adolescents in the United States. J Pain 15:925-933, 2014

14. Hanish AE, Lin-Dyken DC, Han JC: PROMIS sleep disturbance and sleep-related impairment in adolescents: Examining psychometrics using self-report and actigraphy. Nurs Res 66:246-251, 2017

15. Haraldstad K, Sørum R, Eide H, Natvig GK, Helseth S: Pain in children and adolescents: prevalence, impact on daily life, and parents' perception, a school survey. Scand J Caring Sci 25:27-36, 2011

16. Hoftun GB, Romundstad PR, Zwart J-A, Rygg M: Chronic idiopathic pain in adolescence–high prevalence and disability: the young HUNT Study 2008. Pain 152:2259-2266, 2011

17. Huguet A, Miró J: The severity of chronic pediatric pain: An Epidemiological Study. J Pain 9:226-236, 2008

18. Jones GT, Botello AP: Pain in children. Croft P, Blyth FM, van der Windt D, editors. Pain in children. Chronic Pain Epidemiol from Aetiol to Public Heal 159-176, 2010

19. King S, Chambers CT, Huguet A, MacNevin RC, McGrath PJ, Parker L, MacDonald AJ: The epidemiology of chronic pain in children and adolescents revisited: a systematic review. Pain 152:2729-2738, 2011

20. Könning A, Rosenthal N, Brown D, Stahlschmidt L, Wager J: Severity of chronic pain in German adolescent school students: A cross-sectional study. Clin J Pain 37:118-125, 2021

21. Kröner-Herwig B, Gassmann J, Van Gessel H, Vath N: Multiple pains in children and adolescents: A risk factor analysis in a longitudinal study. J Pediatr Psychol 36:420-432, 2011

22. Lalloo C, Harris LR, Hundert AS, Berard R, Cafazzo J, Connelly M, Feldman BM, Houghton K, Huber A, Laxer RM, Luca N, Schmeling H, Spiegel L, Tucker LB, Pham Q, Davies-Chalmers CC, Stinson JN: The iCanCope pain self-management application for adolescents with juvenile idiopathic arthritis: a pilot randomized controlled trial. Rheumatology 60:196-206, 2021

23. Luntamo T, Sourander A, Santalahti P, Aromaa M, Helenius H: Prevalence changes of pain, sleep problems and fatigue among 8-year-old children: years 1989, 1999, and 2005. J Pediatr Psychol 37:307-318, 2012

24. Maes M, Van den Noortgate W, Fustolo-Gunnink SF, Rassart J, Luyckx K, Goossens L: Loneliness in children and adolescents with chronic physical conditions: A meta-analysis. J Pediatr Psychol 42:622-635, 2017

25. Mills SEE, Nicolson KP, Smith BH: Chronic pain: A review of its epidemiology and associated factors in population-based studies. Br J Anaesth 123:e273-e283, 2019

26. Miró J, de la Vega R, Tomé-Pires C, Sánchez-Rodríguez E, Castarlenas E, Jensen MP, Engel JM: Pain extent and function in youth with physical disabilities. J Pain Res 10:113-120, 2017

27. Miró J, Gertz KJ, Carter GT, Jensen MP: Pain location and intensity impacts function in persons with myotonic dystrophy type 1 and facioscapulohumeral dystrophy with chronic pain. Muscle and Nerve 49:900-905, 2014

28. Miró J, Huguet A, Nieto R: Predictive factors of chronic pediatric pain and disability: A Delphi poll. J pain Off J Am Pain Soc 8:774-792, 2007

29. Miró J, Mcgrath PJ, Finley GA, Walco GA: Pediatric chronic pain programs : Current and ideal practice. Pain Rep 2:e613, 2017

30. Miró J, Micó JA, Reinoso-Barbero F: The management of pediatric chronic pain in Spain: A web-based survey study. Curr Med Res Opin 37:303-310, 2021

31. Miró J, Reinoso-Barbero F, Escribano J, Martí L: El tratamiento del dolor en población infantojuvenil en España: datos de una encuesta sobre los programas especializados existentes. Rev Esp Salud Pública 93:e1-11, 2019

32. Morgan EM, Mara CA, Huang B, Barnett K, Carle AC, Farrell JE, Cook KF: Establishing clinical meaning and defining important differences for Patient-Reported Outcomes Measurement Information System (PROMIS®)) measures in juvenile idiopathic arthritis using standard setting with patients, parents, and providers. Qual life Res 26:565-586, 2017

33. O'Connell N: Clinical management in an evidence vacuum: pharmacological management of children with persistent pain. Cochrane Database Syst Rev 6:ED000135, 2019. https://doi.org/10.1002/14651858.ED000135

34. Oliva EM, Midboe AM, Lewis ET, Henderson PT, Dalton AL, Im JJ, Seal K, Paik MC, Trafton JA: Sex differences in chronic pain management practices for patients receiving opioids from the veterans health administration. Pain Med 16:112-118, 2015

35. Perquin CW, Hazebroek-Kampschreur AA, Hunfeld JA, Bohnen AM, van Suijlekom-Smit LW, Passchier J, van der Wouden JC: Pain in children and adolescents: a common experience. Pain 87:51-58, 2000

36. Petersen S, Brulin C, Bergström E: Recurrent pain symptoms in young schoolchildren are often multiple. Pain 121:145-150, 2006

37. Pitcher MH, Von Korff M, Bushnell MC, Porter L: Prevalence and profile of high-impact chronic pain in the United States. J Pain 20:146-160, 2019

38. Quinn H, Thissen D, Liu Y, Magnus B, Lai J-S, Amtmann D, Varni JW, Gross HE, DeWalt DA: Using item response theory to enrich and expand the PROMIS® pediatric self report banks. Health Qual Life Outcomes 12:160, 2014

39. Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, Keefe FJ, Mogil JS, Ringkamp M, Sluka KA, Song X-J, Stevens B, Sullivan MD, Tutelman PR, Ushida T, Vader K: The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. Pain 161:1976-1982, 2020

40. Roman-Juan J, Roy R, Jensen MP, Miró J: The explanatory role of sedentary screen time and obesity in the increase of chronic back pain among european adolescents: The HBSC Study 2002-2014. Eur J Pain 26:1781-1789, 2022

41. Roy R, Galán S, Sánchez-Rodríguez E, Racine M, Solé E, Jensen MP, Miró J: Cross-national trends of chronic back pain in adolescents: results from the HBSC Study, 2001-2014. J Pain 23:123-130, 2022

42. Skrove M, Romundstad P, Indredavik MS: Chronic multisite pain in adolescent girls and boys with emotional and behavioral problems: the Young-HUNT study. Eur Child Adolesc Psychiatry 24:503-515, 2015

43. Steingrímsdóttir ÓA, Landmark T, Macfarlane GJ, Nielsen CS: Defining chronic pain in epidemiological studies: A systematic review and meta-analysis. Pain 158:2092-2107, 2017

44. Stevens B, Zempsky W: Prevalence and distribution of pain in children, in Stevens BJ, Hathway G, Zempsky W, (eds): Oxford Textbook of Paediatr Pain, Oxford, Oxford University Press, 2021, pp 12-19

45. Stevens BJ, Hathway G, Zempsky W, (eds): Oxford Textbook of Pediatric Pain, Oxford, England, Oxford University Press, 2021

46. Swain MS, Henschke N, Kamper SJ, Gobina I, Ottová-Jordan V, Maher CG: An international survey of pain in adolescents. BMC Public Health 14:1-7, 2014

47. Tomczak M, Tomczak E: The need to report effect size estimates revisited. An overview of some recommended measures of effect size. Trends 1:19-25, 2014

48. Treede R-D, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, Cohen M, Evers S, Finnerup NB, First MB, Giamberardino MA, Kaasa S, Korwisi B, Kosek E, Lavand'homme P, Nicholas M, Perrot S, Scholz J, Schug S, Smith BH, Svensson P, Vlaeyen JWS, Wang S-J: Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). Pain 160:19-27, 2019

49. Tumin D, Drees D, Miller R, Wrona S, Hayes DJ, Tobias JD, Bhalla T: Health care utilization and costs associated with pediatric chronic pain. J Pain 19:973-982, 2018

50. Varni JW, Magnus B, Stucky BD, Liu Y, Quinn H, Thissen D, Gross HE, Huang I-C, DeWalt DA: Psychometric properties of the PROMIS ® pediatric scales: precision, stability, and comparison of different scoring and administration options. Qual life Res 23:1233-1243, 2014

51. Varni JW, Stucky BD, Thissen D, Dewitt EM, Irwin DE, Lai JS, Yeatts K, Dewalt DA: PROMIS pediatric pain interference scale: An item response theory analysis of the pediatric pain item bank. J Pain 11:1109-1119, 2010

52. Vervoort T, Logan DE, Goubert L, De Clercq B, Hublet A: Severity of pediatric pain in relation to school-related functioning and teacher support: An epidemiological study among school-aged children and adolescents. Pain 155:1118-1127, 2014

53. Vetter TR: The epidemiology of pediatric chronic pain, in McClain B, Suresh S, (eds): Handbook of Pediatric Chronic Pina, New York, NY, Springer, 2011, pp 1-14

54. Von Korff M, DeBar LL, Krebs EE, Kerns RD, Deyo RA, Keefe FJ: Graded chronic pain scale revised: mild, bothersome, and high-impact chronic pain. Pain 161:651-661, 2020

55. Von Korff M, Scher AI, Helmick C, Carter-Pokras O, Dodick DW, Goulet J, Hamill-Ruth R, LeResche L, Porter L, Tait R, Terman G, Veasley C, Mackey S: United States National Pain Strategy for Population Research: Concepts, Definitions, and Pilot Data. J Pain 17:1068-1080, 2016

56. Wager J, Brown D, Kupitz A, Rosenthal N, Zernikow B: Prevalence and associated psychosocial and health factors of chronic pain in adolescents: Differences by sex and age. Eur J Pain 24:761-772, 2020

57. Walco GA, Krane EJ, Schmader KE, Weiner DK: Applying a lifespan developmental perspective to chronic pain: Pediatrics to geriatrics. J Pain 17:T108-T117, 2016

58. Walker LS, Dengler-Crish CM, Rippel S, Bruehl S: Functional abdominal pain in childhood and adolescence increases risk for chronic pain in adulthood. Pain 150:568-572, 2010

59. World Health Organization: Guidelines on the Management of Chronic Pain in Children. Geneve, World Health Organization, 2020

60. Zernikow B, Wager J, Hechler T, Hasan C, Rohr U, Dobe M, Meyer A, Hübner-Möhler B, Wamsler C, Blankenburg M: Characteristics of highly impaired children with severe chronic pain: a 5-year retrospective study on 2249 pediatric pain patients. BMC Pediatr 12:582, 2012

4.2. Study II

Immigration background as a risk factor of chronic pain and high-impact chronic pain in children and adolescents living in Spain: differences as a function of age.

Research Paper

PAIN 165 (2024) 1372–1379

PAIN®

Immigration background as a risk factor of chronic pain and high-impact chronic pain in children and adolescents living in Spain: differences as a function of age

Josep Roman-Juan[a,b], Elisabet Sánchez-Rodríguez[a,b], Ester Solé[a,b], Elena Castarlenas[a,b], Mark P. Jensen[c], Jordi Miró[a,b,*]

Abstract

The number of people immigrating from one country to another is increasing worldwide. Research has shown that immigration background is associated with chronic pain (CP) and pain disability in adults. However, research in this issue in children and adolescents has yielded inconsistent results. The aims of this study were to examine (1) the association between immigration background, CP, high-impact chronic pain (HICP) in a community sample of children and adolescents; and (2) the extent these associations differed as a function of sex and age. Participants of this cross-sectional study were 1115 school children and adolescents (mean age = 11.67; 56% girls). Participants were asked to provide sociodemographic information and respond to a survey including measures of pain (location, extension, frequency, intensity, and interference). Results showed that having an immigration background was associated with a greater prevalence of CP (OR = 1.91, p <.001) and HICP (OR = 2.55, p <. 01). Furthermore, the association between immigration background and CP was higher in children (OR = 6.92, p <.001) and younger adolescents (OR = 1.66, p <.05) than in older adolescents. Children and adolescents with an immigration background are at higher risk for having CP -especially younger children- and HICP. More resources should be allocated in the prevention of CP and HICP in children and adolescents with an immigration background.

Keywords: Chronic pain, High-impact chronic pain, Children, Adolescents, Immigration background

1. Introduction

Immigration is a growing phenomenon worldwide that is often associated with social conflicts, persecution, poor living environments, and lack of personal safety.[54,65] In 2020, the number of international immigrants was estimated to be almost 281 million; 15% of these individuals were children and adolescents.[29]

Research has shown that having an immigration background is associated with poorer health in adults, including chronic pain (CP) and related disability.[4,7,23,46,64] However, studies examining these associations in children and adolescents have shown inconclusive findings. For example, one study found 2 times higher rates of abdominal pain in children with an immigration background compared with children with a local background,[1] and one study found immigration background to be positively associated with recurrent headaches and abdominal pain in adolescents.[26] Two other studies found lower rates of recurrent pain in children and adolescents with an immigration background when compared with those without an immigration background.[8,36] In addition, 2 other studies found no significant associations between immigration background, CP prevalence, and CP severity in adolescents.[21,63]

Considering the worldwide increase in the number of immigrant children and adolescents, the findings indicating significant positive associations between immigration background and CP in adults, and the potential negative role of immigration background in the development of CP and related disability in children and adolescents, it is important to better understand the association of immigration background and CP in young individuals. Such knowledge could be used to inform the development of new and better tailored strategies to help prevent and treat CP and pain-related disability. Increased knowledge in this area could also be used to inform more effective advocacy and system planning strategies for immigrant children and adolescents.

Given these considerations, this study sought to advance our understanding of the association between immigration background and CP using a large community sample of children and adolescents living in Spain. Specifically, we sought to examine (1) the association between immigration background and the presence of CP and high-impact chronic pain (HICP) and (2) the extent to which these associations differed as a function of sex

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

[a] *Unit for the Study and Treatment of Pain—ALGOS, Research Center for Behavior Assessment (CRAMC), Department of Psychology, Universitat Rovira i Virgili, Catalonia, Spain,* [b] *Institut d'Investigació Sanitària Pere Virgili, Universitat Rovira i Virgili, Catalonia, Spain,* [c] *Department of Rehabilitation Medicine, University of Washington, Seattle, WA, United States*

**Corresponding author. Address: Departament de Psicología, Universitat Rovira i Virgili, Carretera de Valls, s/n, 43007 Tarragona, Spain. Tel.: +34-977558179; fax: +34-977558088. E-mail address: jordi.miro@urv.cat (J. Miró).*

http://dx.doi.org/10.1097/j.pain.0000000000003142

and age. On the basis of prior research showing significant associations between having an immigration background and several negative health-related outcomes in children and adolescents,[30,49,50] as well as findings showing significant associations between immigration background and both the presence of CP and its impact in adults,[4,7,23,46,64] we hypothesized that participants with an immigration background would have higher rates of CP and HICP than participants with a local background. Furthermore, considering the higher prevalence of CP[17,20,62] and HICP[33] among girls and older adolescents, we hypothesized that sex and age would moderate the association between having an immigration background and CP and HICP.

2. Method

2.1. Procedure and participants

The data for the analyses conducted in this study came from an initial assessment of an ongoing longitudinal epidemiological project that included a sample of schoolchildren recruited from 10 schools in Reus, Catalonia (Spain). A paper presenting the primary findings for this study has been published.[33] However, that paper did not examine the association between having an immigration background and pain-related variables, which is the focus of this paper. All schoolchildren aged 8 to 18 years that were able to read, write, and speak Spanish were eligible. In order to be included, both students and their parents needed to provide their assent and informed consent. Participating children were asked to respond a paper-and-pencil survey during a period of time when they were attending school. For their participation in this assessment, they received a gym sack and a calendar valued at 3€. The study was conducted in compliance with established human research ethics standards and was approved by the Institute for Health Research ethics committee of the *Universitat Rovira i Virgili* (*Institut d'Investigació Sanitària Pere Virgili; ref.: 136/2018)*.

For the survey study, 1142 schoolchildren (36% of the potential sample of 3167 schoolchildren) provided data for the initial survey. Of these, 1115 (99% of those participating) provided data for the data analysis (see Miró et al.[33] for additional information about the survey study procedures).

2.2. Measures

2.2.1. Demographic characteristics

Participants were asked to provide information regarding their sex and age. In addition, participants were asked to provide information about their birth country and the birth country of their parents. Based on the participants' developmental stage[37] and consistent with procedures used in previous similar studies (eg, Wager et al.[63]), participants aged below 10 years were considered to be "children," participants aged 10 to 14 years were considered to be "younger adolescents," and participants aged 14 to 18 years were considered to be "older adolescents." On the basis of previous epidemiological studies[24,43,63] and the guidelines of International and European organizations (such as the International Office for Migrants and the European Commission[34,55]), children and adolescents who were born outside of Spain and with at least one of their parents also born in another country (also known as first-generation immigrants) were considered to have an immigration background. Additionally, children and adolescents born in Spain but with both parents born in another country (also known as second-generation immigrants) were also considered to have an immigration background.

2.2.2. Pain characteristics

Participants were asked whether they had experienced pain in the last 3 months. If yes, they were asked to provide information about the *pain location(s)* using a pain site checklist with 11 specific locations (ie, head, neck, chest, shoulders, back, arms, hands, bottom/hips, belly/pelvis, legs, and feet) and an "other" category. This pain checklist has been used in previous studies.[5,31,32] Participants reporting more than one pain location were considered to have multisite pain. For each selected pain location, participants were then asked to report the *pain frequency* in the last 3 months using a 5-point Likert scale (1 = "every day," 2 = "more than once a week," 3 = "once a week," 4 = "once or twice times per month," 5 = "once in the last 3 months"). Participants were classified as experiencing CP if they reported pain at least once a week for at least 3 months.[17,21,42,44,63,66]

2.2.3. Pain-related interference

Participants were asked to respond to the Spanish version of the 8-item Pediatric Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference scale v2.0 (PROMIS-PI).[57] With this scale, respondents are asked to indicate how often pain has interfered with their physical, psychological, and social functioning over the past 7 days with each response measured on a 5-point Likert scale (1= "never" to 5= "almost always"). Like most PROMIS measures, the response to the Pain Interference items are scored as T-scores, with a mean of 50 points and an SD of 10 in the normative sample. Previous studies have shown that the pediatric form of the PROMIS-PI provides a reliable and valid measure of pain interference when used in children and adolescents as young as 8 years.[57] In the current sample, the internal consistency (Cronbach alpha) was 0.86, indicating good reliability. On the basis of the definition of HICP provided by Von Korff et al.[61] and consistent with procedures used in previous epidemiological research,[33] participants who reported experiencing CP were classified as having HICP if PROMIS-PI T-scores were ≥65.

2.3. Data analysis

We first computed descriptive statistics for the demographic and study variables to describe the sample characteristics. To test the 2 study hypotheses, we planned two 3-stage hierarchical multiple logistic regressions: one with the presence of CP as the criterion variable and one with the presence of HICP as the criterion variable. Assumptions of multicollinearity among the predictors were assessed for both regression analyses by examining the variance inflation factors associated with each predictor. Both regression analyses followed the same strategy: we entered immigration background, sex, and age group variables as a block in step 1. All variables were entered as dummy-coded variables with not having an immigration background, being male, and being a child as the reference categories, respectively. We then entered the first-order interactions (ie, Immigration Background × Sex and Immigration Background × Age Group) and the second-order interactions (ie, Immigration Background × Sex × Age Group) in steps 2 and 3, respectively. In the event that the second-order interaction was significant, we planned to compute and examine the prevalence rates (%) of CP and HICP separately

for boys and girls in the different immigration background groups and for each of the 3 age groups (ie, children, younger adolescents, and older adolescents). If the second-order interaction was not significant, we planned to follow-up any significant first-order interaction. The Hosmer–Lemeshow test and the Nagelkerke R^2 were used to evaluate the fit of the logistic regression models. A 2-tailed significance level of $P < 0.05$ was defined as statistically significant. All data analyses were conducted using STATA 14 (Stata Corp, TX) and Jamovi version 2.2 (The Jamovi Project, 2021).

3. Results

3.1. Description of the study sample

Table 1 summarizes demographic and pain-related characteristics of the 1115 participating schoolchildren. The mean age of this sample was 11.67 years (SD = 2.47, range = 8-18 years), and more than half of the participants were girls (57%). Of the total number of participants, 36 (3%) were first-generation immigrants and 123 (11%) were second-generation immigrants. Therefore, 159 (14%) participants were considered to have an immigration background. Almost half of all the participants' sample (N = 510; 46%) met criteria for having CP, and 11% of these (N = 52; 5% of the total sample) met criteria for having HICP. There were no differences in sex ($\chi^2_{(1)} = 0.25$; $P > 0.05$) or age ($\chi^2_{(2)} = 4.21$; $P > 0.05$) between participants with and without an immigration background (**Table 2**).

Table 1

Demographic and pain-related characteristics of the sample (N = 1115).

	N	%	Mean	SD	Range
Sex					
Male	485	44			
Female	630	57			
Age*			11.67	2.47	8-18
Age groups*					
Children	247	22	8.52	0.51	7-9
Younger adolescents	591	53	11.40	1.10	10-13
Older adolescents	276	25	15.06	1.13	14-18
Immigration background†					
No	939	84			
Yes	159	14			
First-generation immigrants	36	3			
Second-generation immigrants	123	11			
Pain in the last 3 mo	989	89			
Chronic pain‡	510	46			
Chronic pain locations (n = 510)					
Head§	201	39			
Neck‖	102	20			
Chest/breast¶	43	8			
Shoulders#	83	16			
Back**	180	35			
Arms††	48	9			
Hands††	42	8			
Bottom/hips††	23	5			
Belly/pelvis**	106	21			
Legs‡‡	122	24			
Feet††	114	22			
Other§§	46	9			
Pain interference (n = 510)‖‖			53.58	9.03	34-78
High-impact chronic pain (n = 510)‖‖	52	11			

* to §: *n* varies because of nonresponses.
* n = 1114 (missing values = 1).
† n = 1098 (missing values = 17).
‡ n = 1068 (missing values = 47).
§ n = (missing values = 5).
‖ n = (missing values = 7).
¶ n = (missing values = 1).
# n = (missing values = 3).
** n = (missing values = 8).
†† n = (missing values = 2).
‡‡ n = (missing values = 6).
§§ n = (missing values = 4).
‖‖ n = 483 (missing values = 27).

3.2. Assumption testing

No violations of multicollinearity were identified in any regression model; variance inflation values were all <10.0 (from 1.66 to 3.58 for the logistic regression with CP as the criterion variable and from 1.10 to 4.42 for the logistic regression with HICP as the criterion variable), indicating that multicollinearity would not bias the findings.[14]

3.3. Logistic regression analyses

3.3.1. Chronic pain

Table 3 shows the results of the 3-stage hierarchical multiple logistic regression using the presence of CP as the criterion variable. The block containing the main effects (step 1) made a significant contribution to the model, explaining an 11% of the variance of CP ($\chi^2 = 90.95$; $df = 4$; $P < 0.001$). As can be seen, immigration background ($\chi^2 = 12.56$; $df = 1$; $P < 0.001$), sex ($\chi^2 = 12.30$; $df = 1$; $P < 0.001$), and age ($\chi^2 = 65.98$; $df = 2$; $P < 0.001$) were all significantly associated with meeting criteria for having CP. Specifically, participants with an immigration background, girls, and adolescents (younger and older) had significantly higher odds of meeting criteria for having CP compared with nonimmigrant participants, boys, and children, respectively.

The block containing the first-order interactions (step 2) also made a significant contribution to the model, explaining an additional 2% of the variance of CP (χ^2 change = 17.49; $df = 3$; $P < 0.001$), with the Immigration Background × Age Group ($\chi^2 = 17.49$; $df = 2$; $P < 0.001$) interaction effect emerging as significant. A closer examination of the coefficients indicated that the effect of immigration background on CP was lower as the age of participant increased. The Immigration Background × Sex × Age Group interaction (step 3) was not significant. The Hosmer–Lemeshow goodness-of-fit statistic was C = 9.94 ($df = 6$, $P = 0.13$), indicating that there was a good fit for the final model including the first-order interactions (step 2).

Table 4 provides information on the prevalence of CP as a function of immigration background. As can be seen, the prevalence of CP is higher in participants with an immigration background compared with those without an immigration background. **Table 4** also provides information on the prevalence of CP separately for children, young adolescents, and older adolescents for the 2 immigration background groups. As can be seen, the prevalence of CP is higher in children and younger adolescents with an immigration background compared with those without an immigration background, but these rates become similar in the oldest group of adolescents. **Table 5** shows the odds ratio for having CP in participants with an immigration background compared with those without an immigration background (reference category) in all age groups. Results indicated that younger participants (ie, those in the "children" and "younger adolescents" categories) with an

Table 2

Distribution of sex and age groups by immigration background.

	Local background (N = 939)	Immigration background (N = 159)
	n (%)	n (%)
Sex		
Male	408 (43)	68 (43)
Female	531 (57)	91 (57)
Age groups		
Children	206 (22)	34 (22)
Younger adolescents	489 (52)	95 (59)
Older adolescents	243 (26)	30 (19)

immigration background had significantly higher odds of meeting criteria for having CP compared with those who were not.

3.3.2. High-impact chronic pain

Table 6 summarizes the results of the 3-stage hierarchical multiple logistic regression analysis with HICP as the criterion variable. The block containing the main effects (step 1) made a significant contribution to the model, explaining a 9% of the variance of HICP ($\chi^2 = 29.25$; $df = 4$; $P < 0.001$). As can be seen, immigration background ($\chi^2 = 6.87$; $df = 1$; $P < 0.01$) and sex ($\chi^2 = 19.40$; $df = 1$; $P < 0.001$) were significantly associated with meeting criteria for having HICP. Specifically, participants with an immigration background and girls had significantly higher odds of meeting criteria for having HICP compared with nonimmigrant participants and boys, respectively. Participants' age was not associated with meeting criteria for having HICP. The block containing the first-order interactions (step 2) and the block containing the second-order interactions (step 3) were not significant. The Hosmer–Lemeshow goodness-of-fit statistic was C = 3.77 ($df = 7$, $P = 0.58$), indicating that there was a good fit for the final model including the block of main effects (step 1).

Table 7 provides information on the prevalence of HICP as a function of immigration background. As can be seen, the prevalence of HICP is higher in participants with an immigration background compared with those without an immigration background.

4. Discussion

This study yielded 2 primary findings. First, and consistent with the first study hypothesis, the rates of CP—except in older adolescents—and HICP were higher in participants with an immigration background compared with those with a local background. Second, and partially supporting the second study hypothesis, participants' age moderated the association between immigration background and CP; specifically, the difference in the prevalence of CP between participants with an immigration background and those with a local background was more pronounced among children and young adolescents and less disparate among older adolescents.

Table 3

Multiple logistic regression analysis with chronic pain as the criterion variable (N = 1050).

Step and variables	Total R^2	R^2 change	χ^2 change	χ^2†	OR (95% CI)
Step 1: Main effects	0.11	0.11	90.95***		
Immigration background				12.56***	
No (ref.)					—
Yes					1.91 (1.33-2.75)***
Sex				12.30***	
Male (ref.)					—
Female					1.58 (1.22-2.04)***
Age group				65.98***	
Children (ref.)					—
Younger adolescent					2.10 (1.49-2.96)***
Older adolescent					4.73 (3.19-7.00)***
Step 2: First-order interactions	0.13	0.02	17.49***		
Immigration background × sex				0.15	
Male with a local background (ref.)					—
Female with an immigration background					1.16 (0.56-2.39)
Immigration background × age group				17.49***	
Children with a local background (ref.)					—
Younger adolescent with an immigration background					0.22 (0.09-0.56)**
Older adolescent with an immigration background					0.09 (0.03-0.30)***
Step 3: Second-order interaction	0.14	0.01	8.20		

**$P < 0.01$.
***$P < 0.001$.
† Omnibus likelihood ratio χ^2 tests.
CI, confidence interval; OR, odds ratio.

Table 4

Number and percent of participants with chronic pain by immigration background and age groups (N = 1050).

	Local background (N = 897)	Immigration background (N = 153)
Total	411 (46)	91 (59)
Age groups		
Children	41 (22)	22 (66)
Younger adolescents	212 (44)	52 (57)
Older adolescents	158 (66)	17 (59)

There are several potential explanations for the differences in the prevalence of CP between children and adolescents with and without an immigration background. First, children and adolescents with an immigration background, and in particular first-generation immigrants, might be exposed to adverse events associated with the country of origin (eg, violence and poverty[54,65]) and the country of destination (eg, discrimination, peer aggression, and bullying[41,49,50]). There is mounting evidence showing that adverse childhood experiences increase the risk for CP.[12,27,35] Second, first-generation immigrant children can face challenges in adapting to a new society and its cultural environment that can result in higher levels of psychological distress,[2,6,13] which could then contribute to the presence and severity of CP.[3,25,33,47,56,63] However, both child's specific ethnic background and the receiving country they are brought up in need to be considered as differentially contributing to these effects.[48] A similar potential explanation could apply to second-generation immigrants. Although these individuals are not directly exposed to adverse events associated with the immigration process, they are still more vulnerable to adverse events such as peer aggression and bullying[49,50] and are more likely to experience psychological distress problems than their counterparts without an immigration background,[49] which have all been associated with CP.[9,28,63]

Research on the association between immigration background and CP in children and adolescents has found conflicting results. One study conducted in Germany showed no significant association[63]; 2 studies, one conducted in Germany and another conducted in Sweden, showed lower rates of recurrent pain in children of immigrant families[8,36]; and 2 studies, one conducted in Sweden and another conducted in Finland, reported higher rates of pain in children with an immigration background.[1,26] Consistent with these latter results, we found that participants with an immigration background had almost 2 times higher odds of reporting CP compared with participants with a local background. The discrepancies in research findings may stem from variations in the definition of immigration background. In the current study, participants were classified as having an immigration background if they were born in another country and had at least one parent not born in Spain or if they were born in Spain and both parents had been born outside Spain. Other researchers only considered the country of birth of the parents[36] or only considered first-generation immigrants.[26] Moreover, the participants' country of birth is another potential factor contributing to the conflicting findings because the risk factors associated with being an immigrant may vary depending on the country of origin. For example, immigrants in Germany predominantly originate from Turkey, Syria, and Romania, whereas immigrants in Sweden come mostly from Syria and Iraq, in Finland from Russia, Iraq, and Somalia, and in Spain from Morocco, Colombia, and Ecuador.[53] Furthermore, cross-national variations in the prevalence of CP[10] suggest that social factors associated with the country of destination may also play a role. Additional research with nationally representative samples of multiple countries using homogenous definitions of immigration is warranted to clarify the association between immigration status and CP.

Consistent with our hypothesis, we found higher rates of HICP in children and adolescents with an immigration background than in those with a local background. Thus, our results suggest that children and adolescents with an immigration background not only are at an increased risk of CP but also of CP that severely impacts on their life and function. This finding contrasts with the one reported by Könning et al.,[21] who found no differences in immigration background among the most severe cases of individuals with CP.

To our knowledge, only one study has tested the moderating effects of sex and age on the association between immigration background and CP. Wager et al.,[63] using a sample of adolescents aged 10 to 18 years living in Germany, found no significant moderating effects of sex or age. In contrast, we found that participants' age moderated the effect of immigration status on CP. Specifically, we found that the difference in the prevalence of CP between participants with and without immigration background was higher for participants of younger age, but these rates were less disparate between older adolescents with and without immigration background. In view of these results, it might be hypothesized that children and younger adolescents with an immigration background, and specifically first-generation immigrants, are more vulnerable to the potential adverse events associated with immigration compared with the older ones. In relation to this, eg, younger age at migration has been associated with a greater risk of mood disorders in children.[19,39] Furthermore, adverse events associated with immigration background such as bullying victimization decrease at older ages,[50] which could partially explain why the rates of CP become similar in older adolescents with and without immigration background. Additional research is needed to examine these hypotheses.

The findings have important financial and clinical implications. Research has shown that CP has detrimental effects across many domains of children and adolescents' lives[51] and that these detrimental effects are higher for those with CP that is of high impact.[33] Furthermore, it is well known that CP conditions in children and adolescents result in a significant economic burden to society[11,45] and that individuals with HICP account for the largest share of the economic costs associated with CP.[60]

Table 5

Odds ratio for chronic pain in participants with an immigration background relative to participants with a local background (N = 1050).

	OR (95% CI)
Age groups	
Children	6.92 (3.10-15.46)***
Younger adolescents	1.66 (1.06-2.61)*
Older adolescents	0.72 (0.33-1.57)

*$P < 0.05$.
***$P < 0.001$.
CI, confidence interval; OR, odds ratio.

Table 6

Multiple logistic regression analysis with high-impact chronic pain as the criterion variable (N = 1025).

Step and variables	Total R^2	R^2 change	χ^2 change	χ^2†	OR (95% CI)
Step 1: Main effects	0.09	0.09	29.25***		
Immigration background				6.87**	
No (ref.)					—
Yes					2.55 (1.32-4.92)**
Sex				19.40***	
Male (ref.)					—
Female					4.77 (2.12-10.73)***
Age group				2.11	
Children (ref.)					—
Younger adolescent					1.28 (0.54-3.03)
Older adolescent					1.85 (0.74-4.61)
Step 2: First-order interactions	0.09	0.00	2.01		
Step 3: Second-order interaction	0.11	0.02	6.49		

**$P < 0.01$.
***$P < 0.001$.
† Omnibus likelihood ratio χ^2 tests.
CI, confidence interval; OR, odds ratio.

Indeed, high rates of health service use have been documented for youth with CP around the world,[16,22,38,52,59] and there are some studies reporting that children and adolescents with an immigration background with CP are more likely to seek medical help for their pain issues than their counterparts with a local background.[15,58] Therefore, if the findings reported here are found to be reliable when examined in additional samples of children, and if the number of children and adolescents with an immigration background continues to increase, the economic burden associated with CP in children and adolescents could also be expected to increase. Also, if the findings regarding the role of age on the association between immigration and CP and HICP are replicated in future studies, this would suggest that children and younger adolescents with an immigration background may be at higher risk for having CP. The findings therefore suggest that there may be a need to provide greater resources to children and adolescents with an immigration background, perhaps especially younger children.

This study has limitations. First, the data from this study were collected from a convenience sample of children and adolescents, and only 36% of the parents approached consented to their children participating. This response rate is lower than similar studies using school-based samples.[17,40,63] Second, the sample of participants with an immigration background identified here may not be representative of all children in Spain with an immigration background. For example, 14% of our sample had an immigration background compared with 20% to 30% nationally, according to official statistics.[18] Potential reasons for this discrepancy may be related to the study's sampling method. For example, the requirement for written literacy in Spanish may have reduced participation of first-generation immigrant parents. Additionally, obtaining data in school settings might have excluded individuals with higher family care responsibilities.

Table 7

Number and percent of participants with high-impact chronic pain by immigration background (N = 1025).

	Local background (N = 881)	Immigration background (N = 144)
No high-impact chronic pain	845 (96)	130 (90)
High-impact chronic pain	36 (4)	14 (10)

Future research should explore alternative sampling strategies, such as accessing community samples through immigration registers or partnerships with immigrant organizations. Third, the low sample of participants with an immigration background did not allow to study the potentially different effects of first-generation and second-generation immigrants on CP and HICP separately. The findings therefore need to be replicated in other samples—ideally samples that are more representative of the population as a whole—to determine their generalizability and reliability. Similarly, future studies could compare CP and HICP rates among immigrants to other groups with similar socioeconomic status (SES) who are not immigrants. This comparison could provide valuable insights into the unique contribution of immigration status vs other factors associated with SES. Fourth, because of the cross-sectional design used, causal relationships between immigration background and future CP and HICP cannot be inferred. Longitudinal studies assessing immigration background's predictive power on pain and related domains are needed.

Despite the study's limitations, this study contributes valuable insights into the association between immigration background and CP and HICP in children and adolescents. The findings that children and adolescent with an immigration background in Spain report higher rates of CP, especially younger children, and HICP provides information that could be used by stakeholders interested in improving the quality of life of this population.

Conflict of interest statement

The authors have no conflicts of interest to declare.

Acknowledgments

This work was partly funded by grants from the Spanish Ministry of Economy, Industry and Competitiveness (RTI2018-09870-B-I00; RED2022-134869-T), the European Regional Development Fund (ERDF), and the Government of Catalonia (AGAUR; 2021SGR-730). E.S.-R.'s work is supported by a grant from the Spanish Ministry of Science and Innovation (PID2020-113869RA-I00). E.S.'s work is supported by a grant from the Spanish Ministry of Science and Innovation (MCIN/AEI/10.13039/501100011033). J.R.-J. is supported by a doctoral grant from MINECO (PRE2019-089283). J.M.'s work is

supported by ICREA-Acadèmia. The Chair in Pediatric Pain is supported by Fundación Grünenthal.

Article history:
Received 10 January 2023
Received in revised form 7 September 2023
Accepted 30 October 2023
Available online 2 January 2024

References

[1] Alfven G. Socioeconomic status as a cause and consequence of psychosomatic symptoms from adolescence to adulthood. Acta Paediatr Int J Paediatrics 1993;82:580–7.
[2] Belhadj Kouider E, Koglin U, Petermann F. Emotional and behavioral problems in migrant children and adolescents in American countries: a systematic review. J Immigr Minor Health 2015;17:1240–58.
[3] Brattberg G. Do pain problems in young school children persist into early adulthood? A 13-year follow-up. Eur J Pain 2004;8:187–99.
[4] Bui Q, Doescher M, Takeuchi D, Taylor V. Immigration, acculturation and chronic back and neck problems among Latino-Americans. J Immigr Minor Health 2011;13:194–201.
[5] de la Vega R, Racine M, Sánchez-Rodríguez E, Tomé-Pires C, Castarlenas E, Jensen MP, Miró J. Pain extent, pain intensity, and sleep quality in adolescents and young adults. Pain Med 2016;17:1971–7.
[6] Dimitrova R, Bender M, Vijver F. Advances in immigrant family research. New York, NY: Springer, 2014.
[7] Dragioti E, Tsamakis K, Larsson B, Gerdle B. Predictive association between immigration status and chronic pain in the general population: results from the SwePain cohort. BMC Public Health 2020;20:1462.
[8] Du Y, Knopf H, Zhuang W, Ellert U. Pain perceived in a national community sample of German children and adolescents. Eur J Pain 2011;15:649–57.
[9] Fales JL, Murphy LK, Rights JD, Palermo TM. Daily peer victimization experiences of adolescents with and without chronic pain: associations with mood, sleep, pain, and activity limitations. J Pain 2020;21:97–107.
[10] Gobina I, Villberg J, Välimaa R, Tynjälä J, Whitehead R, Cosma A, Brooks F, Cavallo F, Ng K, de Matos MG, Villerusa A. Prevalence of self-reported chronic pain among adolescents: evidence from 42 countries and regions. Eur J Pain 2019;23:316–26.
[11] Groenewald CB, Wright DR, Palermo TM. Health care expenditures associated with pediatric pain-related conditions in the United States. PAIN 2015;156:951–7.
[12] Groenewald CB, Murray CB, Palermo TM. Adverse childhood experiences and chronic pain among children and adolescents in the United States. Pain Rep 2020;5:e839.
[13] Gualdi-Russo E, Toselli S, Masotti S, Marzouk D, Sundquist K, Sundquist J. Health, growth and psychosocial adaptation of immigrant children. Eur J Public Health 2014;24(suppl 1):16–25.
[14] Hair JF, Black WC, Babin BJ, Anderson RE. Canonical correlation: a supplement to multivariate data analysis. Multivariate data analysis: a global perspective. 7th ed. Upper Saddle River, NJ: Pearson Prentice Hall Publishing, 2010.
[15] Hirschfeld G, Wager J, Zernikow B. Physician consultation in young children with recurrent pain—a population-based study. PeerJ 2015;3:e916.
[16] Hoekman DR, Rutten JMTM, Vlieger AM, Benninga MA, Dijkgraaf MGW. Annual costs of care for pediatric irritable bowel syndrome, functional abdominal pain, and functional abdominal pain syndrome. J Pediatr 2015;167:1103–8.e2.
[17] Huguet A, Miró J. The severity of chronic pediatric pain: an epidemiological study. J Pain 2008;9:226–36.
[18] Inchley J, Currie D, Budisavljevic S, Torsheim T, Jåstad A, Cosma A, Kelly C, Arnarsson ÁM. Spotlight on adolescent health and well-being. Geneva, Switzerland: World Health Organization, 2018;1:58.
[19] Islam F. Immigrating to Canada during early childhood associated with increased risk for mood disorders. Commun Ment Health J 2015;51:723–32.
[20] King S, Chambers CT, Huguet A, MacNevin RC, McGrath PJ, Parker L, MacDonald AJ. The epidemiology of chronic pain in children and adolescents revisited: a systematic review. PAIN 2011;152:2729–38.
[21] Könning A, Rosenthal N, Brown D, Stahlschmidt L, Wager J. Severity of chronic pain in German adolescent school students: a cross-sectional study. Clin J Pain 2021;37:118–25.
[22] Könning A, Rosenthal N, Friese M, Hirschfeld G, Brown D, Wager J. Factors associated with physician consultation and medication use in children and adolescents with chronic pain: a scoping review and original data. Eur J Pain 2021;25:88–106.
[23] Kurita GP, Sjøgren P, Juel K, Højsted J, Ekholm O. The burden of chronic pain: a cross-sectional survey focussing on diseases, immigration, and opioid use. PAIN 2012;153:2332–8.
[24] Lange M, Kamtsiuris P, Lange C, Schaffrath Rosario A, Stolzenberg H, Lampert T. Sociodemographic characteristics in the German Health Interview and Examination Survey for Children and Adolescents (KiGGS)—operationalisation and public health significance, taking as an example the assessment of general state of health. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2007;50:578–89.
[25] Larsson B, Sund AM. Emotional/behavioural, social correlates and one-year predictors of frequent pains among early adolescents: influences of pain characteristics. Eur J Pain 2007;11:57–65.
[26] Luntamo T, Sourander A, Rihko M, Aromaa M, Helenius H, Koskelainen M, McGrath PJ. Psychosocial determinants of headache, abdominal pain, and sleep problems in a community sample of Finnish adolescents. Eur Child Adolesc Psychiatry 2012;21:301–13.
[27] Mansuri F, Nash MC, Bakour C, Kip K. Adverse childhood experiences (ACEs) and headaches among children: a cross-sectional analysis. Headache 2020;60:735–44.
[28] Marin TJ, Hayden JA, Lewinson R, Mahood Q, Pepler D, Katz J. A systematic review of the prospective relationship between bullying victimization and pain. J Pain Res 2021;14:1875–85.
[29] McAuliffe M, Triandafyllidou A. World migration report 2022. Geneva, Switzerland: International Organization for Migration.
[30] Méroc E, Moreau N, Lebacq T, Dujeu M, Pedroni C, Godin I, Castetbon K. Immigration and adolescent health: the case of a multicultural population. Public Health 2019;175:120–8.
[31] Miró J, Gertz KJ, Carter GT, Jensen MP. Pain location and intensity impacts function in persons with myotonic dystrophy type 1 and facioscapulohumeral dystrophy with chronic pain. Muscle Nerve 2014;49:900–5.
[32] Miró J, De La Vega R, Tomé-Pires C, Sánchez-Rodríguez E, Castarlenas E, Jensen MP, Engel JM. Pain extent and function in youth with physical disabilities. J Pain Res 2017;10:113–20.
[33] Miró J, Roman-Juan J, Sánchez-Rodríguez E, Solé E, Castarlenas E, Jensen MP. Chronic pain and high impact chronic pain in children and adolescents: a cross-sectional study. J Pain 2023;24:812–23.
[34] Naciones Unidas. Glossary on migration no. 34. International Migration Law 2019. Available at: http://medcontent.metapress.com/index/A65RM03P4874243N.pdf%5Cnhttp://www.epim.info/wp-content/uploads/2011/01/iom.pdf. Accessed 22 December 2023.
[35] Nelson S, Beveridge JK, Mychasiuk R, Noel M. Adverse childhood experiences (ACEs) and internalizing mental health, pain, and quality of life in youth with chronic pain: a longitudinal examination. J Pain 2021;22:1210–20.
[36] Östberg V, Alfven G, Hjern A. Living conditions and psychosomatic complaints in Swedish schoolchildren. Acta Paediatr 2006;95:929–34.
[37] Parent A-S, Teilmann G, Juul A, Skakkebaek NE, Toppari J, Bourguignon J-P. The timing of normal puberty and the age Limits of sexual precocity: variations around the world, secular trends, and changes after migration. Endocr Rev 2003;24:668–93.
[38] Park R, Mikami S, Leclair J, Bollom A, Lembo C, Sethi S, Lembo A, Jones M, Cheng V, Friedlander E, Nurko S. Inpatient burden of childhood functional GI disorders in the USA: an analysis of national trends in the USA from 1997 to 2009. Neurogastroenterol Motil 2015;27:684–92.
[39] Patterson B, Kyu HH, Georgiades K. Age at immigration to Canada and the occurrence of mood, anxiety, and substance use disorders. Can J Psychiatry 2013;58:210–7.
[40] Perquin CW, Hazebroek-Kampschreur AAJM, Hunfeld JAM, Bohnen AM, van Suijlekom-Smit LWA, Passchier J, van der Wouden JC. Pain in children and adolescents: a common experience. PAIN 2000;87:51–8.
[41] Pottie K, Dahal G, Georgiades K, Premji K, Hassan G. Do first generation immigrant adolescents face higher rates of bullying, violence and suicidal behaviours than do third generation and native born? J Immigr Minor Health 2015;17:1557–66.
[42] Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, Keefe FJ, Mogil JS, Ringkamp M, Sluka KA, Song X-J, Stevens B, Sullivan MD, Tutelman PR, Ushida T, Vader K. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. PAIN 2020;161:1976–82.
[43] Schwille IJD, Giel KE, Ellert U, Zipfel S, Enck P. A community-based survey of abdominal pain prevalence, characteristics, and health care use among children. Clin Gastroenterol Hepatol 2009;7:1062–8.

[44] Skrove M, Romundstad P, Indredavik MS. Chronic multisite pain in adolescent girls and boys with emotional and behavioral problems: the Young-HUNT study. Eur Child Adolesc Psychiatry 2015;24:503–15.
[45] Sleed M, Eccleston C, Beecham J, Knapp M, Jordan A. The economic impact of chronic pain in adolescence: methodological considerations and a preliminary costs-of-illness study. PAIN 2005;119:183–90.
[46] Soares JJF, Grossi G. Experience of musculoskeletal pain—comparison of immigrant and Swedish patients. Scand J Caring Sci 1999;13:254–66.
[47] Stanford EA, Chambers CT, Biesanz JC, Chen E. The frequency, trajectories and predictors of adolescent recurrent pain: a population-based approach. PAIN 2008;138:11–21.
[48] Stevens GWJM, Vollebergh WAM. Mental health in migrant children. J Child Psychol Psychiatry 2008;49:276–94.
[49] Stevens GWJM, Walsh SD, Huijts T, Maes M, Madsen KR, Cavallo F, Molcho M. An internationally comparative study of immigration and adolescent emotional and behavioral problems: effects of generation and gender. J Adolesc Health 2015;57:587–94.
[50] Stevens GWJM, Boer M, Titzmann PF, Cosma A, Walsh SD. Immigration status and bullying victimization: associations across national and school contexts. J Appl Develop Psychol 2020;66:101075.
[51] Stevens BJ, Hathway G, Zempsky WT. Oxford textbook of pediatric pain. Oxford, England: Oxford University Press, 2021.
[52] Toliver-Sokol M, Murray CB, Wilson AC, Lewandowski A, Palermo TM. Patterns and predictors of health service utilization in adolescents with pain: comparison between a community and a clinical pain sample. J Pain 2011;12:747–55.
[53] Union European. Eurostat. Available: https://ec.europa.eu/eurostat/web/migration-asylum/visualisations. Accessed December 21, 2022.
[54] United Nations, Department of Economic and Social Affairs. International migration report: 2017; 2017.
[55] United Nations Economic Commission for Europe. Conference of European statisticians recommendations for the 2010 censuses of population and housing, 2006. p. 205. Available at: http://www.unece.org/fileadmin/DAM/stats/publications/CES_2010_Census_Recommendations_English.pdf. Accessed 22 December 2023.
[56] van Dijk A, McGrath PA, Pickett W, Van Den Kerkhof EG. Pain and self-reported health in Canadian children. Pain Res Manag 2008;13:407–11.
[57] Varni JW, Stucky BD, Thissen D, Dewitt EM, Irwin DE, Lai JS, Yeatts K, Dewalt DA. PROMIS pediatric pain interference scale: an item response theory analysis of the pediatric pain item bank. J Pain 2010;11:1109–19.
[58] Venepalli NK, Van Tilburg MAL, Whitehead WE. Recurrent abdominal pain: what determines medical consulting behavior? Dig Dis Sci 2006;51:192–201.
[59] Vila M, Kramer T, Obiols JE, Garralda ME. Abdominal pain in British young people: associations, impairment and health care use. J Psychosom Res 2012;73:437–42.
[60] Von Korff M, Scher AI, Helmick C, Carter-Pokras O, Dodick DW, Goulet J, Hamill-Ruth R, LeResche L, Porter L, Tait R, Terman G, Veasley C, Mackey S. United States national pain strategy for population research: concepts, definitions, and pilot data. J Pain 2016;17:1068–80.
[61] Von Korff M, Debar LL, Krebs EE, Kerns RD, Deyo RA, Keefe FJ. Graded chronic pain scale revised: mild, bothersome, and high-impact chronic pain. PAIN 2020;161:651–61.
[62] Wager J, Hechler T, Darlington AS, Hirschfeld G, Vocks S, Zernikow B. Classifying the severity of paediatric chronic pain - an application of the chronic pain grading. Eur J Pain 2013;17:1393–402.
[63] Wager J, Brown D, Kupitz A, Rosenthal N, Zernikow B. Prevalence and associated psychosocial and health factors of chronic pain in adolescents: differences by sex and age. Eur J Pain 2020;24:761–72.
[64] Webb R, Brammah T, Lunt M, Urwin M, Allison T, Symmons D. Prevalence and predictors of intense, chronic, and disabling neck and back pain in the UK general population. Spine (Phila Pa 1976) 2003;28:1195–202.
[65] World Health Organization. Promoting the health of refugees and migrants—72nd world health assembly. Vol. 1, 2019. p. 1–13. Available at: http://www.unhcr.org/uk/figures-at-a-glance.html. Accessed 22 December 2023.
[66] Zernikow B, Wager J, Hechler T, Hasan C, Rohr U, Dobe M, Meyer A, Hübner-Möhler B, Wamsler C, Blankenburg M. Characteristics of highly impaired children with severe chronic pain: a 5-year retrospective study on 2249 pediatric pain patients. BMC Pediatr 2012;12:54.

4.3. Study III

The increase in early menarche is associated with the increase of chronic back pain in female adolescents: The HBSC study 2002-2014.

The increase in early menarche is associated with the increase of chronic back pain in female adolescents: The HBSC study 2002-2014

Josep Roman-Juan, MSc,[a,b] Mark P. Jensen, PhD,[c] and Jordi Miró, PhD[a,b]

[a] Universitat Rovira i Virgili, Unit for the Study and Treatment of Pain – ALGOS, Research Center for Behavior Assessment (CRAMC), Department of Psychology, Catalonia, Spain
[b] Institut d'Investigació Sanitària Pere Virgili; Universitat Rovira i Virgili, Catalonia, Spain
[c] Department of Rehabilitation Medicine, University of Washington, Seattle, WA, USA

Correspondence:
Jordi Miró
Departament de Psicologia
Universitat Rovira i Virgili
Carretera de Valls, s/n
43007 Tarragona
Spain

E-mail: jordi.miro@urv.cat
ORCID: 0000-0002-1998-6653

Tel.: +34-977558179
Fax: +34-977558088

Running title: Early menarche and chronic back pain

Abstract

Objective: Research has shown that there has been an increase in the prevalence of chronic back pain in adolescents, especially in female adolescents. The purpose of the current study was to test the hypothesis that the observed increase in the prevalence of early menarche in female adolescents is contributing to the increase in the prevalence of chronic back pain over time in this population.

Methods: Cross-sectional data from 251,390 female adolescents from 27 countries/regions were drawn from the HBSC questionnaire-based surveys conducted in 2002, 2006, 2010 and 2014. The Karlson–Holm–Breen method was used to examine the explanatory role of the increase in the prevalence of early menarche on the increase in the prevalence of chronic back pain whilst controlling for socioeconomic status, physical activity, body mass index, and psychological symptoms.

Results: The increase in the prevalence of early menarche between 2002 and 2014 was associated with the increase in the prevalence of chronic back pain ($p < 0.001$). The percent of chronic back pain prevalence increase accounted for by the increase in early menarche was 2.2%.

Conclusions: The increase in the prevalence of chronic back pain in female adolescents observed over the last decade may be explained, in part, by the decrease in the age of menarche. This finding, coupled with research showing a decline in early menarche worldwide, highlights the need to delve deeper into the underlying mechanisms of the association between early menarche and pain – particularly chronic back pain – in female adolescents.

Keywords: Chronic back pain; Adolescents; Early menarche; Prevalence

INTRODUCTION

Chronic back pain in adolescence is a highly prevalent,[1] disabling,[2] and costly condition,[3] and is associated with a greater risk of impairment into adulthood.[4] Recent studies have shown that there has been an increase in the prevalence of chronic back pain in adolescents over the last decades,[1] and that this increase has been higher in female than in male adolescents.[5]

Research suggests that the increase in a number of life-style-related factors (e.g., time spent in sedentary screen-related activities and obesity),[6] as well as increases in sleep disturbance and psychological distress [7] may have contributed to the observed increase in the prevalence of chronic back pain in this population. However, the findings of these studies only account for a small percentage of the increases in pain prevalence in adolescents, and the causes of the increase in chronic back pain prevalence remain poorly understood. Additional research that identifies the factors associated with this increase is therefore warranted, as this could provide valuable knowledge for prevention purposes.

In female adolescents, another factor that has the potential to explain the observed increases in chronic back pain prevalence is the decline in the mean menarcheal age (i.e., age of the first menstruation) that has also been observed over the last decades.[8] In support of this hypothesis, there is research showing that an earlier age of first menarche is associated with higher levels of sex-related hormones during puberty (e.g., estradiol/estrogen),[9] which have been suggested to have a

pronociceptive effect.[10,11] Moreover, several studies have shown that earlier menarche onset is associated with a higher prevalence of somatic complaints among female adolescents,[12] including chronic pain.[13]

Given these considerations, the aim of this study was to test the hypothesis that the increase in the prevalence of early menarche in female adolescents is contributing to the increase in the prevalence of chronic back pain in this population, over and above the effects of other factors associated with early menarche and back pain, such as socioeconomic status,[14,15] body mass index (BMI),[16,17] psychological symptoms (e.g., depressive symptoms),[7,18] and physical activity.[19,20]

METHOD

Study Design, Setting, and Participants

Data for the current analyses were retrieved from the HBSC study, an international, repeated cross-sectional study initiated by the World Health Organization in 1983-1984. The HBSC collects data about adolescents' health behaviors and well-being indicators across multiple countries and regions of Europe and North America. Participating countries collect these data every four years from independent, nationally representative samples of boys and girls aged 11, 13, and 15 years, using multi-stage stratified random cluster sampling, with school classes or schools as the sampling unit. Study participation is voluntary and anonymous. Data collection is conducted through standardized self-administered questionnaires in classroom settings. The HBSC study adheres to ethical consent procedures and secures institutional consent in compliance with local requirements from schools, parents, and

adolescents, either through active or passive informed consent/assent processes. Only consenting adolescents whose parents did not object to their child participating are included in the study. Additional details regarding the methodology of the HBSC study can be found elsewhere.[21]

To test the study hypothesis, we retrieved data from 801,648 adolescents across surveys conducted in 2001/2, 2005/6, 2009/10, and 2013/14. In these analyses, data from the survey conducted in 2017/18 were not used because questions about menarche were not included in that survey. Participating countries were eligible for the present analyses if they had collected data on the age of menarche and back pain in the four survey years. Although a number of papers have been published using these data,[8,17,22,23] none of the published papers have examined whether the increase in early menarche contributes to the increase in the prevalence of chronic back pain.

This study was conducted according to the STROBE guidelines for cross-sectional studies.[24]

Variables and measures

Independent variable

Survey year. The variable representing the time of assessment was the survey year (i.e., 2001/02, 2005/06, 2009/10, and 2013/14). Following the procedure of prior studies using data from the HBSC study,[7] survey year was treated as a continuous variable, with values ranging from 1 (“2002”) to 4 (“2014”).

Dependent variable

Chronic back pain. The information regarding the experience of chronic pain back was based on the survey participant's responses to the back pain item of the HBSC symptom checklist (HBSC-SCL).[25] With the HBSC-SCL, respondents are asked to respond to the question "In the last 6 months, how often have you had the following…?" with respect to eight different symptoms – including back pain – using a 5-point scale (1 = "About every day," 2 = "More than once a week," 3 = "About every week," 4 = "About every month," and 5 = "Rarely or never"). Following the procedure used in prior studies using the HBSC-SCL, [5–7] the presence of chronic back pain was deemed positive if adolescents reported having back pain weekly or more often over the last 6 months.

Mediator variable

Early menarche. The variable representing the age of menarche was computed based on the survey respondents' answer to the question, "Have you begun to menstruate (have periods)?" with response options being "No, I have not yet begun to menstruate" and "Yes, I began at the age of _ years and _ months." Given that menarche onset varies among different populations, there is not a universally accepted age cut-off for classifying individuals having early menarche.[26] Therefore, classification should be determined in the context of the specific population under investigation. In line with the approach employed by Kløven and colleagues,[13] we adopted a 25th percentile cut-off, rounded to the nearest whole year, to define early menarche in this study. This turned out to be

11.33 years. Therefore, in this study's population, early menarche was defined as occurring before the age of 11.

Control variables

On the basis of prior research on potential factors associated with early menarche and chronic back pain,[7,15–20,27] participants' socioeconomic status, physical activity, body mass index, and psychological symptoms were included as control variables in the current study.

Socioeconomic status. Information regarding the participants' socioeconomic status was extracted from the Family Affluence Scale II (FAS II).[28] With the FAS II, participants' are asked "Does your family own a car, van or truck?" with response options being (1) "No," (2) "Yes, one," and (3) "Yes, two;" "Do you have your own bedroom for yourself?" with response options being (1) "Yes" and (2) "No;" "During the past 12 months, how many times did you travel away on holiday/ vacation with your family?" with response options being (1) "Not at all," (2) "Once," (3) "Twice," and (4) "More than twice;" and "How many computers does your family own?" with response options being (1) "None," (2) "One," (3) "Two," and (4) "More than two." Responses to the items are summed into a total score, which is then converted into proportional rankings, reflecting the comparative wealth status of participants in their respective residential countries. Using this approach, adolescents were classified into three categories within each country and region: the bottom 20% (low affluence), the middle 60% (medium affluence), and the top 20% (high affluence).[29]

Physical activity. The participants' responses to the question "Over the past 7 days (week), on how many days were you physically active

for a total of at least 60 min per day?" was used as the measure of physical activity. The response options to this question range from (1) "0 days" to (7) "7 days." The question was preceded by explanatory text which defined physical activity as "Any activity that increases your heart rate and makes you get out of breath some of the time."[30]

Body mass index (BMI). Participants' self-reported their body height (cm) and weight (kg). These were used to calculate participants' body mass index (BMI) using the kg/m2 formula.

Psychological symptoms. The variable used as an indicator of psychological symptoms was computed based on the participant's responses to the four items of the HBSC-SCL assessing psychological symptoms (i.e., feeling low, irritability or bad temper, feeling nervous, and sleep difficulties).[25,31] Following the procedures used by prior researchers using the HBSC-SCL,[7] and in line with research demonstrating the validity of these items as a unidimensional measure of psychological symptoms in school-aged children,[31] we conducted reverse recoding on participants' responses to each item (range: 0 to 4; higher scores indicating a greater presence of each psychological symptom) and then we grouped these four items to create a single, composite measure of psychological symptoms (range: 0-16). Higher scores on this measures indicate a greater frequency of psychological symptoms. For the current sample, Cronbach's α = .73, indicating good internal consistency.

Data preparation and Analysis

Data preparation included removing: (1) cases from countries that did not provide information on back pain and/or menarche in each of the

four measurement periods (i.e., Austria, Armenia, Albania, Austria, Bulgaria, Denmark, Greenland, Iceland, Lithuania, Luxembourg, Malta, Poland, Republic of Moldova, Romania, Russia, Slovakia, Turkey, and United States of America); (2) male adolescents; (3) female adolescents who did not provide information about their age or were under the age of 11, given that the determination of early menarche status was not possible in this age group; and (4) female adolescents aged ≥11 who did not provide answers to all the primary study variables (i.e., menarche and back pain).

Means and standard deviations for continuous variables and number and percentages for categorical variables were computed to describe the study sample as a whole and between the four survey years (i.e., 2002, 2006, 2010, and 2014). Two logistic regression models, one with chronic back pain as the criterion variable, and the other with early menarche as the criterion variable, were fitted to evaluate the statistical significance of the increase in the prevalence of chronic back pain and early menarche between 2002 and 2014. In both models, survey year was introduced as a continuous independent variable. Additionally, a third logistic regression model with chronic back pain as the criterion variable and early menarche as the independent variable was fitted to evaluate their statistical association. The contribution of the increase in early menarche to the increase in the prevalence of chronic back pain between 2002 and 2014 was examined using the Karlson-Holm-Breen (KHB) method.[32,33] With this method, we estimated the confidence intervals for the total, direct, and specific indirect effect of survey year (i.e., predictor variable) to chronic back pain (i.e., outcome variable) through early menarche (i.e., mediator

variable). The significance of the indirect effect was determined through the examination of confidence intervals that were calculated using a bias-corrected bootstrapping procedure with *n* = 10,000 subsamples. This indirect effect of early menarche on the association between survey year and chronic back pain was considered significant if the 95% confidence interval did not encompass zero. The KHB method is particularly suitable for examining mediation in non-linear models[32,33] and has been previously used to examine the contribution of increases in screen time and obesity on the increasing trend of chronic back pain in adolescents.[6] Participants' socioeconomic status, level of physical activity, BMI, and level of psychological symptoms were included to account for the potential confounding effects of these variables. Cluster-robust standard errors, accounting for the nesting of adolescents within countries, were used in all analyses. Missing data were handled using list-wise deletion. All statistical analyses were conducted using STATA 14 (Stata Corp., Texas, USA).

RESULTS

As noted previously, we first removed data from countries that did not participate in the four survey waves that are the focus of this study or did not provide data on age of menarche and back pain (n = 240,685). Data from the remaining male adolescents (n = 275,265), female adolescents that did not provide information about their age or were under the age of 11, (n = 4,692); female adolescents aged ≥11 who did not provide answers to all the primary study variables (i.e., menarche and back pain; n = 29616) were removed. Thus, the final sample consisted of 251,390 adolescents from 27 countries.

Results

Table 1 provides a summary of the study sample. As can be seen, the mean age of adolescents was 13.65 (SD = 1.63) and the sample size was similar across the four survey waves. The weighted prevalence of early menarche was 3.5% in 2002, 4.3% in 2004, 5.4% in 2010, and 5.3% in 2014. The weighted prevalence of chronic back pain was 20.7% in 2002, 22.2% in 2004, 23.2% in 2010, and 25.0% in 2014. The significance of an increasing trend over time in both early menarche (B = .02, z = 5.67, p<.001, 95% confidence interval [CI] =.01 - .03) and chronic back pain (B = .04, z = 6.96, p<.001, 95%CI = .03 - .05) was confirmed in the current sample. Furthermore, there was a positive and statistically significant association between early menarche and chronic back pain, such that girls with early menarche had a 5.6% higher odds of reporting chronic back pain than girls who did not have early menarche (OR = 1.56, z = 13.15, p<.001, 95%CI = 1.46 – 1.66). This association remained significant after controlling for socioeconomic status, BMI, physical activity, and psychological symptoms (OR = 1.22, z = 6.01, p<.001, 95%CI = 1.14 – 1.30).

Table 1. Description of the study sample (weighted estimates; N = 251,390).

Variable	N/M	%/SD
Survey year, N and %		
2002	59,960	23.8
2006	62,103	24.8
2010	64,594	25.7
2014	64,733	25.7

Age, N and %		
11-year-olds	77,709	30.9
13-year-olds	86,641	34.4
15-year-olds	87,040	34.7
Socioeconomic status,[a] N and %		
Low	44,654	18.2
Medium	150,872	61.9
High	47,944	19.8
Physical activity,[b] N and %		
0	10,948	4.5
1	22,243	9.1
2	41,826	17.1
3	45,863	18.7
4	38,909	15.9
5	32,944	13.5
6	19,991	8.2
7	32,088	13.1
BMI,[c] M and SD	19.37	3.3
Psychological symptoms,[d] M and SD	5.42	4.1
Early menarche, N and %		
Yes	11,517	4.6
No	239,873	95.4
Chronic back pain, N and %		
Yes	57,348	22.8

No	194,042	77.2
Country/region of residence, N and %		
Belgium Flemish	8,963	3.6
Belgium French	8,275	3.3
Canada	16,162	6.5
Croatia	9,882	3.9
Czech Republic	9,174	3.6
England	9,370	3.7
Estonia	7,198	2.9
Finland	9,234	3.7
France	12,589	5.0
Germany	10,531	4.2
Greece	8,210	3.3
Hungary	7,854	3.1
Ireland	7,724	3.1
Israel	8,132	3.2
Italy	7,965	3.2
Latvia	8,183	3.3
Macedonia	8,134	3.2
Netherlands	6,416	2.5
Norway	8,000	3.2
Portugal	7,980	3.2
Scotland	10,571	4.2
Slovenia	9,438	3.8

Spain	13,472	5.4
Sweden	10,672	4.2
Switzerland	10,170	4.0
Ukraine	8,486	3.2
Wales	8,605	3.4

Note*:* Sample size varies due to non-responses. BMI = Body mass index. N = Number; M = Mean; SD = Standard deviation.

[a]*n* = 243,470 (missing = 7,920); [b]*n* = 244,812 (missing = 6,578); [c]*n* = 206,774 (missing = 44,616); [d]*n* = 247,611 (missing = 3,779).

Table 2 shows the decomposition of the total effect of survey year on chronic back pain into its direct and indirect effect through early menarche while controlling for socioeconomic status, BMI, physical activity, and psychological symptoms. As can be seen, the results supported the mediation effect of early menarche as explaining, at least in part, the increase in the prevalence of back pain observed over time. The total effect of the survey year on chronic back pain was 1.02 times larger than the direct effect, and 2.2% of the total effect was due to early menarche.

Table 2. Decomposition of the total effects of survey year on chronic back pain through early menarche.

	B	*SE robust*	*z*	*P*-value	*CIbca (LL)*	*CIbca (UL)*
Survey year						
Total effect	.012	.003	3.62	<.001	.005	.02
Direct effect	.011	.003	3.54	<.001	.005	.02
Indirect effect	.0003	.00007	3.31	.001	.0001	.0004

Note*:* N for analysis is 193,929. Findings adjusted for socioeconomic status, body mass index, physical activity, and psychological symptoms. SE = Standard error; CIbca (LL) = lower limit of a 95% confidence interval; CIbca (UL) = upper limit.

DISCUSSION

The findings confirmed the study hypothesis that the decrease in the mean age of menarche over time significantly contributes to the observed increase in the prevalence of chronic back pain in female adolescents. This finding adds to the growing body of research examining the factors contributing to the increase in the prevalence of chronic back pain among adolescents.[6,7]

Several studies have found a significant association between early age of menarche and the prevalence of chronic pain in children and adolescents.[8,13] In relation to this, it has been observed that girls experiencing early menarche tend to have higher levels of estrogen, a hormonal pattern that may persist even after a 5-year period.[9,34] In addition, research findings suggest that estradiol – a key estrogen hormone – might

exert a nociceptive effect,[10,11,35] potentially increasing the risk for developing chronic pain. This hormonal link provides a plausible biological mechanism that may explain the observed association between early menarche and chronic back pain in female adolescents. Further investigation into the interplay between hormonal fluctuations and pain perception could offer valuable insights into the increasing prevalence and complex etiology of chronic back pain in adolescents.

In addition to the potential direct physiological-based effects of early menarche on the prevalence and severity of chronic back pain in female adolescents, it is possible that early menarche may elevate the risk of chronic back pain through other psychosocial factors. For example, menarche can be viewed as a stressful event associated with significant physical and lifestyle changes and altered expectations from the environment. Experiencing menarche early could therefore require significant coping efforts before the young woman is emotionally ready.[36] Consistent with this possibility, there is research showing that female adolescents with early menarche endorse higher levels of psychological distress (e.g., depressive symptoms)[18] which in turn are associated with the presence of chronic pain.[1,37,38] Also consistent with this hypothesis are the findings from a recent study showing that an increase in adolescents' psychological symptoms was significantly associated with the increase in the prevalence of chronic back pain in female adolescents.[7]

Furthermore, taking into account findings showing that early menarche is associated with higher BMI,[17] and research showing that the increase in the levels of BMI contribute to the increase in the prevalence of

chronic back pain in adolescents over the last decade,[6] it is possible that the observed decrease in the mean menarcheal age over the last decades may be associated with an increase in BMI in this population, which may then contribute to the observed rise in chronic back pain in female adolescents. Additionally, there is research showing that female adolescents reporting early menarche also report higher rates of bullying victimization,[23] and there is evidence of higher rates of chronic pain, including chronic back pain, among children and adolescents experiencing bullying victimization.[39] A greater understanding of the complex interplay between early menarche, BMI, bullying, stress, and chronic pain could inform interventions that could help to treat and/or reduce the risk of developing chronic back pain in female adolescents.

This study has a number of limitations that should be considered when interpreting the results. Perhaps the most notable is the cross-sectional design of the HBSC study, which precludes drawing causal conclusions from the analyses. Longitudinal studies examining the temporal sequence of the association between menarche onset and subsequent chronic back pain are needed to determine the temporal sequencing of these variables. Moreover, the reliance on self-reported measures for assessing early menarche and chronic back pain introduces the potential for recall bias. However, self-reported information on these variables is generally accepted as valid and reliable, particularly in large epidemiological studies.[40] Third, although we controlled for several possible confounders, the unavailability of other possible confounding variables, such as self-identified race and ethnicity and immigration status, in the

HBSC study limits our ability to consider their influence. Lastly, the findings of this study may not generalize to adolescent girls in populations not represented in the HBSC study.

Despite the study's limitations, the findings provide new information regarding the factors that may underly the observed increase in the prevalence of chronic back pain in female adolescents. The finding that early menarche contributes to the increase in the prevalence of chronic back pain over time, coupled with research showing a decline in early menarche [12] underscores the need to delve deeper into the underlying mechanisms of the association between early menarche and pain -particularly chronic back pain- in female adolescents.

Acknowledgements: HBSC is an international study carried out in collaboration with WHO/EURO. The International Coordinator of the 2005/06 to 2013/14 surveys was Prof. Candace Currie and the Data Bank Manager was Prof. Oddrun Samdal. The surveys were conducted by Principal Investigator in 27 countries: Flemish Belgium (Maxim Dierckens and Katrijn Delaruelle), French Belgium (Katia Castetbon), Croatia (Ivana Pavic Simetin), Denmark (Katrine Rich Madsen), England (Fiona Brooks and Ellen Klemera), Estonia (Leila Oja), Finland (Leena Paakkari and Nelli Lyyra), France (Emmanuelle Godeau), Germany (Matthias Richter), Greece (Anna Kokkevi), Hungary (Ágnes Németh), Ireland (Saoirse Nic Gabhainn), Israel (Yossi Harel-Fisch), Italy (Alessio Vieno), Latvia (Iveta Pudule), Lithuania (Kastytis Šmigelskas), Macedonia (Lina Kostarova Unkovska), the Netherlands (Gonneke Stevens and Saskia van Dorsselaer), Poland (Joanna Mazur and Agnieszka Malkowska-Szkutnik),

Portugal (Tania Gaspar), Russia (Anna Matochkina), Scotland (Jo Inchley), Slovenia (Helena Jericek), Spain (Carmen Moreno and Francisco Rivera), Sweden (Petra Löfstedt), Switzerland (Hervé Kuendig and Marina Delgrande), and Wales (Chris Roberts).

Conflicts of Interest and Source of Funding: The authors declare no financial or other relationships that might lead to a conflict of interest related to this study. This work was partly funded by grants from the Spanish Ministry of Economy, Industry and Competitiveness (RTI2018-09870-B-I00; RED2022-134869-T), the European Regional Development Fund (ERDF), and the Government of Catalonia (AGAUR; 2021SGR-730). JR-J is supported by a doctoral grant from MINECO (PRE2019-089283). JM's work is supported by ICREA-Acadèmia. The Chair in Pediatric Pain is supported by Fundación Grünenthal.

REFERENCES

1. Miró J, Roman-Juan J, Sánchez-Rodríguez E, Solé E, Castarlenas E, Jensen MP. Chronic Pain and High Impact Chronic Pain in Children and Adolescents: A Cross-Sectional Study. *J Pain*. 2023;24(5):812-823. doi:10.1016/j.jpain.2022.12.007

2. MacDonald J, Stuart E, Rodenberg R. Musculoskeletal low back pain in school-aged children a review. *JAMA Pediatr*. 2017;171(3):280-287. doi:10.1001/jamapediatrics.2016.3334

3. Kitschen A, Wahidie D, Meyer D, et al. Cost-of-illness and Economic Evaluation of Interventions in Children and Adolescents with Chronic Pain. *Clin J Pain*. Published online January 25, 2024. doi:10.1097/AJP.0000000000001199

4. Hestbaek L, Leboeuf-Yde C, Kyvik KO. Is comorbidity in adolescence a predictor for adult low back pain? A prospective study of a young population. *BMC Musculoskelet Disord*. 2006;7. doi:10.1186/1471-2474-7-29

5. Roy R, Galán S, Sánchez-Rodríguez E, et al. Cross-National Trends of Chronic Back Pain in Adolescents: Results From the HBSC Study, 2001-2014. *Journal of Pain*. 2022;23(1):123-130. doi:10.1016/j.jpain.2021.07.002

6. Roman-Juan J, Roy R, Jensen MP, Miró J. The explanatory role of sedentary screen time and obesity in the increase of chronic back pain amongst European adolescents: The HBSC study 2002–2014. *European Journal of Pain (United Kingdom)*. 2022;26(8):1781-1789. doi:10.1002/ejp.2003

7. Roman-Juan J, Jensen MP, Miró J. Increases in Sleep Difficulties and Psychological Symptoms are Associated with the Increase of Chronic Back Pain in Adolescents: The HBSC Study 2002-2018. *J Pain*. Published online 2023. doi: 10.1016/j.jpain.2023.09.004

8. Lian Q, Li R, Elgar FJ, Su Q. Early physical maturation and subjective health complaints in adolescent girls: A pooled cross-sectional analysis. *J Epidemiol Community Health (1978)*. 2022;77(2):108-114. doi:10.1136/jech-2022-219547

9. Hamajima N, Hirose K, Tajima K, et al. Menarche, menopause, and breast cancer risk: Individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies. *Lancet Oncol*. 2012;13(11):1141-1151. doi:10.1016/S1470-2045(12)70425-4

10. Craft RM, Mogil JS, Maria Aloisi A. Sex differences in pain and analgesia: the role of gonadal hormones. *European Journal of Pain*. 2004;8(5):397-411. doi:https://doi.org/10.1016/j.ejpain.2004.01.003

11. Bartley EJ, Fillingim RB. Sex differences in pain: a brief review of clinical and experimental findings. *Br J Anaesth*. 2013;111(1):52-58. doi:10.1093/bja/aet127

12. Lian Q, Li R, Elgar FJ, Su Q. Early physical maturation and subjective health complaints in adolescent girls: a pooled cross-sectional analysis. *J Epidemiol Community Health (1978)*. 2023;77(2):108. doi:10.1136/jech-2022-219547

13. Kløven B, Hoftun GB, Romundstad PR, Rygg M. Relationship between pubertal timing and chronic nonspecific pain in adolescent girls: The Young-HUNT3 study (2006-2008). *PAIN*. 2017;158(8):1554-1560. doi:10.1097/j.pain.0000000000000950

14. Posner RB. Early menarche: A review of research on trends in timing, racial differences, etiology and psychosocial consequences. *Sex Roles*. 2006;54(5-6):315-322. doi:10.1007/s11199-006-9003-5

15. Madsen KM, Holstein BE, Madsen KR. Recurrent headache, stomachache, and backpain among adolescents: association with exposure to bullying and parents' socioeconomic status. *Scand J Pain*. Published online 2023. doi:10.1515/sjpain-2022-0144

16. Palmer AJ, Poveda JL, Martinez-Laguna D, et al. Childhood overweight and obesity and back pain risk: A cohort study of 466 997 children. *BMJ Open*. 2020;10(9). doi:10.1136/bmjopen-2019-036023

17. Currie C, Ahluwalia N, Godeau E, Nic Gabhainn S, Due P, Currie DB. Is Obesity at Individual and National Level Associated With Lower Age at Menarche? Evidence From 34 Countries in the Health Behaviour in School-aged Children Study. *Journal of Adolescent Health*. 2012;50(6):621-626. doi:10.1016/j.jadohealth.2011.10.254

18. Sequeira ME, Lewis SJ, Bonilla C, Smith GD, Joinson C. Association of timing of menarche with depressive symptoms and depression in adolescence: Mendelian randomisation study. *British Journal of Psychiatry*. 2017;210(1):39-46. doi:10.1192/bjp.bp.115.168617

19. Calthorpe L, Brage S, Ong KK. Systematic review and meta-analysis of the association between childhood physical activity and age at menarche. *Acta Paediatrica, International Journal of Paediatrics*. 2019;108(6):1008-1015. doi:10.1111/apa.14711

20. Swain MS, Henschke N, Kamper SJ, Gobina I, Ottová-Jordan V, Maher CG. Pain and moderate to vigorous physical activity in adolescence: An international population-based survey. *Pain Medicine (United States)*. 2016;17(5):813-819. doi:10.1111/pme.12923

21. Currie C, Inchley J, Molcho M, Lenzi M, Veselska Z, Wild F. Health behaviour in school-aged children (HBSC) study protocol: background, methodology and mandatory items for the 2018/19 survey. Published online 2018.

22. Steppan M, Whitehead R, McEachran J, Currie C. Family composition and age at menarche: Findings from the international Health Behaviour in School-aged Children study. *Reprod Health*. 2019;16(1):176. doi:10.1186/s12978-019-0822-6

23. Su Q, Chen Z, Li R, Elgar FJ, Liu Z, Lian Q. Association Between Early Menarche and School Bullying. *Journal of Adolescent Health*. 2018;63(2):213-218. doi:https://doi.org/10.1016/j.jadohealth.2018.02.008

24. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. *The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies*. Vol 370.; 2007. www.plosmedicine.org

25. Haugland S, Wold B. Subjective health complaints in adolescence - Reliability and validity of survey methods. *J Adolesc*. 2001;24(5):611-624. doi:10.1006/jado.2000.0393

26. Parent AS, Teilmann G, Juul A, Skakkebaek NE, Toppari J, Bourguignon JP. The Timing of Normal Puberty and the Age Limits of Sexual Precocity: Variations around the World, Secular Trends, and Changes after Migration. *Endocr Rev*. 2003;24(5):668-693. doi:10.1210/er.2002-0019

27. Hestbaek L, Leboeuf-Yde C, Kyvik KO. Are lifestyle-factors in adolescence predictors for adult low back pain? A cross-sectional and prospective study of young twins. *BMC Musculoskelet Disord*. 2006;7:1-8. doi:10.1186/1471-2474-7-27

28. Currie C, Molcho M, Boyce W, Holstein B, Torsheim T, Richter M. Researching health inequalities in adolescents: The development of the Health Behaviour in School-Aged Children (HBSC) Family Affluence Scale. *Soc Sci Med*. 2008;66(6):1429-1436. doi:10.1016/j.socscimed.2007.11.024

29. Cosma A, Stevens G, Martin G, et al. Cross-National Time Trends in Adolescent Mental Well-Being From 2002 to 2018 and the Explanatory Role

of Schoolwork Pressure. *Journal of Adolescent Health*. 2020;66(6):S50-S58. doi:10.1016/j.jadohealth.2020.02.010

30. Prochaska JJ, Sallis JF, Long B. A Physical Activity Screening Measure for Use With Adolescents in Primary Care. *Arch Pediatr Adolesc Med*. 2001;155(5):554-559. doi:10.1001/archpedi.155.5.554

31. Gariepy G, McKinnon B, Sentenac M, Elgar FJ. Validity and Reliability of a Brief Symptom Checklist to Measure Psychological Health in School-Aged Children. *Child Indic Res*. 2016;9(2):471-484. doi:10.1007/s12187-015-9326-2

32. Kohler U, Karlson KB, Holm A. Comparing coefficients of nested nonlinear probability models. *Stata Journal*. 2011;11(3):420-438. doi:10.1177/1536867x1101100306

33. Breen R, Karlson KB, Holm A. Total, Direct, and Indirect Effects in Logit and Probit Models. *Sociol Methods Res*. 2013;42(2):164-191. doi:10.1177/0049124113494572

34. Emaus A, Espetvedt S, Veierød MB, et al. 17-beta-estradiol in relation to age at menarche and adult obesity in premenopausal women. *Hum Reprod*. 2008;23(4):919-927. doi:10.1093/humrep/dem432

35. Aloisi AM. Gonadal Hormones and Sex Differences in Pain Reactivity. *Clin J Pain*. 2003;19(3).

36. Mendle J, Turkheimer E, Emery RE. Detrimental psychological outcomes associated with early pubertal timing in adolescent girls. *Developmental Review*. 2007;27(2):151-171. doi:10.1016/j.dr.2006.11.001

37. Wager J, Brown D, Kupitz A, Rosenthal N, Zernikow B. Prevalence and associated psychosocial and health factors of chronic pain in adolescents:

Differences by sex and age. *European Journal of Pain (United Kingdom)*. 2020;24(4):761-772. doi:10.1002/ejp.1526

38. Miró J, Huguet A, Nieto R. Predictive factors of chronic pediatric pain and disability: a Delphi poll. *The journal of pain official journal of the American Pain Society*. 2007;8(10):774-792.

39. Solé E, Roman-Juan J, Sánchez-Rodríguez E, Castarlenas E, Jensen MP, Miró J. School bullying and peer relationships in children with chronic pain. *Pain*. Published online November 28, 2023. doi:101097/j.pain.0000000000003118

40. Jormanainen E, Fröjd S, Marttunen M, Kaltiala-Heino R. Is pubertal timing associated with involvement in bullying in middle adolescence? *Health Psychol Behav Med*. 2014;2(1):144-159. doi:10.1080/21642850.2014.881259

4.4. Study IV

The explanatory role of sedentary screen time and obesity in the increase of chronic back pain amongst European adolescents: The HBSC study 2002–2014.

Received: 8 November 2021 | Revised: 15 June 2022 | Accepted: 26 June 2022

DOI: 10.1002/ejp.2003

EJP European Journal of Pain

ORIGINAL ARTICLE

The explanatory role of sedentary screen time and obesity in the increase of chronic back pain amongst European adolescents: The HBSC study 2002–2014

Josep Roman-Juan[1,2] | **Rubén Roy**[1,2] | **Mark P. Jensen**[3] | **Jordi Miró**[1,2]

[1]Universitat Rovira i Virgili, Unit for the Study and Treatment of Pain – ALGOS, Research Center for Behavior Assessment (CRAMC), Department of Psychology, Catalonia, Spain

[2]Institut d'Investigació Sanitària Pere Virgili, Universitat Rovira i Virgili, Catalonia, Spain

[3]Department of Rehabilitation Medicine, University of Washington, Seattle, Washington, USA

Correspondence
Jordi Miró, Departament de Psicologia, Universitat Rovira i Virgili, Carretera de Valls, s/n, 43007 Tarragona, Spain.
Email: jordi.miro@urv.cat

Funding information
MINECO; ICREA-Acadèmia; Fundación Grünenthal, Universitat Rovira i Virgili; the Government of Catalonia, Grant/Award Number: 2017SGR-1321; the European Regional Development Fund; Spanish Ministry of Economy, Industry and Competitiveness, Grant/Award Number: RED2018-102546-T and RTI2018-09870-B-I00

Abstract

Background: Previous research has shown that chronic back pain amongst European adolescents is increasing. Determining the factors associated with this increasing trend is crucial for developing prevention strategies. In this study, we used data from the Health Behaviour in School-aged Children (HBSC) survey to examine whether increases in screen time and/or obesity between 2002 and 2014 were associated with the increase in the prevalence of chronic back pain amongst European adolescents during the 12-year period.

Methods: Data from 423,092 adolescents from 27 European countries/regions were drawn from the HBSC questionnaire-based surveys conducted in 2002, 2006, 2010 and 2014. The Karlson–Holm–Breen method was used to examine the explanatory role of increases in screen time and obesity on the increase in the prevalence of chronic back pain whilst controlling for sex and age.

Results: Increases in both screen time and obesity between 2002 and 2014 were associated with increases in the prevalence of chronic back pain ($p < 0.001$). The percent of chronic back pain prevalence increase accounted for by screen time and obesity was 3.98% and 1.65%, respectively.

Conclusions: The increase in the prevalence of chronic back pain amongst European adolescents may be explained, in part, by the rising trends in both sedentary screen time and obesity. The fact that screen time and obesity only accounted for a small part of the increase in the prevalence of chronic back pain indicates that other unmeasured factors also play a role.

Significance: More screen time and obesity are slightly associated with more chronic back pain (CBP) prevalence in adolescents across the WHO European Region. The findings may be used to identify ways to prevent or reduce the rising trend of CBP in adolescents.

1 | INTRODUCTION

Research has shown that chronic back pain interferes with function in adolescents (Bejia et al., 2005; Huguet et al., 2009; Jones et al., 2004) and has an enormous societal impact (Groenewald et al., 2015; Ochsmann et al., 2010). Research has also shown that adolescents with low back pain are more likely to experience low back pain in their adulthood (Brattberg, 2004; Hestbaek, Leboeuf-Yde, & Kyvik, 2006; Hestbaek, Leboeuf-Yde, Kyvik, & Manniche, 2006; Jeffries et al., 2007). Moreover, low back pain causes more global disability than any other of the 291 conditions studied in the Global Burden of Disease Study (Hoy et al., 2014; Wu et al., 2020).

Recent findings show that the prevalence of chronic back pain amongst European adolescents is increasing. For example, Roy and colleagues (Roy et al., 2021) examined pooled data from 33 countries, mainly European, of the Health Behaviour amongst School-aged Children (HBSC) cross-sectional survey conducted from 2002 to 2014 and found that the prevalence of self-reported chronic back pain had steadily increased from 18.3% to 21.6% across the 12-year period. Determining the factors that account for such an increase in the prevalence of chronic back pain amongst children and adolescents is important for policy-makers to improve the development and implementation of preventive and treatment strategies.

Another recent report from the World Health Organization Regional Office for Europe using data from the HBSC study (Inchley et al., 2017) revealed two additional worrisome findings. First, there has been a rapid increase (from 2002 to 2014) in the time adolescents have been spending in sedentary screen-based activities, with almost 90% of European adolescents exceeding the recommendations of 2-h screen time daily in 2014 (Ghekiere et al., 2018). Second, the number of obese adolescents had also increased in many European countries and regions during this period, reaching an average prevalence of 19% of adolescents above the normal weight in 2014 (Inchley et al., 2017).

Time spent in sedentary screen-based activities—such as computer use, tablet, smartphones and TVs—has been repeatedly associated with multiple health complaints and conditions, including back pain, in adolescents (Bento et al., 2020; Hakala et al., 2012; Joergensen et al., 2021; Keane et al., 2017; Lemes et al., 2021; Silva et al., 2017; Torsheim et al., 2010). There is also mounting evidence showing a significant positive association between obesity and low back pain in adolescents (Hershkovich et al., 2013; Hestbaek, Leboeuf-Yde, & Kyvik, 2006; Hestbaek, Leboeuf-Yde, Kyvik, & Manniche, 2006; Palmer et al., 2020; Paulis et al., 2014). Considering these findings as a group, it is reasonable to hypothesize that the increasing rates of screen time and obesity may be associated, in part at least, with the increase of chronic back pain prevalence in European adolescents. Here, we used data from the international HBSC survey collected during the four most recent waves (2001/2, 2005/6, 2009/10 and 2013/14) to test this hypothesis.

2 | METHOD

2.1 | Study design, setting and sample

The Health Behaviour amongst School-aged Children (HBSC) study is a World Health Organization collaborative cross-sectional study that aims to monitor the health and well-being of adolescents across Europe and North America using a standardized methodological approach (Currie et al., 2014). Data have been collected every 4 years since 1983/1984 in school settings from independent, nationally representative samples of 11-, 13- and 15-year-old boys and girls in each participating country/region. Participants are recruited via multistage stratified random cluster sampling, with school classes or the school as the sampling unit. Each country/region obtained approval to conduct the survey from an ethics review board or a country/region-specific equivalent regulatory body. Further information about the methodology of the HBSC study is available elsewhere (Currie et al., 2014; Roberts et al., 2009). For this study, secondary data from 801,648 adolescents were retrieved from four consecutive waves, covering the period between 2002 and 2014 (i.e. 2001/2, 2005/6, 2009/10 and 2013/14).

2.2 | Measures

2.2.1 | Chronic back pain

The presence of chronic back pain was extracted from participants' responses to one of the questions of the HBSC Symptom Checklist (HBSC-SCL), an 8-item symptom checklist developed for the HBSC survey which has been found to provide reliable and valid measures of subjective health complaints (Haugland & Wold, 2001). The HBSC-SCL asks the participant to respond to the question 'In the last 6 months: how often have you had the following...?' on a variety of physical and emotional symptoms (i.e. headache, stomach ache, backache, dizziness, feeling low, irritability/bad temper, nervousness and sleeping difficulties). Answer categories for each question are as follows: (1) 'About every day,' (2) 'More than once a week,' (3) 'About every week,' (4) 'About every month,' and (5) 'Rarely or never.' For the purposes of this study,

adolescents who reported having back pain weekly or more often over the last 6 months were considered to have chronic back pain. This dichotomization has been previously used in studies also using items from the HBSC-SCL (Haugland & Wold, 2001; Roy et al., 2021).

2.2.2 | Screen time

The screen time behaviour was extracted from the participants' responses to three different questions: (1) 'How many hours a day, in your free time, do you usually spend watching TV, videos, DVDs and other entertainment on a screen?'; (2) 'How many hours a day, in your free time, do you usually spend playing games on a computer, games console, tablet (like iPad) or smartphone or other electronic devices (not only including moving or fitness games)?' and (3) 'How many hours a day, in your free time, do you usually spend using electronic devices such as computers, tablets (like iPad) or smartphones for other purposes, for example, homework, emailing, tweeting, Facebook, chatting, surfing the internet?' Each question asked participants about their screen behaviour separately for weekdays and weekends with nine response options: (1) 'None at all,' (2) 'About half an hour,' (3) 'About 1 hour a day,' (4) 'About 2 hours a day,' (5) 'About 3 hours a day,' (6) 'About 4 hours a day,' (7) 'About 5 hours a day,' (8) 'About 6 hours a day,' and (9) 'About 7 or more hours a day.' Participants' answers to the three questions were treated as continuous (i.e. 'None at all' = 0, 'Half an hour a day' = 0.5, 'About an hour a day' = 1.0, etc.) in order to compute a sum score measuring screen time for week and weekend days separately. This sum score was then used to create a weighted average mean (i.e. mean = [5 × weekday +2 weekend day]/7 days; Rey-López et al., 2010) to reflect the average daily screen time. A cutoff at 2 h/day was set to extract an additional dichotomized variable to conform the current international health guidelines for screen time, that is exceeding 2-h daily screen time (coded as '1') or not (coded as '0'; American Academy of Pediatrics: Children, adolescents and television, 2001).

2.2.3 | Obesity

The participants' self-reported body height (cm) and body weight (kg) were used to calculate participants' body mass index (BMI) according to the kg/m^2 formula. We then used the WHO's gender-specific BMI-for-age growth charts (De Onis et al., 2007) to determine adolescents' weight status according to their chronological age (i.e. the difference between the date of administration of the HBSC questionnaire and participants' self-reported month and year of birth). Obesity was defined by the >97th percentile on the gender-specific BMI-for-age growth charts (De Onis et al., 2007; De Onis & Lobstein, 2010).

2.3 | Data analysis

Because this study focused on European countries, we first eliminated data belonging to participants from non-European countries (i.e. Canada and the United States of America). We also eliminated data from European countries that did not participate in the four survey waves (i.e. Albania, Armenia, Bulgaria, Iceland, Luxemburg, Malta, Moldova, Romania, Slovakia and Turkey) and from European countries that did not provide data on each variable of interest for each of the four survey waves (i.e. Austria, Czech Republic, Greenland, Norway and Ukraine). We then removed data from respondents who had not provided answers to all the study variables. For the remaining participants, we computed the number and percentages of all categorical variables, and mean and standard deviations of all continuous variables, across the four measurement periods (i.e. 2002, 2006, 2010 and 2014) for descriptive purposes. Logistic regression models including survey year as a continuous variable and sex and age as control variables were fitted to evaluate the significance of time trends for each of the three outcomes (i.e. screen time, obesity and chronic back pain). Then, to address the study's aim, for chronic back pain, a second model was run that included screen time and obesity to examine the explanatory role of both variables on the trend of chronic back pain. Additionally, the interaction term between screen time and obesity was introduced in a third model to study if the interaction contributed to the explanation of chronic back pain over time. The Karlson-Holm-Breen (KHB) method (Breen et al., 2013; Kohler et al., 2011) was used to decompose the total effect of survey year (i.e. time) on chronic back pain into its direct part (unmediated) and indirect part (mediated) running through screen time and obesity whilst adjusting for sex and age. This method also displays the decomposition of the indirect effect through multiple mediators and calculates the proportion of the total association that is due to each mediator (Kohler et al., 2011). The KHB method is appropriate for examining mediation in non-linear models (Breen et al., 2013; Kohler et al., 2011) and has previously been used to examine the contribution of diverse factors (e.g. daily smoking, truancy) on the decreasing trend of heavy episodic drinking in Nordic countries (Raitasalo et al., 2021). In our study, the KHB method provided an estimate of the contribution of screen time and obesity on the increasing trend of chronic back pain. In all analyses, cluster-robust standard errors (adjusting for adolescents being nested within countries) were used. Statistical significance was set at $p < 0.05$.

All statistical analyses were conducted using STATA 14 (StataCorp.).

3 | RESULTS

3.1 | Sample characteristics

As noted previously, we first removed data belonging to participants from the two non-European countries ($n = 54{,}332$), from the 10 European countries that did not participate in the four waves that are the focus of this study ($n = 115{,}373$) and from the five European countries that did not provide data on each variable of interest for each of the four survey waves ($n = 78{,}705$). Data from the remaining respondents who had not provided answers to all the study variables were also removed ($n = 130{,}146$). Thus, the final sample consisted of 423,092 adolescents (52.77% of the total/initial sample) from 27 European countries or regions ($M_{age} = 13.67$; $SD_{age} = 1.65$; Range = 10.16–17.16; girls = 51.21%). As shown in Table 1, there was a similar sample size amongst the four survey waves and the age- and sex-related groups. Table 2 provides an overview of the prevalence of screen time, obesity and chronic back pain across the 4 survey years.

TABLE 1 Sample descriptives

Age	Mean: 13.67 years (SD: 1.65 years)		
		N	%
Age groups	11 years old	130,257	30.79
	13 years old	143,610	33.94
	15 years old	149,225	35.27
Sex	Females	216,706	51.22
	Males	206,386	48.78
Year of survey	2002	107,791	25.48
	2006	108,842	25.73
	2010	102,687	24.27
	2014	103,772	24.53
Country or region of residence	Belgium (Flemish)	16,508	3.90
	Belgium (French)	12,390	2.93
	Croatia	19,231	4.55
	Denmark	14,882	3.52
	England	8837	2.09
	Estonia	14,702	3.47
	Finland	21,080	4.98
	France	22,588	5.34
	Germany	19,035	4.50
	Greece	15,381	3.64
	Hungry	14,485	3.42
	Ireland	4652	1.10
	Israel	14,526	3.43
	Italy	14,980	3.54
	Latvia	15,500	3.66
	Lithuania	15,335	3.62
	Netherlands	14,331	3.39
	Macedonia	14,621	3.46
	Poland	19,009	4.49
	Portugal	13,578	3.21
	Russian Federation	22,072	5.22
	Scotland	8600	2.03
	Slovenia	18,000	4.25
	Spain	21,264	5.03
	Sweden	17,921	4.24
	Switzerland	19,681	4.65
	Wales	9903	2.34

3.2 | Regression analysis

Logistic regression analysis showed a significant albeit small linear increase over time (i.e. survey year) in screen time ($\beta = 0.059$; $p < 0.001$; 95%IC = 0.035–0.085) and obesity ($\beta = 0.025$; $p < 0.001$; 95%IC = 0.012–0.038).

Results for chronic back pain are presented in Table 3. Logistic regression analysis showed a linear increase over time in the prevalence of chronic back pain (Model 1), and screen time and obesity were associated with an increased likelihood of chronic back pain (Model 2). In addition, by adding screen time and obesity to the model, the survey year effect was slightly reduced but remained significant (Model 2). Results of the interaction effect between screen time and obesity (Model 3) did not emerge as significant; therefore, they are not reported here.

Table 4 displays the mediation of the association between time (i.e. survey year) and chronic back pain through screen time and obesity whilst controlling for sex and age. The model demonstrates a significant indirect and direct effect of survey year on chronic back pain, showing that screen time and obesity explained, in part, the increase in the prevalence of chronic back pain over time. The total effect of the survey year on chronic back pain was 1.06 times larger than the direct effect, and 5.62% of the total effect was due to screen time and obesity.

Table 5 displays the analysis disentangling the mediating effects of screen time and obesity on the trend in chronic back pain. The contribution of each mediator to the indirect effect is displayed in the 'Indirect effect' column, and the column labelled 'Confounding percentage' shows how much the effect of time (i.e. survey year) is due to each mediator.

TABLE 2 Prevalence of screen time, obesity and chronic back pain across the four survey waves

	2002	2006	2010	2014
Mean screen hours per day (SD)	3.99 (2.40)	5.58 (3.66)	6.05 (3.87)	6.40 (4.28)
Screen time (% exceeding 2 h/day)	80.18	87.77	89.76	88.59
BMI (mean; SD)	19.13 (3.22)	19.39 (3.29)	19.50 (3.39)	19.56 (3.46)
Obesity (% PC > 97)	4.02	4.45	5.18	5.25
Back pain (%)				
Rarely or never	65.05	64.27	62.26	59.04
About every month	16.89	16.83	17.84	18.76
About every week	7.72	7.81	8.46	9.26
More than once a week	5.82	6.08	6.22	7.07
About every day	4.52	5.00	5.22	5.87
Chronic back pain (%)	18.06	18.89	19.90	22.20

Abbreviation: BMI, body mass index.

TABLE 3 Association between survey year, screen time, obesity and chronic back pain

	Model 1			Model 2		
	β	95%CI	*p*-value	*β*	95%CI	*p*-value
Survey year	0.021	0.015–0.027	<0.001	0.019	0.014–0.026	<0.001
Screen time (ref = less than 2 h/day)				0.125	0.075–0.175	<0.001
Obesity (ref = nonobese)				0.314	0.258–0.370	<0.001

Note: Findings adjusted for sex and age.

TABLE 4 Decomposition of the total effects of the survey year on chronic back pain

	β (95% CI)	*p*-value
Survey year		
Total	0.021 (0.015–0.027)	<0.001
Direct	0.019 (0.014–0.026)	<0.001
Indirect	0.001 (0.000–0.002)	<0.001
Components of the difference		
	β (S.E.)	
Screen time	0.0008412 (0.000245)	
Obesity	0.0003485 (0.000092)	

Note: Findings adjusted for sex and age.

TABLE 5 The contribution of screen time and obesity on the trend of chronic back pain

	Indirect effect (%)	Confounding percentage (%)
Screen time	70.71	3.98
Obesity	29.29	1.65

Note: Findings adjusted for sex and age.

4 | DISCUSSION

The key finding of this study is that the rising trends in sedentary screen time and obesity are slightly associated with an increase in the prevalence of chronic back pain in European adolescents. The data showed that sedentary screen time accounted for up to 3.98% of the variance in the upward trend of chronic back pain, and obesity accounted for up to 1.65%. These results are consistent with those from previous studies showing positive significant associations between back pain in adolescents and both screen time (e.g. Bento et al., 2020; Keane et al., 2017; Lemes et al., 2021; Silva et al., 2017; Torsheim et al., 2010) and obesity (e.g. Hershkovich et al., 2013; Hestbaek, Leboeuf-Yde, & Kyvik, 2006; Hestbaek, Leboeuf-Yde, Kyvik, & Manniche, 2006; Palmer et al., 2020; Paulis et al., 2014). The results of this study confirm and extend preliminary findings with a wider, international and heterogeneous sample of adolescents.

These findings have relevant public health and economic implications. If the trend for increasing obesity and sedentary screen time in adolescents keeps growing, as reported by recent studies (e.g. Ghekiere et al., 2018;

Inchley et al., 2017), then is more likely that the number of adolescents with chronic back pain will also increase. In this event, an increase in adults with chronic back pain could also be anticipated, given that adolescents with a history of back pain are more likely to have back pain in their adulthood (Brattberg, 2004; Hestbaek, Leboeuf-Yde, & Kyvik, 2006; Hestbaek, Leboeuf-Yde, Kyvik, & Manniche, 2006; Jeffries et al., 2007). If the findings are confirmed in future studies, this growing trend in the prevalence of chronic back pain in adolescents (and adults) will contribute to an increase of needed resources at the education, health and economic levels of the European countries and regions. Indeed, more healthcare professionals and specialized treatment programmes will be required to meet the needs of the growing number of individuals with chronic back pain. When implemented, these actions will lead to a greater demand for economic resources to address the increase in spending.

The findings of this study provide additional support for the importance of implementing public health measures to reduce sedentary screen time and prevent obesity in youth. In this regard, the promotion of a more physically active lifestyle amongst adolescents is crucial. The benefits of regular moderate-to-vigorous physical activity for adolescents are numerous, including a decrease in depressive symptoms, reduced blood pressure and obesity and increased bone mineral density (Janssen & LeBlanc, 2010). Despite the limited research in this field, a recent systematic review of observational studies found moderate evidence for a U-shape relationship between physical activity and low back pain in children and adolescents (Kędra et al., 2020), suggesting the possibility that a moderate level of physical activity has a protective effect against low back pain (Kędra et al., 2020). In fact, regular physical activity, in addition to postural education and hygiene, and engagement in formal physical therapy exercises have been suggested for the treatment and prevention of low back pain in children and adolescents (Landry et al., 2015). However, the extent to which these interventions prevent back pain in younger samples needs to be more systematically studied.

This study has several limitations that must be considered when interpreting the results. First, the data available for the current analyses were limited to just a few of the many factors that are thought to contribute to the complex experience that is chronic back pain. The fact that both the rising prevalence in sedentary screen time and obesity only accounted for a small part of the increase in the prevalence of chronic back pain amongst the participants indicates that there are other unmeasured variables which are important. We now know that the rates of mental health problems and sleep difficulties amongst children and adolescents have been increasing in the last decades (Collishaw, 2015; Fleming et al., 2014; Ghekiere et al., 2018). Research has shown that both of these are risk factors of back pain in children and adolescents (Beynon et al., 2019; Kamper et al., 2016). Additional research to evaluate the role of these and other factors play in back pain is needed. Second, this study is based on cross-sectional data, which enables us to only establish associations amongst variables but not causation. Indeed, it could be argued that the increase in time spent in sedentary screen-based activities is a consequence of the increase in the prevalence of chronic back pain, which, in turn, may facilitate weight gain and obesity. Therefore, longitudinal studies examining the temporal sequence, which is a necessary condition to establish causal relationships, are needed to determine the direction of the effects. Third, the study only used self-reported measures to assess screen time, body height and body weight, and chronic back pain. Self-report measures are known to be influenced by social desirability and recall bias. Although self-reported information about these variables is also known to have acceptable validity and reliability (Aasvee et al., 2015; Bobakova et al., 2015; Haugland & Wold, 2001; Liu et al., 2010; Rey-López et al., 2010; Schmitz et al., 2004), research that also included objective measures of these variables would help to increase overall trust in the findings.

Despite the study's limitation, this is the first study to our knowledge that examines the explanatory role of two specific factors in the rising trend of chronic back pain, using a representative sample of European adolescents. In addition, the finding that both increases in sedentary screen time and obesity are slightly associated with the rising rates of chronic back pain in this population provides important new information that may be useful for policymakers, healthcare professionals and researchers, as we work to evaluate and improve public health measures that can reduce the prevalence and impact of low back pain in adolescents.

AUTHOR CONTRIBUTIONS

JR-J originated the idea, analysed the data, interpreted the results and wrote the first draft of the manuscript. RR contributed to the statistical analysis and revised the drafting manuscript. MJ and JM contributed to the conception and design of the study and revised and edited subsequent drafts of the manuscript. All authors discussed the results and commented on the manuscript.

ACKNOWLEDGEMENTS

HBSC is an international study carried out in collaboration with WHO/EURO. The International Coordinator of

the 2005/06 to 2013/14 surveys was Prof. Candace Currie and the Data Bank Manager was Prof. Oddrun Samdal. The surveys were conducted by Principal Investigator in 27 countries: Flemish Belgium (Maxim Dierckens and Katrijn Delaruelle), French Belgium (Katia Castetbon), Croatia (Ivana Pavic Simetin), Denmark (Katrine Rich Madsen), England (Fiona Brooks and Ellen Klemera), Estonia (Leila Oja), Finland (Leena Paakkari and Nelli Lyyra), France (Emmanuelle Godeau), Germany (Matthias Richter), Greece (Anna Kokkevi), Hungary (Ágnes Németh), Ireland (Saoirse Nic Gabhainn), Israel (Yossi Harel-Fisch), Italy (Alessio Vieno), Latvia (Iveta Pudule), Lithuania (Kastytis Šmigelskas), Macedonia (Lina Kostarova Unkovska), the Netherlands (Gonneke Stevens and Saskia van Dorsselaer), Poland (Joanna Mazur and Agnieszka Malkowska-Szkutnik), Portugal (Tania Gaspar), Russia (Anna Matochkina), Scotland (Jo Inchley), Slovenia (Helena Jericek), Spain (Carmen Moreno and Francisco Rivera), Sweden (Petra Löfstedt), Switzerland (Hervé Kuendig and Marina Delgrande) and Wales (Chris Roberts).

FUNDING INFORMATION

This work was partly funded by grants from the Spanish Ministry of Economy, Industry and Competitiveness (RTI2018-09870-B-I00; RED2018-102546-T), the European Regional Development Fund (ERDF), the Government of Catalonia (AGAUR; 2017SGR-1321), Fundación Grünenthal, Universitat Rovira i Virgili (PFR program) and ICREA-Acadèmia. JR-J and RR are supported by doctoral grants from MINECO.

CONFLICT OF INTEREST

The authors declare no financial or other relationships that might lead to a conflict of interest related to this study.

ORCID

Jordi Miró https://orcid.org/0000-0002-1998-6653

REFERENCES

Aasvee, K., Rasmussen, M., Kelly, C., Kurvinen, E., Giacchi, M. V., & Ahluwalia, N. (2015). Validity of self-reported height and weight for estimating prevalence of overweight among Estonian adolescents: The health behaviour in school-aged children study. *BMC Research Notes*, *8*(1), 606. https://doi.org/10.1186/s13104-015-1587-9

American Academy of Pediatrics. Committee on Public Education. (2001). American Academy of Pediatrics: Children, adolescents, and television. *Pediatrics*, *107*(2), 423–426. https://doi.org/10.1542/peds.107.2.423

Bejia, I., Abid, N., Salem, K. B., Letaief, M., Younes, M., Touzi, M., & Bergaoui, N. (2005). Low back pain in a cohort of 622 Tunisian schoolchildren and adolescents: An epidemiological study. *European Spine Journal*, *14*(4), 331–336. https://doi.org/10.1007/s00586-004-0785-2

Bento, T. P. F., Cornelio, G. P., Perrucini, P. O., Simeão, S. F. A. P., de Conti, M. H. S., & de Vitta, A. (2020). Low back pain in adolescents and association with sociodemographic factors, electronic devices, physical activity and mental health. *Jornal de Pediatria*, *96*(6), 717–724. https://doi.org/10.1016/j.jped.2019.07.008

Beynon, A. M., Hebert, J. J., Lebouef-Yde, C., & Walker, B. F. (2019). Potential risk factors and triggers for back pain in children and young adults. A scoping review, part II: Unclear or mixed types of back pain. *Chiropractic & Manual Therapies*, *27*(1), 1–12. https://doi.org/10.1186/s12998-019-0280-9

Bobakova, D., Hamrik, Z., Badura, P., Sigmundova, D., Nalecz, H., & Kalman, M. (2015). Test–retest reliability of selected physical activity and sedentary behaviour HBSC items in The Czech Republic, Slovakia and Poland. *International Journal of Public Health*, *60*(1), 59–67. https://doi.org/10.1007/s00038-014-0628-9

Brattberg, G. (2004). Do pain problems in young school children persist into early adulthood? A 13-year follow-up. *European Journal of Pain*, *8*(3), 187–199. https://doi.org/https://doi.org/10.1016/j.ejpain.2003.08.001

Breen, R., Karlson, K. B., & Holm, A. (2013). Total, direct, and indirect effects in logit and probit models. *Sociological Methods & Research*, *42*(2), 164–191. https://doi.org/10.1177/0049124113494572

Collishaw, S. (2015). Annual research review: Secular trends in child and adolescent mental health. *Journal of Child Psychology and Psychiatry*, *56*(3), 370–393. https://doi.org/10.1111/jcpp.12372

Currie, C., Inchley, J., Molcho, M., Lenzi, M., Veselska, Z., & Wild, F. (2014). Health behaviour in school-aged children (HBSC) study protocol: Background, methodology and mandatory items for the 2013/14 survey. Retrieved from http://www.hbsc.org/methods/

De Onis, M., & Lobstein, T. (2010). Defining obesity risk status in the general childhood population: Which cut-offs should we use? *International Journal of Pediatric Obesity*, *5*(6), 458–460. https://doi.org/10.3109/17477161003615583

De Onis, M., Onyango, A. W., Borghi, E., Siyam, A., Nishida, C., & Siekmann, J. (2007). Development of a WHO growth reference for school-aged children and adolescents. *Bulletin of the World Health Organization*, *85*(9), 660–667. https://doi.org/10.2471/BLT.07.043497

Fleming, T. M., Clark, T., Denny, S., Bullen, P., Crengle, S., Peiris-John, R., Robinson, E., Rossen, F. V., Sheridan, J., & Lucassen, M. (2014). Stability and change in the mental health of New Zealand secondary school students 2007-2012: Results from the national adolescent health surveys. *Australian and New Zealand Journal of Psychiatry*, *48*(5), 472–480. https://doi.org/10.1177/0004867413514489

Ghekiere, A., Van Cauwenberg, J., Vandendriessche, A., Inchley, J., Gaspar de Matos, M., Borraccino, A., Gobina, I., Tynjälä, J., Deforche, B., & De Clercq, B. (2018). Trends in sleeping difficulties among European adolescents: Are these associated with physical inactivity and excessive screen time? *International Journal of Public Health*, *64*(4), 487–498. https://doi.org/10.1007/s00038-018-1188-1

Groenewald, C. B., Wright, D. R., & Palermo, T. M. (2015). Health care expenditures associated with pediatric pain-related conditions in the United States. *Pain*, *156*(5), 951–957. https://doi.org/10.1097/j.pain.0000000000000137

Hakala, P. T., Saarni, L. A., Punamäki, R.-L., Wallenius, M. A., Nygård, C.-H., & Rimpelä, A. H. (2012). Musculoskeletal symptoms and computer use among Finnish adolescents - pain intensity and inconvenience to everyday life: A cross-sectional study. *BMC Musculoskeletal Disorders*, *13*(1), 41. https://doi.org/10.1186/1471-2474-13-41

Haugland, S., & Wold, B. (2001). Subjective health complaints in adolescence - reliability and validity of survey methods. *Journal of Adolescence*, *24*(5), 611–624. https://doi.org/10.1006/jado.2000.0393

Hershkovich, O., Friedlander, A., Gordon, B., Arzi, H., Derazne, E., Tzur, D., Shamis, A., & Afek, A. (2013). Associations of body mass index and body height with low back pain in 829,791 adolescents. *American Journal of Epidemiology*, *178*(4), 603–609. https://doi.org/10.1093/aje/kwt019

Hestbaek, L., Leboeuf-Yde, C., & Kyvik, K. O. (2006). Are lifestyle-factors in adolescence predictors for adult low back pain? A cross-sectional and prospective study of young twins. *BMC Musculoskeletal Disorders*, *7*, 1–8. https://doi.org/10.1186/1471-2474-7-27

Hestbaek, L., Leboeuf-Yde, C., Kyvik, K. O., & Manniche, C. (2006). The course of low back pain from adolescence to adulthood: Eight-year follow-up of 9600 twins. *Spine*, *31*(4): 468– 472. Retrieved from https://journals.lww.com/spinejournal/Fulltext/2006/02150/The_Course_of_Low_Back_Pain_From_Adolescence_to.17.aspx

Hoy, D., March, L., Brooks, P., Blyth, F., Woolf, A., Bain, C., Williams, G., Smith, E., Vos, T., Barendregt, J., Murray, C., Burstein, R., & Buchbinder, R. (2014). The global burden of low back pain: Estimates from the global burden of disease 2010 study. *Annals of the Rheumatic Diseases*, *73*(6), 968–974. https://doi.org/10.1136/annrheumdis-2013-204428

Huguet, A., Eccleston, C., Miró, J., & Gauntlett-Gilbert, J. (2009). Young people making sense of pain: Cognitive appraisal, function, and pain in 8-16 year old children. *European Journal of Pain*, *13*(7), 751–759. https://doi.org/10.1016/j.ejpain.2008.07.011

Inchley, J., Currie, D., Jewell, J., Breda, J., & Barnekow, V. (2017). Adolescent obesity and related behaviours: Trends and inequalities in the WHO region 2002-2014, observations from the health behaviour in school-aged children (HBSC) WHO collaborative cross-national study. *World Health Organization, Regional Office for Europe*, *130*(4), 207–217. Retrieved from http://www.euro.who.int/__data/assets/pdf_file/0019/339211/WHO_ObesityReport_2017_v3.pdf

Janssen, I., & LeBlanc, A. G. (2010). Systematic review of the health benefits of physical activity and fitness in school-aged children and youth. *International Journal of Behavioral Nutrition and Physical Activity*, *7*(1), 40. https://doi.org/10.1186/1479-5868-7-40

Jeffries, L. J., Milanese, S. F., & Grimmer-Somers, K. A. (2007). Epidemiology of adolescent spinal pain: A systematic overview of the research literature. *Spine*, *32*(23):2630–2637. Retrieved from https://journals.lww.com/spinejournal/Fulltext/2007/11010/Epidemiology_of_Adolescent_Spinal_Pain__A.20.aspx

Joergensen, A. C., Strandberg-Larsen, K., Andersen, P. K., Hestbaek, L., & Andersen, A.-M. N. (2021). Spinal pain in pre-adolescence and the relation with screen time and physical activity behavior. *BMC Musculoskeletal Disorders*, *22*(1), 1–10. https://doi.org/10.1186/s12891-021-04263-z

Jones, M. A., Stratton, G., Reilly, T., & Unnithan, V. B. (2004). A school-based survey of recurrent non-specific low-back pain prevalence and consequences in children. *Health Education Research*, *19*(3), 284–289. https://doi.org/10.1093/her/cyg025

Kamper, S. J., Yamato, T. P., & Williams, C. M. (2016). The prevalence, risk factors, prognosis and treatment for back pain in children and adolescents: An overview of systematic reviews. *Best Practice & Research: Clinical Rheumatology*, *30*(6), 1021–1036. https://doi.org/10.1016/j.berh.2017.04.003

Keane, E., Kelly, C., Molcho, M., & Nic Gabhainn, S. (2017). Physical activity, screen time and the risk of subjective health complaints in school-aged children. *Preventive Medicine*, *96*, 21–27. https://doi.org/10.1016/j.ypmed.2016.12.011

Kędra, A., Plandowska, M., Kędra, P., & Czaprowski, D. (2020). Physical activity and low back pain in children and adolescents: A systematic review. *European Spine Journal*, *0123456789*, 946–956. https://doi.org/10.1007/s00586-020-06575-5

Kohler, U., Karlson, K. B., & Holm, A. (2011). Comparing coefficients of nested nonlinear probability models. *Stata Journal*, *11*(3), 420–438. https://doi.org/10.1177/1536867x1101100306

Landry, B. W., Fischer, P. R., Driscoll, S. W., Koch, K. M., Harbeck-Weber, C., Mack, K. J., Wilder, R. T., Bauer, B. A., & Brandenburg, J. E. (2015). Managing chronic pain in children and adolescents: A clinical review. *PM&R*, *7*(11), S295–S315. https://doi.org/10.1016/j.pmrj.2015.09.006

Lemes, Í. R., Oliveira, C. B., Silva, G. C. R., Pinto, R. Z., Tebar, W. R., & Christofaro, D. G. (2021). Association of sedentary behavior and early engagement in physical activity with low back pain in adolescents: A cross-sectional epidemiological study. *European Spine Journal*, *0123456789*, 152–158. https://doi.org/10.1007/s00586-021-07004-x

Liu, Y., Wang, M., Tynjälä, J., Lv, Y., Villberg, J., Zhang, Z., & Kannas, L. (2010). Test-retest reliability of selected items of health behaviour in school-aged children (HBSC) survey questionnaire in Beijing, China. *BMC Medical Research Methodology*, *10*(1), 73. https://doi.org/10.1186/1471-2288-10-73

Ochsmann, E. B., Escobar Pinzón, C. L., Letzel, S., Kraus, T., Michaelis, M., & Muenster, E. (2010). Prevalence of diagnosis and direct treatment costs of back disorders in 644,773 children and youths in Germany. *BMC Musculoskeletal Disorders*, *11*(1), 193. https://doi.org/10.1186/1471-2474-11-193

Palmer, A. J., Poveda, J. L., Martinez-Laguna, D., Reyes, C., De Bont, J., Silman, A., Carr, A. J., Duarte-Salles, T., & Prieto-Alhambra, D. (2020). Childhood overweight and obesity and back pain risk: A cohort study of 466 997 children. *BMJ Open*, *10*(9), e036023. https://doi.org/10.1136/bmjopen-2019-036023

Paulis, W. D., Silva, S., Koes, B. W., & Van Middelkoop, M. (2014). Overweight and obesity are associated with musculoskeletal complaints as early as childhood: A systematic review. *Obesity Reviews*, *15*(1), 52–67. https://doi.org/10.1111/obr.12067

Raitasalo, K., Kraus, L., Bye, E. K., Karlsson, P., Tigerstedt, C., Törrönen, J., & Raninen, J. (2021). Similar countries, similar factors? Studying the decline of heavy episodic drinking in adolescents in Finland, Norway and Sweden. *Addiction*, *116*(1), 62–71. https://doi.org/10.1111/add.15089

Rey-López, J. P., Vicente-Rodriguez, G., Ortega, F. B., Ruiz, J. R., Martinez-Gómez, D., De Henauw, S., Manios, Y., Molnar,

D., Polito, A., Verloigne, M., Castillo, M. J., Sjöström, M., De Bourdeaudhuij, I., & Moreno, L. A. (2010). Sedentary patterns and media availability in European adolescents: The HELENA study. *Preventive Medicine*, *51*(1), 50–55. https://doi.org/10.1016/j.ypmed.2010.03.013

Roberts, C., Freeman, J., Samdal, O., Schnohr, C. W., de Looze, M. E., Nic Gabhainn, S., Iannotti, R., Rasmussen, M., & International HBSC Study Group. (2009). The health behaviour in school-aged children (HBSC) study: Methodological developments and current tensions. *International Journal of Public Health*, *54*(S2), 140–150. https://doi.org/10.1007/s00038-009-5405-9

Roy, R., Galán, S., Sánchez-Rodríguez, E., Racine, M., Solé, E., Jensen, M. P., & Miró, J. (2021). Cross-National Trends of chronic back pain in adolescents: Results from the HBSC study, 2001-2014. *The Journal of Pain*, *23*(1), 123–130. https://doi.org/10.1016/j.jpain.2021.07.002

Schmitz, K. H., Harnack, L., Fulton, J. E., Jacobs, D. R., Jr., Gao, S., Lytle, L. A., & Van Coevering, P. (2004). Reliability and validity of a brief questionnaire to assess television viewing and computer use by middle school children. *Journal of School Health*, *74*(9), 370–377. https://doi.org/10.1111/j.1746-1561.2004.tb06632.x

Silva, A., Sa-Couto, P., Queirós, A., Neto, M., & Rocha, N. P. (2017). Pain, pain intensity and pain disability in high school students are differently associated with physical activity, screening hours and sleep. *BMC Musculoskeletal Disorders*, *18*(1), 1–11. https://doi.org/10.1186/s12891-017-1557-6

Torsheim, T., Eriksson, L., Schnohr, C. W., Hansen, F., Bjarnason, T., & Valimaa, R. (2010). Screen-based activities and physical complaints among adolescents from the Nordic countries. *BMC Public Health*, *10*, 324. Retrieved from http://queens.ezp1.qub.ac.uk/login?url=http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed9&AN=20534116%5Cnhttp://resolver.ebscohost.com/openurl?sid=OVID:embase&id=pmid:20534116&id=doi:&issn=1471-2458&isbn=&volume=10&issue=&spage=324

Wu, A., March, L., Zheng, X., Huang, J., Wang, X., Zhao, J., Blyth, F. M., Smith, E., Buchbinder, R., & Hoy, D. (2020). Global low back pain prevalence and years lived with disability from 1990 to 2017: Estimates from the global burden of disease study 2017. *Annals of Translational Medicine*, *8*(6), 299. https://doi.org/10.21037/atm.2020.02.175

How to cite this article: Roman-Juan, J., Roy, R., Jensen, M. P., & Miró, J. (2022). The explanatory role of sedentary screen time and obesity in the increase of chronic back pain amongst European adolescents: The HBSC study 2002–2014. *European Journal of Pain*, *00*, 1–9. https://doi.org/10.1002/ejp.2003

4.5. Study V

Increases in Sleep Difficulties and Psychological Symptoms are Associated with the Increase of Chronic Back Pain in Adolescents: The HBSC Study 2002 to 2018.

USASP
US ASSOCIATION FOR THE STUDY OF PAIN
PUBLISHED BY ELSEVIER
The Journal of Pain, Vol xxx, No. xxx (xxxx), xxxx: pp xxx–xxx
Available online at www.jpain.org and www.sciencedirect.com

Original Reports

Increases in Sleep Difficulties and Psychological Symptoms are Associated With the Increase of Chronic Back Pain in Adolescents: The HBSC Study 2002 to 2018

Josep Roman-Juan,*,† Mark P. Jensen,‡ and Jordi Miró*,†

*Universitat Rovira i Virgili, Tarragona, Spain, †Unit for the Study and Treatment of Pain—ALGOS, Research Center for Behavior Assessment (CRAMC), Department of Psychology, URV, Institut d'Investigació Sanitària Pere Virgili, Universitat Rovira i Virgili, Tarragona, Spain, ‡Department of Rehabilitation Medicine, University of Washington, Seattle, Washington

Abstract: **Cross-national research using data from the Health Behavior in School-aged Children (HBSC) survey showed an increase in the prevalence of chronic back pain from 2002 to 2014. However, it is unknown if this trend has persisted beyond 2014. The aims of this study were to 1) determine if the prevalence of chronic back pain in girls and boys aged 11, 13, and 15 continued to increase from 2014 to 2018 and if this was the case, 2) examine whether this increase in the prevalence of chronic back pain between 2002 and 2018 was explained indirectly by increases in sleep difficulties and psychological symptoms. Data from 7,89,596 adolescents retrieved from 5 waves of the HBSC survey conducted in 2002, 2006, 2010, 2014, and 2018 in 32 countries/regions were used. Logistic regressions and path analyses were conducted. Results showed an overall increase of .5% in the prevalence of chronic back pain between 2014 and 2018, ranging from .4% for 15-year-old girls to 1.3% for 11-year-old boys, indicating a continued overall increase in chronic back pain in adolescents beyond 2014. For 13-year-old girls and for 15-year-old girls and boys, the increase in the prevalence of chronic back pain between 2002 and 2018 was partially mediated by increases in sleep difficulties, which in turn were associated with increases in psychological symptoms. The findings provide important information that may aid stakeholders in enhancing public health initiatives to prevent or reduce the increasing trend in the prevalence of chronic back pain in adolescents.**

Perspective: ***This study shows that chronic back pain prevalence continues to increase among adolescents, with sleep difficulties and psychological symptoms contributing significantly to this trend. The findings provide insights that may inform strategies to prevent or reduce the increasing trend of chronic back pain in adolescents.***

Key Words: *Chronic back pain, prevalence, adolescents, sleep difficulties, psychological symptoms*

Back pain can have negative effects on the everyday functioning of adolescents.[1,2] Furthermore, back pain in adolescents can take a chronic course, which incurs a significant negative economic impact[3,4] and is associated with a greater risk of impairment into adulthood.[5]

Received March 10, 2023; Received in revised form August 7, 2023; Accepted September 3, 2023
This work was partly funded by grants from the Spanish Ministry of Economy, Industry, and Competitiveness (RED2022-134869-T), the European Regional Development Fund (ERDF), and the Government of Catalonia (AGAUR; 2021SGR-730). J.R-J. is supported by a doctoral grant from MINECO (PRE2019-089283). J.M.'s work is supported by ICREA-Acadèmia. The Chair in Pediatric Pain is supported by Fundación Grünenthal.
The authors declare no financial or other relationships that might lead to a conflict of interest related to this study.
Address reprint requests to Jordi Miró, Departament de Psicología, Universitat Rovira i Virgili, Carretera de Valls, s/n 43007 Tarragona, Spain. E-mail: jordi.miro@urv.cat

1526-5900/$36.00

https://doi.org/10.1016/j.jpain.2023.09.004

Research has shown that the prevalence of chronic back pain among adolescents has increased over the past few decades. For example, a study conducted by Roy et al[6] using data from the Health Behavior in School-aged Children (HBSC) study reported an increase of 3% in the prevalence of chronic back pain among adolescents from 2002 to 2014. This increase was especially higher in girls and older adolescents.[6] However, it is not known if the increasing trend in the prevalence of chronic back pain has persisted beyond 2014. Providing updated estimates of chronic back pain is important given its association with disability, decreased quality of life, and increased health care costs both in adolescents and adults.[1,2,7–13] Furthermore, if the prevalence of chronic back pain has increased since 2014, then it would be important to identify the factors that are contributing to this increase. This knowledge could be used by policymakers and other stakeholders interested in the development and implementation of preventive and treatment strategies for chronic back pain in this population.

In a recent study, we found that increases in time spent in sedentary screen-based activities (eg, playing computer games or using a smartphone) and obesity between 2002 and 2014 were significantly associated with the increase in the prevalence of chronic back pain across the 12-year period.[14] However, these increases in sedentary screen-based activities and obesity only accounted for 5% of the variance of the increase in back pain prevalence. There are clearly other factors that are playing a role in this increase. Two possible factors could be an increase in sleep disturbances and psychological symptoms. In relation to this, research has shown that both sleep difficulties[15] and psychological symptoms (eg, psychological distress[16-18]) have increased over the last few decades. Furthermore, a substantial body of evidence suggests that sleep disturbance is a robust predictor of future pain-related issues,[19-23] and that psychological symptoms could mediate this relationship.[24-28] It is important to test whether increases in sleep difficulties and psychological symptoms are associated with increases in chronic back pain prevalence, given that both factors are potentially amenable to interventions. Furthermore, to fully understand these relationships, it is essential to examine these associations while considering the variations in the prevalence of these problems by sex and age.[29-32]

Given these considerations, this study had 2 aims. First, using data from the international HBSC survey collected during the 5 most recent waves (2001/2, 2005/6, 2009/10, 2013/14, and 2017/18), we examined if the overall prevalence of chronic back pain in adolescent girls and boys aged 11, 13, and 15 continued to increase from 2014 to 2018. Second, if an increase in the prevalence of chronic back pain was identified, we examined if the increase in the prevalence of chronic back pain from 2002 to 2018 was explained indirectly by the increase in sleep difficulties and increases in psychological symptoms. Based on previous research, we hypothesized that 1) the overall prevalence of chronic back pain among adolescent girls and boys aged 11, 13, and 15 in 2018 would be significantly higher than in 2014 and that 2) over the 16-year time period, increases in sleep disturbance would be associated with increases in psychological symptoms, which in turn would be associated with the increase in prevalence of chronic back pain.

Methods

Study Design, Setting, and Sample

The HBSC study is a collaborative cross-sectional study conducted by the World Health Organization in multiple countries and regions of Europe and North America. The study was conducted at 4-year intervals beginning in 1983 to 1984, with the objective of obtaining data on the health behaviors and well-being of adolescents utilizing a standardized research protocol. Participating countries collect data from independent, nationally representative samples of boys and girls aged 11, 13, and 15 years, using multistage stratified random cluster sampling, with school classes or schools as the sampling unit. Participation in the study is voluntary and anonymous, and data are collected through standardized self-administered questionnaires administered in classrooms. The survey was conducted after obtaining approval from an ethics review board or a country/region-specific regulatory body in each participating country. Ethical consent procedures were followed, and institutional consent was obtained based on local requirements from schools, parents, and adolescents, either through active or passive informed consent/assent. Only consenting adolescents whose parents did not object were included in the study. Additional information about the methodology of the HBSC study can be found elsewhere.[33,34]

For the purposes of this study, only countries that provided data on back pain, psychological symptoms, and sleep difficulties in each of the 5 most recent waves of the HBSC study (ie, 2001/2, 2005/6, 2009/10, 2013/14, and 2017/18) were included. With these restrictions, we were able to use data from 8,26,563 participants from 32 different countries/regions (including Austria, Belgium Flemish, Belgium French, Canada, Croatia, Czech Republic, Denmark, England, Estonia, France, Germany, Greece, Greenland, Hungary, Ireland, Israel, Italy, Latvia, Lithuania, Macedonia, Netherlands, Norway, Poland, Portugal, Russia, Scotland, Slovenia, Spain, Sweden, Switzerland, Ukraine, and Wales). Five percent (36,967) of the participants were excluded because of missing data, leaving data from 7,89,596 children and adolescents available for the current analyses. The characteristics of the sample are presented in Table 1.

Variables and Measures

Independent Variable

Survey year. The variable representing the time of assessment was the survey year (ie, 2001/02, 2005/06, 2009/10, 2013/14, and 2017/18). To create a continuous variable, a value of 1 was assigned to the survey year

Table 1. Description of the Study Sample (Weighted Estimates; N = 7,89,596)

VARIABLE	N/M	%/SD
Survey year		
2002	1,44,870	18.4
2006	1,56,442	19.8
2010	1,59,493	20.2
2014	1,61,142	20.4
2018	1,67,649	21.2
Sex		
Boys	3,84,022	48.8
Girls	4,05,574	51.2
Age		
11-year-olds	2,55,603	32.4
13-year-olds	2,71,973	34.3
15-year-olds	2,62,019	33.3
Socioeconomic status*		
Low	1,30,488	17.3
Medium	4,63,669	61.7
High	1,56,084	21.0
School pressure†	2.26	.03
Sleep difficulties	1.10	.05
Psychological symptoms	3.75	.11
Chronic back pain		
Yes	1,61,718	20.5
No	6,27,878	79.5
Country/region of residence		
Austria	21,215	2.7
Belgium Flemish	22,988	2.9
Belgium French	23,248	2.9
Canada	49,771	6.3
Croatia	25,355	3.2
Czech Republic	29,778	3.8
Denmark	20,760	2.6
England	22,052	2.8
Estonia	21,157	2.7
France	35,046	4.4
Germany	27,534	3.5
Greece	19,876	2.5
Greenland	4,764	.6
Hungary	19,561	2.5
Ireland	19,552	2.5
Israel	26,698	3.4
Italy	20,970	2.7
Latvia	21,204	2.7
Lithuania	25,559	3.2
Macedonia	16,427	2.1
Netherlands	21,483	2.7
Norway	19,789	2.5
Poland	25,297	3.2
Portugal	21,187	2.7
Russia	29,374	3.7
Scotland	27,386	3.5
Slovenia	24,720	3.1
Spain	33,360	4.2
Sweden	25,900	3.3
Switzerland	29,129	3.7
Ukraine	25,062	3.1
Wales	33,394	4.2

NOTE. Sample size varies due to nonresponses.
SD, Standard deviation.
*n = 7,50,241 (missing = 39,355).
†n = 7,74,952 (missing = 14,644).

2002 and incremented the value by 1 for each subsequent survey year, up to a value of 5 for the survey year 2018.

Dependent Variable and Mediator Variables

Chronic back pain, psychological symptoms, and sleep difficulties. The information regarding the experience of chronic pain, back pain, psychological symptoms, and sleep difficulties was extracted from the HBSC symptom checklist (HBSC-SCL).[35] With the HBSC-SCL, participants are asked to respond to the question "In the last 6 months, how often have you had the following…?" with respect to 8 different symptoms using a 5-point scale (1 = "About every day," 2 = "More than once a week," 3 = "About every week," 4 = "About every month," and 5 = "Rarely or never"). Four of the items assess somatic symptoms (ie, headache, stomach ache, backache, and feeling dizzy), and 4 items assess psychological symptoms (ie, feeling low, irritability or bad temper, feeling nervous, and sleep difficulties[35-37]). We used responses to the item assessing back pain and the 4 items assessing psychological symptoms to address the study's aims. On the basis of prior research using the HBSC-SCL,[6,14] adolescents who reported having back pain weekly or more often over the last 6 months were considered to have chronic back pain. In addition, we grouped the items of "feeling low," "irritability or bad temper," and "feeling nervous" as a single, composite measure of psychological symptoms based on prior research showing that these 3 items, in addition to "sleep difficulties," provide a single valid measure of psychological health in school-aged children.[36] For the purposes of the current study, and following Vandendriessche et al's[38] procedure, the item assessing sleep difficulties was left out from the measure of psychological symptoms, allowing sleep to be assessed as a domain distinct from psychological function. In the current sample, the measure of psychological symptoms after leaving out the sleep difficulties item showed a slightly better internal consistency (as reflected by Cronbach's alpha) moving from $\alpha = .74$ to $\alpha = .76$. Response categories of the items conforming the measures of psychological symptoms (ie, feeling low, irritability or bad temper, and feeling nervous) and sleep difficulties were reverse recorded (0–4) so that higher scores indicated a higher frequency of each symptom; that is, worse psychological function and more sleep difficulties. A total score for the psychological symptoms measure was created by summing the responses to each item (range 0–12).

Confounders

Socioeconomic status. Socioeconomic status was assessed using the Family Affluence Scale (FAS). This instrument has been updated through survey years of the HBSC study to account for the changing societal

patterns of consumption and lifestyles of families and adolescents. In survey years 2002 to 2014, the FAS-II version[39] was used. This version includes 4 items asking about the number of cars and computers in the household, whether adolescents have their own bedroom, and the number of overseas holidays taken. In survey years 2014 and 2018, the FAS-III[40] was used. This version includes 2 additional items regarding the number of bathrooms and whether adolescents have a dishwasher at home. For both versions of the FAS, the sum of these scores was transformed into proportional ranks, indicating the relative family affluence of the adolescents in their residential country. By this method, young people were categorized into groups of the lowest 20% (low affluence), middle 60% (medium affluence), and highest 20% (high affluence) within each country and region.

School pressure. Participants were asked to respond the question "How pressured do you feel by the schoolwork you have to do?" with response options being 1 = "not at all" 2 = "a little" 3 = "some" and 4 = "a lot." The responses were recorded from 0 to 3, with a higher score indicating more perceived school pressure.[17]

Data Analyses

We first computed percentages, means, and standard errors of the 3 variables of interest (ie, chronic back pain, sleep difficulties, and psychological symptoms) across the 5 measurement periods (ie, 2001/2, 2005/6, 2009/10, 2013/14, and 2017/18). We then fitted 2 linear regression models, 1 with sleep difficulties as the criterion variable and 1 with psychological symptoms as the criterion variable, to evaluate the statistical significance of the observed increases between 2002 and 2018 in both conditions. In both, the survey year was introduced as the independent variable. Then, to test the first study hypothesis (ie, that the prevalence of chronic back pain has continued to increase past 2014), we compared the prevalence of chronic back pain in 2014 with the prevalence of chronic back pain in 2018 using logistic regression analysis. In the event that the first hypothesis was supported, we planned to conduct a path analysis to test if the increase in the prevalence of chronic back pain from 2002 to 2018 was explained indirectly by increases in sleep difficulties, which, in turn, may be associated with increases in psychological symptoms (ie, a serial mediation analysis). This approach is consistent with those taken by prior studies in this area that have used survey years as a predictor variable in mediation analyses, demonstrating its usefulness in examining trends over time.[14,17,41]

Path analysis establishes a structural model by postulating predetermined hypothesized relationships among variables and utilizes a sequence of multiple regression analyses to statistically represent and analyze the specified pathways. Although path analysis suggests the presence of a causal relationship, the directionality of the relationship cannot be established in cross-sectional designs, such as the one used in this study, due to the possibility of causal influence in the opposite direction or the presence of unmeasured third variables. Therefore, the current study used path analysis to test whether the data aligned with the hypothesis but could not draw definitive conclusions about the direction or timing of the effects.

In this path analysis, the survey year was entered as the independent variable, sleep difficulties as the first mediator, psychological symptoms as the second mediator, and chronic back pain as the dependent variable. Survey year, sleep difficulties, and psychological symptoms were entered as continuous variables, whereas chronic back pain was entered as a dichotomous variable. A bootstrap estimation approach with 10,000 samples was used to examine the hypothesized indirect pathways. To address the effects of potential confounders, path analyses were adjusted for participants' socioeconomic status and school pressure. All analyses were stratified by sex/age subgroups (ie, 11-, 13-, and 15-year-old boys and girls). Cluster robust standard errors (adjusting for adolescents being nested within countries) and survey weights were used to account for the complex sampling method. A 2-tailed significance level of $P < .05$ was defined as statistically significant. Specific model fit indices are reported, including the Root Mean Square Error of Approximation (RMSEA), the Standardized Root Mean Square Residual (SRMR), and the Comparative Fit Index (CFI). A good fit is typically indicated by RMSEA values less than .06, SRMR values less than .08, and CFI values greater than .90.[42] Listwise deletion was used to handle missing data. All analyses were conducted using STATA 14 (StataCorp; College Station, TX).

Results

Differences in the Prevalence of Chronic Back Pain Between 2014 and 2018

Table 2 provides an overview of the prevalence of chronic back pain across the 5 survey waves. As can be seen, the overall prevalence of chronic back pain in 2018 was slightly higher (22.2%) than the prevalence of chronic back pain in 2014 (21.6%). This increase in the prevalence of chronic back pain between 2014 and 2018, albeit small, was statistically significant across all subgroups considered and ranged from .4% for 15-year-old girls to 1.3% for 11-year-old boys.

Increases in Sleep Difficulties and Psychological Symptoms Between 2002 and 2018

Table 3 provides an overview of the frequency of sleep difficulties and psychological symptoms across the 5 survey waves. Results from the linear regression analyses indicated that both the overall frequency of sleep difficulties ($b = .018$, standard error (SE) = .004, $t = 4.50$, $P < .001$) and psychological symptoms ($b = .020$, SE = .002, $t = 10.94$, $P < .001$) increased from 2002 and 2018. The findings showed that whereas the increase in the frequency of sleep difficulties was consistent for all

Table 2. Prevalence of Chronic Back Pain Over Survey Years With Standard Errors (Weighted Estimates)

	Prevalence (%)					*2014 (ref) vs 2018*			*2002 to 2018*		
	2002	*2006*	*2010*	*2014*	*2018*	*OR*	*95% CI*	*P*	*B*	*95% CI*	*P*
Total	18.38 (.01)	19.41 (.01)	20.47 (.01)	21.59 (.01)	22.16 (.01)	1.05	1.03 to 1.07	< .001	.015	.01 to .02	< .001
Subgroups											
11-year-olds											
Girls	14.86 (.01)	15.26 (.01)	15.90 (.01)	16.23 (.01)	17.03 (.01)	1.06	1.01 to 1.11	.017	.010	.004 to .02	.001
Boys	13.04 (.01)	13.72 (.01)	14.06 (.01)	13.87 (.01)	15.18 (.01)	1.11	1.05 to 1.17	< .001	.010	.002 to .02	.010
13-year-olds											
Girls	19.99 (.01)	20.84 (.01)	21.45 (.01)	24.45 (.01)	24.97 (.01)	1.04	1.01 to 1.07	.020	.019	.01 to .02	< .001
Boys	16.83 (.01)	17.30 (.01)	17.94 (.01)	18.04 (.01)	19.24 (.01)	1.08	1.03 to 1.13	.001	.010	.002 to .02	.012
15-year-olds											
Girls	24.92 (.01)	26.82 (.01)	29.42 (.01)	32.09 (.01)	32.54 (.01)	1.03	1.02 to 1.05	.032	.024	.02 to .03	< .001
Boys	20.80 (.01)	21.46 (.01)	23.02 (.01)	23.67 (.01)	24.38 (.01)	1.04	1.02 to 1.09	.001	.013	.007 to .02	< .001

CI, confidence interval; OR, odds ratio.

Table 3. Mean of Sleep Difficulties and Psychological Symptoms Over Survey Years With Standard Errors (Weighted Estimates) and Linear Trends

	Mean					*2002 to 2018*	
	2002	*2006*	*2010*	*2014*	*2018*	*B*	*P*
Sleep difficulties (robust SE)							
Total	.97 (.04)	.99 (.05)	1.08 (.05)	1.15 (.06)	1.30 (.05)	.021	< .001
Subgroups							
11-year-olds							
Girls	1.01 (.06)	.98 (.06)	1.09 (.06)	1.10 (.06)	1.32 (.06)	.019	< .001
Boys	.94 (.06)	.91 (.05)	.98 (.05)	1.02 (.05)	1.21 (.05)	.016	< .001
13-year-olds							
Girls	1.03 (.05)	1.06 (.06)	1.18 (.06)	1.29 (.07)	1.46 (.05)	.027	< .001
Boys	.85 (.04)	.86 (.04)	.95 (.04)	.98 (.05)	1.14 (.04)	.018	< .001
15-year-olds							
Girls	1.23 (.05)	1.18 (.06)	1.30 (.06)	1.45 (.07)	1.55 (.05)	.028	< .001
Boys	.84 (.04)	.90 (.04)	.98 (.05)	1.05 (.05)	1.14 (.04)	.019	< .001
Psychological symptoms (robust SE)							
Total	3.76 (.13)	3.65 (.14)	3.53 (.12)	3.69 (.10)	4.09 (.10)	.019	.001
Subgroups							
11-year-olds							
Girls	3.42 (.12)	3.23 (.14)	3.19 (.12)	3.19 (.12)	3.52 (.11)	.004	.436
Boys	3.08 (.13)	2.88 (.12)	2.78 (.11)	2.76 (.11)	3.16 (.11)	.003	.632
13-year-olds							
Girls	4.23 (.15)	4.15 (.15)	4.03 (.13)	4.37 (.12)	4.82 (.11)	.036	< .001
Boys	3.33 (.13)	3.18 (.12)	3.07 (.11)	3.04 (.10)	3.51 (.11)	.007	.164
15-year-olds							
Girls	4.85 (.18)	4.83 (.17)	4.63 (.16)	5.20 (.11)	5.64 (.12)	.050	< .001
Boys	3.58 (.14)	3.47 (.13)	3.33 (.12)	3.42 (.10)	3.84 (.12)	.013	.041

SE, standard error.

subgroups considered, the increase in the frequency of psychological symptoms was statistically significant only for 13-year-old girls and 15-year-old boys and girls. Based on these results, 3 path analyses were conducted to test the second study hypothesis: 1 for 13-year-old girls, 1 for 15-year-old girls, and 1 for 15-year-old boys.

Path Analysis

Fig 1 presents path coefficients of the model for the increase in the prevalence of chronic back pain between 2002 and 2018 for 13-year-old girls and for 15-year-old girls and boys. As can be seen, the path from survey year to sleep difficulties was statistically significant for all subgroups considered (13-year-old girls: $B = .024$, $SE = .002$, $P < .001$; 15-year-old girls: $B = .025$, $SE = .002$, $P < .001$; 15-year-old boys: $B = .018$, $SE = .002$, $P < .001$), indicating a significant increase in sleep difficulties between 2002 and 2018. Furthermore, more sleep difficulties were significantly associated with more frequent psychological symptoms (13-year-old girls: $B = .844$, $SE = .029$, $P < .001$; 15-year-old girls: $B = .854$, $SE = .025$, $P < .001$; 15-year-old boys: $B = .858$, $SE = .034$, $P < .001$) which, in turn, were significantly associated with a higher prevalence of chronic back pain (13-year-old girls: $B = .167$, $SE = .006$, $P < .001$; 15-year-old girls: $B = .155$, $SE = .006$, $P < .001$; 15-year-old boys: $B = .189$, SE

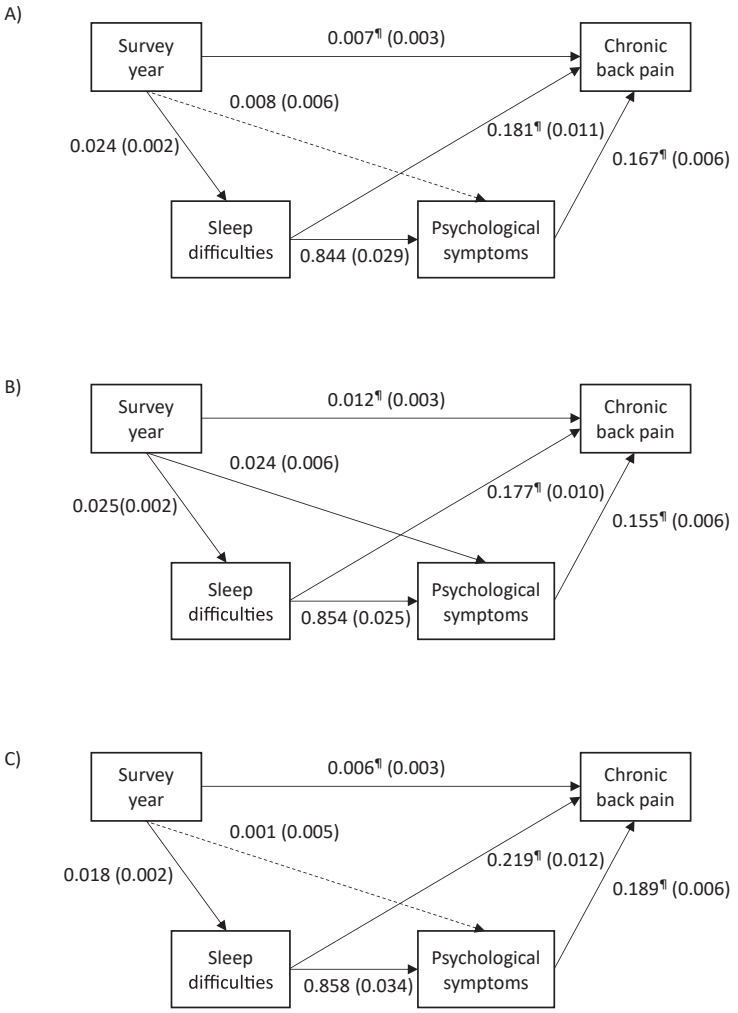


Figure 1. Path analysis testing whether the increase in the prevalence of chronic back pain from 2002 to 2018 was explained indirectly by the increase in the frequency of sleep difficulties, which, in turn, were associated with increases in the frequency of psychological symptoms for 13-year-old girls (**A**) and for 15-year-old girls (**B**) and boys (**C**). Black solid lines indicate significant direct paths ($P < .05$). The gray dotted line indicates nonsignificant direct path ($P > .05$). *Note.* ¶Regression coefficients are on a log-odds metric.

= .006, $P < .001$). The indirect pathway from survey year to psychological symptoms was statistically significant for all subgroups considered (13-year-old girls: $B = .020$, $SE = .002$, 95% confidence interval (CI) = .017–.024, 10,000 bootstrap resamples, $P < .001$; 15-year-old girls: $B = .022$, SE =;.002, 95% CI = .018–.025, 10,000 bootstrap resamples, $P < .001$; 15-year-old boys: $B = .016$, $SE = .002$, 95% CI = .012–.019, 10,000 bootstrap resamples, $P < .001$), indicating that increases in sleep difficulties mediated the increase in psychological symptoms over time. This mediation effect was found to be total for 13-year-old girls and 15-year-old boys and partial for 15-year-old girls. The indirect pathway from survey year to chronic back pain through sleep difficulties and psychological symptoms was statistically significant (13-year-old girls: $B = .003$, $SE = .0003$, 95% CI = .003–.004, 10,000 bootstrap resamples, $P < .001$; 15-year-old girls: $B = .003$, $SE = .0003$, 95% CI = .003–.004, 10,000 bootstrap resamples $P < .001$; 15-year-old boys: $B = .003$, $SE = .0003$, 95% CI = .002–.004, 10,000 bootstrap resamples $P < .001$), hence supporting the purposed model for the increase in the prevalence of chronic back pain between 2002 and 2018. Overall model fit indices indicated a good fit for all models (13-year-old girls: RMSEA = .00, SRMR = .00, CFI = 1.00; 15-year-old girls: RMSEA = .00, SRMR = .00, CFI = 1.00; 15-year-old boys: RMSEA = .00, SRMR = .00, CFI = 1.00).

Conclusions

This large cross-sectional study combined data from 7,89,596 adolescents from 32 countries over 16 years

(2002–2018) to determine 1) if there was a continued increase in the overall prevalence of chronic back pain in adolescents from 2014 to 2018 considering sex and age; and 2) if the increase in the prevalence of chronic back pain from 2002 to 2018 was explained indirectly by the increase in the frequency of sleep difficulties and psychological symptoms.

The study findings confirmed a small increase of .5% in the prevalence of chronic back pain among adolescents between 2014 and 2018. This increase ranged from .4% for 15-year-old girls to 1.3% for 11-year-old boys and indicated that the prevalence of chronic back pain has continued increasing in this population beyond 2014. Overall, the data suggest that the prevalence of chronic back pain in this population has increased by 4% in the last 2 decades, with 22% of adolescents in 2018 reporting chronic back pain compared to 18% in 2002. This is a concerning finding, given the abundance of evidence that chronic pain conditions—and chronic back pain in particular—in adolescents impose a significant economic burden on health care systems.[3,4,43] Moreover, it is well-documented that back pain or low back pain in adolescents is positively associated with back pain in adulthood,[44-46] which is the leading cause of disability worldwide.[8,13] Therefore, if the findings reported here are replicated, it could be anticipated that the negative economic impact associated with this condition, both in adolescents and adults, will also increase. That said, however, the findings also suggested that the rate of increase in the prevalence of chronic back pain between 2014 and 2018 was lower than increases in prior successive waves of the HBSC study—for example, from 19.4% to 20.5% between 2006 and 2010; from 20.5% to 21.6% between 2010 and 2014. In any case, the findings support the importance of continuing to monitor the trends in back pain prevalence rates in children and, if possible, take steps to reduce this prevalence.

Consistent with the second study hypothesis, the findings also showed that for girls aged 13 and for girls and boys aged 15, the increase in the prevalence of chronic back pain between 2002 and 2018 was partially indirectly explained by the increase in the frequency of sleep difficulties, which were associated with increases in the frequency of psychological symptoms. This finding is consistent with research indicating that sleep problems are a prospective predictor of chronic pain problems,[19,21,22] and that psychological symptoms may serve as mediators in this association.[24-26,28] Moreover, these results provide valuable insights into the potential mechanisms underlying the increase in the prevalence of chronic back pain in adolescents, particularly in girls and older adolescents. However, while the results confirmed the study hypotheses, it is important to exercise caution in interpreting the findings due to the divergent temporal trends observed in chronic back pain, sleep difficulties, and psychological symptoms. While the frequency of sleep difficulties and the prevalence of chronic back pain exhibited a consistent upward trend across survey waves, the frequency of psychological symptoms displayed a different pattern. It is worth noting that psychological symptoms are influenced by various contextual and individual factors that were not measured in the current study. These factors could potentially contribute to the observed fluctuations or the absence of a steady increase in psychological symptoms. For example, a recent study examining temporal over time bullying victimization—which has been associated with poor mental health outcomes in adolescents[47]—reported a general decrease in bullying victimization rates across several countries over time. This could partially explain the findings of this study. This possibility should be tested in future studies.

Based on these findings as a group, it is possible that if the upward trends in sleep difficulties and psychological symptoms continue,[15-18] the prevalence of chronic back pain is likely to increase. This is particularly relevant in light of the recent coronavirus disease 19 (COVID-19) pandemic, as studies have shown an increase in sleep problems[48-50] and mental health problems such as anxiety and depressive symptoms[51-53] in children and adolescents. Furthermore, as a result of the COVID-19 pandemic, there have been changes in daily routines, such as increased time spent in screen time activities,[54] which has been associated with multiple health complaints in adolescents, including back pain.[14,55-57] Taken together, the findings raise the possibility that the prevalence of chronic back pain may have increased during the years of COVID-19 lockdown measures,[58,59] and underscore the importance of continuing to monitor back prevalence rates.

The study findings reinforce the importance of implementing public health interventions to promote mental health and prevent sleep problems in adolescents. Considering that adolescents spend most of their waking time in school, educational institutions are well-positioned to play a significant role in delivering such interventions. In this regard, whole-school interventions, that is, comprehensive programs or strategies that are implemented across an entire school with collaboration and coordination among all stakeholders within the school community, including teachers, administrators, students, and parents, aimed at enhancing students' development of social and emotional skills have shown promising results for improving emotional well-being and reducing internalizing symptoms.[60] Furthermore, school-based sleep education programs have been shown to be effective at increasing adolescents' sleep knowledge[61] and produce short-term benefits on sleep-related outcomes such as sleep duration.[62] However, the extent to which these interventions prevent the development of back pain and chronic back pain or their impact on adolescents needs to be systematically studied.

The results of this study should be considered in light of several limitations. First, the HBSC study data are cross-sectional at each time point, allowing only for tests of concurrent associations among variables; these data cannot be used to test for and confirm causal relationships. For example, although insufficient sleep can precede and maintain pain, pain can also interfere with the ability to initiate and maintain sleep.[63] Therefore, and in support of the increasing body of research suggesting a bidirectional relationship between sleep disturbance and chronic pain,[20,27,64] it could be argued that increases in sleep difficulties are a possible consequence of the increase in the prevalence of chronic back pain. Longitudinal research is

needed to evaluate the potential for causal relationships between sleep, psychological function, and chronic back pain. Second, the study was limited to the measures that were used for the HBCS study, which only included a subset of the many factors that are thought to contribute to the complex experience of chronic back pain. Moreover, the HBSC collects self-report data, which is based, at least in part, on the respondents' memories. Although this is the most commonly used method in chronic pain survey studies, it may lead to overestimation of rates and associations among study variables.[65] The utilization of objective measures of sleep, such as actigraphy and polysomnography, and the inclusion of measures of psychological symptoms reported by multiple sources (eg, parents) would have enhanced the rigor of the study findings. Furthermore, our study would also have benefitted from incorporating other, more specific measures of psychological symptoms such as depressive symptoms or anxiety. Future research should include additional sources of data for assessing the variables assessed here when possible. Additionally, while our path analysis accounted for confounding variables associated with chronic back pain, sleep difficulties, and psychological symptoms, it is important to note that potential confounding effects of unmeasured factors, including the influence of the delay in sleep phase/chronotype, may still exist. The delay in sleep phase/chronotype, which is particularly prominent during adolescence, has been previously linked to psychological symptoms, sleep difficulties, and pain in existing studies.[66-68] Therefore, the impact of this particular factor on the observed relationships should be studied in future research, if possible. Future research should also consider the potential moderating role of adolescents' sex when investigating the effects of sleep disturbance on pain rather than considering it solely as a confounding variable; there is a growing body of evidence indicating that these effects may differ between boys and girls.[69] Finally, the HBSC survey does not collect data on self-identified race and ethnicity, which may prevent the generalizability of our findings to populations with different racial and ethnic backgrounds.

Despite the study's limitations, the findings provide important new information regarding the rising trend in the prevalence of chronic back pain among adolescents. Moreover, the finding that increases in sleep difficulties and psychological symptoms are significantly linked with the increasing rates of chronic back pain in this population, particularly in girls and older adolescents, provides important information that may aid policymakers, health care professionals, and researchers in assessing and enhancing public health initiatives that aim to reduce the occurrence and effects of chronic back pain in adolescents.

Acknowledgments

Health Behaviour in School-aged Children is an international study carried out in collaboration with the World Health Organization Regional Office for Europe. The International Coordinator was Jo Inchley (University of Glasgow) for the 2018 survey and Candace Currie (Glasgow Caledonian University) for the 2002 to 2014 surveys. The Data Bank Manager was Professor Oddrun Samdal (University of Bergen). The survey data included in this study were conducted by the following principal investigators in the 32 countries: Austria (Rosemarie Felder-Puig and Wolfgang Dür), Flemish Belgium (Bart De Clercq, Carine Vereecken, Anne Hublet, and Lea Maes), French Belgium (Katia Castetbon and Danielle Piette), Canada (William Pickett, Wendy Craig, John Freeman, and William Boyce), Croatia (Ivana Pavic Simetin and Marina Kuzman), Czech Republic (Michal Kalman and Ladislav Csemy), Denmark (Mette Rasmussen and Pernille Due), England (Fiona Brooks, Ellen Klemera, and Antony Morgan), Estonia (Leila Oja, Katrin Aasvee, and Mai Kaser), France (Emmanuelle Godeau), Germany (Matthias Richter, Petra Kolip, Ulrike Ravens-Sieberer, and Klaus Hurrelmann), Greece (Anna Kokkevi), Greenland (Birgit Niclasen), Hungary (Ágnes Németh and Anna Aszmann), Ireland (Saoirse Nic Gabhainn), Israel (Yossi Harel-Fisch), Italy (Franco Cavallo), Latvia (Iveta Pudule), Lithuania (Kastytis Smigelskas and Apolinaras Zaborskis), North Macedonia (Lina Kostarova Unkovska), the Netherlands (Gonneke Stevens, Saskia van Dorsselaer, Wilma Vollebergh, and Tom de Bogt), Norway (Oddrun Samdal), Poland (Joanna Mazur and Barbara Woynarowska), Portugal (Margarida Gaspar de Matos), Romania (Adriana Baban), Russia (Anna Matochkina, Oleg Churganov, and Alexander Komkov), Scotland (Jo Inchley and Candace Currie), Slovenia (Helena Jericek and Eva Stergar), Spain (Carmen Moreno), Sweden (Petra Löfstedt, Lilly Augustine, and Ulla Marklund), Switzerland (Marina Delgrande-Jordan, Hervé Kuendig, Emmanuel Kuntsche, and Holger Schmid), Ukraine (Olga Balakireva), and Wales (Chris Roberts).

References

1. Bejia I, Abid N, Salem KB, Letaief M, Younes M, Touzi M, Bergaoui N: Low back pain in a cohort of 622 Tunisian schoolchildren and adolescents: An epidemiological study. Eur Spine J 14:331-336, 2005. https://doi.org/10.1007/s00586-004-0785-2

2. MacDonald J, Stuart E, Rodenberg R: Musculoskeletal low back pain in school-aged children a review. JAMA Pediatr 171:280-287, 2017. https://doi.org/10.1001/jamapediatrics.2016.3334

3. Groenewald CB, Wright DR, Palermo TM: Health care expenditures associated with pediatric pain-related conditions in the United States. Pain 156:951-957, 2015. https://doi.org/10.2217/pmt.14.52

4. Ochsmann EB, Escobar Pinzón CL, Letzel S, Kraus T, Michaelis M, Muenster E: Prevalence of diagnosis and direct treatment costs of back disorders in 644,773 children and youths in Germany. BMC Musculoskelet Disord 11:193, 2010. https://doi.org/10.1186/1471-2474-11-193

5. Hestbaek L, Leboeuf-Yde C, Kyvik KO: Is comorbidity in adolescence a predictor for adult low back pain? A

prospective study of a young population. BMC Musculoskelet Disord 29:1-7, 2006. https://doi.org/10.1186/1471-2474-7-29

6. Roy R, Galán S, Sánchez-Rodríguez E, Racine M, Solé E, Jensen MP, Miró J: Cross-national trends of chronic back pain in adolescents: Results from the HBSC Study, 2001-2014. J Pain 23:123-130, 2021. https://doi.org/10.1016/j.jpain.2021.07.002

7. Groenewald CB, Essner BS, Wright D, Fesinmeyer MD, Palermo TM: The economic costs of chronic pain among a cohort of treatment-seeking adolescents in the United States. J Pain 15:925-933, 2014. https://doi.org/10.1016/j.jpain.2014.06.002

8. Hoy D, Bain C, Williams G, March L, Brooks P, Blyth F, Woolf A, Vos T, Buchbinder R: A systematic review of the global prevalence of low back pain. Arthritis Rheum 64:2028-2037, 2012. https://doi.org/10.1002/art.34347

9. Lynch AM, Kashikar-Zuck S, Goldschneider KR, Jones BA: Psychosocial risks for disability in children with chronic back pain. J Pain 7:244-251, 2006

10. Martin BI, Deyo RA, Mirza SK, Turner JA, Comstock BA, Hollingworth W, Sullivan SD: Expenditures and health status among adults with back and neck problems. JAMA 299:656-664, 2008. https://doi.org/10.1001/jama.299.6.656

11. Roth-Isigkeit A, Thyen U, Stöven H, Schwarzenberger J, Schmucker P: Pain among children and adolescents: Restrictions in daily living and triggering factors. Pediatrics 115:152-162, 2005. https://doi.org/10.1542/peds.2004-0682

12. Sjölie AN: Psychosocial correlates of low-back pain in adolescents. Eur Spine J 11:582-588, 2002. https://doi.org/10.1007/s00586-002-0412-z

13. Wu A, March L, Zheng X, Huang J, Wang X, Zhao J, Blyth FM, Smith E, Buchbinder R, Hoy D: Global low back pain prevalence and years lived with disability from 1990 to 2017: Estimates from the Global Burden of Disease Study 2017. Ann Transl Med 8:299, 2020. https://doi.org/10.21037/atm.2020.02.175

14. Roman-Juan J, Roy R, Jensen MP, Miró J: The explanatory role of sedentary screen time and obesity in the increase of chronic back pain amongst European adolescents: The HBSC study 2002–2014. Eur J Pain 26:1781-1789, 2022

15. Ghekiere A, Van Cauwenberg J, Vandendriessche A, Inchley J, Gaspar de Matos M, Borraccino A, Gobina I, Tynjälä J, Deforche B, De Clercq B: Trends in sleeping difficulties among European adolescents: Are these associated with physical inactivity and excessive screen time. Int J Public Health 64:487-498, 2018. https://doi.org/10.1007/s00038-018-1188-1

16. Collishaw S: Annual research review: Secular trends in child and adolescent mental health. J Child Psychol Psychiatry 56:370-393, 2015. https://doi.org/10.1111/jcpp.12372

17. Cosma A, Stevens G, Martin G, Duinhof EL, Walsh SD, Garcia-Moya I, Költő A, Gobina I, Canale N, Catunda C, Inchley J, de Looze M: Cross-national time trends in adolescent mental well-being from 2002 to 2018 and the explanatory role of schoolwork pressure. J Adolesc Health 66:S50-S58, 2020. https://doi.org/10.1016/j.jadohealth.2020.02.010

18. Fleming TM, Clark T, Denny S, Bullen P, Crengle S, Peiris-John R, Robinson E, Rossen FV, Sheridan J, Lucassen M: Stability and change in the mental health of New Zealand secondary school students 2007-2012: Results from the national adolescent health surveys. Aust N Z J Psychiatry 48:472-480, 2014. https://doi.org/10.1177/0004867413514489

19. Afolalu EF, Ramlee F, Tang NKY: Effects of sleep changes on pain-related health outcomes in the general population: A systematic review of longitudinal studies with exploratory meta-analysis. Sleep Med Rev 39:92-97, 2018. https://doi.org/10.1016/j.smrv.2017.08.001

20. Allen JM, Graef DM, Ehrentraut JH, Tynes BL, Crabtree VM: Sleep and pain in pediatric illness: A conceptual review. CNS Neurosci Ther 22:880-893, 2016. https://doi.org/10.1111/cns.12583

21. Bonvanie IJ, Oldehinkel AJ, Rosmalen JGM, Janssens KAM: Sleep problems and pain: A longitudinal cohort study in emerging adults. Pain 157:957-963, 2016. https://doi.org/10.1097/j.pain.0000000000000466

22. Incledon E, O'Connor M, Giallo R, Chalkiadis GA, Palermo TM: Child and family antecedents of pain during the transition to adolescence: A longitudinal population-based study. J Pain 17:1174-1182, 2016. https://doi.org/10.1016/j.jpain.2016.07.005

23. Kamper SJ, Yamato TP, Williams CM: The prevalence, risk factors, prognosis and treatment for back pain in children and adolescents: An overview of systematic reviews. Best Pract Res Clin Rheumatol 30:1021-1036, 2016. https://doi.org/10.1016/j.berh.2017.04.003

24. Arnison T, Schrooten MGS, Hesser H, Jansson-Fröjmark M, Persson J: Longitudinal, bidirectional relationships of insomnia symptoms and musculoskeletal pain across adolescence: The mediating role of mood. Pain 163:287-298, 2022. https://doi.org/10.1097/j.pain.0000000000002334

25. Burgess HJ, Burns JW, Buvanendran A, Gupta R, Chont M, Kennedy M, Bruehl S: Associations between sleep disturbance and chronic pain intensity and function: A test of direct and indirect pathways. Clin J Pain 35:569-576, 2019. https://doi.org/10.1097/AJP.0000000000000711

26. Pavlova M, Ference J, Hancock M, Noel M: Disentangling the sleep-pain relationship in pediatric chronic pain: The mediating role of internalizing mental health symptoms. Pain Res Manag :1586921. https://doi.org/10.1155/2017/1586921, 2017.

27. Valrie CR, Bromberg MH, Palermo T, Schanberg LE: A systematic review of sleep in pediatric pain populations. J Dev Behav Pediatr :120-128, 2013. https://doi.org/10.1097/DBP.0b013e31827d5848

28. Whibley D, Alkandari N, Kristensen K, Barnish M, Rzewuska M, Druce KL, Tang NKY: Sleep and Pain: A systematic review of studies of mediation. Clin J Pain 35:544-558, 2019. https://doi.org/10.1097/AJP.0000000000000697

29. Donskoy I, Loghmanee D: Insomnia in adolescence. Med Sci 6:72, 2018

30. Hysing M, Pallesen S, Stormark KM, Lundervold AJ, Sivertsen B: Sleep patterns and insomnia among adolescents: A population-based study. J Sleep Res 22:549-556, 2013. https://doi.org/10.1111/jsr.12055

31. King S, Chambers CT, Huguet A, MacNevin RC, McGrath PJ, Parker L, MacDonald AJ: The epidemiology of chronic pain in children and adolescents revisited: A systematic review. Pain 152:2729-2738, 2011. https://doi.org/10.1016/j.pain.2011.07.016

32. Merikangas KR, Nakamura EF, Kessler RC: Epidemiology of mental disorders in children and adolescents. Dialog Clin Neurosci 1:7-20, 2022

33. Currie C, Inchley J, Molcho M, Lenzi M, Veselska Z, Wild F: Health behaviour in school-aged children (HBSC) study protocol: Background, methodology and mandatory items for the 2018/19 survey. Child Adolesc Health Res Unit 2018.

34. Roberts C, Freeman J, Samdal O, Schnohr CW, Looze ME, Nic Gabhainn S, Iannotti R, Rasmussen M, Dür W, Piette D, Vasileva L, Boyce W, Kuzman M, Csémy L, Due P, Morgan A, Tynjälä J, Godeau E, Ravens-Sieberer U, Kokkevi A, Niclasen B, Németh Á, Bjarnason T, Harel-Fisch Y, Cavallo F, Pudule I, Zaborskis A, Wagener Y, Massa M, Vollebergh W, Samdal O, Mazur J, de Matos MG, Baban A, Komkov A, Currie C, Morvicova E, Jericek H, Rodriguez CM, Marklund U, Kuntsche E, Unkovska LK, Ercan O, Balakireva O, Iannotti R: The Health Behaviour in School-aged Children (HBSC) study: Methodological developments and current tensions. Int J Public Health 54:140-150, 2009

35. Haugland S, Wold B: Subjective health complaints in adolescence - Reliability and validity of survey methods. J Adolesc 24:611-624, 2001. https://doi.org/10.1006/jado.2000.0393

36. Gariepy G, McKinnon B, Sentenac M, Elgar FJ: Validity and reliability of a brief symptom checklist to measure psychological health in school-aged children. Child Indic Res 9:471-484, 2016. https://doi.org/10.1007/s12187-015-9326-2

37. Hetland J, Torsheim T, Aarø LE: Subjective health complaints in adolescence: Dimensional structure and variation across gender and age. Scand J Public Health 30:223-230, 2002

38. Vandendriessche A, Ghekiere A, Van Cauwenberg J, De Clercq B, Dhondt K, Desmet A, Tynjälä J, Verloigne M, Deforche B: Does sleep mediate the association between school pressure, physical activity, screen time, and psychological symptoms in early adolescents? A 12-country study. Int J Environ Res Public Health 16:1072, 2019. https://doi.org/10.3390/ijerph16061072

39. Currie C, Molcho M, Boyce W, Holstein B, Torsheim T, Richter M: Researching health inequalities in adolescents: The development of the Health Behaviour in School-Aged Children (HBSC) Family Affluence Scale. Soc Sci Med 66:1429-1436, 2008. https://doi.org/10.1016/j.socscimed.2007.11.024

40. Torsheim T, Cavallo F, Levin KA, Schnohr C, Mazur J, Niclasen B, Currie C: Psychometric validation of the revised family affluence scale: A latent variable approach. Child Indic Res 9:771-784, 2016. https://doi.org/10.1007/s12187-015-9339-x

41. Raitasalo K, Kraus L, Bye EK, Karlsson P, Tigerstedt C, Törrönen J, Raninen J: Similar countries, similar factors? Studying the decline of heavy episodic drinking in adolescents in Finland, Norway and Sweden. Addiction 116:62-71, 2021. https://doi.org/10.1111/add.15089

42. Kline RB: Principles and Practice of Structural Equation Modeling. New York, Guilford Publications; 2023

43. Tumin D, Drees D, Miller R, Wrona S, Hayes D, Tobias JD, Bhalla T: Health care utilization and costs associated with pediatric chronic pain. J Pain 19:973-982, 2018. https://doi.org/10.1016/j.jpain.2018.03.012

44. Brattberg G: Do pain problems in young school children persist into early adulthood? A 13-year follow-up. Eur J Pain 8:187-199, 2004. https://doi.org/10.1016/j.ejpain.2003.08.001

45. Hestbaek L, Leboeuf-Yde C, Kyvik KO, Manniche C: The course of low back pain from adolescence to adulthood: Eight-year follow-up of 9600 twins. Spine 31:468-472, 2006. https://doi.org/10.1097/01.brs.0000199958.04073.d9

46. Jeffries LJ, Milanese SF, Grimmer-Somers KA: Epidemiology of adolescent spinal pain: A systematic overview of the research literature. Spine 32:2630-2637, 2007. https://doi.org/10.1097/BRS.0b013e318158d70b 2630-2367

47. Halliday S, Gregory T, Taylor A, Digenis C, Turnbull D: The impact of bullying victimization in early adolescence on subsequent psychosocial and academic outcomes across the adolescent period: A systematic review. J Sch Violence 20:351-373, 2021. https://doi.org/10.1016/j.lanepe.2021.100093

48. Bothe K, Schabus M, Eigl E-S, Kerbl R, Hoedlmoser K: Self-reported changes in sleep patterns and behavior in children and adolescents during COVID-19. Sci Rep 12:20412, 2022. https://doi.org/10.1038/s41598-022-24509-7

49. Bruni O, Malorgio E, Doria M, Finotti E, Spruyt K, Melegari MG, Villa MP, Ferri R: Changes in sleep patterns and disturbances in children and adolescents in Italy during the Covid-19 outbreak. Sleep Med 91:166-174, 2022. https://doi.org/10.1016/j.sleep.2021.02.003

50. Sharma M, Aggarwal S, Madaan P, Saini L, Bhutani M: Impact of COVID-19 pandemic on sleep in children and adolescents: A systematic review and meta-analysis. Sleep Med 84:259-267, 2021. https://doi.org/10.1016/j.sleep.2021.06.002

51. Hafstad GS, Sætren SS, Wentzel-Larsen T, Augusti E-M: Adolescents' symptoms of anxiety and depression before and during the Covid-19 outbreak – A prospective population-based study of teenagers in Norway. The Lancet Regional Health. Europe 5:100093. https://doi.org/10.1016/j.lanepe.2021.100093, 2021.

52. Hawes MT, Szenczy AK, Klein DN, Hajcak G, Nelson BD: Increases in depression and anxiety symptoms in adolescents and young adults during the COVID-19 pandemic. Psychol Med 52:3222-3230, 2022. https://doi.org/10.1017/S0033291720005358

53. Panchal U, Salazar de Pablo G, Franco M, Moreno C, Parellada M, Arango C, Fusar-Poli P: The impact of COVID-19 lockdown on child and adolescent mental health: Systematic review. Eur Child Adolesc Psychiatry 32:1151-1177, 2021. https://doi.org/10.1007/s00787-021-01856-w

54. Cellini N, Canale N, Mioni G, Costa S: Changes in sleep pattern, sense of time and digital media use during COVID-19 lockdown in Italy. J Sleep Res 29:e13074. https://doi.org/10.1111/jsr.13074, 2020.

55. Bento TPF, Cornelio GP, Perrucini PO, Simeão SFAP, de Conti MHS, de Vitta A: Low back pain in adolescents and association with sociodemographic factors, electronic devices, physical activity and mental health. J Pediatr 96:717-724, 2020. https://doi.org/10.1016/j.jped.2019.07.008

56. Joergensen AC, Strandberg-Larsen K, Andersen PK, Hestbaek L, Andersen A-MN: Spinal pain in pre-adolescence and the relation with screen time and physical activity behavior. BMC Musculoskelet Disord 22:1-10, 2021. https://doi.org/10.1186/s12891-021-04263-z

57. Lemes ÍR, Oliveira CB, Silva GCR, Pinto RZ, Tebar WR, Christofaro DG: Association of sedentary behavior and early engagement in physical activity with low back pain in adolescents: A cross-sectional epidemiological study. Eur Spine J 31:1-7, 2021. https://doi.org/10.1007/s00586-021-07004-x

58. Clauw DJ, Häuser W, Cohen SP, Fitzcharles MA: Considering the potential for an increase in chronic pain after the COVID-19 pandemic. Pain 161:1694-1697, 2020

59. Papalia GF, Petrucci G, Russo F, Ambrosio L, Vadalà G, Iavicoli S, Papalia R, Denaro V: COVID-19 pandemic increases the impact of low back pain: A systematic review and metanalysis. Int J Environ Res Public Health 19:4599, 2022. https://doi.org/10.3390/ijerph19084599

60. Goldberg JM, Sklad M, Elfrink TR, Schreurs KMG, Bohlmeijer ET, Clarke AM: Effectiveness of interventions adopting a whole school approach to enhancing social and emotional development: A meta-analysis. European Journal of Psychology of Education 34:755-782, 2019. https://doi.org/10.1007/s10212-018-0406-9 755–722

61. Rigney G, Watson A, Gazmararian J, Blunden S: Update on school-based sleep education programs: how far have we come and what has Australia contributed to the field. Sleep Med 80:134-157, 2021. https://doi.org/10.1016/j.sleep.2021.01.061

62. Chung KF, Chan MS, Lam YY, Lai CSY, Yeung WF: School-based sleep education programs for short sleep duration in adolescents: A systematic review and meta-analysis. J School Health 87:401-408, 2017. https://doi.org/10.1111/josh.12509

63. Lautenbacher S, Kundermann B, Krieg J-C: Sleep deprivation and pain perception. Sleep Med Rev 10:357-369, 2006

64. Albinni B, de Zambotti M, Iacovides S, Baker FC, King CD: The complexities of the sleep-pain relationship in adolescents: A critical review. Sleep Med Rev 67:101715 https://doi.org/10.1016/j.smrv.2022.101715, 2023.

65. Steingrímsdóttir ÓA, Landmark T, Macfarlane GJ, Nielsen CS: Defining chronic pain in epidemiological studies: A systematic review and meta-analysis. Pain 158:2092-2107, 2017. https://doi.org/10.1097/j.pain.0000000000001009

66. Arnison T, Schrooten MGS, Bauducco S, Jansson-Fröjmark M, Persson J: Sleep phase and pre-sleep arousal predicted co-developmental trajectories of pain and insomnia within adolescence. Sci Rep 12:4480, 2022. https://doi.org/10.1038/s41598-022-08207-y

67. Bauducco S, Richardson C, Gradisar M: Chronotype, circadian rhythms and mood. Curr Opin 34:77-83, 2020. https://doi.org/10.1016/j.copsyc.2019.09.002

68. Palada V, Gilron I, Canlon B, Svensson CI, Kalso E: The circadian clock at the intercept of sleep and pain. Pain 161:894-900, 2020. https://doi.org/10.1097/j.pain.0000000000001786

69. Christensen J, Noel M, Mychasiuk R: Neurobiological mechanisms underlying the sleep-pain relationship in adolescence: A review. Neurosci Biobehav Rev 96:401-413, 2019. https://doi.org/10.1016/j.neubiorev.2018.11.006

4.6. Study VI

Validation of the pediatric version of the Graded Chronic Pain Scale Revised in school-aged children and adolescents.

Research Paper

PAIN®

Validation of the pediatric version of the Graded Chronic Pain Scale Revised in school-aged children and adolescents

Josep Roman-Juan[a], Ester Solé[a], Elisabet Sánchez-Rodríguez[a], Elena Castarlenas[a], Mark P. Jensen[b], Jordi Miró[a,*]

Abstract

The Graded Chronic Pain Scale (GCPS) was originally developed to grade the severity of chronic pain conditions in adults. A revised version of this instrument (ie, GCPS-R) has been developed for use with adults to account for advances in pain metrics and new operational definitions of chronic pain and high-impact chronic pain. The purpose of the current study was to adapt the GCPS-R for use with pediatric samples (P-GCPS-R) and evaluate the adapted measure's concurrent validity. One thousand five hundred sixty-four school-aged children and adolescents (55% girls; 8-18 years) completed the P-GCPS-R and provided responses to measures of physical health, anxiety and depressive symptoms, maladaptive pain coping strategies, and activity limitations. Results showed that 14% of participants had chronic pain, of which 37% (5% of the whole sample) had mild chronic pain, 45% (6% of the whole sample) bothersome chronic pain, and 18% (3% of the whole sample) high-impact chronic pain. Participants without chronic pain and those with mild chronic pain showed no significant between-group differences in any of the study measures. Participants with bothersome chronic pain and high-impact chronic pain reported worse physical health, more anxiety and depressive symptoms, pain catastrophizing, and activity limitations than those with mild chronic pain. Participants with high-impact chronic pain reported more activity limitations than those with bothersome chronic pain. The findings support the concurrent validity of the P-GCPS-R for use with pediatric samples.

Keywords: Chronic pain, Chronic pain severity, P-GCPS-R, Children, Adolescents

1. Introduction

The Graded Chronic Pain Scale (GCPS[34]) was developed to classify the severity of pain conditions in adults and has a great deal of evidence supporting its reliability and validity.[5,6,17] Moreover, several studies support the applicability and validity of adapted versions of the GCPS to grade the severity of chronic pain in children and adolescents.[15,18,33,37,39]

Given recent advances in pain metrics as well as new operational definitions of chronic pain and high-impact chronic pain,[3,4,28,35] Von Korff et al.[36] recently developed and validated a revised version of the GCPS: the Graded Chronic Pain Scale-Revised (GCPS-R). The GCPS-R uses 5 items to grade the severity of chronic pain into 4 grades: "chronic pain absent" (grade 0), "mild chronic pain" (grade 1), "bothersome chronic pain" (grade 2), and "high-impact chronic pain" (grade 3). The GCPS-R's advantages over the original GCPS include simpler test items and a simpler scoring system than the latter.[36] Furthermore, the GCPS-R allows for the identification of individuals with chronic pain, facilitating direct comparison of the frequencies and correlates of chronic pain in epidemiological research,[18] which is crucial to understand the prevalence and impact of chronic pain.[2]

In support of the concurrent validity of the GCPS-R scores, Von Korff et al.[36] found statistically significant between-group differences in individuals classified as having different chronic pain grades in measures of health status, pain coping beliefs, activity limitations, and opioid use in a sample of adults enrolled in a healthcare plan. These differences were mostly found between individuals with bothersome chronic pain or high-impact chronic pain and individuals without chronic pain or with mild chronic pain. Individuals with mild chronic pain differed from those without chronic pain only in opioid use, whereas activity limitations were the distinguishing factor between individuals experiencing bothersome and high-impact chronic pain. Based on these findings, Von Korff et al.[36] noted that more research to evaluate the concurrent validity of the GCPS-R scores is needed, including research in diverse populations. However, to the best of our knowledge, no such research has been conducted with children and adolescents.

The aims of the current study were to (1) adapt the GCPS-R for its use with pediatric samples and to (2) evaluate its concurrent validity in a community sample of school-aged children and adolescents. Based on prior research in adults,[36] we hypothesized that (1) children and adolescents with mild chronic pain would report similar levels of health, use of maladaptive pain coping strategies, and activity limitations to

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

[a] *Unit for the Study and Treatment of Pain—ALGOS, Department of Psychology, Research Center for Behavior Assessment (CRAMC), Universitat Rovira i Virgili, Catalonia, Spain,* [b] *Department of Rehabilitation Medicine, University of Washington, Seattle, WA, United States*

**Corresponding author. Address: Departament de Psicología, Universitat Rovira i Virgili, Carretera de Valls, s/n, 43007 Tarragona, Spain. Tel.: +34-977558179; fax: +34-977558088. E-mail address: jordi.miro@urv.cat (J. Miró).*

PAIN 00 (2023) 1–9

http://dx.doi.org/10.1097/j.pain.0000000000002965

those without chronic pain; (2) children and adolescents with bothersome chronic pain and high-impact chronic pain would report significantly worse health, more use of maladaptive coping pain strategies, and higher activity limitations than those without chronic pain or with mild chronic pain; and (3) children and adolescents with high-impact chronic pain would report significantly higher activity limitations than those with bothersome chronic pain.

2. Method

2.1. Procedure and participants

This cross-sectional study uses data from the initial assessment of a sample of children and adolescents recruited between February and June 2022 for their participation in the EPIDOL project (second wave), an ongoing longitudinal epidemiological study of pain in children and adolescents conducted in the South East of Catalonia (Spain[24]). Data for the current analyses were collected at 20 schools from 3 different areas that agreed to participate in the study, which represent a 67% of the total number of schools initially approached (n = 30). All students aged between 8 and 18 years who were able to read, write, and speak Spanish were eligible to participate in the study. To participate, both the students and their parents needed to provide informed assent and consent, respectively. Students who met the study eligibility criteria were asked to respond a paper-and-pencil survey while at school. The participants were given a gym sack and a calendar valued in €3 each for their participation. The Ethics Committee of the Universitat Rovira i Virgili approved the study (*Institut d'Investigació Sanitària Pere Virgili; ref.: 136/2018*).

Of the 5328 students who were eligible and invited to participate, 1721 expressed a willingness to participate and received consent from their parents. Of these, 1564 (30% of those eligible) provided complete or mostly complete data. The data from these participants were used in the analyses for this study.

2.2. Variables and measures

2.2.1. Demographic variables

All participants were asked to provide information about their sex at birth, age, and school grade.

2.2.2. Graded Chronic Pain Scale-Revised

As noted previously, the GCPS-R[36] classifies chronic pain severity using 5 items. The first item aims to identify individuals with chronic pain and asks respondents to report: "In the past 3 months, how often did you have pain?" with response options "never," "some days," "most days," and "every day." The second item aims to identify individuals with high-impact chronic pain and asks respondents the following question: "Over the past 3 months, how often did pain limit your life or work activities?" with response options "never," "some days," "most days," and "every day." Items 3, 4, and 5 assess pain intensity and interference over the past 7 days and are taken from the *Pain, Enjoyment and General Activities* scale (PEG[20]). Specifically, item 3 asks "What number best describes your pain, on average?" Respondents are then asked to respond to this question using a 0 to 10 Numerical Rating Scale (NRS) where 0 = "no pain" and 10 = "pain as bad as you can imagine." Item 4 asks "During the past 7 days, what number best describes how pain has interfered with your enjoyment of life?" Respondents then rate the frequency of interference with life enjoyment on a 0 to 10 NRS where 0 = "does not interfere" and 10 = "completely interferes." Item 5 asks "During the past 7 days, what number best describes how pain has interfered with your general activities," and the associated 0 to 10 NRS endpoints are 0 = "does not interfere" and 10 = "completely interferes." The responses to items 3, 4, and 5 are summed to compute a PEG total score that ranges from 0 to 30. Finally, although it is not used to grade the severity of chronic pain, the GCPS-R includes an additional item (item 6) that asks respondents, "Are you not working or unable to work due to pain or a pain condition?" with the response options of "yes" or "no."

2.2.3. Adaptation of the Graded Chronic Pain Scale-Revised for use in pediatric populations

Because the GCPS-R was developed to be used with adults, the items were revised for administration to a pediatric population by a group of 5 clinicians and researchers with a breadth and depth of experience in the study and treatment of children and adolescents with chronic pain, including the development and validation of assessment instruments to be used with these samples. They included a basic science researcher, 2 clinical health psychologists, a pediatric pain psychologist, and an expert in behavioral assessment and measurement. The resulting measure was called the Pediatric Graded Chronic Pain Scale-Revised (P-GCPS-R). The following specific adaptations were made:

(1) An additional response option ("half of the days") for items 1 (ie, "In the past 3 months, how often did you have pain?") and 2 (ie, "Over the past 3 months, how often did pain limit your life or work?") was added, so that the options were now "never," "some days," "half of the days," "most days," and "every day." The rational for the inclusion of this additional response option was to be more accurate in the assessment of pain and related disability.
(2) Because children and adolescents are rarely employed, and most attend school, item 2 was modified to ask participants about the interference of pain on their school activities (ie, "Over the past 3 months, how often did pain limit your life or school activities?").
(3) Item 6 (ie, "Are you not working or unable to work due to pain or a pain condition?") was modified, again because children rarely work (ie, "Are you not attending school or unable to attend school due to pain or a pain condition?"). Although, as noted above, item 6 is not used to rate the severity of chronic pain[36]; this additional item, however, has clinical relevance for identifying children and adolescents who do not or cannot attend school because of pain. However, because our sample consisted of schoolchildren and adolescents, and all participants that provided data on the P-GCPS-R were able to attend school at the original time of data collection, item 6 was not administered to participants in this study.

Because our sample was composed of Spanish-speaking school children and adolescents, all of the P-GCPS-R items were translated into Spanish using a back-translation procedure.[25,38] One of the benefits of this procedure is that it helps to ensure that the final translated measure is culturally appropriate.[38] This procedure was conducted in 3 steps: first, 2 bilingual psychologists fluent in Spanish and English translated the items into Spanish; subsequently, a professional translator who was not familiar with the original version of the GCPS-R, back translated the Spanish version of the items into English; last, the English

back translation was reviewed by one of the GCPS-R developers to ensure consistency with the intended meaning of the original items. No changes were needed. This process has been used in previous research.[14,26] Before the administration of the questionnaire, the comprehensibility of the adapted items was tested with 5 children and adolescents randomly selected from the study sample. **Figure 1** shows the items of the P-GCPS-R.

Following the scoring algorithm of the GCPS-R,[36] participants responses to the P-GCPS-R were classified in grade 0 (chronic pain absent) if they reported no pain over the past 3 months or reported pain that is not present on most days or every day. The remaining participants who reported chronic pain (ie, pain in most days or every day over the past 3 months) were classified in grades 1, 2, and 3. Among those, participants who reported that pain did not limit their life or school activities on most days or every day and with PEG total scores below 12 were classified in grade 1 (mild chronic pain); participants who reported that pain did not limit their life or school activities on most days or every day and with PEG total scores equal or above 12 were classified in grade 2 (bothersome chronic pain); and participants who reported that pain limited their life or school activities on most days or every day were classified in grade 3 (high-impact chronic pain), regardless of their PEG scores. **Figure 2** provides a summary of the P-GCPS-R scoring procedures.

2.2.4. Health status

2.2.4.1. Physical health

The Spanish versions of the 4-item Mobility and Fatigue scales from the Patient-Reported Outcomes Measurement Information System (PROMIS) Pediatric-25 Profile Form v.2 and the 4-item PROMIS pediatric sleep disturbance short form V1.0 were used to assess participants perceived physical health. With these forms,

1. In the past 3 months, how many times did you have pain?

☐ Never ☐ Most days

☐ Some days ☐ Every day

☐ Half the days

2. Over the past 3 months, how often did pain limit your life or school activities?

☐ Never ☐ Most days

☐ Some days ☐ Every day

☐ Half the days

Now think about the pain you have had over the past 7 days...

3. On average, which number best describes your pain?

0	1	2	3	4	5	6	7	8	9	10

No pain — A lot of pain

4. During the past 7 days, which number best describes how pain has interfered with your ability to have fun?

0	1	2	3	4	5	6	7	8	9	10

Does not interfere — Interferes completely

5. During the past 7 days, which number best describes how pain has interfered with your overall activity?

0	1	2	3	4	5	6	7	8	9	10

Does not interfere — Interferes completely

6. Are you not attending school or not able to attend school due to pain or a pain condition?

☐ Yes ☐ No

Figure 1. Adaptation of the Graded Chronic Pain Scale-Revised for its use with pediatric samples.

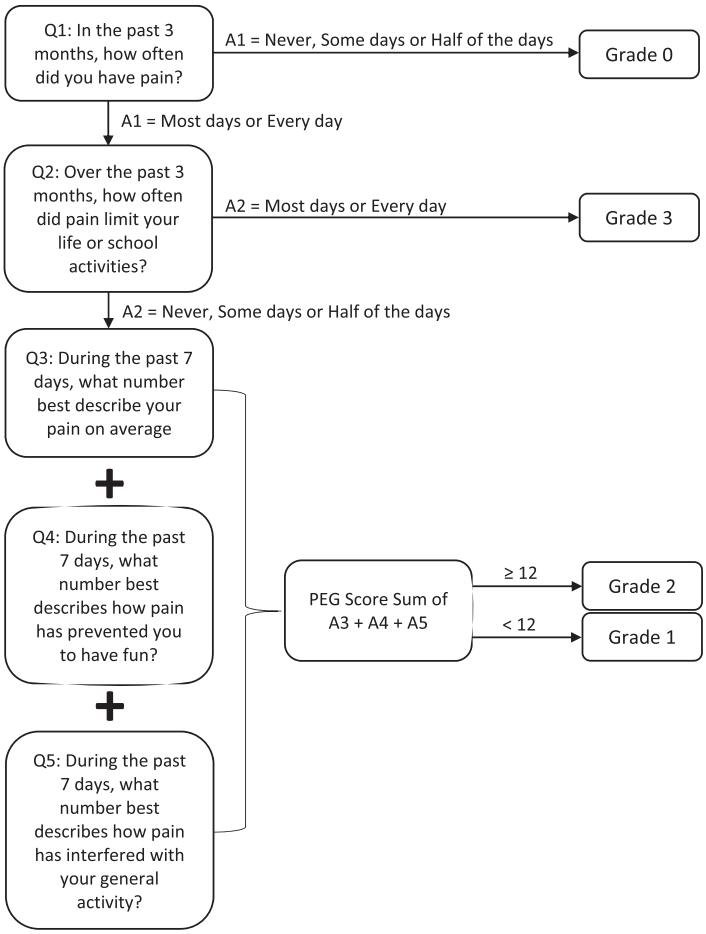


Figure 2. Calculation method for the Graded Chronic Pain Scale-Revised as per Von Korff et al.[36] PEG indicates Pain, Enjoyment and General Activities Scale. Grade 0 = chronic pain absent; grade 1 = mild chronic pain; grade 2 = bothersome chronic pain; grade 3 = high-impact chronic pain.

respondents are asked to indicate how often they had experienced different physical problems related with each domain over the past 7 days using a 5-point Likert scale ranging from 1 ("never") to 5 ("very often"). Scores are based on a T-score distribution with a mean of 50 points and a SD of 10 in the normative sample. Lower scores in the mobility short form reflect more frequent mobility problems. Higher scores in the fatigue and sleep short forms reflect more frequent fatigue and sleep problems, respectively. Pediatric PROMIS measures have been shown to provide valid and reliable information in individuals aged 8 to 17 years.[32] In the current sample, Cronbach alpha of the mobility, fatigue, and sleep short forms were 0.67, 0.84, and 0.86, respectively, indicating borderline acceptable to good internal consistency.

2.2.4.2. Anxiety and depressive symptoms severity

The Spanish versions of the 4-item Anxiety and Depression scales from the PROMIS Pediatric-25 Profile Form v.2 were used to assess participants' anxiety and depressive symptoms. With these forms, respondents are asked to indicate how often they had experienced different anxiety and depressive symptoms over the past 7 days using a 5-point Likert scale ranging from 1 ("never") to 5 ("very often"). Scores are based on a T-score distribution with a mean of 50 points and a SD of 10 in the normative sample. Higher scores in the anxiety and depression short forms reflect more frequent anxiety and depressive symptoms, respectively. Pediatric PROMIS measures have been shown to provide valid and reliable information in individuals aged 8 to 17 years.[32] In the current sample, Cronbach alpha of the anxiety and depression short forms were 0.85 and 0.86, respectively, indicating good internal consistency.

2.2.5. Maladaptive pain coping strategies

2.2.5.1. Pain catastrophizing

The Catalan/Spanish version of the 13-item Pain Catastrophizing Scale for children (PCS-C)[30] was used to assess pain catastrophizing. The PCS-C reflects a variety of negative thoughts and feelings about the child experience in 3 domains: rumination (sample item, "I cannot keep it [pain] out of my mind"),

magnification (sample item, "I am afraid that pain will get worse"), and helplessness (sample item, "There is nothing I can do to reduce pain"). Respondents indicate the extent to which they have these thoughts when in pain on a 0 ("not at all") to 4 ("extremely") Likert scale. Reponses are summed to create a total score that can range from 0 to 52, with higher scores indicating more frequent catastrophizing pain beliefs. The Catalan/Spanish version of the PCS-C has been shown to provide valid and reliable information about pain catastrophizing when used with children and adolescents.[30] In the current sample, Cronbach alpha of the PCS-C was 0.88, indicating good internal consistency.

2.2.5.2. Externalizing pain coping

The externalizing subscale of the Catalan/Spanish version of the 36-item Pain Coping Questionnaire (PCQ[16]) was used to assess frequency of the use of externalizing as a pain coping strategy. With the PCQ, respondents are asked to rate how often they engage in each pain coping response when they are in pain using a 5-point Likert scale from 0 ("never") to 4 ("very often"). A sample item from the externalizing subscale is "get mad and throw or hit something." The Catalan/Spanish version of the PCQ has been shown to provide valid and reliable scores when used to measure pain coping strategies in children and adolescents.[16,29] In the current sample, Cronbach alpha of the PCQ-Externalizing was 0.77, indicating adequate internal consistency.

2.2.6. Activity limitations

2.2.6.1. Number of schooldays missed due to pain

Participants were asked to respond to the question, "In the last 3 months, how many days did you miss school because of pain?" Self-reports of school absenteeism in adolescents with chronic pain have been found to be consistent with objective school reports of school absenteeism.[22]

2.3. Data analyses

To describe the sample and study variables, we first computed the means and standard deviations (for continuous variables) and number and percentages (for categorical variables) of the demographic and study variables. Next, we computed the number and rates of participants in each chronic pain grade in the sample. We then used analyses of covariance (ANCOVA) to examine the hypothesized differences in the measures of health status, maladaptive coping strategies, and activity limitations as a function of chronic pain grade classification, while controlling for the participants' sex and age. Post hoc comparisons were made using Bonferroni tests. For any statistically significant findings, we computed estimates of effect sizes using (1) the partial η^2 for ANCOVAs (small effect: $\eta^2_P = 0.01$, medium effect: $\eta^2_P = 0.06$; large effect: $\eta^2_P = 0.14$) and (2) Cohen *d* (small effect: $d = 0.2$; medium effect: $d = 0.6$; large effect: $d = 0.8$) for univariate *t* tests.[1] Statistical significance was set at $P < 0.05$. Data analyses were conducted using STATA 14 (Stata Corp, College Station, TX).

3. Results

3.1. Sample characteristics

Table 1 provides a summary of the characteristics of the 1564 participants. As can be seen, the mean age of this sample was 11.1 years (SD = 2.5; age range = 8-18 years), and a little more than a half of the participants were girls (55%).

Table 1
Sample characteristics (N = 1564).

Variable (range)	M	SD	N	%
Demographics				
Sex*				
Male			703	45
Female			856	55
Age (8-18)	11.08	2.51		
Health status indicators				
Mobility (PROMIS)† (20-80)	48.23	8.91		
Fatigue (PROMIS)‡ (20-80)	49.57	11.16		
Sleep disturbance (PROMIS)§ (20-80)	55.03	12.16		
Anxiety (PROMIS)‖ (20-80)	51.94	11.80		
Depression (PROMIS)† (20-80)	52.30	11.26		
Maladaptive pain coping strategies				
Pain catastrophizing (PCS-C)¶ (0-52)	18.97	11.24		
Externalizing pain coping (PCQ)# (1-5)	1.78	0.87		
Activity limitations				
Pain-related school absence**	2.21	4.09		

Sample size varies due to nonresponses.
* n = 1559 (missing = 5).
† n = 1532 (missing = 32).
‡ n = 1531 (missing = 33).
§ n = 1500 (missing = 64).
‖ n = 1535 (missing = 29).
¶ n = 1397 (missing = 167).
# n = 1464 (missing = 100).
** n = 1494 (missing = 90).
PCQ, Pain Coping Questionnaire; PROMIS, Patient-Reported Outcomes Measurement Information System Pediatric Measure; PCS-C, Pain Catastrophizing Scale for Children.

Table 2 shows GCPS-R classification results. As can be seen, a total of 1348 participants (86%) did not report chronic pain and were classified by the GCPS-R in Grade 0 (chronic pain absent). Regardless of the impact, a total of 216 participants (14%) were classified as having chronic pain; that is, pain that had been occurred on most days or every day over the past 3 months. Eighty of these participants (37%; 5% of the total sample) were classified by the GCPS-R in grade 1 (low-impact chronic pain), 98 (45%; 6% of the total sample) were classified in grade 2 (bothersome chronic pain), and 38 (18%; 3% of the total sample) were classified in grade 3 (high-impact chronic pain).

3.2. Health status, use of maladaptive pain coping strategies, and activity limitation as a function of chronic pain grade

Children and adolescents with bothersome and high-impact chronic pain endorsed having lower levels of health (ie, as reflected by worse measures of physical mobility, fatigue, sleep disturbance, anxiety, and depressive symptoms severity) than those with mild chronic pain and without chronic pain. Furthermore, children and adolescents with bothersome and high-impact chronic pain endorsed using maladaptive coping strategies (ie, pain catastrophizing and externalizing pain coping responses) more often and having more severe activity limitations (ie, higher number of school days missed due to pain in the past 3 months) than those with mild chronic pain and without chronic pain. The between-group differences in health status, in using maladaptive coping strategies and in activity limitations, were statistically significant (all $P < 0.001$), with effects size ranging from small to moderate (η^2 range, 0.03-0.06; see **Table 3**).

Table 2

Response to the items of the Pediatric Graded Chronic Pain Scale-Revised.

	N	%	M	SD
Item 1: pain in the past 3 mo (all participants, N = 1564)				
Never	208	13		
Some days	1017	65		
Half of the days	123	8		
Most days	158	10		
Every day	58	4		
Chronic pain	216	14		
Item 2: pain limits life or school activities (participants with chronic pain, N = 216)				
Never	51	24		
Some days	104	47		
Half of the days	23	11		
Most days	31	14		
Every day	7	3		
Item 3: pain intensity (0-10, participants with chronic pain, N = 216)			6.11	2.42
Item 4: pain interfered with enjoyment of life (0-10, participants with chronic pain, N = 216)			3.79	2.87
Item 5: pain interfered with general activity (0-10, participants with chronic pain, N = 216)			4.06	3.07
PEG sum score (participants with chronic pain, N = 216)			13.96	6.94
P-GCPS-R (N = 1564)				
0–no chronic pain	1348	86		
1–mild chronic pain	80	5		
2–bothersome chronic pain	98	6		
3–high-impact chronic pain	38	3		

PEG, sum of items 3, 4, and 5; P-GCPS-R, Pediatric Graded Chronic Pain Scale-Revised.

3.2.1. Children and adolescents with mild chronic pain (grade 1) compared with those without chronic pain (grade 0)

Post hoc comparisons between children and adolescents with mild chronic pain and those without chronic pain showed no statistically significant differences in any of the health status indicators (mobility: $t = 0.31$, $P > 0.05$; fatigue: $t = -0.07$, $P > 0.05$; sleep disturbance: $t = -1.10$, $P > 0.05$; anxiety: $t = -1.59$, $P < 0.05$; and depression: $t = -0.82$, $P < 0.05$), in the use of maladaptive coping strategies (catastrophizing: $t = -0.79$, $P > 0.05$ and externalizing: $t = -1.24$, $P > 0.05$) and in activity limitations (number of missed school days due to pain: $t = 0.029$, $P > 0.05$).

3.2.2. Children and adolescents with bothersome chronic pain (grade 2) and high-impact chronic pain (grade 3) compared with those with mild chronic pain (grade 1)

Post hoc comparisons showed that, compared with children and adolescents with mild chronic pain, those with bothersome chronic pain had significantly worse scores in all of the health status indicators (mobility: $t = 3.34$, $P = 0.005$, $d = 0.51$; fatigue: $t = -4.48$, $P < 0.001$, $d = -0.68$; sleep disturbance: $t = -3.56$, $P = 0.002$, $d = -0.54$; anxiety: $t = -2.72$, $P = 0.040$, $d = -0.41$; depression: $t = -4.01$, $P < 0.001$, $d = -0.61$) and higher activity limitations (number of missed school days due to pain: $t = -3.43$, $P = 0.004$, $d = -0.53$). In addition, children and adolescents with high-impact chronic pain reported significantly worse scores in all study health status indicators (mobility: $t = 4.55$, $P < 0.001$, $d = 0.93$; fatigue: $t = -4.19$, $P < 0.001$, $d = -0.84$; sleep disturbance: $t = -2.77$, $P = 0.33$, $d = -0.57$; anxiety: $t = -3.52$, $P = 0.003$, $d = -0.71$; and depression: $t = -3.90$, $P < 0.001$, $d = -0.81$) and higher activity limitations (number of missed school days due to pain: $t = -6.26$, $P < 0.001$, $d = -1.30$) compared with those with mild chronic pain. The effect sizes for these differences were in the medium to large range (ie, 0.51-1.30[1]).

Differences regarding maladaptive pain coping strategies were less consistent. Post hoc analyses showed significantly higher scores with borderline to large effect sizes in pain catastrophizing in children and adolescents with bothersome chronic pain ($t = -4.43$, $P < 0.001$, $d = -0.70$) and high-impact chronic pain ($t = -5.16$, $P < 0.001$, $d = -1.06$) in contrast with those with mild chronic pain. However, although children and adolescents with bothersome chronic pain and high-impact chronic pain had higher scores in externalizing pain coping compared with those with mild chronic pain, these differences were not statistically significant ($t = -2.42$, $P = 0.094$; and $t = -2.32$, $P = 0.121$, respectively).

3.2.3. Children and adolescents with high-impact chronic pain (grade 3) compared with those with bothersome chronic pain (grade 2)

Post hoc analyses revealed no statistically significant differences between children and adolescents with high-impact chronic pain and those with bothersome chronic pain neither in any of the study health status indicators (mobility: $t = 2.09$, $P > 0.05$; fatigue: $t = -0.79$, $P > 0.05$; sleep disturbance: $t = -0.13$, $P > 0.05$; anxiety: $t = -1.51$, $P > 0.05$; and depression: $t = -0.97$, $P > 0.$ 05) nor in the use of maladaptive coping strategies (catastrophizing: $t = -1.81$, $P > 0.05$ and externalizing: $t = -0.56$, $P > 0.05$). However, children and adolescents with high-impact chronic pain reported statistically significantly more activity limitations (number of missed school days due to pain: $t = 3.70$, $P < 0.001$, $d = -0.77$) than those with bothersome chronic pain.

4. Discussion

To the best of our knowledge, the current study is the first to adapt the GCPS-R[36] for use in pediatric samples (P-GCPS-R) and assess its concurrent validity using a community sample of school-aged children and adolescents. We found that with the P-GCPS-R most participants (86%) were classified in grade 0 (chronic pain absent). Of the participants with chronic pain, 37% were classified in grade 1 (low-impact chronic pain), 45% in grade 2 (bothersome chronic pain), and 18% in grade 3 (high-impact chronic pain).

The concurrent validity of the P-GCPS-R scores was supported by the magnitude and directions of the differences between participants classified in different grades in measures of health status, in the use of maladaptive pain coping strategies, and in activity limitations. Specifically, and consistent with the study hypotheses, (1) there were no significant differences between participants without chronic pain and participants with mild chronic pain in any of the study measures, (2) there were moderate-to-large differences between participants without chronic pain or with mild chronic pain and those with bothersome chronic pain or high-impact chronic pain in most study measures,

Table 3

Mean and standard deviation (in parenthesis) of health indicators, activity limitations, and negative pain-coping beliefs by chronic pain grade and analyses of covariance statistics controlling for participants' age and sex (N = 1564).

	Grade 0: chronic pain absent	Grade 1: mild chronic pain	Grade 2: moderate chronic pain	Grade 3: high-impact chronic pain	*df*	F	P (η_p^2)
Health status indicators							
Mobility (PROMIS)*	48.70 (8.76)	48.53 (8.89)	44.62 (8.95)	40.49 (8.75)	3, 1526	16.03	<0.001 (0.03)
Fatigue (PROMIS)†	48.83 (10.82)	48.72 (10.23)	57.16 (11.96)	57.49 (12.94)	3, 1525	24.00	<0.001 (0.05)
Sleep disturbance (PROMIS)‡	54.19 (11.90)	55.50 (12.31)	63.02 (11.76)	61.91 (12.23)	3, 1494	20.57	<0.001 (0.04)
Anxiety (PROMIS)§	51.12 (11.43)	52.89 (11.58)	58.74 (12.79)	61.27 (13.17)	3, 1529	21.23	<0.001 (0.04)
Depression (PROMIS)*	51.48 (10.81)	52.13 (10.67)	60.15 (11.75)	60.43 (15.17)	3, 1526	25.25	<0.001 (0.05)
Maladaptive pain coping							
Pain catastrophizing (PCS-C)‖	18.08 (10.80)	18.57 (10.84)	26.14 (11.99)	30.26 (12.25)	3, 1391	28.47	<0.001 (0.06)
Externalizing pain coping (PCQ)¶	1.96 (0.72)	2.09 (0.71)	2.55 (0.85)	2.75 (0.93)	3, 1458	27.22	<0.001 (0.06)
Activity limitations							
No. of missed school days due to pain#	1.89 (3.28)	1.54 (2.31)	3.59 (5.82)	6.44 (12.35)	3, 1488	20.51	<0.001 (0.04)

* n = 1532 (missing = 32).
† n = 1531 (missing = 33).
‡ n = 1500 (missing = 64).
§ n = 1535 (missing = 29).
‖ n = 1397 (missing = 167).
¶ n = 1464 (missing = 100).
# n = 1494 (missing = 90).
PCQ, Pain Coping Questionnaire; PCS-C, Pain Catastrophizing Scale for Children; PROMIS, Patient-Reported Outcomes Measurement Information System Pediatric Measure.

such that children and adolescents classified in grades 2 and 3 reported poorer health status, catastrophized more about their pain, and reported more activity limitations compared with those classified in grades 0 and 1; and (3) participants with high-impact chronic pain only differed from those with bothersome chronic pain on activity limitations, which were significantly higher in participants with high-impact chronic pain. These findings are consistent with those found by Von Korff et al.[36] in adults and suggest that, despite their chronic pain condition, children and adolescents with mild chronic pain have a similar health status to those without chronic pain and do not experience major activity limitations due to pain. Furthermore, although bothersome chronic pain and high-impact chronic pain seem to have similar negative effects on the overall health status of children and adolescents, the latter is associated with more activity limitations than the former, which is consistent with the current definition of high-impact chronic pain.[2,16,34]

This study represents an important step forward in the development of tools for assessing pediatric chronic pain. If additional studies confirm the findings, this would show that the P-GCPS-R would be a valuable valid measure for identifying children and adolescents with chronic pain and differentiating those who, despite their chronic pain condition, do not experience major activity limitations from those who are more severely impaired by their pain. This is important for treatment and cost planning purposes. According to a recent review, between 31% and 70% of children and adolescents with chronic pain seek healthcare for their pain[19] and those with a higher chronic pain severity are the ones most likely to seek medical treatment.[18,37] Thus, the P-GCPS-R could be used to identify those with high-impact chronic pain, providing insight into the proportion of children and adolescents with chronic pain who are likely to seek medical care. This information in turn could be used to estimate the cost of treating this group, based on previous studies of healthcare costs related to pediatric chronic pain.[12,13,31] Noteworthy, the GCPS-R is being increasingly used in studies of adults with different chronic pain conditions, further emphasizing the potential value of a pediatric version of this measure.[10,11,14,26]

The use of the P-GCPS-R would also facilitate comparability of data across different pediatric samples in future research. Previous studies using adapted versions of the original GCPS have reported discrepancies in the proportions of youths with different grades of chronic pain.[15,18,33,37,39] The variations in the definition of chronic pain used in these studies has been suggested as a potential explanation for these discrepancies.[18] By enabling a standard way to identify youth with chronic pain, the P-GCPS-R could help to overcome this issue.

Furthermore, if replicated in clinical settings, the P-GCPS-R could be used as a valid approach to screen for chronic pain severity in pediatric pain patients and to monitor changes in pain over time. Pain severity has been posited as one of the most important outcome domains to be assessed in when providing clinical care to children with pain.[27] Moreover, the classification of children with varying levels of chronic pain severity could potentially provide valuable data for informing treatment decisions, although specific treatment recommendations would require a more comprehensive assessment than that provided by the P-GCPS-R alone. Although there has been an improvement in the treatment of pediatric chronic pain over the last decades[23] and there are currently a variety of treatments that have been shown to be effective for reducing the severity and negative impact of chronic pain in children and adolescents,[8,23] there is a tendency to provide all individuals with chronic pain with the same treatment. Given that chronic pain does not affect children and adolescents equally,[24] it stands to reason that treatment for chronic pain should not be the same for all individuals.

With reference to the above, we found that the largest differences between children and adolescents with mild chronic and bothersome chronic pain were found in measures of fatigue, depression, and pain catastrophizing. We also found that the most predominant difference between children and adolescents with high-impact chronic and mild chronic pain was found in activity limitations, although moderate-to-large differences were also found in measures of physical health, psychological symptoms, and pain catastrophizing. Therefore, and in line with what was speculated by Von Korff et al.,[36] children and

adolescents with bothersome chronic pain could benefit from psychological interventions addressing psychological distress and pain catastrophizing such as cognitive-behavioral therapy,[7] whereas those with high-impact chronic pain might require additional treatments and strategies that also address the behavioral consequences of the pain problem. For example, promoting engagement in value-based actions through acceptance and commitment therapy and providing parental training to reinforce a child's adaptive behaviors, such as regular school attendance, may be effective strategies.[9,21] Future clinical trials using the P-GCPS-R to classify pediatric pain patients on enrollment in chronic pain treatments are necessary to evaluate the effectiveness of various treatment strategies for different levels of pain severity.

The study findings should be considered in light of several limitations. First, the data were collected from a convenience sample of children and adolescents, and the participation rate was relatively low (30%). This potentially limits the generalizability of the findings. Second, given the cross-sectional nature of the study, the P-GCPS-R's test–retest reliability and predictive validity could not be evaluated. Longitudinal research evaluating the P-GCPS-R would, therefore, be useful. Third, a large number of measures were administered for this study, which could have led to respondents' fatigue and thus could reduce the accuracy of responses, especially in younger children. Despite this, the findings from this study are very similar to those found in studies with adults and are consistent with the study's hypothesis. Therefore, even if the study procedures resulted in some fatigue for some of the participants, this did not appear to have a significant impact on the study findings. Fourth, the measure of activity limitations used in the study was a single question asking participants to note the number of days missed from school due to pain. The evaluation of the concurrent validity P-GCPS-R's scores would have been strengthened with additional measures of pain-related activity limitations (eg, limitations in leisure activities or social activities). In addition, the measure of pain-related absenteeism relied on the participants' memories about school attendance over the prior 3 months, which may have introduced some recall bias. However, as noted previously, prior research in adolescents with chronic pain found that adolescent self-report of school absenteeism was consistent with objective school reports of school absenteeism.[22]

Despite the study's limitations, the results provide important new evidence regarding the concurrent validity of the P-GCPS-R scores for use with pediatric samples. The findings support the measure for use by researchers seeking to expand knowledge regarding the prevalence and impact of chronic pain in children and adolescents, knowledge of which can be used by policymakers and other stakeholders interested in better understanding the potential need for interventions and cost planning purposes. If additional studies confirm these findings in clinical settings and other samples of children, the P-GCPS-R could potentially be regarded and used as a tool to help guide and tailor interventions for children and adolescents with chronic pain. Furthermore, if widely adopted in epidemiology studies with pediatric samples, the P-GCPS-R would facilitate greater comparability of findings across studies and help identify general needs of this population.

Conflict of interest statement

The authors declare no financial or other relationships that might lead to a conflict of interest related to this study.

Acknowledgements

This work was partly funded by grants from the Spanish Ministry of Economy, Industry and Competitiveness (RTI2018-09870-B-I00; RED2022-134869-T), the European Regional Development Fund (ERDF), and the Government of Catalonia (AGAUR; 2021SGR-730). E. Sánchez-Rodríguez work is supported by a grant from the Spanish Ministry of Science and Innovation (PID2020-113869RA-I00). E. Solé work is supported by a grant from the Spanish Ministry of Science and Innovation (PID2020-114146RJ-I00). J. Roman-Juan is supported by a doctoral grant from MINECO (PRE2019-089283). J. Miró work is supported by ICREA-Acadèmia. The Chair in Pediatric Pain is supported by Fundación Grünenthal.

Article history:
Received 8 February 2023
Received in revised form 30 March 2023
Accepted 13 April 2023
Available online 12 July 2023

References

[1] Cohen J. The effect size. New Jersey: Lawrence Erlbaum Associates, 1988.
[2] Croft P, Blyth FM, van der Windt D. Chronic pain epidemiology: from aetiology to public health. Oxford, United Kingdom: Oxford University Press, 2010.
[3] Dahlhamer J, Lucas J, Zelaya C, Nahin R, Mackey S, DeBar L, Kerns R, von Korff M, Porter L, Helmick C. Prevalence of chronic pain and high-impact chronic pain among adults—United States, 2016. MMWR Morb Mortal Weekly Rep 2018;67:1001–6.
[4] Deyo RA, Dworkin SF, Amtmann D, Andersson G, Borenstein D, Carragee E, Carrino J, Chou R, Cook K, Delitto A, Goertz C, Khalsa P, Loeser J, MacKey S, Panagis J, Rainville J, Tosteson T, Turk D, von Korff M, Weiner DK. Report of the NIH task force on research standards for chronic low back pain. J Pain 2014;15:569–85.
[5] Dunn KM, Croft PR, Main CJ, von Korff M. A prognostic approach to defining chronic pain: replication in a UK primary care low back pain population. PAIN 2008;135:48–54.
[6] Elliott AM, Smith BH, Smith CW, Chambers AW. Changes in chronic pain severity over time: the Chronic Pain Grade as a valid measure. PAIN 2000; 88:303–8.
[7] Fisher E, Heathcote L, Palermo TM, de C Williams AC, Lau J, Eccleston C. Systematic review and meta-analysis of psychological therapies for children with chronic pain. J Pediatr Psychol 2014;39:763–82.
[8] Fisher E, Law E, Dudeney J, Palermo TM, Stewart G, Eccleston C. Psychological therapies for the management of chronic and recurrent pain in children and adolescents. Cochrane Database Syst Rev 2018;9:CD003968.
[9] Gauntlett-Gilbert J, Connell H, Clinch J, Mccracken LM. Acceptance and values-based treatment of adolescents with chronic pain: outcomes and their relationship to acceptance. J Pediatr Psychol 2013;38:72–81.
[10] George SZ, Bolognesi MP, Bhavsar NA, Penrose CT, Horn ME. Chronic pain prevalence and factors associated with high impact chronic pain following total joint arthroplasty: an observational study. J Pain 2022;23: 450–8.
[11] George SZ, Bolognesi MP, Ryan SP, Horn ME. Sleep disturbance, dyspnea, and anxiety following total joint arthroplasty: an observational study. J Orthop Surg Res 2022;17:396.
[12] Groenewald CB, Palermo TM. The price of pain: the economics of chronic adolescent pain. Pain Manag 2015;5:61–4.
[13] Groenewald CB, Essner BS, Wright D, Fesinmeyer MD, Palermo TM. The economic costs of chronic pain among a cohort of treatment-seeking adolescents in the United States. J Pain 2014;15:925–33.
[14] Hietaharju M, Näpänkangas R, Sipilä K, Teerijoki-Oksa T, Tanner J, Kemppainen P, Tolvanen M, Suvinen T. Importance of the graded chronic pain scale as a biopsychosocial screening instrument in TMD pain patient subtyping. J Oral Facial Pain Headache 2021;35:303–16.
[15] Huguet A, Miró J. The severity of chronic pediatric pain: an epidemiological study. J Pain 2008;9:226–36.
[16] Huguet A, Miró J, Nieto R. The factor structure and factorial invariance of the Pain-Coping Questionnaire across age: evidence from community-based samples of children and adults. Eur J Pain 2009;13:879–89.

[17] Klasen BW, Hallner D, Schaub C, Willburger R, Hasenbring M. Validation and reliability of the German version of the Chronic Pain Grade questionnaire in primary care back pain patients. Psychosoc Med 2004;1:Doc07.
[18] Könning A, Rosenthal N, Brown D, Stahlschmidt L, Wager J. Severity of chronic pain in German adolescent school students: a cross-sectional study. Clin J Pain 2021;37:118–25.
[19] Könning A, Rosenthal N, Friese M, Hirschfeld G, Brown D, Wager J. Factors associated with physician consultation and medication use in children and adolescents with chronic pain: a scoping review and original data. Eur J Pain 2021;25:88–106.
[20] Krebs EE, Lorenz KA, Bair MJ, Damush TM, Wu J, Sutherland JM, Asch SM, Kroenke K. Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference. J Gen Intern Med 2009;24:733–8.
[21] Law E, Fisher E, Eccleston C, Bartlett J, Palermo TM. Psychological interventions for parents of children and adolescents with chronic illness. Cochrane Database Syst Rev 2015;4:CD009660.
[22] Logan DE, Simons LE, Stein MJ, Chastain L. School impairment in adolescents with chronic pain. J Pain 2008;9:407–16.
[23] Miró J, McGrath PJ, Finley GA, Walco GA. Pediatric chronic pain programs: current and ideal practice. Pain Rep 2017;2:e613.
[24] Miró J, Roman-Juan J, Sánchez-Rodríguez E, Solé E, Castarlenas E, Jensen MP. Chronic pain and high impact chronic pain in children and adolescents: a cross-sectional study. J Pain 2023;24:812–23.
[25] Miró J. Translation, validation, and adaptation of an instrument to assess the information-seeking style of coping with stress: the Spanish version of the Miller Behavioral Style Scale. Personal Individ Diff 1997;23:909–12.
[26] Özden F, Özkeskin M, Bakırhan S, Karaman ÖN, Aydoğmuş H. The reliability and validity of the Turkish version of the graded chronic pain scale in patients with chronic low back pain. Eur Spine J 2021;30:2955–61.
[27] Palermo TM, Walco GA, Paladhi UR, Birnie KA, Crombez G, Vega R, Eccleston C, Kashikar-Zuck S, Stone AL. Core outcome set for pediatric chronic pain clinical trials: results from a Delphi poll and consensus meeting. PAIN 2021;162:2539–47.
[28] Pitcher MH, von Korff M, Bushnell MC, Porter L. Prevalence and profile of high-impact chronic pain in the United States. J Pain 2019;20:146–60.
[29] Sánchez-Rodríguez E, Solé E, Tomé-Pires C, Galán S, Racine M, Jensen MP, Miró J. Are attitudes about pain related to coping strategies used by adolescents in the community? Scand J Pain 2019;19:513–21.
[30] Solé E, Castarlenas E, Miró J. A Catalan adaptation and validation of the pain catastrophizing scale for children. Psychol Assess 2016;28:e119–26.
[31] Tumin D, Drees D, Miller R, Wrona S, Hayes D Jr., Tobias JD, Bhalla T. Health care utilization and costs associated with pediatric chronic pain. J Pain 2018;19:973–82.
[32] Varni JW, Magnus B, Stucky BD, Liu Y, Quinn H, Thissen D, Gross HE, Huang I-C, DeWalt DA. Psychometric properties of the PROMIS ® pediatric scales: precision, stability, and comparison of different scoring and administration options. Qual Life Res 2014;23:1233–43.
[33] Vervoort T, Logan DE, Goubert L, de Clercq B, Hublet A. Severity of pediatric pain in relation to school-related functioning and teacher support: an epidemiological study among school-aged children and adolescents. PAIN 2014;155:1118–27.
[34] Von Korff M, Ormel J, Keefe FJ, Dworkin SF. Grading the severity of chronic pain. PAIN 1992;50:133–49.
[35] Von Korff M, Scher AI, Helmick C, Carter-Pokras O, Dodick DW, Goulet J, Hamill-Ruth R, LeResche L, Porter L, Tait R, Terman G, Veasley C, Mackey S. United States national pain strategy for population research: concepts, definitions, and pilot data. J Pain 2016;17:1068–80.
[36] Von Korff M, Debar LL, Krebs EE, Kerns RD, Deyo RA, Keefe FJ. Graded chronic pain scale revised: mild, bothersome, and high-impact chronic pain. PAIN 2020;161:651–61.
[37] Wager J, Hechler T, Darlington AS, Hirschfeld G, Vocks S, Zernikow B. Classifying the severity of paediatric chronic pain—an application of the chronic pain grading. Eur J Pain 2013;17:1393–402.
[38] Wild D, Grove A, Martin M, Eremenco S, McElroy S, Verjee-Lorenz A, Erikson P. Principles of good practice for the translation and cultural adaptation process for patient-reported outcomes (PRO) measures: report of the ISPOR task force for translation and cultural adaptation. Value Health 2005;8:94–104.
[39] Wurm M, Anniko M, Tillfors M, Flink I, Boersma K. Musculoskeletal pain in early adolescence: a longitudinal examination of pain prevalence and the role of peer-related stress, worry, and gender. J Psychosomatic Res 2018;111:76–82.

4.7. Study VII

Fatigue, sleep disturbance, and pain interference in children and adolescents with chronic pain: a longitudinal study.

Fatigue, sleep disturbance, and pain interference in children and adolescents with chronic pain: a longitudinal study

Josep Roman-Juan[a,b], Guillermo Ceniza-Bordallo[c], Elisabet Sánchez-Rodríguez[a,b], Mark P. Jensen[d], Jordi Miró[a,b]

[a] Universitat Rovira i Virgili, Unit for the Study and Treatment of Pain – ALGOS, Research Center for Behavior Assessment (CRAMC), Department of Psychology, Catalonia, Spain
[b] Institut d'Investigació Sanitària Pere Virgili; Universitat Rovira i Virgili, Catalonia, Spain
[c] Faculty of Nursing, Physiotherapy and Podiatry. University Complutense of Madrid. Madrid, Spain.
[d] Department of Rehabilitation Medicine, University of Washington, Seattle, WA, USA

Correspondence:
Jordi Miró
Departament de Psicología
Universitat Rovira i Virgili
Carretera de Valls, s/n
43007 Tarragona
Spain

jordi.miro@urv.cat

Tel.: +34-977558179
Fax: +34-977558088

Number of text pages: 30
Number of tables: 5
Number of figures: 2

Disclosure/Conflict of interest information: The authors declare no financial or other relationships that might lead to a conflict of interest related to this study.

Data availability: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Abstract

Research has shown that pain and sleep disturbance often co-occur and influence each other over time in children and adolescents with chronic pain. Longitudinal studies examining the underlying mechanisms of this association are scarce and have mainly focused on the role of internalizing mental health symptoms and mood. This longitudinal study aimed to determine if fatigue underlies the co-occurrence and mutual maintenance of sleep disturbance and pain over time in children and adolescents with chronic pain. Participants of this study were 355 school-aged children and adolescents (mean age = 11.63; 67% female) with chronic pain. Participants provided sociodemographic information and responded a survey including measures of pain (duration, intensity, interference), sleep disturbance, and fatigue at first assessment and 12 months later. Partially latent cross-lagged structural equation panel models revealed that sleep disturbance, pain intensity, and pain interference co-occurred at both time points. Higher levels of sleep disturbance, pain intensity, and pain interference at first assessment predicted higher levels of sleep disturbance, pain intensity, and pain interference at follow-up, respectively. Higher levels of pain interference at first assessment predicted higher levels of sleep disturbance at follow-up while controlling for initial levels of sleep disturbance. Furthermore, fatigue was found to mediate the association between first assessment and follow-up sleep disturbance, the association between first assessment and follow-up pain interference, and the association between first assessment pain interference and follow-up sleep

disturbance. These findings highlight the need to assess and address fatigue in children and adolescents with chronic pain and sleep disturbance.
Keywords: Chronic pain; Children; Adolescents; Sleep disturbance; Fatigue; Structural equation modelling.

INTRODUCTION

Chronic pain in children and adolescents is a prevalent [12,24] and disabling condition [15,18,35,38] that often co-occurs with sleep disturbance [9,19]. Several studies show that the prevalence of severe sleep-related issues exceeds 50% in this population [23,26,27]. The association between chronic pain and sleep disturbance has been proposed to be bidirectional [21,46], and recent findings both in adults [11] and children and adolescents [1] suggest that the effect of sleep disturbance on pain may be stronger than *vice versa*.

The conceptual model developed by Valrie and colleagues [46] suggests that psychological and physiological factors may underlie the co-occurrence and maintenance of pain and sleep disturbance in children and adolescents with chronic pain. To date, research has largely focused on the role of psychological factors such as mood [1] and internalizing mental health symptoms [28,42] as potential underlying mechanisms.

One additional physiological factor that could help explain the co-occurrence and maintenance of sleep disturbance and pain in children and adolescents with chronic pain over time is fatigue. Existing research has shown that increased fatigue can result from both pain and sleep problems [4,13,49]. Research has also shown that fatigue can be a predictor of subsequent sleep disturbance and pain in children and adolescents with

chronic pain [44]. Moreover, findings from cross-sectional studies are consistent with a mediation effect of fatigue in the association between sleep and pain interference in children and adolescents with chronic pain [50]. However, there is a need for longitudinal research to more systematically examine the role of fatigue in the co-occurrence and mutual maintenance of pain and sleep disturbance among children and adolescents with chronic pain.

Given these considerations, the aim of this study was to better understand the role that fatigue plays in the co-occurrence and maintenance of sleep disturbance and pain over time in children and adolescents with chronic pain. To address this aim, we used data from an ongoing longitudinal survey of children and adolescents with chronic pain to examine: (1) the bidirectional association between sleep disturbance, pain intensity, and pain interference over time; and (2) the mediating role of fatigue in these associations. Based on research showing statistically significant bidirectional positive associations between sleep disturbance and pain in children and adolescents over time [2], and on research showing both cross-sectional and longitudinal positive associations between fatigue and pain intensity and pain interference in children and adolescents with chronic pain [24,44,50], we hypothesized that (1) higher levels of sleep disturbance, pain intensity, and pain interference measured at the initial assessment would predict subsequent increases in sleep disturbance, pain intensity, and pain interference 12 months later, and that (2) fatigue would mediate these associations.

METHOD

Study design and procedure

This longitudinal study uses data from a sample of children and adolescents participating in the EPIDOL project, a longitudinal epidemiological study of pain in children and adolescents conducted in the South East of Catalonia (Spain; [24]). The EPIDOL project underwent participant recruitment and follow-ups twice: once between 2018 and 2020 (pre-COVID) and once between 2022 and 2023 (post-COVID). A number of articles have been published using cross-sectional data from the survey conducted between 2018 and 2020 [24,31,32,41], and the survey conducted after 2022 [33,34]. The data used for the current analyses were exclusively derived from the survey conducted after 2022, and none of the previous articles have addressed the study questions that are the focus of the current analyses.

The data of the first assessment (Time 1) were gathered between February and June 2022 at 20 schools that agreed to participate in the study, which represent a 67% of the total number of schools initially approached (n = 30). Follow-up data (Time 2) were collected 12 months later from 19 of the 20 participating schools (i.e., one of the participating schools opted for not continuing their participation due to constraints related to time availability). At Time 1 and Time 2, eligible students were asked to provide sociodemographic information and fill-in a paper-and-pencil survey with questions about pain-related characteristics, and self-report measures related to sleep disturbance and fatigue. The ethics committee of the

Universitat Rovira i Virgili approved the study (*Institut d'Investigació Sanitària Pere Virgili; ref.: 136/2018)*.

Participants

Eligibility for study participation was limited to students that (1) were aged between 8 and 18 years who expressed their willingness to participate, (2) were able to read, write, and speak Spanish, (3) had parental consent for their participation, (4) and reported experiencing chronic pain (i.e., pain persisting ≥3 months) at Time 1 and Time 2.

Of the 1,721 students who expressed willingness and had parental consent, 738 participants reported experiencing chronic pain and provided either complete or mostly complete data at Time 1. Among these participants, 491 provided data at Time 2, with 355 reporting chronic pain at this time point. This subset of 355 participants constitutes the sample of participants used in the current analysis.

Variables and Measures

Demographic variables

Participants provided information regarding their sex (i.e., boy or girl) and age at Time 1 and Time 2.

Pain Characteristics

At both Time 1 and Time 2, participants were asked to provide information about the characteristics of any pain problem(s) they had experienced in the last 3 months, specifically: location, duration, intensity, and interference. Pain location was evaluated using a pain site checklist which asked about pain in 11 possible locations (i.e., head, neck, chest, shoulders, back, arms, hands, bottom/hips, belly/pelvis, legs, and feet) and

an “other location” category. This classification approach has been used in previous studies [24,37,42]. For each selected pain location, pain duration was evaluated by asking participants whether the pain had persisted for over three months (yes/no). In accordance with the contemporary definition of chronic pain established by the International Association for the Study of Pain [25,45], participants were classified as having chronic pain if they reported pain persisting ≥3 months at any of the specified locations. Average pain intensity in the past seven days was assessed using a 0-10 Numerical Rating Scale (NRS-11) which asks respondents to rate their average pain intensity over this time period from 0 = “No pain” to 10 = “Very much pain”. This version of NRS-11 has shown to provide reliable and valid pain intensity scores when used with children 6 years or over [7]. Pain interference was measured using the Spanish version of the Pediatric Patient-Reported Outcomes Measurement Information System (PROMIS) Pediatric Pain Interference 8a Short Form v2.0 [8,30]. With this form, participants rate the frequency that pain interfered with 8 different activities over the past 7 days using a 5-point Likert scale (1= “Never” to 5= “Almost always”). The pain interference score is computed by summing responses and transforming them to T-scores, with higher scores reflecting greater levels of pain interference. Previous research has demonstrated that pediatric PROMIS measures of pain interference provides valid and reliable information for individuals aged 8 to 17 years [48], including samples of children and adolescents with chronic pain [31,41]. In the current sample, the Cronbach’s alphas of the Pain Interference short form were .86 at both Time 1 and Time 2, indicating good internal consistency.

Sleep disturbance

At both Time 1 and Time 2, participants' sleep disturbance was evaluated with the Spanish versions of the 4-item PROMIS pediatric Sleep Disturbance short form V1.0. With this form, participants rate how often they experienced problems related sleep over the past 7 days using a 5-point Likert scale (1= "Never" to 5= "Almost always"). The sleep disturbance score was computed by summing responses and transforming them to T-scores, with higher scores reflecting more frequent sleep problems. Previous research has demonstrated that pediatric PROMIS measures of sleep disturbance provide valid and reliable information for individuals aged 8 to 17 years [48], including samples of children and adolescents with chronic pain [3,39]. In the current sample, the Cronbach's alphas of the sleep disturbance short form at Time 1 and Time 2 were .89 and .87, respectively, indicating good internal consistency.

Fatigue

At Time 1 only, participants' fatigue was measured using with the Spanish version of the 4-item Fatigue scale from the PROMIS Pediatric-25 Profile Form v.2. With this form, participants are asked to rate how often they experienced different fatigue symptoms over the past 7 days using a 5-point Likert scale (1= "Never" to 5= "Almost always"). The fatigue scores were computed by summing responses and transforming them to T-scores. Higher scores in the fatigue short form indicate higher levels of fatigue. Previous research has shown that pediatric PROMIS measures of fatigue provide valid and reliable information when used with individuals aged 8 to

17 years [48]. In the current sample, the Cronbach's alpha of the fatigue short form was .87, indicating good internal consistency.

Data analysis

We first computed number and percentages (categorical variables) and mean and standard deviations (continuous variables) of the demographic and primary study variables to describe the sample. We then computed bivariate Pearson correlations between the key study variables (i.e., sleep disturbance, pain intensity, pain interference at initial assessment and 12 months, and fatigue) to describe their zero order associations. We also conducted T-tests and computed bivariate correlations to examine the associations between key study variables and participants' biological sex and age, for descriptive purposes.

To address the primary study aim (i.e., to examine the role that fatigue plays in the co-occurrence and maintenance of sleep disturbance and pain over time in children and adolescents with chronic pain), we conducted partial cross-lagged panel structural equation analyses. The analyses were adjusted for participants' sex and age, given their association with key study variables (i.e., sleep disturbance, pain intensity, pain interference, and fatigue; see the Results section for details) at the 12-month assessment point. In order to test the first study hypotheses, in the first model (see Figure 1, top panel) we regressed sleep disturbance, pain intensity, and pain interference assessed at the 12 months assessment on the measures of these domains at the initial assessment. This model examined whether sleep disturbance at first assessment predicted change over time in pain intensity and pain interference while controlling for initial

levels of pain intensity and pain interference. It also examined whether initial levels of pain intensity and pain interference predicted change over time in sleep disturbance while controlling for the effects of initial sleep disturbance.

In order to test the second study hypothesis, we regressed fatigue on sleep disturbance, pain intensity and pain interference at the initial assessment; and sleep disturbance, pain intensity and pain interference at the 12 months assessment on fatigue (see Figure 1, bottom panel). This model examined whether fatigue underlined the associations between sleep disturbance, pain intensity, and pain interference at first assessment and at 12 months. We used a bias-corrected bootstrapping resampling method with n = 10,000 resamples to estimate the 95% confidence intervals for the mediating effect of fatigue on the association between the initial measures of sleep disturbance, pain intensity, and pain interference and the criterion variables assessed 12 months later. In both models, we used maximum likelihood estimation to handle missing data. As measures of goodness of fit, we estimated χ^2, the ratio of χ^2 to degrees of freedom, the root-mean-square error of approximation (RMSEA), and the comparative fit index (CFI). Acceptable fit is usually concluded when $\chi^2/df < 2$ [6], CFI values > 0.90 [14], and RMSEA < 0.08 with a nonsignificant (pClose)[17]. To adhere to the principle of parsimony, we systematically removed paths that were not statistically significant from the model, starting with the least significant ones, based on the Wald test [16]. Subsequent to the removal of nonsignificant paths, we performed a chi-square difference test to confirm

that the trimmed model did not exhibit a significantly poorer fit to the data when compared to the full model.

A two-tailed significance level of $p < .05$ was used to determine that an association was statistically significant. Indirect effects were considered significant if the 95% confidence interval did not include zero. All data analyses were conducted using STATA 14 (Stata Corp., Texas, USA).

RESULTS

Sample descriptives

Table 1 presents the descriptive statistics for the demographic and key study variables at the initial assessment and at 12 months. As can be seen, the average age of the sample at the initial assessment was 11.6 years and more than a half of participants (67%) were female. At both the initial assessment and at 12 months after the initial assessment, the most frequent pain locations were the head (50% and 56%, respectively), back (40% and 49%, respectively), and belly/pelvis (35% and 39%, respectively). Pain intensity and pain interference levels ranged from 0 to 10 and from 34 to 79 (T-score), respectively, at both time points. Sleep disturbance levels ranged from 35 to 78 (T-score) at both time points. Fatigue levels at the initial assessment ranged from 35 to 78 (T-score).

Table 1. Sample characteristics.

Variable	First assessment		12-month assessment	
	M(SD) or N(%)	N	M(SD) or N(%)	N
Sex		355		355
Male	117 (33)		117 (33)	
Female	238 (67)		238 (67)	
Age (8-17)	11.63 (2.27)	355	12.66 (2.29)	355
Pain locations				
Head	176 (50)	355	198 (56)	354
Neck	90 (25)	355	105 (30)	353
Chest/breast	58 (16)	355	63 (18)	353
Shoulders	66 (19)	355	74 (21)	354
Back	143 (40)	355	173 (49)	353
Arms	53 (15)	355	50 (14)	354
Hands	34 (10)	355	44 (12)	353
Bottom/hips	20 (6)	355	35 (10)	354
Belly/pelvis	123 (35)	355	136 (39)	352
Legs	104 (29)	355	115 (33)	353
Feet	95 (27)	355	93 (26)	353
Other location(s)	20 (6)	355	28 (8)	350
Pain intensity (NRS)	4.49 (2.61)	354	4.13 (2.38)	355

Pain interference (PROMIS)	52.76 (9.44)	334	51.30 (9.02)	354
Sleep disturbance (PROMIS)	59.36 (11.94)	345	57.41 (11.45)	357
Fatigue (PROMIS)	52.78 (11.74)	351	-	-

Note: M = Mean; SD = Standard Deviation; PROMIS = Patient-Reported Outcomes Measurement Information System pediatric measure; NRS = Numerical Rating Scale.

The average levels of the key study variables and their standard deviations assessed at both assessment points, as a function of sex, are presented in Table 2. As can be seen, girls reported a significantly higher level of sleep disturbance and pain interference at both the initial assessment and at 12 months, and more fatigue at the initial assessment compared to boys. The difference between girls and boys for pain intensity at both assessment points was not statistically significant.

Table 2. Differences in key variables as a function of participant sex.

Variable	Girls		Boys		*t*	*df*	*P*
	M	SD	M	SD			
T1-Pain intensity (NRS)	4.45	2.51	4.57	2.81	-0.42	352	.336
T2-Pain intensity (NRS)	4.18	2.34	4.03	2.45	0.56	353	.712

T1-Pain interference (PROMIS)	53.99	9.19	50.24	9.47	3.47	332	< .001
T2-Pain interference (PROMIS)	53.00	8.26	47.86	9.52	5.23	352	< .001
T1-Sleep disturbance (PROMIS)	61.28	11.33	55.27,	12.25	4.73	343	< .001
T1-Sleep disturbance (PROMIS)	59.54	10.98	53.04	11.20	5.18	351	< .001
Fatigue (PROMIS)	54.11	12.14	50.09	10.41	3.05	349	.002

Note: T1 = first assessment; T2 = 12 months assessment; M = Mean; SD = Standard Deviation. PROMIS = Patient-Reported Outcomes Measurement Information System pediatric measure; NRS = Numerical Rating Scale.

Bivariate Pearson correlation coefficients between participants' age and the key study variables are shown in Table 3. As can be seen, participant's age was positively and significantly correlated with sleep disturbance and fatigue at both assessment points. All the associations between the pairs of key study variables were positive; most were statistically significant and in the weak (.10 < r < .30; 48%) or moderate (r = .30 to .49; 38%) range.

Table 3. Bivariate Pearson correlation coefficients s between key variables.

Variable	1	2	3	4	5	6	7	8
(1) T1-Pain intensity (NRS)	1	.21‡	.38‡	.11*	.27‡	.04	.29‡	.08
(2) T2-Pain intensity (NRS)		1	.18‡	.30‡	.08	.15†	.18‡	-.01
(3) T1-Pain interference (PROMIS)			1	.42‡	.56‡	.33‡	.68‡	.08
(4) T2-Pain interference (PROMIS)				1	.24‡	.60‡	.35‡	.09
(5) T1-Sleep disturbance (PROMIS)					1	.36‡	.47‡	.16†
(6) T2-Sleep disturbance (PROMIS)						1	.31‡	.11*
(7) Fatigue (PROMIS)							1	.14†
(8) Age								1

Note: T1 = first assessment; T2 = 12 months assessment; PROMIS = Patient-Reported Outcomes Measurement Information System pediatric measure; NRS = Numerical Rating Scale.

*$P < .05$

†$P < .01$

‡$P < .001$

Partial cross-lagged panel structural equation analyses

The first model (Figure 1, top panel) was fully saturated and therefore goodness of fit statistics are omitted because these were perfect. Sleep disturbance at first assessment was not significantly associated with pain interference and pain intensity at 12 months; and pain intensity at first assessment was not significantly associated with sleep disturbance and pain interference at 12 months. Furthermore, sex was not significantly associated with pain intensity at first assessment and at 12 months; and age was not associated with sleep disturbance at 12 months, and pain interference and pain intensity at both assessment points (Supplementary Table 1). In view of these results, and to adhere to the principle of parsimony, these nonsignificant paths were removed from the model.

Fit indices indicated an excellent fit for the trimmed model (see Figure 2, top panel): $\chi^2(8) = 5.52$, $P = .701$, $\chi^2/df = 0.\ 69$, RMSEA = 0.00, 90% confidence interval [CI] for RMSEA = 0.00-0.05, pClose = 0.96, CFI = 1.00. In this model, at both time points, there was a significant positive association between sleep disturbance and pain intensity and pain interference, as well as between pain intensity and pain interference. Sleep disturbance, pain interference, and pain intensity at first assessment all

predicted measures of these domains at the 12 months assessment point. Pain interference at first assessment was significantly associated with pain intensity and sleep disturbance at 12 months, over and above sex and initial levels of sleep disturbance and pain intensity, respectively. Similarly, female sex was significantly associated with higher levels of sleep disturbance and pain interference at 12 months over and above initial levels of sleep disturbance and pain interference, respectively.

The second model including fatigue as a mediator (Figure 1, bottom panel) also showed an excellent fit to the data: $\chi^2(8) = 6.20$, $P = .624$, $\chi^2/df = 0.\ 77$, RMSEA = 0.00, 90% CI for RMSEA = 0.00-0.06, pClose = 0.94, CFI = 1.00. This model yielded no significant associations between fatigue and pain intensity at first assessment, sex, and age. Furthermore, the effect of pain interference at first assessment on sleep disturbance at 12 months became non-significant (Supplementary Table 2). In view of these results, these nonsignificant paths were removed from the model.

The final model including fatigue as a mediator (see Figure 2, bottom panel) continued to show excellent fit to the data: $\chi^2(13) = 13.55$, $P = .406$, $\chi^2/df = 1.\ 04$, RMSEA = 0.01, 90% CI for RMSEA = 0.00-0.06, pClose = 0.92, CFI = 0.99. In this model, pain intensity, pain interference, and sleep disturbance were significantly and positively associated at both time points. Furthermore, higher levels of sleep disturbance and pain interference at first assessment were associated with higher levels of fatigue, which in turn was associated with higher levels of sleep disturbance and pain interference at 12 months over and above sex and initial levels of sleep disturbance and pain interference, respectively. The indirect pathway

from sleep disturbance at initial assessment to sleep disturbance at 12 months through fatigue was statistically significant (*B* = 0.02, SE = 0.01, z = 2.01, *P* = .045, 95% CI = <.0.01 to 0.04), indicating that fatigue mediated the positive association between sleep disturbance at initial assessment and sleep disturbance at 12 months. Similarly, the indirect pathway from pain interference at initial assessment to sleep disturbance at 12 months through fatigue was statistically significant (*B* = 0.13, SE = 0.04, z = 3.03, *P* = .002, 95% CI = 0.04 to 0.21), indicating that fatigue mediated the positive association between pain interference at initial assessment and sleep disturbance at 12 months. Additionally, the indirect pathway from pain interference at initial assessment to pain interference at 12 months through fatigue was also statistically significant (*B* = 0.08, SE = 0.04, z = 2.20, *P* = .027, 95% CI = 0.01 to 0.15), indicating that fatigue mediated the positive association between pain interference at initial assessment and pain interference at 12 months.

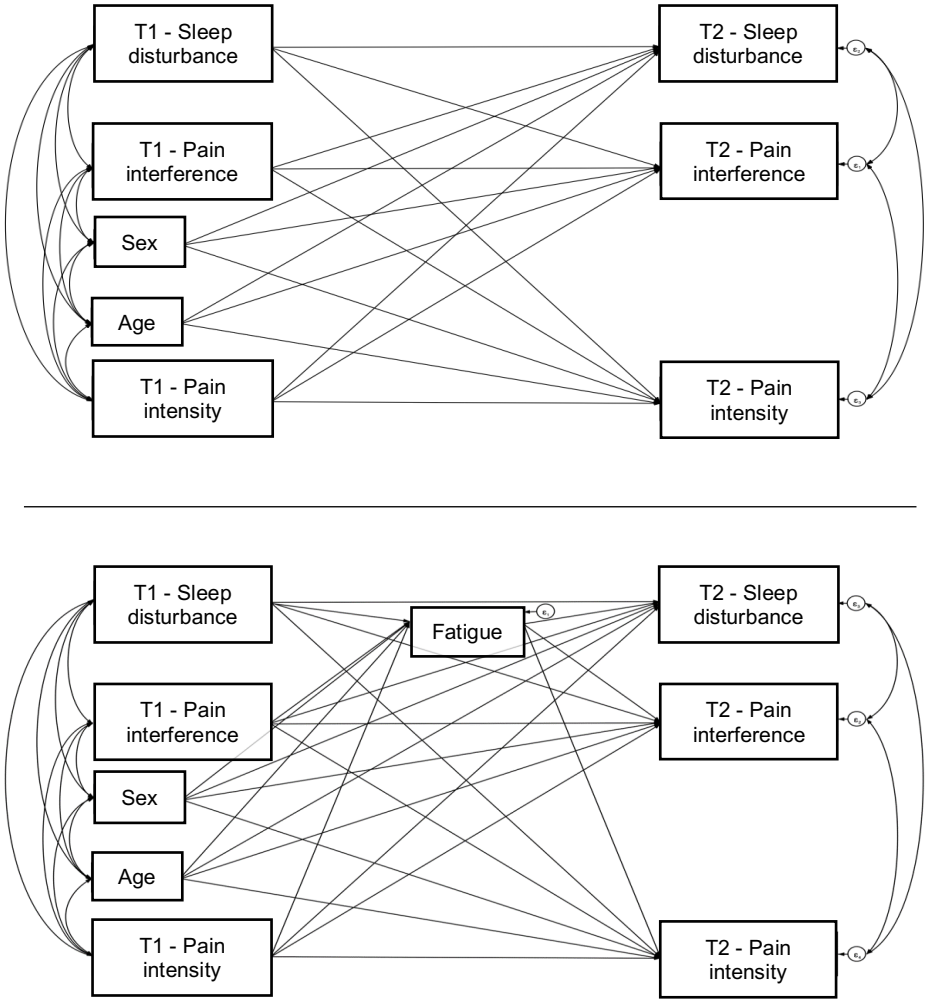


Figure 1. Non-trimmed models of bidirectional associations between sleep disturbance and pain at first assessment (T1) and 12-month follow-up (T2; top panel) and the role of fatigue in the associations between sleep disturbance and pain first assessment (T1) and 12-month follow-up (T2; bottom panel).

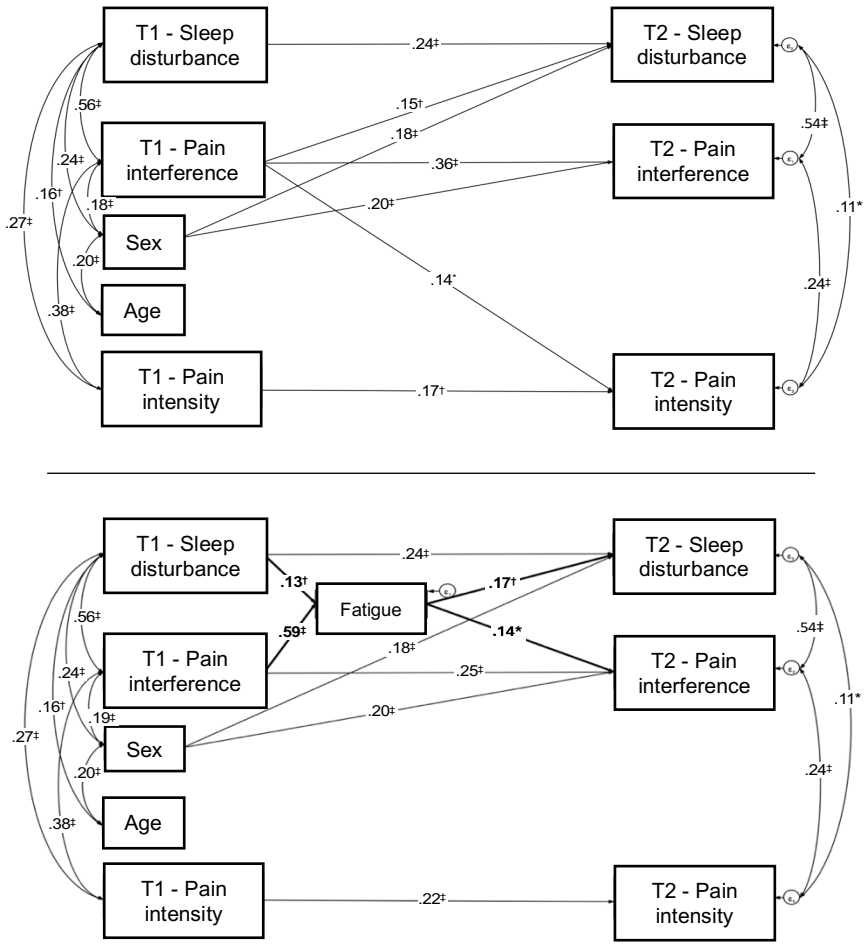


Figure 2. Trimmed models of bidirectional associations between sleep disturbance and pain at first assessment (T1) and 12-month follow-up (T2; top panel) and the role of fatigue in the associations between sleep disturbance and pain first assessment (T1) and 12-month follow-up (T2; bottom panel). Indirect significant paths are in bold font. *P < 0.05, †P < 0.01, ‡P < 0.001.

DISCUSSION

This is the first study to examine the role of fatigue in the co-occurrence and mutual maintenance of sleep disturbance and pain over time in a sample of children and adolescents with chronic pain. We hypothesized that sleep disturbance, pain intensity, and pain interference measured at the initial assessment would predict subsequent sleep disturbance, pain intensity, and pain interference 12 months later; and that fatigue would mediate these associations over time.

The findings did not support the first study hypothesis. Although we found that sleep disturbance and pain co-occurred at both time points – as evidenced by positive associations between sleep disturbance, pain intensity, and pain interference – we did not find evidence for a bidirectional association between pain intensity, pain interference, and sleep disturbance over time. Instead, the findings suggest that pain interference may contribute to future sleep disturbance, but sleep disturbance does not appear to contribute to future pain interference or pain intensity. Moreover, although pain intensity at initial assessment is associated with sleep disturbance and pain interference at initial assessment, pain intensity assessed at the initial assessment does not appear to contribute to pain interference or sleep disturbance 12 months later.

These findings are not consistent with prior research showing that sleep disturbance predicts subsequent pain interference in children and adolescents with chronic pain [29]. Furthermore, the study findings are not consistent with the conceptual model developed by Valrie and colleagues [46] which hypothesizes a reciprocal influence between pain intensity and

sleep disturbance over time in children and adolescents with chronic pain, or with research showing that, in this bidirectional association, the effect of insomnia symptoms on pain (pain intensity, pain interference, and pain frequency) is stronger than *vice versa* [1].

Differences in the study designs used in prior research and the current study might help explain, at least in part, the inconsistent findings. For example, most longitudinal studies reporting significant associations between sleep disturbance and subsequent pain intensity and pain interference in children and adolescents with chronic pain have used a diary design [5,20,47] or a prospective short-term follow-up design [29]. The current study, however, was based on data from a prospective 1-year follow-up design. We know that the temporal distance between assessments is important, because any causal influence of one variable on another likely has a specific time lag associated with that influence [10]. It is possible, for example, that sleep disturbance exerts its largest impact on the next day's or the next week's levels of pain intensity and pain interference, but has relatively little influence over longer time lags. A second issue is that in the current study sleep disturbance was assessed based on the participants' recall of sleep in the past 7 days; hence the measure may reflect the sleep disturbance as a state variable rather than as a trait variable. The latter is more suitable in research studying longer lag times, such as what was studied here [22]. Chronic pain, by definition, is a stable condition [43]. The design of the current study could therefore potentially explain why pain interference at the initial assessment predicted subsequent sleep disturbance 12 months later but not *vice versa* in the

current study. In addition, differences in the sample characteristics between studies might also help to explain any between-study differences. For example, the studies showing significant associations between sleep disturbance and subsequent pain intensity and pain interference used mixed clinical samples of children and adolescents with chronic pain [20,29] and other chronic conditions including sickle cell disease [47] and juvenile idiopathic arthritis [5]. Our study used a community sample of school-attending children and adolescents with chronic pain. It is likely that clinical samples of children and adolescents with chronic pain experience more severe levels of sleep disturbance than children and adolescents with chronic pain recruited from the community [23,26,27,40]. These differences may explain the lack of a statistically significant association between sleep disturbance and subsequent pain intensity and pain interference in the current study sample. Differences in participants' age could also help explain the different findings. For example, Arnison and colleagues [1] used a cohort of healthy adolescents that was older than the one used in this study, and there is research showing that age moderates the association between sleep disturbance and pain-related outcomes (e.g., pain perception; [36]); specifically, that the association between these two factors increases with age.

The findings also showed that fatigue measured at the initial assessment predicted subsequent worse pain interference and sleep disturbance over and above the effects of pain intensity, pain interference, and sleep disturbance measured at the first assessment; hence confirming and extending preliminary longitudinal findings [44]. The unique

contributions of fatigue to sleep disturbance and pain interference in children and adolescents with chronic pain underscore the need to monitor and manage fatigue in this population.

Consistent with the second study hypothesis, fatigue was found to explain a portion of the association found between sleep disturbance at first assessment and at 12 months, and the association between pain interference at first assessment and at 12 months. Specifically, we found that changes over time in both pain interference and sleep disturbance were mediated by fatigue, with higher levels of pain interference and sleep disturbance at first assessment independently contributing to higher levels of fatigue, which, in turn, were associated with increased pain interference and sleep disturbance as measured at 12 months. Additionally, we found that fatigue at first assessment mediated the association found between the initial levels of pain interference and sleep disturbance 12 months later, such that higher levels of pain interference at first assessment were associated with higher levels of fatigue at first assessment, which, in turn, predicted increased sleep disturbance at the 12-months assessment. These findings confirm and extend the preliminary findings from a cross-sectional study in which fatigue was found to explain a statistically significant amount of the variance of the association between pain interference and sleep disturbance in children and adolescents with chronic pain [50]. These findings also contribute to knowledge regarding the complex associations between sleep disturbance, pain intensity, and pain interference in adolescents with chronic pain, and support a conceptual model that suggests that both psychological and physiological factors

mediate the pain-sleep association in this population [46]. If these findings are confirmed by future studies conducted with clinical samples, they would suggest that by targeting the fatigue associated with or due to pain and sleep disturbance in children and adolescents with chronic pain, it might be possible to prevent the worsening of sleep problems and pain interference over time and reduce the impact of pain on subsequent sleep disturbance.

This study has a number of limitations that should be considered when interpreting the results. First, the participants were recruited from a convenience sample of children and adolescents and therefore the generalizability of the findings may be limited. Furthermore, given that participants were selected if chronic pain was present at the initial assessment and 12 months later, and chronic pain was considered to be present if it persisted ≥3 months, the stability of the chronic pain problem between the two assessment points is not known. Future research should examine times points that are closer together, if possible. Second, the cross-lagged panel model testing mediation effects was based on just two timepoints. This limits the ability to test the explanatory/causal role of fatigue in the sleep disturbance-pain interrelationship. Although fatigue at first assessment predicted subsequent sleep disturbance and fatigue, it is unknown if sleep disturbance and pain intensity and pain interference also preceded and predicted fatigue over time. Additional studies using a longitudinal design that allowed for a strict test of these mediation effects, with predictor, mediator, and outcome variables measured on multiple occasions is needed to determine the reliability and generalizability of the findings. Third, all measures used in this study were based on self-report,

which increases the risk that common method variance, may explain some of the significant associations found. Research that also included objective measures of the study variables when possible – such as actigraphy or polysomnography to assess sleep duration – could help to complement and increase the overall validity and reliability in the findings.

Despite the study's limitations, the findings provide important new information regarding the role of fatigue in the association between pain intensity, and pain interference, and sleep disturbance in children and adolescents with chronic pain. The fact that fatigue was shown to explain, at least in part, the co-occurrence and maintenance of pain interference (but not pain intensity) and sleep disturbance over time underscores fatigue as a factor that deserves additional study in children and adolescents with chronic pain.

Acknowledgements: This work was supported by grants from the Spanish Ministry of Economy, Industry and Competitiveness (RTI2018-09870-B-I00; RED2022-134869-T); the European Regional Development Fund (ERDF); and the Government of Catalonia (AGAUR; 2021SGR-730). ES-R's work is supported by a grant from the Spanish Ministry of Science and Innovation (MCIN/AEI/10.13039/501100011033; PID2020-113869RA-I00). JR-J is supported by a doctoral grant from MINECO (PRE2019-089283). JM's work is supported by ICREA-Acadèmia. The Chair in Pediatric Pain is supported by Fundación Grünenthal.

REFERENCES

[1] Arnison T, Schrooten MGS, Hesser H, Jansson-Fröjmark M, Persson J. Longitudinal, bidirectional relationships of insomnia

symptoms and musculoskeletal pain across adolescence: The mediating role of mood. Pain 2022;163:287–298.

[2] Arnison, T., Evans, B., Schrooten, M. G., Persson, J., & Palermo, T. M. Adolescent girls' musculoskeletal pain is more affected by insomnia than boys', and through different psychological pathways. The Journal of Pain 2024;104571.

[3] Bingham CO, Butanis AL, Orbai AM, Jones M, Ruffing V, Lyddiatt A, Schrandt MS, Bykerk VP, Cook KF, Bartlett SJ. Patients and clinicians define symptom levels and meaningful change for PROMIS pain interference and fatigue in RA using bookmarking. Rheumatology (Bulgaria) 2021;60:4306–4314.

[4] Bonvanie IJ, Oldehinkel AJ, Rosmalen JGM, Janssens KAM. Sleep problems and pain: A longitudinal cohort study in emerging adults. Pain 2016;157:957–963.

[5] Bromberg MH, Gil KM, Schanberg LE. Daily sleep quality and mood as predictors of pain in children with juvenile polyarticular arthritis. Health Psychology 2012;31:202–209.

[6] Carmines EG. Analyzing models with unobserved variables. Social measurement: Current issues 1981;80.

[7] Castarlenas E, Jensen MP, von Baeyer CL, Miró J. Psychometric properties of the numerical rating scale to assess self-reported pain intensity in children and adolescents. Clin J Pain 2017;33:376–383.

[8] Ceniza-Bordallo G, Fraile AG, Martín-Casas P, López-de-Uralde-Villanueva I. Validity and reliability of Spanish PROMIS pediatric pain interference short form. J Pediatr Nurs 2022;66:79–85.

[9] Christensen J, Noel M, Mychasiuk R. Neurobiological mechanisms underlying the sleep-pain relationship in adolescence: A review. Neurosci Biobehav Rev 2019;96:401–413.

[10] Cole DA, Maxwell SE. Testing mediational models with longitudinal data: questions and tips in the use of structural equation modeling. J Abnorm Psychol 2003;112:558.

[11] Finan PH, Goodin BR, Smith MT. The association of sleep and pain: An update and a path forward. Journal of Pain 2013;14:1539–1552.

[12] Gobina I, Villberg J, Välimaa R, Tynjälä J, Whitehead R, Cosma A, Brooks F, Cavallo F, Ng K, de Matos MG, Villerusa A. Prevalence of self-reported chronic pain among adolescents: Evidence from 42 countries and regions. European Journal of Pain (United Kingdom) 2019;23:316–326.

[13] Harris AL, Carmona NE, Moss TG, Carney CE. Testing the contiguity of the sleep and fatigue relationship: A daily diary study. Sleep 2021;44.

[14] Hoyle RH. Structural equation modeling: Concepts, issues, and applications. Sage, 1995.

[15] Hunfeld JAM, Perquin CW, Duivenvoorden HJ, Hazebroek-Kampschreur AAJM, Passchier J, Van Suijlekom-Smit LWA, Van Der Wouden JC. Chronic pain and its impact on quality of life in adolescents and their families. J Pediatr Psychol 2001;26:145–153.

[16] Kline RB. Principles and practice of structural equation modeling. Guilford publications, 2023.

[17] Kline RB, Santor DA. Principles & practice of structural equation modelling. Canadian Psychology 1999;40:381.

[18] Könning A, Rosenthal N, Brown D, Stahlschmidt L, Wager J. Severity of Chronic Pain in German Adolescent School Students: A Cross-sectional Study. Clinical Journal of Pain 2021;37:118–125.

[19] de la Vega R, Racine M, Sánchez-Rodríguez E, Tomé-Pires C, Castarlenas E, Jensen MP, Miró J. Pain Extent, Pain Intensity, and Sleep Quality in Adolescents and Young Adults. Pain Medicine 2016;17:1971–1977. doi:10.1093/pm/pnw118.

[20] Lewandowski AS, Palermo TM, Motte SD La, Fu R. Temporal daily associations between pain and sleep in adolescents with chronic pain versus healthy adolescents. Pain 2010;151:220–225.

[21] Lewin DS, Dahl RE. Importance of sleep in the management of pediatric pain. Journal of Developmental and Behavioral Pediatrics 1999;20:201–207.

[22] Little TD. Longitudinal structural equation modeling. Guilford press, 2013.

[23] Long AC, Krishnamurthy V, Palermo TM. Sleep disturbances in school-age children with chronic pain. J Pediatr Psychol 2008;33:258–268.

[24] Miró J, Roman-Juan J, Sánchez-Rodríguez E, Solé E, Castarlenas E, Jensen MP. Chronic Pain and High Impact Chronic Pain in

Children and Adolescents: A Cross-Sectional Study. J Pain 2023;24:812–823. doi:10.1016/j.jpain.2022.12.007.

[25] Nugraha B, Gutenbrunner C, Barke A, Karst M, Schiller J, Schäfer P, Falter S, Korwisi B, Rief W, Treede RD. The IASP classification of chronic pain for ICD-11: Functioning properties of chronic pain. Pain 2019;160:88–94.

[26] Palermo TM, Kiska R. Subjective sleep disturbances in adolescents with chronic pain: Relationship to daily functioning and quality of life. J Pain 2005;6:201–207. doi:https://doi.org/10.1016/j.jpain.2004.12.005.

[27] Palermo TM, Wilson AC, Lewandowski AS, Toliver-Sokol M, Murray CB. Behavioral and psychosocial factors associated with insomnia in adolescents with chronic pain. Pain 2011;152:89–94.

[28] Pavlova M, Ference J, Hancock M, Noel M. Disentangling the Sleep-Pain Relationship in Pediatric Chronic Pain: The Mediating Role of Internalizing Mental Health Symptoms. Pain Res Manag 2017;2017.

[29] Pavlova M, Kopala-Sibley DC, Nania C, Mychasiuk R, Christensen J, McPeak A, Tomfohr-Madsen L, Katz J, Palermo TM, Noel M. Sleep disturbance underlies the co-occurrence of trauma and pediatric chronic pain: A longitudinal examination. Pain 2020;161:821–830.

[30] Quinn H, Thissen D, Liu Y, Magnus B, Lai J, Amtmann D, Varni JW, Gross HE, DeWalt DA. Using item response theory to enrich and

expand the PROMIS® pediatric self report banks. Health Qual Life Outcomes 2014;12:160.

[31] Roman-Juan J, Sánchez-Rodríguez E, Solé E, Castarlenas E, Jensen MP, Miró J. Immigration background as a risk factor of chronic pain and high-impact chronic pain in children and adolescents living in Spain: differences as a function of age. Pain 2024. doi:10.1097/j.pain.0000000000003142.

[32] Roman-Juan J, Sánchez-Rodríguez E, Solé E, Castarlenas E, Jensen MP, Miró J. Psychological factors and pain medication use in adolescents with chronic pain. Pain Medicine 2023:pnad075. doi:10.1093/pm/pnad075.

[33] Roman-Juan J, Solé E, Sánchez-Rodríguez E, Castarlenas E, Jensen MP, Miró J. Adverse Childhood Events and Chronic Pain in Adolescents: The Role of Sleep Disturbance. J Pediatr Psychol 2023:jsad063. doi:10.1093/jpepsy/jsad063.

[34] Roman-Juan J, Solé E, Sánchez-Rodríguez E, Castarlenas E, Jensen MP, Miró J. Validation of the pediatric version of the Graded Chronic Pain Scale Revised in school-aged children and adolescents. Pain 2023. doi:10.1097/j.pain.0000000000002965.

[35] Roth-Isigkeit A, Thyen U, Stöven H, Schwarzenberger J, Schmucker P. Pain among children and adolescents: Restrictions in daily living and triggering factors. Pediatrics 2005;115.

[36] Rouhi S, Topcu J, Egorova-Brumley N, Jordan AS. The impact of sleep disturbance on pain perception: A systematic review

examining the moderating effect of sex and age. Sleep Med Rev 2023;71.

[37] Sánchez-Rodríguez E, Ferreira-Valente A, Pathak A, Solé E, Sharma S, Jensen MP, Miró J. The role of perfectionistic self-presentation in pediatric pain. Int J Environ Res Public Health 2021;18:1–14.

[38] Simons LE, Sieberg CB, Claar RL. Anxiety and functional disability in a large sample of children and adolescents with chronic pain. Pain Res Manag 2012;17:93–97.

[39] Singh A, Panepinto JA. Clinical meaning of PROMIS pain domains for children with sickle cell disease. Blood Adv 2019;3:2244–2249.

[40] Siu Y-F, Chan S, Wong K-M, Wong W-S. The comorbidity of chronic pain and sleep disturbances in a community adolescent sample: prevalence and association with sociodemographic and psychosocial factors. Pain Medicine 2012;13:1292–1303.

[41] Solé E, Roman-Juan J, Sánchez-Rodríguez E, Castarlenas E, Jensen MP, Miró J. School bullying and peer relationships in children with chronic pain. Pain 2023. doi:10.1097/j.pain.0000000000003118.

[42] Solé E, Sharma S, Ferreira-Valente A, Pathak A, Sánchez-Rodríguez E, Jensen MP, Miró J. The Associations between Sleep Disturbance, Psychological Dysfunction, Pain Intensity, and Pain Interference in Children with Chronic Pain. Pain Medicine (United States) 2022;23:1106–1117.

[43] Soltani S, Kopala-Sibley DC, Noel M. The Co-occurrence of Pediatric Chronic Pain and Depression: A Narrative Review and Conceptualization of Mutual Maintenance. Clinical Journal of Pain 2019;35:633–643.

[44] Sommer A, Grothus S, Claus BB, Stahlschmidt L, Wager J. Fatigue in Children and Adolescents: A Population-Based Longitudinal Study on Fatigue and Chronic Pain. J Pediatr Psychol 2023;48:626–635.

[45] Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, Cohen M, Evers S, Finnerup NB, First MB, Giamberardino MA, Kaasa S, Korwisi B, Kosek E, Lavand'Homme P, Nicholas M, Perrot S, Scholz J, Schug S, Smith BH, Svensson P, Vlaeyen JWS, Wang SJ. Chronic pain as a symptom or a disease: The IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). Pain 2019;160:19–27.

[46] Valrie CR, Bromberg MH, Palermo T, Schanberg LE. A systematic review of sleep in pediatric pain populations. Journal of Developmental and Behavioral Pediatrics 2013;34:120–128.

[47] Valrie CR, Gil KM, Redding-Lallinger R, Daeschner C. Brief report: Daily mood as a mediator or moderator of the pain-sleep relationship in children with sickle cell disease. J Pediatr Psychol 2008;33:317–322.

[48] Varni JW, Magnus B, Stucky BD, Liu Y, Quinn H, Thissen D, Gross HE, Huang I-C, DeWalt DA. Psychometric properties of the PROMIS ® pediatric scales: precision, stability, and comparison of

different scoring and administration options. Qual Life Res 2014;23:1233–1243.

[49] Yamada K, Adams H, Ellis T, Clark R, Sully C, Lariviere C, Sullivan MJ. The temporal relation between pain and fatigue in individuals receiving treatment for chronic musculoskeletal pain. BMC Musculoskelet Disord 2022;23.

[50] Yoon IA, Sturgeon JA, Feinstein AB, Bhandari RP. The role of fatigue in functional outcomes for youth with chronic pain. European Journal of Pain (United Kingdom) 2019;23:1548–1562.

Supplementary Table 1. Results from the non-trimmed partial cross-lagged panel structural equation analyses.

Variables	β	SE	z	*P*	95%CI (LL)	95%CI (UP)
T2 – Sleep disturbance						
T1 – Sleep disturbance	.23	.06	3.90	<.001	.11	.35
T1 – Pain interference	.19	.062	3.12	.002	.07	.31
T1 – Pain intensity	-.10	.05	-1.84	.066	-.20	.01
Sex	.16	.05	3.28	.001	.07	.26
Age	.04	.05	0.74	.460	-.06	.13
T2 - Pain interference						
T1 – Sleep disturbance	-.03	.06	-0.47	.636	-.15	.09
T1 – Pain interference	.39	.06	6.52	<.001	.27	.50
T1 – Pain intensity	-.03	.05	-0.54	.592	-.13	.07
Sex	-.03	.05	-0.54	.592	-.13	.07
Age	.03	.05	0.66	.512	-.06	.13
T2 - Pain intensity						
T1 – Sleep disturbance	-.04	.06	-0.56	.572	-.16	.09
T1 – Pain interference	.16	.07	2.40	.017	.03	.29
T1 – Pain intensity	.17	.06	3.10	.002	.06	.28

Sex	.01	.05	0.16	.874	-.10	.11
Age	-.04	.05	-0.71	.475	-.14	.07
Covariates						
T1 – Sleep disturbance → T1 – Pain interference	.56	.04	14.96	<.001	.48	.63
T1 – Sleep disturbance → T1 – Pain intensity	.27	.05	5.36	<.001	.17	.36
T1 – Sleep disturbance → Sex	.24	.05	4.69	<.001	.14	.34
T1 – Sleep disturbance → Age	.16	.05	3.13	.002	.06	.26
T1 – Pain interference → T1 – Pain intensity	.38	.05	8.19	<.001	.29	.48
T1 – Pain interference → Sex	.18	.05	3.53	<.001	.08	.29
T1 – Pain interference → Age	.07	.05	1.30	.193	-.03	.18
T1 – Pain intensity → Sex	-.02	.05	-0.43	.666	-.13	.08
T1 – Pain intensity → Age	.08	.05	1.55	.120	-.02	.18
Sex → Age	.20	.05	3.85	<.001	.10	.30

T2 – Sleep disturbance → T2 – Pain interference	.54	.038	14.21	<.001	.46	.61
T2 – Sleep disturbance → T2 – Pain intensity	.11	.05	2.11	.035	.01	.21
T2 – Pain interference → T2 – Pain intensity	.24	.05	4.79	<.001	.14	.34

Note: 95%CI (LL) = lower limit of a 95% confidence interval; CI (UL) = upper limit; T1 = first assessment; T2 = 12 months assessment.

Supplementary Table 2. Results from the non-trimmed partial cross-lagged panel structural equation analyses including fatigue as a mediator.

Variables	β	SE	z	*P*	95%CI (LL)	95%CI (UP)
T2 – Sleep disturbance						
T1 – Sleep disturbance	.23	.05	4.63	<.001	.13	.33
T1 – Pain interference	.05	.07	0.68	.494	-.09	.18
Fatigue	.15	.06	2.37	.018	.03	.28
Sex	.18	.05	3.65	<.001	.08	.27
T2 - Pain interference						
T1 – Pain interference	.26	.06	3.99	<.001	.13	.39
Fatigue	.14	.06	2.22	.026	.02	.27
Sex	.20	.05	4.26	<.001	.11	.29
T2 - Pain intensity						
T1 – Pain interference	.07	.07	0.95	.340	-.07	.21
T1 – Pain intensity	.17	.05	3.18	.001	.07	.27
Fatigue	.10	.07	1.40	.163	-.04	.23

Fatigue						
T1 – Sleep disturbance	.11	.05	2.34	.019	.02	.21
T1 – Pain interference	.58	.04	12.80	.000	.49	.67
T1 – Pain intensity	.03	.04	0.77	.440	-.05	.12
Sex	.005	.04	0.12	.904	-.08	.09
Age	.07	.04	1.72	.086	-.01	.15
Covariates						
T1 – Sleep disturbance → T1 – Pain interference	.56	.04	14.91	<.001	.48	.63
T1 – Sleep disturbance → T1 – Pain intensity	.27	.05	5.40	<.001	.17	.37
T1 – Sleep disturbance → Sex	.24	.05	4.73	<.001	.14	.34
T1 – Sleep disturbance → Age	.16	.05	3.17	0.002	.06	.27
T1 – Pain interference → T1 – Pain intensity	.38	.05	8.08	<.001	.29	.47
T1 – Pain interference → Sex	.19	.05	3.69	<.001	.09	.29

Sex → Age	.20	.05	3.85	<.001	.10	.30
T2 – Sleep disturbance → T2 – Pain interference	.53	.04	14.03	<.001	.46	.61
T2 – Sleep disturbance → T2 – Pain intensity	.11	.05	1.98	.045	.002	.20
T2 – Pain interference → T2 – Pain intensity	.23	.05	4.68	<.001	.14	.33

Note: 95%CI (LL) = lower limit of a 95% confidence interval; CI (UL) = upper limit; T1 = first assessment; T2 = 12 months assessment.

4.8. Study VIII

Psychological factors and pain medication use in adolescents with chronic pain.

Pain Medicine, 2023, **24**, 1183–1188
https://doi.org/10.1093/pm/pnad075
Advance access publication 21 June 2023
Original Research Article

Psychological factors and pain medication use in adolescents with chronic pain

Josep Roman-Juan, MSc,[1,2] Elisabet Sánchez-Rodríguez, PhD,[1,2] Ester Solé, PhD,[1,2] Elena Castarlenas, PhD,[1,2] Mark P. Jensen, PhD,[3] Jordi Miró, PhD[1,2,*]

[1]Universitat Rovira i Virgili, Unit for the Study and Treatment of Pain—ALGOS, Research Center for Behavior Assessment (CRAMC), Department of Psychology, Tarragona, 43007 Catalonia, Spain
[2]Institut d'Investigació Sanitària Pere Virgili, Universitat Rovira i Virgili, 43204 Catalonia, Spain
[3]Department of Rehabilitation Medicine, University of Washington, Seattle, WA 98104, United States

**Corresponding author:* Departament de Psicologia, Universitat Rovira i Virgili, Carretera de Valls, s/n, 43007 Tarragona, Spain. Email: jordi.miro@urv.cat

Abstract

Objective: The purpose of this study was to examine (1) the associations of anxiety, depressive symptoms, and pain catastrophizing with pain medication use in adolescents with chronic pain and (2) the extent to which these associations differed as a function of adolescents' sex.

Methods: Cross-sectional data from 320 adolescents 12–18 years of age with chronic pain were drawn from an epidemiological study on pediatric chronic pain conducted in Reus (Catalonia, Spain). Participants were asked to provide sociodemographic information and respond to measures assessing pain (location, frequency, intensity, and interference), pain medication use, anxiety, depressive symptoms, and pain catastrophizing. Point biserial correlations were conducted to examine univariate associations between the psychological variables and pain medication use. Hierarchical logistic regression analysis was used to examine these associations while controlling for demographic characteristics, pain intensity, and pain interference.

Results: Anxiety, depressive symptoms, and pain catastrophizing were significantly associated with pain medication use in univariate analyses. Regression analysis identified pain catastrophizing as a unique independent predictor of pain medication use after controlling for the effect of demographic variables (sex and age), pain intensity, and pain interference (odds ratio = 1.1, $P < .05$). No moderating effect of adolescents' sex on the associations between psychological factors and pain medication use was found.

Conclusions: Adolescents with chronic pain with higher levels of pain catastrophizing use pain medications more often. Research to examine the impact of interventions targeting pain catastrophizing on pain medication use among adolescents with chronic pain would be an important next step.

Keywords: adolescents; pain medication; chronic pain; pain catastrophizing

Introduction

Chronic pain is a common health condition in adolescents,[1–3] and between 18% and 65% of adolescents with chronic pain from the general population use pain medications to manage their pain.[4] Research findings also suggest that the frequency of medication use in this population is increasing over time.[5] Although there is clearly a role for pain medications for acute pain, long-term medication use for chronic pediatric pain is not an optimal solution. In fact, the effectiveness of pain medications for pediatric chronic pain has not been demonstrated.[6] Furthermore, some of the most commonly used pain medications, such as nonsteroidal anti-inflammatory drugs (eg, ibuprofen) and analgesic drugs (eg, paracetamol), are associated with several side effects, and their long-term safety is unclear.[7,8] Therefore, an adequate use of pain medications in children and adolescents with chronic pain is of most importance.

Several demographic (eg, sex, age) and pain-related characteristics (eg, pain intensity, pain-related disability, pain frequency, pain extent) have been found to be associated with pain-related medication use in children and adolescents.[4,9–11] When pain medication is used appropriately, it would be reasonable to expect pain-related medication use to vary mostly as a function of pain intensity and pain-related disability. However, if pain medication use is driven by psychological factors (eg, psychological distress, catastrophizing) over and above pain-related factors such as pain intensity, this would suggest the possibility of a misguided use of pain medications. In this case, it would be important to identify those specific psychological factors that contribute to pain medication use, as this would allow for the development of interventions that could reduce misguided medication use and improve pain management.

However, knowledge of the association between psychological factors and pain medication use in adolescents with chronic pain is significantly limited. We are aware of only one study that has examined this issue.[4] The findings from that study showed that anxiety and depressive symptoms were significantly and positively associated with pain medication use in adolescents with chronic pain in univariate analyses. However, this association did not remain significant in multivariate analysis after other pain-related factors had been controlled for, including pain intensity and pain-related disability. Those investigators recommended that future research should continue studying this topic and expand the predictor variables examined to include pain-related cognitive

Received: 3 January 2023. **Revised:** 20 May 2023. **Accepted:** 1 June 2023

factors, such as pain catastrophizing. In support of the possibility that catastrophizing could be associated with pain medication use in children and adolescents, research in adults with chronic pain has shown that pain catastrophizing is associated with pain medication use[12,13] and with inappropriate use of pain medications.[14–16]

Given these issues, the aim of the present study was to evaluate the extent to which anxiety, depressive symptoms, and pain catastrophizing were associated with pain medication use in a community sample of adolescents with chronic pain, both in univariate analyses and with controlling for demographic factors (sex and age) and pain-related factors (pain intensity and pain interference). On the basis of prior research in adolescents[4] and adults,[14–16] we hypothesized significant positive univariate associations between anxiety, depressive symptoms, and pain catastrophizing and pain medication use. We also hypothesized that the associations of anxiety and depressive symptoms with pain medication use would be vitiated by controlling for sex, age, pain intensity, and pain interference, whereas pain catastrophizing would emerge as a significant independent predictor of pain medication use. Additionally, given prior research showing that adolescent girls report higher levels of psychological dysfunction[17,18] and pain medication use,[4] we also hypothesized that sex would have a moderating effect on the associations examined.

Methods

Study design

This study used a cross-sectional observational design. Data were collected between October 2018 and March 2020, before the lockdown due to COVID-19, as an initial assessment of an ongoing longitudinal epidemiological study at 10 schools in the Southeast of Catalonia, Spain (EPIDOL Project). An article presenting the primary findings derived from these data has been published.[3] However, that article did not address the study questions that are the focus of the present article. The ethics committee of the Universitat Rovira i Virgili approved the study (*Institut d'Investigació Sanitària Pere Virgili; ref.: 136/2018*).

Procedure

All parents of schoolchildren in the participant schools who were 8–18 years of age and able to read, write, and speak Spanish received a letter explaining the study and asking them to provide their consent for their children to participate. Schoolchildren's participation required both the students' and parents' assent and consent, respectively. Participating students completed a paper-and-pencil survey during the school day, following the instructions provided by the research staff. For participation in this study, children received a 3€ gym sack and calendar (see Miró et al.[3] for additional information on the procedure).

Participants

For the purposes of the study presented here, only participants who reported chronic pain—defined as pain that had lasted for at least 3 months and that was present at least once a week—and who were 12 years of age or older were included for data analysis, as the younger children were not asked to report on pain medication use.

Variables and measures

Demographic characteristics

Participants were asked to provide information about their sex and age.

Pain characteristics

Participants were asked to provide information about any pain problem they had experienced in the previous 3 months. The frequency of each pain problem was assessed on a 5-point Likert scale (1 = "every day," 2 = "more than once a week," 3 = "once a week," 4 = "one or two times per month," 5 = "once in the last 3 months"). On the basis of previous epidemiology studies, participants were classified as experiencing chronic pain if they reported pain at least once a week for at least 3 months.[2,11,19–23] In addition, those who reported that they had pain during the prior 3 months were provided with a pain site checklist that had been used in previous studies[22,24–26] to assess *pain location*. It included 11 specific locations (ie, head, neck, chest, shoulders, back, arms, hands, bottom/hips, belly/pelvis, legs, feet) and an "other" category. Participants with more than one pain location were considered to have multisite pain. Participants were also asked to rate their usual (average) and maximum *pain intensity* in the prior week for each pain location on a 0–10 numerical rating scale (NRS-11), where 0 = "no pain" and 10 = "very much pain." The NRS-11 has been shown to provide reliable and valid scores when used with children as young as 6 years of age.[27] Following the procedure of prior studies,[4,11,28] for analyses we computed a mean score from the usual (average) and maximum pain intensity scores to represent chronic pain intensity. When participants reported multisite chronic pain, the highest usual (average) and the highest maximum pain intensity scores were selected to calculate chronic pain intensity. When this mean score could not be calculated because of missing values in usual (average) or maximum pain intensity, we chose either the highest maximum or the highest usual (average) pain intensity scores, respectively.

Pain-related interference

Pain interference was assessed with the Spanish version of the 8-item pediatric Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference scale v2.0 (PROMIS-PI).[29] With the PROMIS-PI, respondents are asked to rate how often pain had interfered with their physical, psychological, and social functioning over the prior 7 days, with each response measured on a Likert scale (1 = "never" to 5 = "almost always"). Scores are based on a T-score distribution with a mean of 50 points and a standard deviation of 10. Previous studies have shown that the pediatric form of the PROMIS-PI provides reliable and valid data for pain interference when used in children and adolescents as young as 8 years of age.[29] In the present sample, Cronbach's alpha ($\alpha = 0.86$) indicated good reliability for the PROMIS-PI scale.

Psychological characteristics

Anxiety and depressive symptoms were assessed with the Spanish version of the 4-item short form from the anxiety and depression symptom subscales of the PROMIS Pediatric-25 Profile Form v2.0.[30] Participants were asked to rate the frequency with which they had experienced 4 anxiety symptoms and 4 depressive symptoms in the prior 7 days, with each response measured on a Likert scale (1 = "never" to

5 = "almost always"). Scores for anxiety and depressive symptoms are based on a T-score distribution with a mean of 50 points and a standard deviation of 10. The Pediatric-25 Profile Form scales have been shown to be able to report reliable and valid scores of anxiety and depressive symptoms.[31] In the present sample, Cronbach's alpha for the measures of anxiety ($\alpha = 0.84$) and depressive symptoms ($\alpha = 0.87$) indicated good reliability for these scales.

Pain catastrophizing was assessed with the Spanish version of the Pain Catastrophizing Scale for children (PCS-C).[32,33] The PCS-C is a 13-item measure that use a 5-point Likert scale (0 = "not at all" to 4 = "always") to assess the tendency of children to catastrophize about their pain. Items were summed, yielding a total score ranging from 0 to 52, with higher scores indicating greater pain catastrophizing. Reports from the PCS-C have been shown to be valid and reliable when used with children and adolescents.[32,33] In the present sample, Cronbach's alpha for this scale ($\alpha = 0.87$) indicated good reliability for the PCS-C.

Pain-related medication use

Participants were asked to respond (yes/no) to whether they had taken medications for their pain during the prior 3 months. In the event that a "yes" was chosen, participants were asked to indicate the type of medications they had taken, with the following options: ibuprofen, paracetamol, aspirin, and an "other" option. If the "other" option was chosen, participants were asked to report the specific pain medication they had taken.

Data analysis

We first computed descriptive statistics for the demographic and study variables to describe the sample. Chi-squared analyses were performed to study the associations between specific chronic pain locations and pain medication use for descriptive purposes. Then, to test the hypotheses and study questions about the univariate associations between the study predictors and pain medication use, we computed a series of point-biserial correlation coefficients between the study criterion measure (ie, pain medication use as a dichotomous variable) and the 3 psychological variables (ie, anxiety, depressive symptoms, and pain catastrophizing). Then, to test the hypotheses about the role of psychological variables as predictors of medication use when controlling for sex, age, pain intensity, and pain interference, we conducted a multivariate logistic regression analysis, with (1) pain-related medication use as the criterion variable, (2) adolescents' sex and age and measures of pain intensity and pain interference as control variables, and (3) measures of anxiety, depressive symptoms, and pain catastrophizing as predictors. In these analyses, we first entered sex and age in step 1, measures of pain intensity and pain interference in step 2, and measures of the study predictors (ie, anxiety, depressive symptoms, and pain catastrophizing) in step 3. Finally, to test the hypotheses about the potential moderating effects of adolescents' sex on the associations between psychological factors and pain-related medication use, we entered in step 4 the first-order interaction terms between sex and the 3 psychological factors (sex × anxiety, sex × depressive symptoms, and sex × pain catastrophizing). In the event that any interaction effect between sex and any psychological variable emerged as significant, we planned to compute the zero-order associations between the psychological factor involved and the criterion variable separately for boys and girls. Before conducting the multivariate analysis, we assessed assumptions of multicollinearity of the study predictors to confirm that they met the assumptions for regression. No violations of assumptions were identified, as variance inflation factor values were all less than 2.0 (1.07–1.85), consistent with guidelines.[34] Goodness-of-fit of the multivariable regression was assessed by computing Nagelkerke's R^2 index. A 2-tailed significance level of $P < .05$ was defined as statistically significant. Pairwise deletion was used to handle missing values. All data analyses were conducted in STATA 14 (Stata Corp., Texas, USA).

Results

Sample characteristics

A total of 532 schoolchildren participated. Of those, 320 participants (60%) reported having chronic pain and comprised the final study sample. Table 1 presents the demographic, pain-related, and psychological characteristics of the study sample. More than a half were girls (63%), and the mean age of the participant sample was 14.02 years (SD = 1.61, range = 12–18 years). The most common chronic pain locations in the sample were the back (45%) and the head (44%), and more than a half of participants reported having pain at more than one site (65%). A total of 249 adolescents (78%) reported that they had taken pain medications in the previous 3 months to manage pain. Most frequently, adolescents taking pain medications reported taking nonsteroidal anti-inflammatory drugs (89%) such as ibuprofen or aspirin, followed by non-opioid analgesics (52%) such as paracetamol. Seven percent of adolescents reported taking other medications for their pain, such as calcium channel blockers or antidepressants. The analyses indicated that adolescents who reported pain in the belly/pelvis were more likely to take pain medications—especially nonsteroidal anti-inflammatory drugs—whereas those who reported pain in the shoulders were more likely to take non-opioid analgesics (see Supplementary Table S1).

Associations between the study predictors and pain medication use

Point-biserial correlations revealed weak and positive significant associations between pain medication use and anxiety ($r_{pbis} = 0.15$, $df = 291$, $P = .011$), depressive symptoms ($r_{pbis} = 0.16$, $df = 294$, $P = .007$), and pain catastrophizing ($r_{pbis} = 0.20$, $df = 279$, $P < .001$).

The results of the multivariable logistic regression model predicting pain-related medication use are presented in Table 2. As can be seen, sex and age made a significant 6% contribution to the prediction of pain medication use (χ^2 change = 8.41, $df = 2$, $P = .015$), with this effect being mostly related to sex. Specifically, the odds of pain medication use were almost 3 times higher in female participants than in male participants. Pain intensity and pain interference, as a whole, made an additional significant contribution to the prediction of pain-related medication use (χ^2 change = 6.39, $df = 2$, $P = .041$), accounting for 4% of the variance in the criterion variable. However, this effect was related mostly to pain interference. As can be seen, the odds ratio associated with this analysis indicated that for a 1-unit increase in pain interference score, the odds of reporting pain medication use being positive significantly increased by a factor of 1.

The block of predictors including anxiety, depressive symptoms, and pain catastrophizing made an additional 8% significant contribution to the explanation of the variance in the criterion variable (χ^2 change = 11.94, $df = 3$, $P = .008$). That said, however, a closer look at the odds ratio indicated that only pain catastrophizing made a significant independent contribution (ie, with controlling for the other variables) to this effect. Specifically, for a 1-unit increase in the pain catastrophizing score, the odds of reporting pain medication use being positive significantly increased by a factor of 1.1. No significant interactions between sex and any of the examined psychological factors emerged in the regression analysis predicting pain medication use.

Table 1. Sample characteristics of adolescents with chronic pain ($n = 320$)

	n	%	Mean	SD	Range
Demographics					
Sex					
Male	117	37			
Female	203	63			
Age, years			14.02	1.61	12–18
Chronic pain characteristics					
Pain locations					
Head[a]	141	44			
Neck[b]	69	22			
Chest/breast[c]	25	8			
Shoulders[c]	70	22			
Back[d]	143	45			
Arms[c]	29	9			
Hands[c]	28	9			
Bottom/hips	19	6			
Belly/pelvis[e]	62	19			
Legs[b]	79	25			
Feet[c]	63	20			
Other locations[f]	32	10			
Pain extent					
Single-site chronic pain	111	35			
Multisite chronic pain	209	65			
Pain intensity[g]			6.80	1.88	0–10
Pain interference[h]			53.40	8.83	20–80
Pain medication use[i]	249	78			
Nonsteroidal anti-inflammatory drugs	221	89			
Non-opioid analgesics	130	52			
Other	18	7			
Psychological characteristics					
Anxiety[j]			56.16	10.96	20–80
Depressive symptoms[c]			55.30	11.20	20–80
Pain catastrophizing[k]			21.39	10.57	0–52

[a–f] *n* varies because of nonresponses.
[a] $n = 316$ (missing = 4); [b] $n = 314$ (missing = 6); [c] $n = 319$ (missing = 1); [d] $n = 313$ (missing = 7); [e] $n = 312$ (missing = 8); [f] $n = 317$ (missing = 3); [g] $n = 271$ (missing = 49); [h] $n = 311$ (missing = 9); [i] $n = 296$ (missing = 24); [j] $n = 315$ (missing = 5); [k] $n = 304$ (missing = 16).

Discussion

The aim of this study was to evaluate the associations between measures of three psychological factors (ie, anxiety, depressive symptoms, and pain catastrophizing) and pain medication use and to examine the potential moderating role of sex and age on these associations in a community sample of adolescents with chronic pain. This study provides new data that could help us to better understand the factors that might contribute to pain medication use, prevent inadequate use of pain medications, and thereby improve the management of chronic pain in this population.

In the present study, consistent with the findings from other research studies on chronic pain in adolescents and adults,[4,35,36] and in support of our hypotheses, univariate analyses revealed that anxiety, depressive symptoms, and pain catastrophizing were positively associated with pain medication use. However, and also supporting the study's hypotheses, of the 3 factors examined in the multivariate model, only pain catastrophizing emerged as a statistically significant predictor. These findings suggest that pain catastrophizing could play a unique role in pain medication use, separate from those of pain intensity and pain interference. This finding is consistent with results of studies showing that pain catastrophizing independently contributes to pain medication use, and especially to the use of opioids, in adults with chronic pain.[16,35,37,38] However, to the best of our knowledge, the present study is the first study to report this in a sample of adolescents with chronic pain. Research is needed to confirm this finding and to study whether other pain-related cognitive factors, such as attitudes toward pain and its management (eg, the belief that the individual can control the

Table 2. Multivariate analyses of factors associated with pain medication use ($n = 231$)

	Step 1 OR (95% CI)	Step 2 OR (95% CI)	Step 3 OR (95% CI)	Step 4 OR (95% CI)
Control variables				
Sex (ref: boys)	2.7 (1.3–5.7)**	2.3 (1.1–4.9)*	2.0 (0.9–4.5)	0.5 (0.0–61.8)
Age	1.1 (0.9–1.4)	1.1 (0.9–1.4)	1.1 (0.8–1.4)	1.0 (0.8–1.3)
Pain intensity		1.1 (0.9–1.4)	1.1 (0.9–1.4)	1.1 (0.9–1.4)
Pain interference		1.0 (1.0–1.1)*	1.0 (0.9–1.1)	1.0 (0.9–1.1)
Psychological factors				
Anxiety			1.0 (0.9–1.0)	1.0 (0.9–1.0)
Depressive symptoms			1.0 (0.9–1.1)	1.0 (0.9–1.1)
Pain catastrophizing			1.1 (1.0–1.1)*	1.1 (0.9–1.6)
Interactions				
Sex × anxiety				0.9 (0.9–1.0)
Sex × depression				1.1 (0.9–1.2)
Sex × pain catastrophizing				1.0 (0.9–1.1)
Nalgerke pseudo R^2, %	6.2	10.8	19.1	20.8
Wald χ^2	8.41, $df = 2$, $P = .015$	6.39, $df = 2$, $P = .041$	11.94, $df = 3$, $P = .008$	2.53, $df = 3$, $P = .47$

* $P < .05$.
** $P < .01$.

pain or whether the individual believes in a medical cure for the pain problem), contribute to pain medication use.

Inconsistent with the study hypotheses about interaction effects, we found no moderating effects of sex on the associations between any of the psychological variables and pain medication use. Research in adults with chronic pain has shown that pain catastrophizing appears to have a stronger relationship with opioid prescription in women than in men.[15] Given the inconsistent findings, as well as the limited number of studies on this important issue, further research addressing this question in both youth and adults is warranted.

If the present study findings were replicated, they would raise the possibility that adolescents with chronic pain with higher levels of pain catastrophizing might be using pain medications regardless of their pain intensity and pain interference. If that was the case, it would raise the possibility that these adolescents might be using pain medications misguidedly. In addition, pain medications for children and adolescents with chronic pain represent a substantial cost to health care systems,[39] and medication use–related behavior adopted in adolescence often continues into adulthood.[40] Thus, a misguided use of pain medications in adolescents with chronic pain might contribute to a misguided use of pain medication in adulthood, increasing the already-high financial burden of chronic pain in adults with chronic pain.[41] It is also important to limit any misguided use of pain medications in children and adolescents, given the negative side effects that some of these pain medications can have in this population.[7,8]

The present study findings also highlight the potential importance of interventions addressing pain catastrophizing in adolescents with chronic pain for possibly preventing or limiting misguided pain medication use. Evidence supports the efficacy of psychological interventions for reducing catastrophizing in this population.[42] At a community level, implementing these and similar approaches in school settings could potentially help teach adolescents more adaptive pain coping skills. In support of this idea, school-based educational programs focusing on chronic pain have been shown to promote students' adaptive pain attitudes,[43] as well as both adaptive coping strategies and pain cognition changes.[44] However, the extent to which these interventions also prevent misguided medication use needs to be systematically studied.

Several limitations should be considered in the interpretation of the findings of this study. First, we used a cross-sectional design. This precludes any causal conclusions. Therefore, longitudinal studies examining the temporal sequences of changes in pain medication use and catastrophizing, which are a necessary condition to establish causal relationships, are needed to determine the direction of the effects. Second, the data for this study were collected from a convenience sample of children and adolescents from the community. Thus, the sample might or might not be representative of the population of youth with chronic pain, including both those receiving and those not receiving active pain treatment in pain clinics. Research is therefore needed to determine the generalizability of the study findings. Fourth, the definition of pain medication use in this study was fairly liberal (ie, one pain medication intake in the prior 3 months). Different findings might have emerged if the participants had needed to take more pain medications to be classified as pain medication users. In addition, assessing pain medication differently (for example, asking about frequency of pain medication intakes or number of intakes per month or week) could have resulted in different findings. Future research should include more precise ways of assessing pain medication intake, as different psychosocial factors could become relevant depending on the patients' characteristics (eg, being an episodic vs persistent pain medication user).

Despite the study's limitations, the findings provide new information that helps us to better understand the factors associated with more pain medication use in adolescents with chronic pain. The finding that pain catastrophizing predicted pain medication use over and above pain intensity and pain interference raises the possibility that adolescents with higher levels of pain catastrophizing could be using pain medications misguidedly. Research to examine the impact of interventions targeting pain catastrophizing on pain medication use is warranted.

Supplementary material

Supplementary material is available at *Pain Medicine* online.

Funding

This work was partly funded by grants from the Spanish Ministry of Economy, Industry and Competitiveness (RTI2018-09870-B-I00; RED2022-134869-T), the European Regional Development Fund (ERDF), and the Government of Catalonia (AGAUR; 2021SGR-730). E.S.-R.'s work is supported by a grant from the Spanish Ministry of Science and Innovation (PID2020-113869RA-I00). E.S.'s work is supported by a grant from the Spanish Ministry of Science and Innovation (MCIN/AEI/10.13039/501100011033). J.R.-J. is supported by a doctoral grant from MINECO (PRE2019-089283). J.M.'s work is supported by ICREA-Acadèmia. The Chair in Pediatric Pain is supported by Fundación Grünenthal.

Conflicts of interest: The authors declare no financial or other relationships that might lead to a conflict of interest related to this study.

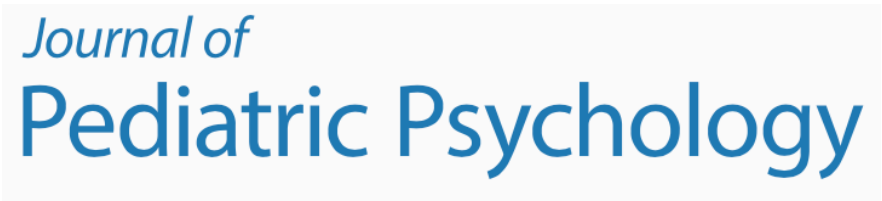
References

1. Gobina I, Villberg J, Välimaa R, et al. Prevalence of self-reported chronic pain among adolescents: evidence from 42 countries and regions. Eur J Pain. 2019;23(2):316-326.
2. Wager J, Brown D, Kupitz A, Rosenthal N, Zernikow B. Prevalence and associated psychosocial and health factors of chronic pain in adolescents: differences by sex and age. Eur J Pain. 2020;24(4):761-772.
3. Miró J, Roman-Juan J, Sánchez-Rodríguez E, Solé E, Castarlenas E, Jensen MP. Chronic pain and high impact chronic pain in children and adolescents: a cross-sectional study. J Pain. 2022;24(5):812-823.
4. Könning A, Rosenthal N, Friese M, Hirschfeld G, Brown D, Wager J. Factors associated with physician consultation and medication use in children and adolescents with chronic pain: a scoping review and original data. Eur J Pain. 2021;25(1):88-106.
5. Kaufman EL, Tress J, Sherry DD. Trends in medicalization of children with amplified musculoskeletal pain syndrome. Pain Med. 2017;18(5):825-831.
6. Eccleston C, Fisher E, Cooper TE, et al. Pharmacological interventions for chronic pain in children: an overview of systematic reviews. Pain. 2019;160(8):1698-1707.

7. Cooper TE, Fisher E, Anderson B, Willkinson N, Williams DG, Eccleston C. Paracetamol (acetaminophen) for chronic non-cancer pain in children and adolescents. Cochrane Database Syst Rev. 2017;(8):CD012539.
8. Eccleston C, Cooper TE, Fisher E, Anderson B, Willkinson N. Non-steroidal anti-inflammatory drugs (NSAIDs) for chronic non-cancer pain in children and adolescents (Review). Cochrane Database Syst Rev. 2017;(8):CD012537.
9. Perquin CW, Hazebroek-Kampschreur AAJM, Hunfeld JAM, van Suijlekom-Smit LWA, Passchier J, Van der Wouden JC. Chronic pain among children and adolescents: physician consultation and medication use. Clin J Pain. 2000;16(3):229-235.
10. Du Y, Ellert U, Zhuang W, Knopf H. Analgesic use in a national community sample of German children and adolescents. Eur J Pain. 2012;16(6):934-943.
11. Huguet A, Miró J. The severity of chronic pediatric pain: an epidemiological study. J Pain. 2008;9(3):226-236.
12. Elphinston RA, Sullivan MJL, Sterling M, et al. Pain medication beliefs mediate the relationship between pain catastrophizing and opioid prescription use in patients with chronic non-cancer pain. J Pain. 2022;23(3):379-389.
13. Severeijns R, Vlaeyen JWS, van den Hout MA, Picavet HSJ. Pain catastrophizing is associated with health indices in musculoskeletal pain: a cross-sectional study in the Dutch community. Health Psychol. 2004;23(1):49-57.
14. Martel MO, Wasan AD, Jamison RN, Edwards RR. Catastrophic thinking and increased risk for prescription opioid misuse in patients with chronic pain. Drug Alcohol Depend. 2013;132(1-2):335-341.
15. Sharifzadeh Y, Kao M-C, Sturgeon JA, Rico TJ, Mackey S, Darnall BD. Pain catastrophizing moderates relationships between pain intensity and opioid prescription. Anesthesiology. 2017;127(1):136-146.
16. Lazaridou A, Franceschelli O, Buliteanu A, Cornelius M, Edwards RR, Jamison RN. Influence of catastrophizing on pain intensity, disability, side effects, and opioid misuse among pain patients in primary care. J Appl Biobehav Res. 2017;22(1):1-13.
17. Beesdo K, Pine DS, Lieb R, Wittchen H-U. Incidence and risk patterns of anxiety and depressive disorders and categorization of generalized anxiety disorder. Arch Gen Psychiatry. 2010;67(1):47-57.
18. Merikangas KR, Nakamura EF, Kessler RC. Epidemiology of mental disorders in children and adolescents. Dialogues Clin Neurosci. 2009;11(1):7-20.
19. Könning A, Rosenthal N, Brown D, Stahlschmidt L, Wager J. Severity of chronic pain in German adolescent school students: a cross-sectional study. Clin J Pain. 2021;37(2):118-125.
20. Skrove M, Romundstad P, Indredavik MS. Chronic multisite pain in adolescent girls and boys with emotional and behavioral problems: The Young-HUNT study. Eur Child Adolesc Psychiatry. 2015;24(5):503-515.
21. Zernikow B, Wager J, Hechler T, et al. Characteristics of highly impaired children with severe chronic pain: A 5-year retrospective study on 2249 pediatric pain patients. BMC Pediatr. 2012;12(1):54.
22. Miró J, Roman-Juan J, Sánchez-Rodríguez E, Solé E, Castarlenas E, Jensen MP. Chronic pain and high impact chronic pain in children and adolescents: a cross-sectional study. J Pain.
23. Nugraha B, Gutenbrunner C, Barke A, et al.; IASP Taskforce for the Classification of Chronic Pain The IASP classification of chronic pain for ICD-11: Functioning properties of chronic pain. Pain. 2019;160(1):88-94.
24. de la Vega R, Racine M, Sánchez-Rodríguez E, et al. Pain extent, pain intensity, and sleep quality in adolescents and young adults. Pain Med. 2016;17(11):1971-1977.
25. Miró J, Gertz KJ, Carter GT, Jensen MP. Pain location and intensity impacts function in persons with myotonic dystrophy type 1 and facioscapulohumeral dystrophy with chronic pain. Muscle Nerve. 2014;49(6):900-905.
26. Miró J, De La Vega R, Tomé-Pires C, et al. Pain extent and function in youth with physical disabilities. J Pain Res. 2017;10:113-120.
27. Castarlenas E, Jensen MP, Baeyer V, Miró CL. J. Psychometric properties of the numerical rating scale to assess self-reported pain intensity in children and adolescents. Clin J Pain. 2017;33(4):376-383.
28. Wager J, Hechler T, Darlington AS, Hirschfeld G, Vocks S, Zernikow B. Classifying the severity of paediatric chronic pain—an application of the chronic pain grading. Eur J Pain. 2013;17(9):1393-1402.
29. Varni JW, Stucky BD, Thissen D, et al. PROMIS pediatric pain interference scale: an item response theory analysis of the pediatric pain item bank. J Pain. 2010;11(11):1109-1119.
30. Varni JW, Magnus B, Stucky BD, et al. Psychometric properties of the PROMIS® pediatric scales: precision, stability, and comparison of different scoring and administration options. Qual Life Res. 2014;23(4):1233-1243.
31. Quinn H, Thissen D, Liu Y, et al. Using item response theory to enrich and expand the PROMIS® pediatric self report banks. Health Qual Life Outcomes. 2014;12:160.
32. Crombez G, Bijttebier P, Eccleston C, et al. The child version of the Pain Catastrophizing Scale (PCS-C): a preliminary validation. Pain. 2003;104(3):639-646.
33. Solé E, Castarlenas E, Miró J. A Catalan adaptation and validation of the Pain Catastrophizing Scale for children. Psychol Assess. 2016;28(6):e119-e126.
34. Kutner MH, Nachtsheim CJ, Neter J. Applied linear regression models. Boston: McGraw-Hill; 2005.
35. Arteta J, Cobos B, Hu Y, Jordan K, Howard K. Evaluation of how depression and anxiety mediate the relationship between pain catastrophizing and prescription opioid misuse in a chronic pain population. Pain Med (United States). 2016;17(2):295-303.
36. Hah JM, Sturgeon JA, Zocca J, Sharifzadeh Y, Mackey SC. Factors associated with prescription opioid misuse in a cross-sectional cohort of patients with chronic non-cancer pain. J Pain Res. 2017;10:979-987.
37. Martel MO, Edwards RR, Jamison RN. The relative contribution of pain and psychological factors to opioid misuse: a 6-month observational study. Am Psychol. 2020;75(6):772-783.
38. Morasco BJ, Turk DC, Donovan DM, Dobscha SK. Risk for prescription opioid misuse among patients with a history of substance use disorder. Drug Alcohol Depend. 2013;127(1-3):193-199.
39. Groenewald CB, Wright DR, Palermo TM. Health care expenditures associated with pediatric pain-related conditions in the United States. Pain. 2015;156(5):951-957.
40. Andersen A, Holstein BE, Due P, Holme Hansen E. Medicine use for headache in adolescence predicts medicine use for headache in young adulthood. Pharmacoepidemiol Drug Saf. 2009;16:228-228.
41. Rasu RS, Vouthy K, Crowl AN, et al. Cost of pain medication to treat adult patients with nonmalignant chronic pain in the United States. J Manag Care Spec Pharm. 2014;20(9):921-928.
42. Fisher E, Law E, Dudeney J, Palermo TM, Stewart G, Eccleston C. Psychological therapies for the management of chronic and recurrent pain in children and adolescents. Cochrane Database Syst Rev. 2018;(9):CD003968.
43. Martí L, Castarlenas E, Solé E, de la Vega R, Miró J. Video-based pain education in schools: a study with adolescents. Clin J Pain. 2021;37(3):199-205.
44. Mittinty MM, Vanlint S, Stocks N, Mittinty MN, Moseley GL. Exploring effect of pain education on chronic pain patients' expectation of recovery and pain intensity. Scand J Pain. 2018;18(2):211-219.

4.9. Study IX

Adverse childhood events and chronic pain in adolescents: the role of sleep disturbance.



Journal of Pediatric Psychology, 2023, **00**, 1–9
https://doi.org/10.1093/jpepsy/jsad063
Original Research Article

OXFORD

Adverse Childhood Events and Chronic Pain in Adolescents: The Role of Sleep Disturbance

Josep Roman-Juan [1,2] MSc, Ester Solé,[1,2] PhD, Elisabet Sánchez-Rodríguez [1,2] PhD, Elena Castarlenas,[1,2] PhD, Mark P. Jensen,[3] PhD, and Jordi Miró [1,2,*] PhD

[1]Universitat Rovira i Virgili, Spain
[2]Department of Psychology, Unit for the Study and Treatment of Pain—ALGOS, Research Center for Behavior Assessment (CRAMC), Spain
[3]Department of Rehabilitation Medicine, University of Washington, USA

*All correspondence concerning this article should be addressed to Jordi Miró, PhD, Departament de Psicología, Universitat Rovira i Virgili, Carretera de Valls, s/n, 43007 Tarragona, Spain. E-mail: jordi.miro@urv.cat

Abstract

Objectives: This study aimed to (1) examine the extent to which the association between exposure to adverse childhood events (ACEs) and having chronic pain in adolescents is explained by the association between exposure to ACEs and sleep disturbance and (2) explore the role of sleep disturbance in the association between exposure to ACEs and anxiety and depressive symptoms in adolescents with chronic pain.

Methods: Cross-sectional data from 469 adolescents aged 13–18 years old were drawn from an epidemiological study on pediatric chronic pain conducted in Catalonia (Spain). Participants provided self-reports of demographic characteristics, exposure to ACEs, pain characteristics, sleep disturbance, anxiety, and depressive symptoms. Mediation and moderation models were conducted.

Results: Sleep disturbance explained a significant amount of the variance in the association between exposure to ACEs and the presence of chronic pain. Moreover, sleep disturbance explained a significant amount of the variance in the association between exposure to ACEs and depressive symptoms and moderated the association between exposure to ACEs and anxiety in adolescents with chronic pain.

Conclusion: The study findings suggest the possibility that addressing sleep disturbance in adolescents exposed to ACEs may help to prevent the development of chronic pain, anxiety, and depressive symptoms in those adolescents who already have chronic pain.

Keywords: adolescents; adverse childhood events; anxiety; chronic pain; depressive symptoms; sleep disturbance.

Introduction

Adverse childhood events (ACEs) refer to a wide range of experiences (e.g., abuse, neglect, household dysfunction) that occur before the age of 18 years and can exert a significant negative impact on the individual (Centers for Disease Control and Prevention, 2019). Research indicates that ACEs are prevalent in the general population (Gilbert et al., 2015; Merrick et al., 2018), with nearly half of children and adolescents being exposed to one or more ACE during their childhood (Bethell et al., 2014; Crouch et al., 2019).

Research has shown that children and adolescents who have been exposed to ACEs have twice the rates of chronic pain, compared to those with no reported ACEs, with this association increasing in a graded dose–response fashion (Groenewald et al., 2020). Groenewald and colleagues (2020) recommended that future research should seek to identify the mechanisms that might explain this association. Specifically, they suggested that posttraumatic stress symptoms such as sleep disturbance—which along with hypervigilance, constitutes one of the four symptom clusters utilized to diagnose posttraumatic stress disorder (American Psychiatric Association, 2013)—could serve as potential mediators of the association between exposure to ACEs and chronic pain. This hypothesis aligns with a conceptual model proposing that posttraumatic stress symptoms, including sleep disturbance, could potentially lead to the development of chronic pain by increasing pain sensitivity and decreasing the child's ability to cope adaptively with pain (Holley et al., 2016). Furthermore, research has shown that exposure to trauma is associated with a generalized state of physiological and neurobiological hyperarousal that contributes to the development of sleep disturbance (Riemann et al., 2010; Sinha, 2016). Also, there is mounting research suggesting that sleep problems are a reliable predictor of chronic pain in children and adolescents (for a review see, Finanet al., 2013).

On the other hand, research has shown that a history of exposure to ACEs is not a reliable predictor of pain-related outcomes, including pain intensity and pain interference, in youth with chronic pain (Nelson et al., 2017, 2018, 2021). However, exposure to ACEs has been shown to be associated with psychological symptoms such as anxiety and depressive symptoms in this population in both cross-sectional (Nelson et al., 2018) and longitudinal studies (Nelson et al., 2021). In addition, these associations have been found to be moderated by posttraumatic stress symptoms. For example, in one study, Nelson et al. (2021) found that the association between exposure to ACEs and anxiety and depressive symptoms was exacerbated by the child's posttraumatic stress symptoms in a sample of children with chronic pain. However, the specific role of sleep disturbance in the relationship between exposure to ACEs and anxiety and depressive symptoms in youth with chronic pain has yet to be determined.

Given that sleep disturbance is a modifiable consequence of ACEs, it would be important to examine how these factors

Received: May 22, 2023. **Revised:** September 7, 2023. **Accepted:** September 8, 2023

interact in order to understand the association between ACEs and chronic pain, as well as between a history of exposure to ACEs and anxiety and depressive symptoms in youth with chronic pain. This knowledge could aid in reducing the risk of developing chronic pain—which is a highly prevalent condition among children and adolescents worldwide (Gobina et al., 2019; Roy et al., 2021)—and preventing anxiety and depressive symptoms in youth with chronic pain who have been exposed to ACEs.

Given these considerations, the current study had two aims. First, we sought to determine the extent to which sleep disturbance indirectly explained the association between the number of ACEs and chronic pain in adolescents. Based on the conceptual model developed by Holley et al. (2016), research showing a higher prevalence of chronic pain and sleep disturbance in children and adolescents exposed to ACEs compared to those who are not exposed to ACEs (Groenewald et al., 2020; Wang et al., 2016), and research consistently showing a positive association between sleep disturbance and the development chronic pain in children and adolescents (Finan et al., 2013), we hypothesized that sleep disturbance would explain a significant amount of the variance in the association between the number of ACEs and the presence of chronic pain. Second, we sought to determine the extent to which the severity of sleep disturbance indirectly explained the associations between the number of ACEs and anxiety and depressive symptoms in adolescents with chronic pain. Given the data showing that posttraumatic stress symptoms mediate the exposure to trauma and pain-related outcomes in adults with chronic low back pain (Pegram et al., 2017) and that posttraumatic stress symptoms moderate the association between exposure to ACEs and anxiety and depressive symptoms in adolescents with chronic pain (Nelson et al., 2021), we explored two alternative models: (1) that sleep disturbance severity would explain a significant amount of the variance of the positive association between the number of ACEs and both anxiety and depressive symptoms and (2) that sleep disturbance would moderate the association between the number of ACEs and both anxiety and depressive symptoms, such that those with a higher score on a measure of sleep disturbance would evidence a stronger association between the number of ACEs and anxiety and depressive symptoms than those with a lower score on a measure of sleep disturbance.

Methods

Study Design and Participants

This cross-sectional study uses data from the initial assessment of a sample of children and adolescents participating in the EPIDOL project, an ongoing epidemiological study of pain in children and adolescents conducted in the Southeast of Catalonia (Miró et al., 2023). This project was designed to determine the factors contributing to the development and maintenance of chronic pain in children and adolescents. In addition, although the study did not focus specifically on posttraumatic stress disorders, data on ACEs and sleep disturbance were also collected.

Inclusion criteria for the current study were as follows: (1) being at least 13 years old and (2) being able to read, write, and speak Spanish. Exclusion criteria were having any cognitive impairment that would limit the ability to participate. The rationale for including youth aged 13 years old or older is that the measure of ACEs used in this study was designed to be used by individuals aged 13–19 years old.

In total, 469 schoolchildren 13 years old or older took part in the EPIDOL project, and this is the sample of participants that provided data for this study.

Procedure

Data for the current analyses were collected between February and June of 2022 at 20 schools located at the Southeast of Catalonia, representing 67% of the total number of schools initially approached ($n = 30$). All parents of schoolchildren aged between 8 and 18 attending these schools ($N = 5{,}328$) were sent a letter explaining the EPIDOL project and asked to provide consent for their child to participate. In total, 1,721 parents agreed that their children could participate in the study. Of these, 1,564 schoolchildren provided complete or mostly complete data (see Roman-Juan et al., 2023 for a detailed description of the whole sample). Participating students received a gym sack and a calendar for their participation (approximate value = €3 each). As noted previously, only those aged 13 years old or older, whose parents provided consent, took part in the study; the total sample size of participants in this study is $N = 469$. Data were obtained using a paper-and-pencil survey that was administered during the school day. The ethics committee of the Universitat Rovira i Virgili approved the study (*Institut d'Investigació Sanitària Pere Virgili*; ref.: 136/2018).

Measures

Demographic Variables

All participants were asked to provide information about their age and biological sex at birth.

Chronic Pain and Pain Intensity

The presence/absence of chronic pain and (for those with chronic pain) average pain intensity was assessed using the first and second items of the pediatric version of the Graded Chronic Pain Scale-Revised (Von Korff et al., 2020), recently adapted and validated in a sample of children and adolescents (Roman-Juan et al., 2023). The first item asks individuals, "In the past 3 months, how many times did you have pain?" with response options "Never," "Some days," "Most days," and "Every day." Following the procedure described by Roman-Juan et al. (2023), a participant was considered to have chronic pain if they reported pain most days or every day. The second item asks participants to rate the intensity of their average pain in the past 7 days by asking them, "On average, which number best describes your pain?" with response options ranging from 0 = *No pain* to 10 = *A lot of pain*.

Adverse Childhood Experiences

Adverse childhood experiences were assessed using the Center for Youth Wellness Adverse Childhood Experiences Questionnaire Teen Self-Report (CYW ACE-Q Teen SR; Purewal et al., 2016). With this questionnaire, respondents are asked to indicate the number of times they have been exposed to 19 events at any point since they were born. In order to maintain consistency with previous research that has assessed ACEs in the general youth population (Groenewald et al., 2020), in this study, we used nine items that included: (1) "Your parents or guardians were separated or divorced;" (2) "You lived with a household member who served time in

jail or prison;" (3) "You lived with a household member who was depressed, mentally ill or attempted suicide;" (4) "You saw or heard household members hurt or threaten to hurt each other;" (5) "A household member swore at, insulted, humiliated, or put you down in a way that scared you or a household member acted in a way that made you afraid that you might be physically hurt;" (6) "More than once, you went without food, clothing, a place to live, or had no one to protect you;" (7) "You lived with someone who had a problem with drinking or using drugs;" (8) "You have lived with a parent or guardian who died;" and (9) "You have often been treated badly because of race, sexual orientation, place of birth, disability or religion." Following the procedure described by Nelson et al. (2021), we modified the original questionnaire in such a way that all ACEs were categorized as binary (Yes/No). A total score ranging from 0 to 9 was then computed by summing all the positive responses, which reflected the number of ACEs experienced by each participant. We used the Spanish version of the CYW ACE-Q Teen SR available at https://centerforyouthwellness.org/aceq-pdf/.

Sleep Disturbance

Sleep disturbance was assessed using the Spanish version of the 4-item PROMIS pediatric Sleep Disturbance short form V1.0. With this form, respondents are asked to indicate how often they experienced four different sleep issues over the past 7 days using a 5-point Likert scale (1 = "Never," 2 = "Almost never," 3 = "Sometimes," 4 = "Often," 5 = "Almost always"). Sample items are "I had difficulty falling asleep" and "I slept through the night" (negatively scored). Raw scores are transformed to T-scores, with a mean of 50 points and an *SD* of 10 in the normative sample. Higher scores reflect more frequent sleep disturbance. Pediatric PROMIS measures have been shown to provide valid and reliable information in individuals aged 8–17 years (Varni et al., 2014). The internal consistency of the scores of this short form in the sample of adolescents as a whole was good (Cronbach's alpha = .89) and in the group of adolescents with chronic pain was excellent (Cronbach's alpha = .90).

Anxiety and Depressive Symptoms

Anxiety and depressive symptoms were assessed using the Spanish versions of the 4-item Anxiety and Depression scales from the PROMIS Pediatric-25 Profile Form v.2. With these forms, respondents are asked to indicate how often they experienced different anxiety and depressive symptoms over the past 7 days using a 5-point Likert (1 = *Never*, 2 = *Almost never*, 3 = *Sometimes*, 4 = *Often*, 5 = *Almost always*). Sample items from the Anxiety short form include "I felt like something awful might happen" and "I felt nervous." Sample items from the Depression short form include "I felt everything in my life went wrong" and "I felt lonely." Raw scores are transformed to T-scores with a mean of 50 points and an *SD* of 10 in the normative sample. Higher scores on these measures reflect more frequent anxiety and depressive symptoms, respectively. Pediatric PROMIS measures have been shown to provide valid and reliable information in individuals aged 8–17 years (Varni et al., 2014). The internal consistency of the scores of the Anxiety and Depression short forms for the group of adolescents with chronic pain was good (Cronbach's alphas = .84 and .88, respectively).

Data Analysis

For descriptive purposes, categorical variables were described using frequency statistics, while mean values and *SD*s were calculated for continuous variables. Before conducting the planned analyses, the normality of the distributions of the study variables (i.e., skewness and kurtosis) was evaluated. No violations of normality were identified. We then computed and examined the associations between key variables to justify their inclusion in mediation analyses. Specifically, before testing the study hypothesis, independent samples *t*-tests were computed to evaluate differences in the number of ACEs and sleep disturbance between adolescents with and without chronic pain, and a bivariate Pearson correlation was computed to evaluate the association between the number of ACEs and sleep disturbance using the sample of adolescents as a whole. In addition, before addressing the second study aim, bivariate Pearson correlations were computed to evaluate the associations between the number of ACEs, sleep disturbance, anxiety, and depressive symptoms in the group of adolescents with chronic pain. T-tests, chi-square tests, and bivariate Pearson correlations were also used to assess differences in key outcome variables as a function of sociodemographic variables (i.e., sex and age) and pain intensity.

Although mediation models were tested, it is important to keep in mind that the data used for these analyses are cross-sectional. Thus, we were unable to test for true mediation (i.e., that the impacts of a predictor variable on a criterion variable are explained by the impacts of that variable on a mediator). Instead, in this study, we used mediation analyses to determine if the (concurrent) association between the number of ACEs and the three study criterion variables is explained by the associations between the number of ACEs and the severity of sleep disturbance. A positive finding would support the possibility of true mediation, but not confirm it.

To test the first study hypothesis, one mediation analysis was conducted using the whole sample of adolescents to estimate the total, direct, and specific indirect associations between the number of ACEs and the presence of chronic pain explained by sleep disturbance. In this model, the number of ACEs was introduced as a continuous independent variable, the presence of chronic pain was introduced as a binary-coded dependent variable (i.e., yes/no), and sleep disturbance as a continuous mediator variable.

To address the second study aim, for both key dependent variables (i.e., anxiety and depressive symptoms), two mediation and two moderation analyses were conducted with the group of adolescents with chronic pain. In all models, the number of ACEs was introduced as an independent continuous variable and anxiety and depressive symptoms as dependent continuous variables. Sleep disturbance was introduced as a continuous mediator variable in all mediation models and as a continuous moderator variable in all moderation models. Mediation analyses estimated the total, direct, and specific indirect associations between the number of ACEs and anxiety and depressive symptoms explained by sleep disturbance. Moderation analyses examined whether the variable sleep disturbance moderates the associations between ACEs and anxiety and depressive symptoms. In order to interpret any interaction effect emerging as significant, we planned to use the simple slopes analysis technique recommended by Hayes and Rockwood (2017). This approach involves computing regression lines that depict the effect of the independent

variable (i.e., ACEs) on the dependent variable (i.e., anxiety and depressive symptoms) at different levels of the moderator variable (i.e., sleep disturbance). In mediation analyses, bootstrapping methods with $n = 10{,}000$ resamples were used to estimate the 95% confidence intervals of the indirect effects. Indirect effects were considered significant if the 95% confidence interval did not cross zero. In moderation analyses, a two-tailed significance level of $p < .05$ was defined as statistically significant. Pair-wise deletion was used for all analyses. Adequacy of the chronic pain sample size for the planned analyses was examined using a post hoc power analysis in a statistical power analysis program (G*power; Erdfelder et al., 1996). This power analysis was based on the observed sample size, observed effect size, and alpha level (i.e., 0.05) used in the study.

All analyses were conducted using the Statistical Package for the Social Sciences (SPSS), version 28. Mediation and moderation models were tested using the PROCESS macro v.4.2 for SPSS developed by Hayes (http://afhayes.com/introduction-to-mediation-moderation-and-conditional-process-analysis.html).

Availability of the Data

Data available on request.

Results

Sample Characteristics

Characteristics of the study sample are presented in Table I. As can be seen, the sample included a greater number of girls than boys, and the mean age of participants was 14.28 years ($SD = 1.74$; age range = 13–18). Among all participants, 56% ($N = 263$) reported that they had experienced at least one ACE and 19% ($N = 88$) reported having chronic pain. There were no significant differences as a function of sex ($\chi^2(1) = 2.72$, $p = .099$) and age between participants with chronic pain and participants without chronic pain ($t(467) = 0.88$, $p = .380$). Therefore, in the mediation model with chronic pain as the dependent variable, we did not control for participants' sex and age. Participants with chronic pain reported statistically significantly higher levels of anxiety ($t(463) = 3.94$, $p < .001$) and depressive symptoms ($t(464) = -4.29$, $p < .001$) compared to participants without chronic pain.

Participants in the chronic pain group reported an average level of pain intensity over the past 7 days of 5.82/10 ($SD = 1.97$), and 73% ($n = 63$) reported that they had experienced at least one ACE ($M = 1.58$; $SD = 1.52$). Girls reported more anxiety ($M = 50.77$, $SD = 11.19$ vs $M = 61.68$, $SD = 10.38$, $t(84) = -4.81$, $p = < .001$) and depressive symptoms ($M = 51.55$, $SD = 12.03$ vs $M = 63.90$, $SD = 10.18$, $t(85) = -4.81$, $p = < .001$) than boys. Participants' age and pain intensity were not significantly associated with anxiety (age: $r(84) = .08$, $p = .450$; pain intensity: $r(84) = .15$, $p = .163$) or depressive symptoms (age: $r(85) = .16$, $p = .145$; pain intensity: $r(85) = .09$, $p = .392$). Therefore, the mediation and moderation models with anxiety and depressive symptoms as dependent variables only controlled for the participants' sex.

The adequacy of the chronic pain sample size for the planned analyses was confirmed. For both outcomes (i.e., anxiety and depressive symptoms), power analysis yielded a very high level of power (.99), indicating that the sample size of the chronic pain subsample was adequate to detect significant effects with a high degree of confidence.

Bivariate Associations Between the Number of ACEs, Sleep Disturbance, and Chronic Pain

Adolescents with chronic pain reported a greater number of ACEs compared to those without chronic pain ($t(467) = -3.05$, $p = .002$). Adolescents with chronic pain reported

Table I. Characteristics of the Entire Sample of Adolescents, the Subsample of Adolescents Without Chronic Pain, and the Subsample of Adolescents With Chronic Pain

	Study Sample ($n = 469$)				Adolescents Without Chronic Pain ($n = 381$)				Adolescents With Chronic Pain ($n = 88$)			
Variable (Range)	N	%	M	SD	N	% within subsample	M	SD	N	% within subsample	M	SD
Sex identified at birth												
Male	202	43			171	45			31	35		
Female	267	57			210	55			51	65		
Age (range, 13–18)	469		14.28	1.74	381		14.32	1.76	88		14.14	1.69
Anxiety symptoms (PROMIS; range, 36–80)	465[a]		53.47	11.33	379[b]		52.50	11.00	86[c]		57.75	11.85
Depression symptoms (PROMIS; range, 38–79)	466[d]		54.71	11.74	379[b]		53.62	11.33	87[e]		59.50	12.33
Sleep disturbance (PROMIS; range, 39–79)	464[f]		57.12	11.97	377[g]		55.70	11.52	87[e]		63.24	11.99
History of ACEs												
Yes	263	56			200	52			63	72		
No	206	44			181	48			25	28		
Number of ACEs (CYW-ACE-Q Teen SR; range, 0–7)	469		1.17	1.42	381		1.07	1.38	88		1.58	1.52
Pain intensity (range, 0–10)	466[a]		3.68	2.47	378[h]		3.27	2.27	88		5.82	1.97

Note. Sample size varies due to non-responses. *PROMIS* = Patient-Reported Outcomes Measurement Information System pediatric measure; *CYW-ACE-Q Teen SR* = Center for Youth Wellness Adverse Childhood Experiences Questionnaire Teen Self-Report.
[a] $n = 465$ (missing = 4).
[b] $n = 379$ (missing = 2).
[c] $n = 86$ (missing = 2).
[d] $n = 466$ (missing = 3).
[e] $n = 87$ (missing = 1).
[f] $n = 464$ (missing = 5).
[g] $n = 377$ (missing = 4).
[h] $n = 378$ (missing = 3).

greater sleep disturbance than those without chronic pain ($t(462) = 5.46$, $p < .001$). The number of ACEs and sleep disturbance were positively and significantly associated ($n = 464$, $r = .318$, $p < .001$).

Bivariate Correlations Between the Number of ACEs, Sleep Disturbance, Anxiety, and Depressive Symptoms in Adolescents With Chronic Pain

Table II presents the bivariate Pearson correlations between key variables and dependent variables. As can be seen, among participants with chronic pain, the number of ACEs and sleep disturbance were positively and significantly associated with anxiety and depressive symptoms. The number of ACEs was also positively and significantly correlated with sleep disturbance.

Association Between the Number of ACEs and Chronic Pain Explained by Sleep Disturbance

Table III presents the results of the mediation analysis examining total, direct, and specific indirect associations between the number of ACEs and chronic pain explained by sleep disturbance. In this analysis, the *a* coefficient denotes the association between the number of ACEs and sleep disturbance; the *b* coefficient denotes the association between sleep disturbance and having chronic pain; the *c* coefficient denotes the association between the number of ACEs and having chronic pain without the inclusion of the mediator variable (i.e., total association); and the *c'* coefficient denotes the association between the number of ACEs and having chronic pain after the mediator variable was included in the model (i.e., direct effect). The product-of-coefficients (*a*b*) were calculated using bootstrapping methods ($n = 10{,}000$ bootstrap resamples) in order to estimate the indirect association between the number of ACEs and having chronic pain explained by sleep disturbance.

Table II. Bivariate Correlations Between Key Variables in the Sample of Adolescents With Chronic Pain (N = 88)

	1.	2.	3.	4.
1. Number of ACEs	–			
2. Sleep disturbance	.25*	–		
	$n = 87$			
3. Anxiety symptoms	.30**	.39***	–	
	$n = 86$	$n = 85$		
4. Depressive symptoms	.34**	.55***	.62***	–
	$n = 87$	$n = 86$	$n = 86$	

* $p < .05$, ** $p < .01$, *** $p < .001$.

Table III. Results of the Tested Association Between the Number of ACEs and Chronic Pain Explained by Sleep Disturbance Using the Whole Sample of Adolescents

Model	*B*	*SE*	*t/z*	*p*	PCI (LL)	PCI (UL)
Chronic pain						
Number of ACEs → sleep disturbance (*a*)	2.66	0.37	7.21	<.001	1.96	3.39
Sleep disturbance → chronic pain (*b*)	0.06[a]	0.01	5.12	<.001	0.03	0.08
Number of ACEs → chronic pain (*c*)	0.23[a]	0.08	2.97	.003	0.08	0.04
Number of ACEs → chronic pain (*c'*)	0.11[a]	0.08	1.28	.20	−0.06	0.27
Number of ACEs → sleep disturbance → chronic pain (*a * b*)	0.14[a]	0.04			0.07	0.22

Note. *N* for analysis is 464 cases. Number of ACEs was the independent variable. Chronic pain was the dependent variable. Sleep disturbance was the mediator variable. *PCI (LL)* = lower limit of a 95% percentile confidence interval; *PCI (UL)* = upper limit of a 95% percentile confidence interval.
[a] Regression coefficients are on a log-odds metric.

As can be seen, the findings support a mediation model in which sleep disturbance explained a significant amount of the association between the number of ACEs and having chronic pain ($n = 464$, $B = 0.14$, $SE = 0.01$, 95% percentile confidence interval [PCI] = 0.07–0.22). After including sleep disturbance in the model, the association between the number of ACEs and having chronic pain (i.e., direct effect) became nonsignificant, hence consistent with the conclusion that the association between both variables is explained by sleep disturbance.

Association Between the Number of ACEs and Anxiety and Depressive Symptoms Explained by Sleep Disturbance in Adolescents With Chronic Pain

Table IV shows two separate analyses examining total, direct, and specific indirect associations between the number of ACEs and anxiety and depressive symptoms, respectively, explained by sleep disturbance while controlling for adolescents' sex. As can be seen, the results did not support the mediation model in which sleep disturbance explained the association between the number of ACEs and anxiety in adolescents with chronic pain. However, support for a model in which sleep disturbance explained the association between the number of ACEs and depressive symptoms in adolescents with chronic pain was found ($n = 84$, $B = 0.845$, $SE = 0.330$, 95% PCI = 0.262–1.550). After including sleep disturbance in the model, the association between the number of ACEs and depressive symptoms (i.e., direct effect) became nonsignificant, hence consistent with the conclusion that the association between both variables is explained by sleep disturbance.

Sleep Disturbance as a Moderator of the Association Between the Number of ACEs and Anxiety and Depressive Symptoms in Adolescents With Chronic Pain

Two separate models were conducted to test whether sleep disturbance moderates the association between the number of ACEs and anxiety and depressive symptoms while controlling for adolescents' sex. For anxiety symptoms, results indicated that the interaction effect of the number of ACEs × sleep disturbance was statistically significant ($n = 83$, $t = 2.29$, $SE = 0.06$, $p = .003$). The simple slopes analysis was conducted to better understand the significant interaction. This analysis revealed that the positive association between the number of ACEs and anxiety symptoms was statistically significant specifically for those adolescents with levels of sleep disturbance $\geq 1SD$ above the mean ($\beta = 0.63$, $t = 3.13$, $p = .008$). However, for adolescents with sleep disturbance levels $\leq 1SD$ below the mean ($\beta = -0.38$, $t = 1.98$, $p = .065$) and those with a mean sleep disturbance ($\beta = 0.21$, $t = 1.57$ $p = .122$), this association was not statistically significant (see

Table IV. Results of the Tested Associations Between the Number of ACEs and Anxiety and Depressive Symptoms Explained by Sleep Disturbance in the Sample of Adolescents With Chronic Pain

Model	*B*	*SE*	*t*	*p*	PCI (LL)	PCI (UL)
Anxiety symptoms						
Number of ACEs → sleep disturbance (*a*)	1.61	0.80	2.02	.045	0.02	3.19
Sleep disturbance → anxiety symptoms (*b*)	0.22	0.10	2.17	.033	0.02	0.42
Number of ACEs → anxiety symptoms (*c*)	1.87	0.75	2.51	.014	0.39	3.36
Number of ACEs → anxiety symptoms (*c′*)	1.52	0.75	2.03	.045	0.03	3.01
Number of ACEs → sleep disturbance → anxiety symptoms (*a*b*)	0.35	0.23			−0.02	0.87
Depressive symptoms						
Number of ACEs → sleep disturbance (*a*)	1.98	0.81	2.44	.017	0.36	3.60
Sleep disturbance → depressive symptoms (*b*)	0.43	0.09	4.66	<.001	0.24	0.61
Number of ACEs → depressive symptoms (*c*)	1.79	0.75	2.40	.019	0.031	3.28
Number of ACEs → depressive symptoms (*c′*)	0.95	0.69	1.37	.173	−0.42	2.32
Number of ACEs → sleep disturbance → depressive symptoms (*a * b*)	0.84	0.33			0.26	1.55

Note. *N* for analysis is 83 cases for models including anxiety symptoms and 84 for models including depressive symptoms. The number of ACEs was the independent variable in all models. Anxiety and depressive symptoms were the dependent variables. Sleep disturbance was the mediator variable in all models. PCI (LL) = lower limit of a 95% percentile confidence interval; PCI (UL) = upper limit of a 95% percentile confidence interval.

Figure 1). For depressive symptoms, the data indicated that the number of ACEs × sleep disturbance interaction effect was not statistically significant ($n = 84$, $t = 0.02$, $SE = 0.07$, $p > .05$).

Discussion

This study used a sample of adolescents recruited from the community to examine the role of sleep disturbance—one of the symptoms used to diagnose posttraumatic stress disorders (American Psychiatric Association, 2013)—in the association between exposure to ACEs and the presence of chronic pain, as well as in the association between exposure to ACEs and anxiety and depressive symptoms in adolescents with chronic pain.

The results indicated that more than a half of the entire sample reported having been exposed to ACEs, with more than 70% of the subsample with chronic pain reporting at least one ACE during their childhood. These findings are consistent with previous research examining the prevalence of ACEs and chronic pain in the general youth population (Groenewald et al., 2020; Mansuri et al., 2020). For example, Groenewald et al. (2020), using data from the National Survey of Children's Health conducted in United States, found parental reports of ACE exposure in 50% of children, whereas in those with chronic pain, parents reports about ACE exposure went to over 70% of cases. The high rates of ACEs among adolescents with chronic pain found in this study are also consistent with those reported in clinical samples of youth with chronic pain (Nelson et al., 2018; Nelson & Logan, 2018).

Consistent with the study hypothesis, we also found that sleep disturbance explained a significant amount of the variance in the association between the number of ACEs and the presence of chronic pain in adolescents. This is consistent with prior studies showing a higher prevalence of sleep disturbance in adolescents exposed to ACEs (Wang et al., 2016). In addition, this finding provides empirical support to a conceptual model highlighting the role of sleep disturbance has in the context of posttraumatic stress symptoms and the development of chronic pain in youth (Holley et al., 2016). If this finding is replicated in longitudinal prospective studies, it would raise the possibility that sleep disturbance could be playing a significant role in the development of chronic pain in adolescents who have been exposed to ACEs. Such a finding would support the need for interventions targeting sleep disturbance in adolescents who have experienced ACEs, as a potential strategy to decrease the risk for developing chronic pain in this population.

The study findings are also consistent with previous cross-sectional and longitudinal studies that have reported a significant positive association between the exposure to ACEs and anxiety and depressive symptoms in clinical samples of youth with chronic pain (Nelson et al., 2018, 2021) and extend these findings to children with chronic pain living in the community. Furthermore, the results of this study build upon those reported by Nelson et al. (2021) who found that posttraumatic stress-related symptoms exacerbated the effects of ACEs on anxiety and depressive symptoms and extend them by highlighting the specific role of sleep disturbance in these associations. Specifically, we found that sleep disturbance moderated the association between the number of ACEs and anxiety; that is, the association between the number of ACEs and anxiety was stronger in adolescents with chronic pain that presented higher levels of sleep disturbance compared to those with low levels. Furthermore, we found that sleep disturbance concurrently mediated the association between the number of ACEs and depressive symptoms, hence suggesting the possibility that that sleep disturbance could be playing a significant role in the development of depressive symptoms in adolescents with chronic pain who have been exposed to ACEs. This is consistent with research showing that sleep disturbance (e.g., insomnia) is a consistent predictor of the development of depression (Baglioni et al., 2011) and that the prevalence of sleep disturbance among adolescents exposed to ACEs is higher than in those with no ACEs exposure (Wang et al., 2016).

The study findings, when considered in light of those reported by prior studies (Noel et al., 2018; Pavlova et al., 2020), provide additional evidence of the need to address sleep disturbance in youth with chronic pain who have been exposed to ACEs and who may therefore experience posttraumatic stress symptoms. For example, Noel et al. (2018) and Pavlova et al. (2020) found that sleep disturbance mediated

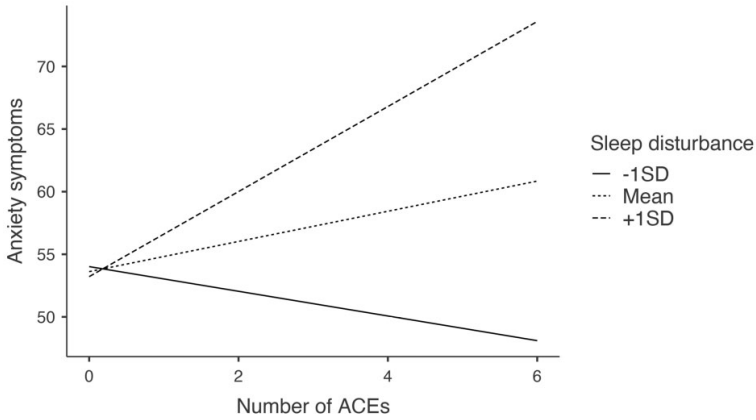


Figure 1. Sleep disturbance as a significant moderator in the association between the number of ACEs and anxiety symptoms in the sample of adolescents with chronic pain. *ACE* = adverse childhood event.

the association between posttraumatic stress symptoms and pain intensity and pain interference in clinical samples of children with chronic pain using cross-sectional and longitudinal data, respectively. Although cross-sectional and longitudinal studies have not found a significant association between the exposure to ACEs and pain-related outcomes in youth with chronic pain (e.g., pain intensity, pain interference; Nelson et al., 2017, 2018, 2021), these studies have found a significant association between exposure to ACEs and anxiety and depressive symptoms in children with chronic pain. This could explain, at least in part, the association between sleep disturbance and chronic pain-related disability (Pavlova et al., 2017). For example, an abundance of research has demonstrated statistically significant associations between measures of psychological dysfunction and pain presence, pain severity, and pain-related disability in youth with chronic pain (Gauntlett-Gilbert & Eccleston, 2007; Kashikar-Zuck et al., 2008; Könning et al., 2021; Huguet & Miró, 2008; Wager et al., 2020). Therefore, as speculated by Nelson et al. (2018), exposure to ACEs could potentially indirectly contribute to the maintenance of chronic pain and pain-related disability through its effects on internalizing mental health problems, which in turn could be influenced by posttraumatic stress symptoms and, specifically, sleep disturbance. Again, longitudinal research that evaluates these possibilities is warranted.

The study has a number of important limitations that should be considered when interpreting the findings. First, this study used cross-sectional data which precludes drawing causal conclusions regarding the associations between the study variables. For example, it is possible that sleep disturbance is a component or manifestation of chronic pain and other psychological symptoms (e.g., anxiety and depressive symptoms) rather than a factor that contributes to the development or maintenance of anxiety and depression. At the same time, and given the cross-sectional nature of the study, the possibility that exposure to ACEs could contribute to elevated anxiety and depressive symptoms, which could in turn impact sleep in adolescents with chronic pain, should be considered. In any case, because the results of the mediation analyses using cross-sectional data cannot be used to test actual (causal) mediation (Maxwell et al., 2011), the current findings can help identify associations that warrant further examination to determine causal relationships in future longitudinal studies. Second, all of the study variables were assessed with self-reported measures. This may have artificially increased the estimates of the associations among the variables through shared method variance. Future research should use additional strategies to assess study variables when possible. For example, diagnostic clinical interviews could be used to assess anxiety and depressive symptoms and objective assessment approaches (e.g., actigraphy; Pavlova et al., 2020) could be used to assess activity level. Additionally, although self-report questionnaires are frequently used to evaluate ACEs, they might not be the most effective method (Bethell et al., 2017; Gerson & Rappaport, 2013; Jones et al., 2009). Moreover, while our measure of ACEs aligns with the approach used in similar population-based studies (Groenewald et al., 2020), it did not include an assessment of items related to physical or sexual abuse, which limits a comprehensive assessment of ACEs in this study. Third, this study focused exclusively on sleep disturbance as one of the multiple components of posttraumatic stress symptoms. It is important for future research to consider other posttraumatic stress symptoms (e.g., hypervigilance, behavioral avoidance), as this will provide a more comprehensive understanding of the impact of ACEs on chronic pain and on psychological symptoms in adolescents with chronic pain. Fourth, we did not study pain-related variables other than pain intensity (e.g., pain location, pain etiology, health history). Therefore, we were not able to determine if any of these influenced the associations between the study variables. Future studies examining the relationships between chronic pain, sleep disturbance, and psychological symptoms in adolescents with chronic pain exposed to ACEs should consider the potential effects of these other pain-related characteristics. Finally, the participants in this study were a convenience sample of schoolchildren, and data on self-identified race, self-identified ethnicity, gender orientation, and socioeconomic status were not collected. As a result, we cannot determine the extent to which the results generalize to the population of children as a whole. Therefore, additional research is needed to study whether any of these, or other, sociodemographic variables play a significant role in the associations found.

Despite the study's limitations, the results provide new and important insights regarding the role of sleep disturbance in the associations between ACE exposure, chronic pain, and anxiety and depressive symptoms in adolescents from the community. In particular, sleep disturbance was found to explain a significant amount of the variance in the associations between the number of ACEs and chronic pain as well as between the number of ACEs and depression symptoms in adolescents with chronic pain. Additionally, the association between the number of ACEs and anxiety was stronger in adolescents with chronic pain that presented higher levels of sleep disturbance compared to those with lower levels. These findings suggest the possibility that addressing sleep disturbance in adolescents exposed to ACEs may prevent chronic pain and anxiety and depressive symptoms in adolescents with chronic pain.

Author Contributions

Josep Roman-Juan (Conceptualization [equal], Formal analysis [lead], Investigation [equal], Project administration [equal], Writing—original draft [lead]), Ester Solé (Investigation [equal], Writing—review & editing [equal]), Elisabet Sánchez-Rodríguez (Investigation, Writing—review & editing [equal]), Elena Castarlenas (Investigation, Writing—review & editing [equal]), Mark P. Jensen (Conceptualization [equal], Formal analysis [equal], Supervision-lead, Writing—review & editing [lead]) and Jordi Miró (Conceptualization [lead], Funding acquisition [lead], Investigation [lead], Methodology [lead], Project administration [equal], Supervision [lead], Writing—review & editing [lead])

Funding

This work was supported by grants from the Spanish Ministry of Economy, Industry and Competitiveness (RTI2018-09870-B-I00; RED2022-134869-T); the European Regional Development Fund (ERDF); and the Government of Catalonia (AGAUR; 2021SGR-730). ES-R's work was supported by a grant from the Spanish Ministry of Science and Innovation (MCIN/AEI/10.13039/501100011033; PID2020-113869RA-I00). ES's work was supported by a grant from the Spanish Ministry of Science and Innovation (MCIN/AEI/10.13039/501100011033; PID2020-114146RJ-I00). JR-J was supported by a doctoral grant from MINECO (PRE2019-089283). JM's work was supported by ICREA-Acadèmia. The Chair in Pediatric Pain is supported by Fundación Grünenthal.

Conflicts of interest

None declared.

References

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. American Psychiatric Association.

Baglioni, C., Battagliese, G., Feige, B., Spiegelhalder, K., Nissen, C., Voderholzer, U., Lombardo, C., & Riemann, D. (2011). Insomnia as a predictor of depression: A meta-analytic evaluation of longitudinal epidemiological studies. *Journal of Affective Disorders*, *135*(1–3), 10–19. https://doi.org/10.1016/j.jad.2011.01.011

Bethell, C. D., Carle, A., Hudziak, J., Gombojav, N., Powers, K., Wade, R., & Braveman, P. (2017). Methods to assess adverse childhood experiences of children and families: Toward approaches to promote child well-being in policy and practice. *Academic Pediatrics*, *17*(7S), S51–S69. https://doi.org/10.1016/j.acap.2017.04.161

Bethell, C. D., Newacheck, P., Hawes, E., & Halfon, N. (2014). Adverse childhood experiences: Assessing the impact on health and school engagement and the mitigating role of resilience. *Health Affairs (Project Hope)*, *33*(12), 2106–2115. https://doi.org/10.1377/hlthaff.2014.0914

Centers for Disease Control and Prevention. (2019). *Preventing Adverse Childhood Experiences (ACEs): Leveraging the Best Available Evidence*. https://www.cdc.gov/violenceprevention/pdf/ACEs-Prevention-Resource_508.pdf

Crouch, E., Probst, J. C., Radcliff, E., Bennett, K. J., & McKinney, S. H. (2019). Prevalence of adverse childhood experiences (ACEs) among US children. *Child Abuse & Neglect*, *92*, 209–218. https://doi.org/10.1016/j.chiabu.2019.04.010

Erdfelder, E., Faul, F., & Buchner, A. (1996). GPOWER: A general power analysis program. *Behavior Research Methods, Instruments & Computers*, *28*(1), 1–11. https://doi.org/10.3758/BF03203630

Finan, P. H., Goodin, B. R., & Smith, M. T. (2013). The association of sleep and pain: An update and a path forward *Journal of Pain*, *14*(12), 1539–1552. https://doi.org/10.1016/j.jpain.2013.08.007

Gauntlett-Gilbert, J., & Eccleston, C. (2007). Disability in adolescents with chronic pain: Patterns and predictors across different domains of functioning. *Pain*, *131*(1–2), 132–141. https://doi.org/10.1016/j.pain.2006.12.021

Gerson, R., & Rappaport, N. (2013). Traumatic stress and posttraumatic stress disorder in youth: Recent research findings on clinical impact, assessment, and treatment. *The Journal of Adolescent Health: Official Publication of the Society for Adolescent Medicine*, *52*(2), 137–143. https://doi.org/10.1016/j.jadohealth.2012.06.018

Gilbert, L. K., Breiding, M. J., Merrick, M. T., Thompson, W. W., Ford, D. C., Dhingra, S. S., & Parks, S. E. (2015). Childhood adversity and adult chronic disease: An update from ten states and the District of Columbia, 2010. *American Journal of Preventive Medicine*, *48*(3), 345–349. https://doi.org/10.1016/j.amepre.2014.09.006

Gobina, I., Villberg, J., Välimaa, R., Tynjälä, J., Whitehead, R., Cosma, A., Brooks, F., Cavallo, F., Ng, K., de Matos, M. G., & Villerusa, A. (2019). Prevalence of self-reported chronic pain among adolescents: Evidence from 42 countries and regions. *European Journal of Pain (London, England)*, *23*(2), 316–326. https://doi.org/10.1002/ejp.1306

Groenewald, C. B., Murray, C. B., & Palermo, T. M. (2020). Adverse childhood experiences and chronic pain among children and adolescents in the United States. *Pain Reports*, *5*(5), e839. https://doi.org/10.1097/PR9.0000000000000839

Hayes, A. F., & Rockwood, N. J. (2017). Regression-based statistical mediation and moderation analysis in clinical research: Observations, recommendations, and implementation. *Behaviour Research and Therapy*, *98*, 39–57. https://doi.org/10.1016/j.brat.2016.11.001

Holley, A. L., Wilson, A. C., Noel, M., & Palermo, T. M. (2016). Posttraumatic stress symptoms in children and adolescents with chronic pain: A topical review of the literature and a proposed framework for future research. *European Journal of Pain (London, England)*, *20*(9), 1371–1383. https://doi.org/10.1002/ejp.879

Huguet, A., & Miró, J. (2008). The severity of chronic pediatric pain: an epidemiological study. *The Journal of Pain*, *9*(3), 226–236. https://doi.org/10.1016/j.jpain.2007.10.015

Jones, G. T., Power, C., & Macfarlane, G. J. (2009). Adverse events in childhood and chronic widespread pain in adult life: Results from the 1958 British Birth Cohort Study. *Pain*, *143*(1–2), 92–96. https://doi.org/10.1016/j.pain.2009.02.003

Kashikar-Zuck, S., Parkins, I. S., Graham, T. B., Lynch, A. M., Passo, M., Johnston, M., Schikler, K. N., Hashkes, P. J., G., Banez, J., Richards, M. M. (2008). *Anxiety, Mood, and Behavioral Disorders*

Among Pediatric Patients With Juvenile Fibromyalgia Syndrome, 24(7), 620–626.

Könning, A., Rosenthal, N., Brown, D., Stahlschmidt, L., & Wager, J. (2021). Severity of chronic pain in German adolescent school students: A cross-sectional study. *The Clinical Journal of Pain*, *37*(2), 118–125. https://doi.org/10.1097/AJP.0000000000000898

Mansuri, F., Nash, M. C., Bakour, C., & Kip, K. (2020). Adverse childhood experiences (ACEs) and headaches among children: A cross-sectional analysis. *Headache*, *60*(4), 735–744. https://doi.org/10.1111/head.13773

Maxwell, S. E., Cole, D. A., & Mitchell, M. A. (2011). Bias in cross-sectional analyses of longitudinal mediation: Partial and complete mediation under an autoregressive model. *Multivariate Behavioral Research*, *46*(5), 816–841. https://doi.org/10.1080/00273171.2011.606716

Merrick, M. T., Ford, D. C., Ports, K. A., & Guinn, A. S. (2018). Prevalence of adverse childhood experiences from the 2011-2014 behavioral risk factor surveillance system in 23 states. *JAMA Pediatrics*, *172*(11), 1038–1044. https://doi.org/10.1001/jamapediatrics.2018.2537

Miró, J., Roman-Juan, J., Sánchez-Rodríguez, E., Solé, E., Castarlenas, E., & Jensen, M. P. (2023). Chronic pain and high impact chronic pain in children and adolescents: A cross-sectional study. *The Journal of Pain*, *24*(5), 812–823. https://doi.org/10.1016/j.jpain.2022.12.007

Nelson, S., Beveridge, J. K., Mychasiuk, R., & Noel, M. (2021). Adverse childhood experiences (ACEs) and internalizing mental health, pain, and quality of life in youth with chronic pain: A longitudinal examination. *The Journal of Pain*, *22*(10), 1210–1220. https://doi.org/10.1016/j.jpain.2021.03.143

Nelson, S., Cunningham, N., Peugh, J., Jagpal, A., Arnold, L. M., Lynch-Jordan, A., & Kashikar-Zuck, S. (2017). Clinical profiles of young adults with juvenile-onset fibromyalgia with and without a history of trauma. *Arthritis Care & Research*, *69*(11), 1636–1643. https://doi.org/10.1002/acr.23192

Nelson, S., & Logan, D. (2018). The role of adverse childhood experiences (ACEs) in school-related impairment in youth with chronic pain. *The Journal of Pain*, *19*(3), S58. https://doi.org/10.1016/j.jpain.2017.12.147

Nelson, S., Simons, L. E., & Logan, D. (2018). The incidence of adverse childhood experiences (ACEs) and their association with pain-related and psychosocial impairment in youth with chronic pain. *The Clinical Journal of Pain*, *34*(5), 402–408. https://doi.org/10.1097/AJP.0000000000000549

Noel, M., Vinall, J., Tomfohr-Madsen, L., Holley, A. L., Wilson, A. C., & Palermo, T. M. (2018). Sleep mediates the association between PTSD symptoms and chronic pain in youth. *The Journal of Pain*, *19*(1), 67–75. https://doi.org/10.1016/j.jpain.2017.09.002

Pavlova, M., Ference, J., Hancock, M., & Noel, M. (2017). Disentangling the sleep-pain relationship in pediatric chronic pain: The mediating role of internalizing mental health symptoms. *Pain Research & Management*, *2017*, 1586921. https://doi.org/10.1155/2017/1586921

Pavlova, M., Kopala-Sibley, D. C., Nania, C., Mychasiuk, R., Christensen, J., McPeak, A., Tomfohr-Madsen, L., Katz, J., Palermo, T. M., & Noel, M. (2020). Sleep disturbance underlies the co-occurrence of trauma and pediatric chronic pain: A longitudinal examination. *Pain*, *161*(4), 821–830. https://doi.org/10.1097/j.pain.0000000000001769

Pegram, S. E., Lumley, M. A., Jasinski, M. J., & Burns, J. W. (2017). Psychological trauma exposure and pain-related outcomes among people with chronic low back pain: Moderated mediation by thought suppression and social constraints. *Annals of Behavioral Medicine: A Publication of the Society of Behavioral Medicine*, *51*(2), 316–320. https://doi.org/10.1007/s12160-016-9838-0

Purewal, S. K., Bucci, M., Gutiérrez Wang, L., Koita, K., Silvério Marques, S., Oh, D., & Burke Harris, N. (2016). Screening for adverse childhood experiences (ACEs) in an integrated pediatric care model. *Zero to Three*, *37*(1), 10–17.

Riemann, D., Spiegelhalder, K., Feige, B., Voderholzer, U., Berger, M., Perlis, M., & Nissen, C. (2010). The hyperarousal model of insomnia: A review of the concept and its evidence. *Sleep Medicine Reviews*, *14*(1), 19–31. https://doi.org/10.1016/j.smrv.2009.04.002

Roman-Juan, J., Solé, E., Sánchez-Rodríguez, E., Castarlenas, E., Jensen, M. P., & Miró, J. (2023). Validation of the pediatric version of the Graded Chronic Pain Scale Revised in school-aged children and adolescents. *Pain*, https://doi.org/10.1097/j.pain.0000000000002965

Roy, R., Galán, S., Sánchez-Rodríguez, E., Racine, M., Solé, E., Jensen, M. P., & Miró, J. (2021). Cross-national trends of chronic back pain in adolescents: Results from the HBSC study, 2001-2014. *The Journal of Pain*, *23*(1), 123–130. https://doi.org/10.1016/j.jpain.2021.07.002

Sinha, S. S. (2016). Trauma-induced insomnia: A novel model for trauma and sleep research. *Sleep Medicine Reviews*, *25*, 74–83. https://doi.org/10.1016/j.smrv.2015.01.008

Varni, J. W., Magnus, B., Stucky, B. D., Liu, Y., Quinn, H., Thissen, D., Gross, H. E., Huang, I.-C., & DeWalt, D. A. (2014). Psychometric properties of the PROMIS ® pediatric scales: precision, stability, and comparison of different scoring and administration options. [Comparative Study, Journal Article, Research Support, N.I.H., Extramural]. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, *23*(4), 1233–1243. https://doi.org/10.1007/s11136-013-0544-0

Von Korff, M., Debar, L. L., Krebs, E. E., Kerns, R. D., Deyo, R. A., & Keefe, F. J. (2020). Graded chronic pain scale revised: Mild, bothersome, and high-impact chronic pain. *Pain*, *161*(3), 651–661. https://doi.org/10.1097/j.pain.0000000000001758

Wager, J., Brown, D., Kupitz, A., Rosenthal, N., & Zernikow, B. (2020). Prevalence and associated psychosocial and health factors of chronic pain in adolescents: Differences by sex and age. *European Journal of Pain (London, England)*, *24*(4), 761–772. https://doi.org/10.1002/ejp.1526

Wang, Y., Raffeld, M. R., Slopen, N., Hale, L., & Dunn, E. C. (2016). Childhood adversity and insomnia in adolescence. *Sleep Medicine*, *21*, 12–18. https://doi.org/10.1016/j.sleep.2016.01.011

5. Discussion

This doctoral dissertation encompasses nine articles with studies dedicated to advancing our understanding of chronic pain among children and adolescents. Studies I-II aimed to describe the prevalence, sociodemographic distribution, and impact of chronic pain. Studies III-V explored the role of some biopsychosocial factors as potentially contributing to the increase in the prevalence of chronic pain among European adolescents (Roy et al., 2022) and discussed potential community-based preventive measures to curb its rise. Study VI focused on the adaptation and validation of the GCPS-R (Von Korff et al., 2020) for assessing chronic pain severity in pediatric samples, thereby furnishing valuable metrics for evaluating this condition in young populations. Finally, studies VII-IX were aimed at providing useful information for the treatment of children and adolescents with chronic pain by determining the influence of several biopsychosocial factors on chronic pain, its daily impact, the use of pharmacological treatment, emotional function, and sleep.

Study I (Miró et al., 2023) showed the concerning prevalence of chronic pain among children and adolescents aged 8-18 living in Spain, with rates reaching 46%. This prevalence aligns with findings from a recent study by Gobina et al. (2019), which reported similar rates in a pooled sample of adolescents from 42 mainly European countries, indicating a pervasive issue. Notably, the prevalence rate observed in Study I exceeds that reported almost two decades ago by Huguet and Miró (2008) in the

same territory and with a similar sample, suggesting a potential increase in chronic pain among youth which aligns with recent studies also reporting significant increases in the prevalence of chronic pain in childhood (Roy et al., 2022). Moreover, the prevalence of high-impact chronic pain, at 5%, surpasses rates observed in the aforementioned study (Huguet & Miró, 2008), suggesting a worrisome trend of increasing severity. This is important given that children and adolescents experiencing high-impact chronic pain are the most likely to seek medical treatment (Könning, Rosenthal, Brown, et al., 2021; Könning, Rosenthal, Friese, et al., 2021) and, therefore, are those who account for the largest share of the economic costs of chronic pain (Von Korff et al., 2016). Study I and Study II underscore the heightened prevalence of chronic pain and high-impact chronic pain among vulnerable groups such as girls, older adolescents, and those with an immigration background, highlighting the urgent need for targeted resource allocation to address their unique needs.

Studies III to V (Roman-Juan et al., 2022; Roman-Juan, Sánchez-Rodríguez, et al., 2023, Roman-Juan, Ceniza-Bordallo, et al., 2024) examined the potential contribution of several biopsychosocial factors to the observed increase in chronic pain prevalence among European adolescents (Roy et al., 2022). Specifically, these studies showed that the increase of early menarche (in female adolescents), sedentary screen-based activities and obesity, and sleep difficulties and psychological distress were associated with the increase in the prevalence of chronic pain in this population. Addressing these factors through community interventions could play a key role in preventing the rising trend in chronic

pain prevalence. For example, community interventions aimed at promoting healthy lifestyle behaviors, providing psychosocial support, and addressing environmental stressors associated with early menarche (e.g., bullying; Su et al., 2018) may offer avenues for preventing chronic pain in female adolescents. Similarly, fostering a more active lifestyle, preventing obesity, and encouraging a healthy sleep could significantly contribute to reducing the prevalence and impact of chronic pain among adolescents.

Recognizing the critical need for a comprehensive assessment of chronic pain severity, Study VI (Roman-Juan, et al., 2023c) adapted the GCPS-R, which was originally developed for adults (Von Korff et al., 2020), for its use with pediatric populations. Through this adaptation, the study confirmed the validity of the pediatric version of the scale, thus providing a potentially reliable and brief tool for evaluating pain severity in pediatric samples with chronic pain. Moreover, if use in large-scale epidemiological studies to identify children and adolescents with high-impact chronic pain who are likely to seek medical care, this tool can provide useful information for cost-planning purposes, drawing on previous studies of healthcare costs related to pediatric chronic pain (Groenewald et al., 2014; Groenewald & Palermo, 2015; Tumin et al., 2018).

Study VIII (Roman-Juan et al., 2024) showed that fatigue may underlie the co-occurrence and maintenance of sleep disturbance and pain interference over time in this population. These findings are consistent with the ones found in previous cross-sectional studies (Sommer et al., 2023) and emphasize the importance of addressing fatigue in the treatment of chronic pain among young individuals. Interventions targeting fatigue

management, such as lifestyle adjustments, cognitive-behavioral therapy, and energy conservation techniques, could prove beneficial in enhancing sleep quality, reducing daily pain impact, and promoting overall well-being and functional outcomes.

Study VIII also showed that pain catastrophizing was associated with the use of pain medication, particularly analgesics and non-steroidal anti-inflammatory drugs, among adolescents with chronic pain, even after accounting for pain intensity and interference. This finding extends prior research examining psychological factors associated with pain medication use in children and adolescents with chronic pain (Könning, Rosenthal, Friese, et al., 2021) and suggests a potential risk of medication misuse among those with high levels of pain catastrophizing. Considering the side effects associated with some of these medications (Fisher et al., 2022) and their unclear long-term safety (Cooper et al., 2017; Eccleston et al., 2017), addressing pain catastrophizing in children and adolescents with chronic pain undergoing pharmacological treatment may be useful to prevent pain medication misuse and associated adverse effects.

Finally, in Study IX (Roman-Juan et al., 2023a), adolescents reporting a higher number of adverse childhood experiences (ACEs) displayed elevated rates of chronic pain. Additionally, those with chronic pain that had experienced a higher number of ACEs exhibited elevated levels of sleep disturbance, anxiety, and depressive symptoms. These findings are consistent with prior research in both the general population (Groenewald, Murray, et al., 2020) and clinical samples (Nelson et al., 2021), highlighting the significant impact of ACEs on emotional function and

sleep in adolescents with chronic pain. Importantly, the study identified sleep disturbance as a significant mediator in the relationship between ACEs and both chronic pain and depressive symptoms in adolescents with chronic pain. Additionally, the association between ACEs and anxiety was particularly pronounced in adolescents with chronic pain experiencing higher levels of sleep disturbance. These findings highlight the potential of addressing sleep disturbances and mitigating the effects of ACEs as preventive measures for chronic pain, anxiety, and depressive symptoms in children and adolescents with chronic pain.

The studies included in this dissertation have several limitations, which must be taken into consideration when interpreting the findings. These limitations are discussed in detail in each study. Overall, it is important to note that the studies that used data from the EPIDOL project relied on a convenience sample of children and adolescents recruited from the community. In addition, some of those initially approached refused to participate. Therefore, it is unclear whether this introduced some bias in the sample of participants.

Secondly, all studies, except for Study VIII, were cross-sectional in nature. While cross-sectional studies are valuable for exploring associations between variables at a single point in time, they inherently limit our ability to establish causal relationships. As such, while these studies provide valuable insights into the relationships between various factors and chronic pain prevalence or severity, caution must be exercised when inferring causality.

Moreover, the studies examining factors contributing to the increase in chronic pain prevalence among European adolescents utilized data from the HBSC study. While these studies offer valuable insights into potential biopsychosocial factors associated with chronic pain, it is essential to acknowledge the inherent limitations of secondary data analysis. The data set may lack certain variables or nuances that could provide a more comprehensive understanding of the phenomenon under investigation. Additionally, cross-sectional data from the HBSC study may limit the depth of analysis and hinder the ability to draw robust conclusions regarding causality.

Despite these limitations, the findings reported in the studies of this doctoral dissertation help to significantly improve our understanding of chronic pain among children and adolescents. They provide key information as to its prevalence, sociodemographic distribution, impact, contributing factors, and assessment. In addition, they also offer valuable information to help improve current treatment practices.

6. Conclusions

The main conclusions of this dissertations are the following:

- The prevalence of chronic pain among children and adolescents is high, indicating a pervasive issue that warrants close attention.
- High-impact chronic pain is particularly concerning, with rates surpassing those reported in previous studies, suggesting an alarming trend of increasing severity.
- Vulnerable groups, including girls, older adolescents, and individuals with an immigration background, report the highest burden of chronic pain and high-impact chronic pain, highlighting the urgent need for allocating additional resources and implementing targeted interventions to address the unique needs of these populations.
- Identified biopsychosocial factors, including early menarche, sedentary behaviors, obesity, sleep disturbance, and psychological distress, are significantly contributing to the increasing prevalence of chronic pain among European adolescents, underscoring the importance of addressing these factors through community-based interventions.
- The P-GCPS-R provides valid information about chronic pain severity when used with children and adolescents. Therefore, it seems to be a valuable tool to classify pediatric samples with chronic pain and to leverage treatment.

- Fatigue may have an important role in the co-occurrence and maintenance of sleep disturbance and pain interference over time in children and adolescents with chronic pain, suggesting that fatigue management should be integrated into interventions for chronic pain.
- Pain catastrophizing is a significant predictor of pain medication use among adolescents with chronic pain, emphasizing the need to address this factor in children and adolescents undergoing pharmacological therapy to prevent pain medication misuse and associated adverse effects.
- Adverse childhood events are associated with chronic pain, sleep disturbances, anxiety, and depressive symptoms among adolescents, highlighting the importance of addressing these factors in preventive and therapeutic interventions.

7. References

Alfven, G. (1993). The covariation of common psychosomatic symptoms among children from socio-economically differing residential areas. An epidemiological study. *Acta Paediatrica*, *82*(5), 484–487. https://doi.org/10.1007/s00127-005-0930-1

Allgaier, A.-K., Frühe, B., Pietsch, K., Saravo, B., Baethmann, M., & Schulte-Körne, G. (2012). Is the Children's Depression Inventory Short version a valid screening tool in pediatric care? A comparison to its full-length version. *Journal of Psychosomatic Research*, *73*(5), 369–374.https://doi.org/ 10.1016/j.jpsychores.2012.08.016

Anttila, P., Metsähonkala, L., & Sillanpää, M. (2006). Long-term trends in the incidence of headache in finnish schoolchildren. *Pediatrics*, *117*(6), 1197–1201. https://doi.org/10.1542/peds.2005-2274

Bandell-Hoekstra, I. E. N. G., Abu-Saad, H. H., Passchier, J., Frederiks, C. M. A., Feron, F. J. M., & Knipschild, P. (2001). Prevalence and characteristics of headache in Dutch schoolchildren. *European Journal of Pain*, *5*(2), 145–153. https://doi.org/10.1053/eujp.2001.0234

Bhandari, R. P., Feinstein, A. B., Huestis, S. E., Krane, E. J., Dunn, A. L., Cohen, L. L., Kao, M. C., Darnall, B. D., & Mackey, S. C. (2016). Pediatric-Collaborative Health Outcomes Information Registry (Peds-CHOIR): A learning health system to guide pediatric pain

References

research and treatment. *PAIN*, *157*(9), 2033–2044. https://doi.org/10.1097/j.pain.0000000000000609

Blaauw, B. A., Dyb, G., Hagen, K., Holmen, T. L., Linde, M., Wentzel-Larsen, T., & Zwart, J.-A. (2015). The relationship of anxiety, depression and behavioral problems with recurrent headache in late adolescence–a Young-HUNT follow-up study. *The Journal of Headache and Pain*, *16*(10). https://doi.org/10.1186/1129-2377-16-10

Breivik, H., Collett, B., Ventafridda, V., Cohen, R., & Gallacher, D. (2006). Survey of chronic pain in Europe: Prevalence, impact on daily life, and treatment. *European Journal of Pain*, *10*(4), 287–333. https://doi.org/10.1016/j.ejpain.2005.06.009

Bromberg, M. H., Law, E. F., & Palermo, T. M. (2017). Suicidal ideation in adolescents with and without chronic pain. *The Clinical Journal of Pain*, *33*(1), 21–27. https://doi.org/10.1097/AJP.0000000000000366

Caqueo-Urízar, A., Urzúa, A., & De Munter, K. (2014). Mental health of indigenous school children in Northern Chile. *BMC Psychiatry*, *14*(11). https://doi.org/10.1186/1471-244X-14-11

Castarlenas, E., Jensen, M. P., Von Baeyer, C. L., & Miró, J. (2017). Psychometric properties of the numerical rating scale to assess self-reported pain intensity in children and adolescents. *Clinical Journal of Pain*, *33*(4), 376–383. https://doi.org/10.1097/AJP.0000000000000406

References

Chambers, C. T., Dol, J., Tutelman, P. R., Langley, C. L., Parker, J. A., Cormier, B. T., Macfarlane, G., Jones, G., Chapman, D., & Proudfoo, N., Grant, A., Marianayagam, J. (in press). The Prevalence of Chronic Pain in Children and Adolescents: A Systematic Review Update and Meta-analysis. *PAIN*. https://doi.org/10.1097/j.pain.0000000000003267

Christoph, M. J., Larson, N. I., Winkler, M. R., Wall, M. M., & Neumark-Sztainer, D. (2019). Longitudinal trajectories and prevalence of meeting dietary guidelines during the transition from adolescence to young adulthood. *The American Journal of Clinical Nutrition*, *109*(3), 656–664. https://doi.org/10.1093/ajcn/nqy333

Claar, R. L., Simons, L. E., & Logan, D. E. (2008). Parental response to children's pain: The moderating impact of children's emotional distress on symptoms and disability. *PAIN*, *138*(1), 172–179. https://doi.org/10.1016/j.pain.2007.12.005

Collett, B., Haanpaa, M., & Kamel, C. (2010). Task force on wait times: Summary and recommendations. *International Association for the Study of Pain.*

Connolly, M. R., Chaudari, J. Y., Yang, X., Ward, N., Kitt, R. A., Herrmann, R. S., Krane, E. J., LeBel, A. A., Smith, S. M., Walco, G. A., Weisman, S. J., Turk, D. C., Dworkin, R. H., & Gewandter, J. S. (2019). Design and Reporting Characteristics of Clinical Trials of Select Chronic and Recurrent Pediatric Pain Conditions: An Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks Systematic Review. *The*

References

Journal of Pain, *20*(4), 394–404. https://doi.org/10.1016/j.jpain.2018.08.007

Cooper, T. E., Heathcote, L. C., Clinch, J., Gold, J. I., Howard, R., Lord, S. M., Schechter, N., Wood, C., & Wiffen, P. J. (2017). Paracetamol (acetaminophen) for chronic non-cancer pain in children and adolescents (Review). *Cochrane Database of Systematic Reviews*, *8*. https://doi.org/10.1002/14651858.CD012535

Croft, P., Blyth, F. M., & van der Windt, D. (2010). *Chronic pain epidemiology: From aetiology to public health*. Oxford University Press.

Cservenka, A., Stein, H., Wilson, A. C., & Nagel, B. J. (2015). Neurobiological Phenotypes of Familial Chronic Pain in Adolescence: A Pilot fMRI Study. *The Journal of Pain*, *16*(9), 913–925. https://doi.org/10.1016/j.jpain.2015.05.013

Dahlhamer, J., Lucas, J., Zelaya, C., Nahin, R., Mackey, S., DeBar, L., Kerns, R., Von Korff, M., Porter, L., & Helmick, C. (2018). Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults—United States, 2016. *Morbidity and Mortality Weekly Report*, *67*(36), 1001–1006. https://doi.org/10.15585/mmwr.mm6736a2

Dampier, C., Palermo, T. M., Darbari, D. S., Hassell, K., Smith, W., & Zempsky, W. (2017). AAPT diagnostic criteria for chronic sickle cell disease pain. *The Journal of Pain*, *18*(5), 490–498. https://doi.org/10.1016/j.jpain.2016.12.016

References

De La Vega, R., & Palermo, T. (2024). *Pediatric Pain Clinics 2024*. http://childpain.org/wp-content/uploads/2024/02/PedPainClinicList_2024_Final.pdf

Deyo, R. A., Dworkin, S. F., Amtmann, D., Andersson, G., Borenstein, D., Carragee, E., Carrino, J., Chou, R., Cook, K., Delitto, A., Goertz, C., Khalsa, P., Loeser, J., MacKey, S., Panagis, J., Rainville, J., Tosteson, T., Turk, D., Von Korff, M., & Weiner, D. K. (2014). Report of the NIH task force on research standards for chronic low back pain. *The Journal of Pain*, *15*(6), 569–585. https://doi.org/10.1016/j.jpain.2014.03.005

Dilini Rajapakse, Christina Liossi, & Richard F Howard. (2014). Presentation and management of chronic pain. *Archives of Disease in Childhood*, *99*(5), 474–480. https://doi.org/10.1136/archdischild-2013-304207

Drissi, I., Woods, W. A., & Woods, C. G. (2020). Understanding the genetic basis of congenital insensitivity to pain. *British Medical Bulletin*, *133*(1), 65–78. https://doi.org/10.1093/bmb/ldaa003

Dunn, K. M., Croft, P. R., Main, C. J., & Von Korff, M. (2008). A prognostic approach to defining chronic pain: Replication in a UK primary care low back pain population. *PAIN*, *135*(1–2), 48–54.

Dworkin, R. H., Turk, D. C., Farrar, J. T., Haythornthwaite, J. A., Jensen, M. P., Katz, N. P., Kerns, R. D., Stucki, G., Allen, R. R., Bellamy, N., Carr, D. B., Chandler, J., Cowan, P., Dionne, R., Galer, B. S., Hertz, S., Jadad, A. R., Kramer, L. D., Manning, D. C., … Witter, J. (2005). Core outcome measures for chronic pain clinical trials: IMMPACT

References

recommendations. *PAIN*, *113*(1), 9–19. https://doi.org/10.1016/j.pain.2004.09.012

Dzau, V. J., & Pizzo, P. A. (2014). Relieving pain in America: Insights from an Institute of Medicine committee. *Jama*, *312*(15), 1507–1508. https://doi.org/10.1001/jama.2014.12986

Eccleston, C., Cooper, T. E., Fisher, E., Anderson, B., & Willkinson, N. (2017). Non-steroidal anti-inflammatory drugs (NSAIDs) for chronic non-cancer pain in children and adolescents (Review). *Cochrane Database of Systematic Reviews*, *8*. https://doi.org/10.1002/14651858.CD012537.pub2

Eccleston, C., Fisher, E., Cooper, T. E., Grégoire, M. C., Heathcote, L. C., Krane, E., Lord, S. M., Sethna, N. F., Anderson, A. K., Anderson, B., Clinch, J., Gray, A. L., Gold, J. I., Howard, R. F., Ljungman, G., Moore, R. A., Schechter, N., Wiffen, P. J., Wilkinson, N. M. R., … Zernikow, B. (2019). Pharmacological interventions for chronic pain in children: An overview of systematic reviews. *PAIN*, *160*(8), 1698–1707. https://doi.org/10.1097/j.pain.0000000000001609

Eccleston, C., Fisher, E., Howard, R. F., Slater, R., Forgeron, P., Palermo, T. M., Birnie, K. A., Anderson, B. J., Chambers, C. T., & Crombez, G. (2021). Delivering transformative action in paediatric pain: A Lancet Child & Adolescent Health Commission. *The Lancet Child & Adolescent Health*, *5*(1), 47–87. https://doi.org/10.1016/S2352-4642(20)30277-7

Eccleston, C., Jordan, A., McCracken, L. M., Sleed, M., Connell, H., & Clinch, J. (2005). The Bath Adolescent Pain Questionnaire

References

(BAPQ): Development and preliminary psychometric evaluation of an instrument to assess the impact of chronic pain on adolescents. *PAIN*, *118*(1–2), 263–270. https://doi.org/10.1016/j.pain.2005.08.025

Eccleston, C., Palermo, T., Williams, A. C. de C., Lewandowski, A., Morley, S., Fisher, E., & Law, E. (2016). Psychological therapies for the management of chronic and recurrent pain in children and adolescents. *Cochrane Database of Systematic Reviews*, *9*. https://doi.org/10.1002/14651858.CD003968.pub5

Emre Ilhan, Verity Pacey, Laura Brown, Kaye Spence, Christ-jan van Ganzewinkel, Rebecca Pillai Riddell, Marsha Campbell-Yeo, Bonnie J Stevens, Mats Eriksson, Vibhuti Shah, Kanwaljeet J S Anand, Carlo Bellieni, Mandy Daly, Celeste Johnston, & Julia Hush. (2022). What is the definition of acute episodic and chronic pain in critically ill neonates and infants? A global, four-stage consensus and validation study. *BMJ Open*, *12*(3), e055255. https://doi.org/10.1136/bmjopen-2021-055255

Essner, B., Noel, M., Myrvik, M., & Palermo, T. (2015). Examination of the factor structure of the Adolescent Sleep–Wake Scale (ASWS). *Behavioral Sleep Medicine*, *13*(4), 296–307. https://doi.org/10.1080/15402002.2014.896253

Fayaz, A., Croft, P., Langford, R. M., Donaldson, L. J., & Jones, G. T. (2016). Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. *BMJ Open*, *6*(6), e10364. https://doi.org/10.1136/bmjopen-2015

References

Fillingim, R. B., Loeser, J. D., Baron, R., & Edwards, R. R. (2016). Assessment of Chronic Pain: Domains, Methods, and Mechanisms. *The Journal of Pain*, *17*(9), T10–T20. https://doi.org/10.1016/j.jpain.2015.08.010

Fisher, E., Heathcote, L. C., Eccleston, C., Simons, L. E., & Palermo, T. M. (2018). Assessment of Pain Anxiety, Pain Catastrophizing, and Fear of Pain in Children and Adolescents With Chronic Pain: A Systematic Review and Meta-Analysis. *Journal of Pediatric Psychology*, *43*(3), 314–325. https://doi.org/10.1093/jpepsy/jsx103

Fisher, E., Villanueva, G., Henschke, N., Nevitt, S. J., Zempsky, W., Probyn, K., Buckley, B., Cooper, T. E., Sethna, N., & Eccleston, C. (2022). Efficacy and safety of pharmacological, physical, and psychological interventions for the management of chronic pain in children: A WHO systematic review and meta-analysis. *PAIN*, *163*(1), E1–E19. https://doi.org/10.1097/j.pain.0000000000002297

Forrest, C. B., Bevans, K. B., Pratiwadi, R., Moon, J., Teneralli, R. E., Minton, J. M., & Tucker, C. A. (2014). Development of the PROMIS® pediatric global health (PGH-7) measure. *Quality of Life Research*, *23*, 1221–1231. https://doi.org/10.1007/s11136-013-0581-8

Forrest, C. B., Meltzer, L. J., Marcus, C. L., de la Motte, A., Kratchman, A., Buysse, D. J., Pilkonis, P. A., Becker, B. D., & Bevans, K. B. (2018). Development and validation of the PROMIS Pediatric Sleep Disturbance and Sleep-Related Impairment item banks. *Sleep*, *41*(6), zsy054. https://doi.org/10.1093/sleep/zsy054

References

Fryer, B. A., Cleary, G., Wickham, S. L., Barr, B. R., & Taylor-Robinson, D. C. (2017). Effect of socioeconomic conditions on frequent complaints of pain in children: Findings from the UK Millennium Cohort Study. *BMJ Paediatrics Open*, *1*(1). https://doi.org/10.1136/bmjpo-2017-000093

Gatchel, R. J., Bo Peng, Y., Peters, M. L., Fuchs, P. N., & Turk, D. C. (2007). The Biopsychosocial Approach to Chronic Pain: Scientific Advances and Future Directions. *Psychological Bulletin*, *133*(4), 581–624. https://doi.org/10.1037/0033-2909.133.4.581

Gobina, I., Villberg, J., Välimaa, R., Tynjälä, J., Whitehead, R., Cosma, A., Brooks, F., Cavallo, F., Ng, K., de Matos, M. G., & Villerusa, A. (2019). Prevalence of self-reported chronic pain among adolescents: Evidence from 42 countries and regions. *European Journal of Pain (United Kingdom)*, *23*(2), 316–326. https://doi.org/10.1002/ejp.1306

Gold, J. I., Mahrer, N. E., Yee, J., & Palermo, T. M. (2009). Pain, Fatigue, and Health-related Quality of Life in Children and Adolescents With Chronic Pain. *The Clinical Journal of Pain*, *25*(5), 407–412. https://doi.org/10.1097/AJP.0b013e318192bfb1

Grimby-Ekman, A., Åberg, M., Torén, K., Brisman, J., Hagberg, M., & Kim, J.-L. (2018). Pain could negatively affect school grades—Swedish middle school students with low school grades most affected. *PLoS ONE*, *13*(12), e0208435. https://doi.org/10.1371/journal.pone.0208435

References

Groenewald, C. B., Essner, B. S., Wright, D., Fesinmeyer, M. D., & Palermo, T. M. (2014). The economic costs of chronic pain among a cohort of treatment-seeking adolescents in the United States. *The Journal of Pain*, *15*(9), 925–933. https://doi.org/10.1016/j.jpain.2014.06.002

Groenewald, C. B., Murray, C. B., & Palermo, T. M. (2020). Adverse childhood experiences and chronic pain among children and adolescents in the United States. *Pain Reports*, *5*(5), e839. https://doi.org/10.1097/PR9.0000000000000839

Groenewald, C. B., & Palermo, T. M. (2015). The price of pain: The economics of chronic adolescent pain. *Pain Management*, *5*(2), 61–64. https://doi.org/10.2217/pmt.14.52

Groenewald, C. B., Tham, S. W., & Palermo, T. M. (2020). Impaired school functioning in children with chronic pain: A national perspective. *Clinical Journal of Pain*, *36*(9), 693–699. https://doi.org/10.1097/AJP.0000000000000850

Guy, W. (1976). *ECDEU assessment manual for psychopharmacology*. US Department of Health, Education, and Welfare, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, National Institute of Mental Health, Psychopharmacology Research Branch, Division of Extramural Research Programs.

Hakala, P., Rimpelä, A., Salminen, J. J., Virtanen, S. M., & Rimpelä, M. (2002). Back, neck, and shoulder pain in Finnish adolescents: National cross sectional surveys. *BMJ*, *325*(7367), 743–746. https://doi.org/10.1136/bmj.325.7367.743

References

Haraldstad, K., Sørum, R., Eide, H., Natvig, G. K., & Helseth, S. (2011). Pain in children and adolescents: Prevalence, impact on daily life, and parents' perception, a school survey. *Scandinavian Journal of Caring Sciences*, *25*(1), 27–36. https://doi.org/10.1111/j.1471-6712.2010.00785.x

Hechler, T., Kanstrup, M., Holley, A. L., Simons, L. E., Wicksell, R., Hirschfeld, G., & Zernikow, B. (2015). Systematic review on intensive interdisciplinary pain treatment of children with chronic pain. *Pediatrics*, *136*(1), 115–127. https://doi.org/10.1542/peds.2014-3319

Herman, P. M., Qureshi, N., Arick, S. D., Edelen, M. O., Hays, R. D., Rodriguez, A., Weir, R. L., & Coulter, I. D. (2023). Definitions of Chronic Low Back Pain From a Scoping Review, and Analyses of Narratives and Self-Reported Health of Adults With Low Back Pain. *The Journal of Pain*, *24*(3), 403–412. https://doi.org/10.1016/j.jpain.2022.10.012

Higgins, K. S., Birnie, K. A., Chambers, C. T., Wilson, A. C., Caes, L., Clark, A. J., Lynch, M., Stinson, J., & Campbell-Yeo, M. (2015). Offspring of parents with chronic pain: A systematic review and meta-analysis of pain, health, psychological, and family outcomes. *PAIN*, *156*(11), 2256–2266. https://doi.org/10.1097/j.pain.0000000000000293

Holley, A. L., Wilson, A. C., Noel, M., & Palermo, T. M. (2016). Post-traumatic stress symptoms in children and adolescents with chronic pain: A topical review of the literature and a proposed

References

framework for future research. *European Journal of Pain (United Kingdom)*, *20*(9), 1371–1383. https://doi.org/10.1002/ejp.879

Holley, A. L., Zhou, C., Wilson, A. C., Hainsworth, K., & Palermo, T. M. (2018). The CALI-9: A brief measure for assessing activity limitations in children and adolescents with chronic pain. *PAIN*, *159*(1), 48–56.

Horst, S., Shelby, G., Anderson, J., Acra, S., Polk, D. B., Saville, B. R., Garber, J., & Walker, L. S. (2014). Predicting persistence of functional abdominal pain from childhood into young adulthood. *Clinical Gastroenterology and Hepatology*, *12*(12), 2026–2032. https://doi.org/10.1016/j.cgh.2014.03.034

Huguet, A., & Miró, J. (2008). The Severity of Chronic Pediatric Pain: An Epidemiological Study. *The Journal of Pain*, *9*(3), 226–236. https://doi.org/10.1016/j.jpain.2007.10.015

Hunfeld, J. A. M., Perquin, C. W., Duivenvoorden, H. J., Hazebroek-Kampschreur, A. A. J. M., Passchier, J., Van Suijlekom-Smit, L. W. A., & Van Der Wouden, J. C. (2001). Chronic pain and its impact on quality of life in adolescents and their families. *Journal of Pediatric Psychology*, *26*(3), 145–153. https://doi.org/10.1093/jpepsy/26.3.145

Incledon, E., O'Connor, M., Giallo, R., Chalkiadis, G. A., & Palermo, T. M. (2016). Child and Family Antecedents of Pain During the Transition to Adolescence: A Longitudinal Population-Based Study. *The Journal of Pain*, *17*(11), 1174–1182. https://doi.org/10.1016/j.jpain.2016.07.005

References

International Association for the Study of Pain. (1979). Pain terms: a list with definitions and notes on usage. Recommended by the IASP Subcommittee on Taxonomy. *PAIN*, *6*(3), 249.

International Association for the Study of Pain. (1994). *IASP Task force on Taxonomy. In Classification of chronic pain: Descriptions of chronic pain syndromes and definitions of pain terms. (2nd edition).* IASP Press.

International Association for the Study of Pain. (2022). Acute pain. Retrieved from https://www.iasp-pain.org/resources/topics/acute-pain/

Irwin, D. E., Stucky, B., Langer, M. M., Thissen, D., DeWitt, E. M., Lai, J.-S., Varni, J. W., Yeatts, K., & DeWalt, D. A. (2010). An item response analysis of the pediatric PROMIS anxiety and depressive symptoms scales. *Quality of Life Research*, *19*, 595–607. https://doi.org/10.1007/s11136-010-9619-3

Jacobson, C. J., Farrell, J. E., Kashikar-Zuck, S., Seid, M., Verkamp, E., & DeWitt, E. M. (2013). Disclosure and self-report of emotional, social, and physical health in children and adolescents with chronic pain—A qualitative study of PROMIS pediatric measures. *Journal of Pediatric Psychology*, *38*(1), 82–93. https://doi.org/10.1093/jpepsy/jss099

James, S. L., Abate, D., Abate, K. H., Abay, S. M., Abbafati, C., Abbasi, N., Abbastabar, H., Abd-Allah, F., Abdela, J., Abdelalim, A., Abdollahpour, I., Abdulkader, R. S., Abebe, Z., Abera, S. F., Abil, O. Z., Abraha, H. N., Abu-Raddad, L. J., Abu-Rmeileh, N. M. E.,

References

Accrombessi, M. M. K., … Murray, C. J. L. (2018). Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. *The Lancet*, *392*(10159), 1789–1858. https://doi.org/10.1016/S0140-6736(18)32279-7

Johansen, A., Romundstad, L., Nielsen, C. S., Schirmer, H., & Stubhaug, A. (2012). Persistent postsurgical pain in a general population: Prevalence and predictors in the Tromsø study. *PAIN*, *153*(7), 1390–1396. https://doi.org/10.1016/j.pain.2012.02.018

Jones, G. T., & Botello, A. P. (2010). Pain in children. In P. Croft, F. M. Blyth, & D. van der Windt (Eds.), *Chronic Pain Epidemiology: From Aetiology to Public Health*. Oxford University Press. https://doi.org/10.1093/acprof:oso/9780199235766.003.0014

Jones, G. T., Silman, A. J., & Macfarlane, G. J. (2003). Predicting the onset of widespread body pain among children. *Arthritis and Rheumatology*, *48*(9), 2615–2621. https://doi.org/10.1002/art.11221

Kashikar-Zuck, S., Cunningham, N., Peugh, J., Black, W. R., Nelson, S., Lynch-Jordan, A. M., Pfeiffer, M., Tran, S. T., Ting, T. V., & Arnold, L. M. (2019). Long-term outcomes of adolescents with juvenile-onset fibromyalgia into adulthood and impact of depressive symptoms on functioning over time. *PAIN*, *160*(2), 433–441. https://doi.org/10.1097/j.pain.0000000000001415

References

Kashikar-Zuck, S., Cunningham, N., Sil, S., Bromberg, M. H., Lynch-Jordan, A. M., Strotman, D., Peugh, J., Noll, J., Ting, T. V., & Powers, S. W. (2014). Long-term outcomes of adolescents with juvenile-onset fibromyalgia in early adulthood. *Pediatrics*, *133*(3), e592–e600. https://doi.org/10.1542/peds.2013-222

Kashikar-Zuck, S., Flowers, S. R., Claar, R. L., Guite, J. W., Logan, D. E., Lynch-Jordan, A. M., Palermo, T. M., & Wilson, A. C. (2011). Clinical utility and validity of the Functional Disability Inventory among a multicenter sample of youth with chronic pain. *Pain*, *152*(7), 1600–1607. https://doi.org/10.1016/j.pain.2011.02.050

Kitschen, A., Wahidie, D., Meyer, D., Rau, L.-M., Ruhe, A.-K., Wager, J., Zernikow, B., & Sauerland, D. (2024). Cost-of-illness and Economic Evaluation of Interventions in Children and Adolescents with Chronic Pain. *The Clinical Journal of Pain*, *40*(5), 306–319. https://doi.org/10.1097/AJP.0000000000001199

Koechlin, H., Locher, C., & Prchal, A. (2020). Talking to children and families about chronic pain: The importance of pain education—An introduction for pediatricians and other health care providers. *Children*, *7*(10), 179. https://doi.org/10.3390/children7100179

Könning, A., Rosenthal, N., Brown, D., Stahlschmidt, L., & Wager, J. (2021). Severity of Chronic Pain in German Adolescent School Students: A Cross-sectional Study. *Clinical Journal of Pain*, *37*(2), 118–125. https://doi.org/10.1097/AJP.0000000000000898

Könning, A., Rosenthal, N., Friese, M., Hirschfeld, G., Brown, D., & Wager, J. (2021). Factors associated with physician consultation and

medication use in children and adolescents with chronic pain: A scoping review and original data. *European Journal of Pain (United Kingdom)*, *25*(1), 88–106. https://doi.org/10.1002/ejp.1661

Larsson, B., Sigurdson, J. F., & Sund, A. M. (2018). Long-term follow-up of a community sample of adolescents with frequent headaches. *The Journal of Headache and Pain*, *19*(79), 1–8. https://doi.org/10.1186/s10194-018-0908-5

Laurell, K., Larsson, B., & Eeg-Olofsson, O. (2004). Prevalence of headache in Swedish schoolchildren, with a focus on tension-type headache. *Cephalalgia*, *24*(5), 380–388. https://doi.org/10.1111/j.1468-2982.2004.00681.x

Laures, E., LaFond, C., Hanrahan, K., Pierce, N., Min, H., & McCarthy, A. M. (2019). Pain Assessment Practices in the Pediatric Intensive Care Unit. *Journal of Pediatric Nursing*, *48*, 55–62. https://doi.org/10.1016/j.pedn.2019.07.005

Law, E., Fisher, E., Eccleston, C., & Palermo, T. M. (2019). Psychological interventions for parents of children and adolescents with chronic illness. *Cochrane Database of Systematic Reviews*, *3*. https://doi.org/10.1002/14651858.CD009660.pub4

Li, R., Gibler, R. C., Rheel, E., Slack, K., & Palermo, T. M. (2023). Recommendations for Patient-Reported Outcomes Measurement Information System pediatric measures in youth with chronic pain: A COnsensus-based Standards for the selection of health Measurement INstruments systematic review of measurement

References

properties. *PAIN*, *165*(2), 258–295. https://doi.org/10.1097/j.pain.0000000000002998

Liossi, C., & Howard, R. F. (2016). Pediatric chronic pain: Biopsychosocial assessment and formulation. *Pediatrics*, *138*(5), e20160331. https://doi.org/10.1542/peds.2016-0331

Long, A. C., Krishnamurthy, V., & Palermo, T. M. (2008). Sleep disturbances in school-age children with chronic pain. *Journal of Pediatric Psychology*, *33*(3), 258–268. https://doi.org/10.1093/jpepsy/jsm129

Luntamo, T., Sourander, A., Rihko, M., Aromaa, M., Helenius, H., Koskelainen, M., & McGrath, P. J. (2012). Psychosocial determinants of headache, abdominal pain, and sleep problems in a community sample of Finnish adolescents. *European Child and Adolescent Psychiatry*, *21*, 301–313. https://doi.org/10.1007/s00787-012-0261-1

Luntamo, T., Sourander, A., Santalahti, P., Aromaa, M., & Helenius, H. (2012). Prevalence changes of pain, sleep problems and fatigue among 8-year-old children: Years 1989, 1999, and 2005. *Journal of Pediatric Psychology*, *37*(3), 307–318. https://doi.org/10.1093/jpepsy/jsr091

Lynch-Jordan, A. M., Sil, S., Peugh, J., Cunningham, N., Kashikar-Zuck, S., & Goldschneider, K. R. (2014). Differential changes in functional disability and pain intensity over the course of psychological treatment for children with chronic pain. *PAIN*, *155*(10), 1955–1961. https://doi.org/10.1016/j.pain.2014.06.008

References

Mackey, S. (2016). Future Directions for Pain Management. Lessons from the Institute of Medicine Pain Report and the National Pain Strategy. *Hand Clinics*, *32*(1), 91–98. https://doi.org/10.1016/j.hcl.2015.08.012

Mano, K. E. J., O'Bryan, E. M., Gibler, R. C., & Beckmann, E. (2019). The co-occurrence of pediatric chronic pain and anxiety: A theoretical review of a developmentally informed shared vulnerability model. *The Clinical Journal of Pain*, *35*(12), 989–1002. https://doi.org/10.1097/AJP.0000000000000763

McGrath, P. J., Walco, G. A., Turk, D. C., Dworkin, R. H., Brown, M. T., Davidson, K., Eccleston, C., Finley, G. A., Goldschneider, K., & Haverkos, L. (2008). Core outcome domains and measures for pediatric acute and chronic/recurrent pain clinical trials: PedIMMPACT recommendations. *The Journal of Pain*, *9*(9), 771–783. https://doi.org/10.1016/j.jpain.2008.04.007

Miller, M. M., Meints, S. M., & Hirsh, A. T. (2018). Catastrophizing, pain, and functional outcomes for children with chronic pain: A meta-analytic review. *PAIN*, *159*, 2442–2460. https://doi.org/10.1097/j.pain.0000000000001342

Miró, J. (2010). Chronic pain: Also a public health problem among younger people? *Revista de La Sociedad Española Del Dolor*, *17*(7), 301–303. https://doi.org/10.1016/j.resed.2010.07.001

Miró, J., McGrath, P. J., Finley, G. A., & Walco, G. A. (2017). Pediatric chronic pain programs: Current and ideal practice. *Pain Reports*, *2*(5), e613. https://doi.org/10.1097/PR9.0000000000000613

References

Miró, J., Roman-Juan, J., Sánchez-Rodríguez, E., Solé, E., Castarlenas, E., & Jensen, M. P. (2023). Chronic Pain and High Impact Chronic Pain in Children and Adolescents: A Cross-Sectional Study. *The Journal of Pain*, *24*(5), 812–823. https://doi.org/10.1016/j.jpain.2022.12.007

Moore, S. V., Davis, M. C., & Lemery-Chalfant, K. (2020). Children's physical pain: Relations with maternal and paternal pain and prediction from maternal depressive symptoms and hope during infancy. *Psychology, Health & Medicine*, *25*(5), 613–622. https://doi.org/10.1080/13548506.2019.1659980

Muthuri, S. G., Kuh, D., & Cooper, R. (2018). Longitudinal profiles of back pain across adulthood and their relationship with childhood factors: Evidence from the 1946 British birth cohort. *PAIN*, *159*(4), 764–774. https://doi.org/10.1097/j.pain.0000000000001143

Nelson, S., Beveridge, J. K., Mychasiuk, R., & Noel, M. (2021). Adverse Childhood Experiences (ACEs) and Internalizing Mental Health, Pain, and Quality of Life in Youth With Chronic Pain: A Longitudinal Examination. *The Journal of Pain*, *22*(10), 1210–1220. https://doi.org/10.1016/j.jpain.2021.03.143

Noel, M., Chambers, C. T., Parker, J. A., Aubrey, K., Tutelman, P. R., Morrongiello, B., Moore, C., McGrath, P. J., Yanchar, N. L., & Von Baeyer, C. L. (2018). Boo-boos as the building blocks of pain expression: An observational examination of parental responses to everyday pain in toddlers. *Canadian Journal of Pain*, *2*(1), 74–86. https://doi.org/10.1080/24740527.2018.1442677

References

Noel, M., Vinall, J., Tomfohr-Madsen, L., Holley, A. L., Wilson, A. C., & Palermo, T. M. (2018). Sleep Mediates the Association Between PTSD Symptoms and Chronic Pain in Youth. *The Journal of Pain*, *19*(1), 67–75. https://doi.org/10.1016/j.jpain.2017.09.002

Palermo, T. (2000). Impact of Recurrent and Chronic Pain on Child and Family Daily Functioning: A Critical Review of the Literature. *Journal of Developmental & Behavioral Pediatrics*, *21*(1), 58–69. https://doi.org/10.1097/00004703-200002000-00011

Palermo, T. (2012). *Cognitive-behavioral therapy for chronic pain in children and adolescents*. Oxford University Press.

Palermo, T. (2020). Pain prevention and management must begin in childhood: The key role of psychological interventions. *PAIN*, *161*, S114–S121. https://doi.org/10.1097/j.pain.0000000000001862

Palermo, T., & Kiska, R. (2005). Subjective sleep disturbances in adolescents with chronic pain: Relationship to daily functioning and quality of life. *The Journal of Pain*, *6*(3), 201–207. https://doi.org/10.1016/j.jpain.2004.12.005

Palermo, T., Li, R., Birnie, K. A., Crombez, G., Eccleston, C., Kashikar-Zuck, S., Stone, A. L., & Walco, G. A. (2024). Updated recommendations on measures for clinical trials in pediatric chronic pain: A multiphase approach from the Core Outcomes in Pediatric Persistent Pain (Core-OPPP) Workgroup. *PAIN*, *165*(5), 1086–1100. https://doi.org/10.1097/j.pain.0000000000003105

Palermo, T. M., Law, E. F., Fales, J., Bromberg, M. H., Jessen-Fiddick, T., & Tai, G. (2016). Internet-delivered cognitive-behavioral treatment

References

for adolescents with chronic pain and their parents: A randomized controlled multicenter trial. *PAIN*, *157*(1), 174–185. https://doi.org/10.1097/j.pain.0000000000000348

Palermo, T. M., Slack, M., Zhou, C., Aaron, R., Fisher, E., & Rodriguez, S. (2019). Waiting for a Pediatric Chronic Pain Clinic Evaluation: A Prospective Study Characterizing Waiting Times and Symptom Trajectories. *The Journal of Pain*, *20*(3), 339–347. https://doi.org/10.1016/j.jpain.2018.09.009

Palermo, T. M., Valrie, C. R., & Karlson, C. W. (2014). Family and parent influences on pediatric chronic pain. *American Psychologist*, *69*(2), 142–152. https://doi.org/10.1037/a0035216

Palermo, T., Walco, G. A., Paladhi, U. R., Birnie, K. A., Crombez, G., Vega, R. de la, Eccleston, C., Kashikar-Zuck, S., & Stone, A. L. (2021). Core outcome set for pediatric chronic pain clinical trials. *PAIN*, *162*(10), 2539–2547. https://doi.org/10.1097/j.pain.0000000000002241

Palermo, T., Wilson, A. C., Lewandowski, A. S., Toliver-Sokol, M., & Murray, C. B. (2011). Behavioral and psychosocial factors associated with insomnia in adolescents with chronic pain. *PAIN*, *152*(1), 89–94. https://doi.org/10.1016/j.pain.2010.09.035

Perquin, C. W., Hazebroek-Kampschreur, A. A. J. M., Hunfeld, J. A. M., Bohnen, A. M., van Suijlekom-Smit, L. W. A., Passchier, J., & van der Wouden, J. C. (2000). Pain in children and adolescents: A common experience. *PAIN*, *87*(1), 51–58. https://doi.org/10.1016/S0304-3959(00)00269-4

References

Pitcher, M. H., Von Korff, M., Bushnell, M. C., & Porter, L. (2019). Prevalence and Profile of High-Impact Chronic Pain in the United States. *The Journal of Pain*, *20*(2), 146–160. https://doi.org/10.1016/j.jpain.2018.07.006

Raja, S. N., Carr, D. B., Cohen, M., Finnerup, N. B., Flor, H., Gibson, S., Keefe, F. J., Mogil, J. S., Ringkamp, M., Sluka, K. A., Song, X. J., Stevens, B., Sullivan, M. D., Tutelman, P. R., Ushida, T., & Vader, K. (2020). The revised International Association for the Study of Pain definition of pain: Concepts, challenges, and compromises. *PAIN*, *161*(9), 1976–1982. https://doi.org/10.1097/j.pain.0000000000001939

Rice, A. S. C., Smith, B. H., & Blyth, F. M. (2016). Pain and the global burden of disease. *PAIN*, *157*(4), 791–796. https://doi.org/10.1097/j.pain.0000000000000454

Richardson, P. A., Birnie, K. A., Harrison, L. E., Rajagopalan, A., & Bhandari, R. P. (2020). Profiling Modifiable Psychosocial Factors Among Children With Chronic Pain: A Person-Centered Methodology. *The Journal of Pain*, *21*(3–4), 467–476. https://doi.org/10.1016/j.jpain.2019.08.015

Roman-Juan, J., Ceniza-Bordallo, G., Sánchez-Rodríguez, E., Jensen, M. P., & Miró, J. (2024). Fatigue, sleep disturbance, and pain interference in children and adolescents with chronic pain: a longitudinal study. *PAIN (under review)*

Roman-Juan, J., Jensen, M. P., & Miró, J. (2024). The increase in early menarche is associated with the increase of chronic back pain in

References

female adolescents: The HBSC study 2002-2014. *Clinical Journal of Pain (under review)*

Roman-Juan, J., Jensen, M. P., & Miró, J. (2023). Increases in Sleep Difficulties and Psychological Symptoms are Associated with the Increase of Chronic Back Pain in Adolescents: The HBSC Study 2002-2018. *The Journal of Pain*, *25*(2), 407–417. https://doi.org/10.1016/j.jpain.2023.09.004

Roman-Juan, J., Roy, R., Jensen, M. P., & Miró, J. (2022). The explanatory role of sedentary screen time and obesity in the increase of chronic back pain amongst European adolescents: The HBSC study 2002–2014. *European Journal of Pain (United Kingdom)*, *26*(8), 1781–1789. https://doi.org/10.1002/ejp.2003

Roman-Juan, J., Sánchez-Rodríguez, E., Solé, E., Castarlenas, E., Jensen, M. P., & Miró, J. (2023). Psychological factors and pain medication use in adolescents with chronic pain. *Pain Medicine*, *24*(10), 1183–1188. https://doi.org/10.1093/pm/pnad075

Roman-Juan, J., Sánchez-Rodríguez, E., Solé, E., Castarlenas, E., Jensen, M. P., & Miró, J. (2024). Immigration background as a risk factor of chronic pain and high-impact chronic pain in children and adolescents living in Spain: Differences as a function of age. *PAIN*, *165*(6), 1372–1379. https://doi.org/10.1097/j.pain.0000000000003142

Roman-Juan, J., Solé, E., Sánchez-Rodríguez, E., Castarlenas, E., Jensen, M. P., & Miró, J. (2023a). Adverse Childhood Events and Chronic Pain in Adolescents: The Role of Sleep Disturbance.

References

Journal of Pediatric Psychology, *48*(11), 931–939. https://doi.org/10.1093/jpepsy/jsad063

Roman-Juan, J., Solé, E., Sánchez-Rodríguez, E., Castarlenas, E., Jensen, M. P., & Miró, J. (2023b). Validation of the pediatric version of the Graded Chronic Pain Scale Revised in school-aged children and adolescents. *PAIN*, *164*(11), 2606–2614. https://doi.org/10.1097/j.pain.0000000000002965

Rosenbloom, B. N., Rabbitts, J. A., & Palermo, T. M. (2017). A developmental perspective on the impact of chronic pain in late adolescence and early adulthood: Implications for assessment and intervention. *PAIN*, *158*(9), 1629–1632. https://doi.org/10.1097/j.pain.0000000000000888

Roth-Isigkeit, A., Thyen, U., Stöven, H., Schwarzenberger, J., & Schmucker, P. (2005). Pain among children and adolescents: Restrictions in daily living and triggering factors. *Pediatrics*, *115*(2), e152–e162. https://doi.org/10.1542/peds.2004-0682

Rovio, S. P., Yang, X., Kankaanpää, A., Aalto, V., Hirvensalo, M., Telama, R., Pahkala, K., Hutri-Kähönen, N., Viikari, J. S., & Raitakari, O. T. (2018). Longitudinal physical activity trajectories from childhood to adulthood and their determinants: The Young Finns Study. *Scandinavian Journal of Medicine & Science in Sports*, *28*(3), 1073–1083. https://doi.org/10.1111/sms.12988

Roy, R., Galán, S., Sánchez-Rodríguez, E., Racine, M., Solé, E., Jensen, M. P., & Miró, J. (2022). Cross-National Trends of Chronic Back Pain in Adolescents: Results From the HBSC Study, 2001-2014.

References

The Journal of Pain, *23*(1), 123–130. https://doi.org/10.1016/j.jpain.2021.07.002

Siddall, P. J., & Cousins, M. J. (2004). Persistent pain as a disease entity: Implications for clinical management. *Anesthesia & Analgesia*, *99*(2), 510–520. https://doi.org/10.1213/01.ANE.0000133383.17666.3A

Sillanpää, M., & Saarinen, M. M. (2017). Long term outcome of childhood onset headache: A prospective community study. *Cephalalgia*, *38*(6), 1159–1166. https://doi.org/10.1177/0333102417727536

Simons, L., Pielech, M., Erpelding, N., Linnman, C., Moulton, E., Sava, S., Lebel, A., Serrano, P., Sethna, N., & Berde, C. (2014). The responsive amygdala: Treatment-induced alterations in functional connectivity in pediatric complex regional pain syndrome. *PAIN*, *155*(9), 1727–1742.

Sinclair, C. M., Meredith, P., Strong, J., & Feeney, R. (2016). Personal and contextual factors affecting the functional ability of children and adolescents with chronic pain: A systematic review. *Journal of Developmental & Behavioral Pediatrics*, *37*(4), 327–342. https://doi.org/10.1097/DBP.0000000000000300

Smith, B. H., Fors, E. A., Korwisi, B., Barke, A., Cameron, P., Colvin, L., Richardson, C., Rief, W., & Treede, R. D. (2019). The IASP classification of chronic pain for ICD-11: Applicability in primary care. *PAIN*, *160*(1), 83–87. https://doi.org/10.1097/j.pain.0000000000001360

References

Solé, E., Roman-Juan, J., Sánchez-Rodríguez, E., Castarlenas, E., Jensen, M. P., & Miró, J. (2023). School bullying and peer relationships in children with chronic pain. *PAIN*, *165*(5), 1169–1176. https://doi.org/10.1097/j.pain.0000000000003118

Solé, E., Sharma, S., Ferreira-Valente, A., Pathak, A., Sánchez-Rodríguez, E., Jensen, M. P., & Miró, J. (2022). The Associations between Sleep Disturbance, Psychological Dysfunction, Pain Intensity, and Pain Interference in Children with Chronic Pain. *Pain Medicine (United States)*, *23*(6), 1106–1117. https://doi.org/10.1093/pm/pnab333

Soltani, S., Kopala-Sibley, D. C., & Noel, M. (2019). The Co-occurrence of Pediatric Chronic Pain and Depression: A Narrative Review and Conceptualization of Mutual Maintenance. *Clinical Journal of Pain*, *35*(7), 633–643. https://doi.org/10.1097/AJP.0000000000000723

Soltani, S., Noel, M., Bernier, E., & Kopala-Sibley, D. C. (2023). Pain and insomnia as risk factors for first lifetime onsets of anxiety, depression, and suicidality in adolescence. *PAIN*, *164*(8), 1810–1819. https://doi.org/10.1097/j.pain.0000000000002879

Sommer, A., Grothus, S., Claus, B. B., Stahlschmidt, L., & Wager, J. (2023). Fatigue in Children and Adolescents: A Population-Based Longitudinal Study on Fatigue and Chronic Pain. *The Journal of Pediatric Psychology*, *48*(7), 626–635. https://doi.org/10.1093/jpepsy/jsad026

Stanford, E. A., Chambers, C. T., Biesanz, J. C., & Chen, E. (2008). The frequency, trajectories and predictors of adolescent recurrent pain:

References

A population-based approach. *PAIN*, *138*(1), 11–21. https://doi.org/10.1016/j.pain.2007.10.032

Stone, A. L., & Wilson, A. C. (2016). Transmission of risk from parents with chronic pain to offspring: An integrative conceptual model. *PAIN*, *157*(12), 2628–2639. https://doi.org/10.1097/j.pain.0000000000000637

Su, Q., Chen, Z., Li, R., Elgar, F. J., Liu, Z., & Lian, Q. (2018). Association Between Early Menarche and School Bullying. *Journal of Adolescent Health*, *63*(2), 213–218. https://doi.org/10.1016/j.jadohealth.2018.02.008

Sufrinko, A. M., Valrie, C. R., Lanzo, L., Bond, K. E., Trout, K. L., Ladd, R. E., & Everhart, D. E. (2015). Empirical validation of a short version of the Adolescent Sleep–Wake Scale using a sample of ethnically diverse adolescents from an economically disadvantage community. *Sleep Medicine*, *16*(10), 1204–1206.

Sullivan, M. J. L., Thorn, B., Haythornthwaite, J. A., Keefe, F., Martin, M., Bradley, L. A., & Lefebvre, J. C. (2001). Theoretical perspectives on the relation between catastrophizing and pain. *The Clinical Journal of Pain*, *17*(1), 52–64.

Swain, M. S., Henschke, N., Kamper, S. J., Gobina, I., Ottová-Jordan, V., & Maher, C. G. (2016). Pain and moderate to vigorous physical activity in adolescence: An international population-based survey. *Pain Medicine (United States)*, *17*(5), 813–819. https://doi.org/10.1111/pme.12923

References

Tegethoff, M., Belardi, A., Stalujanis, E., & Meinlschmidt, G. (2015). Comorbidity of mental disorders and chronic pain: Chronology of onset in adolescents of a national representative cohort. *The Journal of Pain*, *16*(10), 1054–1064.

Tracey, I., & Bushnell, M. C. (2009). How Neuroimaging Studies Have Challenged Us to Rethink: Is Chronic Pain a Disease? *The Journal of Pain*, *10*(11), 1113–1120. https://doi.org/10.1016/j.jpain.2009.09.001

Treede, R. D., Rief, W., Barke, A., Aziz, Q., Bennett, M. I., Benoliel, R., Cohen, M., Evers, S., Finnerup, N. B., First, M. B., Giamberardino, M. A., Kaasa, S., Korwisi, B., Kosek, E., Lavand'Homme, P., Nicholas, M., Perrot, S., Scholz, J., Schug, S., … Wang, S. J. (2019). Chronic pain as a symptom or a disease: The IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). *PAIN*, *160*(1), 19–27. https://doi.org/10.1097/j.pain.0000000000001384

Treede, R. D., Rief, W., Barke, A., Aziz, Q., Bennett, M. I., Benoliel, R., Cohen, M., Evers, S., Finnerup, N. B., First, M. B., Giamberardino, M. A., Kaasa, S., Kosek, E., Lavand'homme, P., Nicholas, M., Perrot, S., Scholz, J., Schug, S., Smith, B. H., … Wang, S. J. (2015). A classification of chronic pain for ICD-11. *PAIN*, *156*(6), 1003–1007. https://doi.org/10.1097/j.pain.0000000000000160

Tumin, D., Drees, D., Miller, R., Wrona, S., Hayes Jr., D., Tobias, J. D., & Bhalla, T. (2018). Health Care Utilization and Costs Associated

References

With Pediatric Chronic Pain. *The Journal of Pain*, *19*(9), 973–982. https://doi.org/10.1016/j.jpain.2018.03.012

Turk, D. C., Wilson, H., Swanson, K. S., Ebert, M., & Kerns, R. (2011). The biopsychosocial model of pain and pain management. In *Behavioral and psychopharmacologic pain management* (pp. 16–43). Cambridge University Press.

Varni, J. W., Magnus, B., Stucky, B. D., Liu, Y., Quinn, H., Thissen, D., Gross, H. E., Huang, I.-C., & DeWalt, D. A. (2014). Psychometric properties of the PROMIS ® pediatric scales: Precision, stability, and comparison of different scoring and administration options. *Quality of Life Research : An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, *23*(4), 1233–1243. https://doi.org/10.1007/s11136-013-0544-0

Varni, J. W., Seid, M., & Kurtin, P. S. (2001). PedsQL™ 4.0: Reliability and validity of the Pediatric Quality of Life Inventory™ Version 4.0 Generic Core Scales in healthy and patient populations. *Medical Care*, *39*(8), 800–812. https://doi.org/10.1097/00005650-200108000-00006

Varni, J. W., Stucky, B. D., Thissen, D., Dewitt, E. M., Irwin, D. E., Lai, J. S., Yeatts, K., & Dewalt, D. A. (2010). PROMIS pediatric pain interference scale: An item response theory analysis of the pediatric pain item bank. *The Journal of Pain*, *11*(11), 1109–1119. https://doi.org/10.1016/j.jpain.2010.02.005

Vervoort, T., Logan, D. E., Goubert, L., De Clercq, B., & Hublet, A. (2014). Severity of pediatric pain in relation to school-related functioning

References

and teacher support: An epidemiological study among school-aged children and adolescents. *PAIN*, *155*(6), 1118–1127. https://doi.org/10.1016/j.pain.2014.02.021

Von Korff, M. (2011). Assessment of chronic pain in epidemiological and health services research: Empirical bases and new directions. In *Handbook of pain assessment, 3rd ed.* (pp. 455–473). The Guilford Press.

Von Korff, M., Debar, L. L., Krebs, E. E., Kerns, R. D., Deyo, R. A., & Keefe, F. J. (2020). Graded chronic pain scale revised: Mild, bothersome, and high-impact chronic pain. *PAIN*, *161*(3), 651–661. https://doi.org/10.1097/j.pain.0000000000001758

Von Korff, M., & Dunn, K. M. (2008). Chronic pain reconsidered. *PAIN*, *138*(2), 267–276. https://doi.org/10.1016/j.pain.2007.12.010

Von Korff, M., Ormel, J., Keefe, F. J., & Dworkin, S. F. (1992). Grading the severity of chronic pain. *PAIN*, *50*(2), 133–149. https://doi.org/10.1016/0304-3959(92)90154-4

Von Korff, M., Scher, A. I., Helmick, C., Carter-Pokras, O., Dodick, D. W., Goulet, J., Hamill-Ruth, R., LeResche, L., Porter, L., Tait, R., Terman, G., Veasley, C., & Mackey, S. (2016). United States National Pain Strategy for Population Research: Concepts, Definitions, and Pilot Data. *The Journal of Pain*, *17*(10), 1068–1080. https://doi.org/10.1016/j.jpain.2016.06.009

Vowles, K. E., Rosser, B., Januszewicz, P., Morlion, B., Evers, S., & Eccleston, C. (2014). Everyday pain, analgesic beliefs and analgesic behaviours in Europe and Russia: an epidemiological

References

survey and analysis. *European Journal of Hospital Pharmacy: Science and Practice*, *21*(1), 39-44.

Wager, J., Brown, D., Kupitz, A., Rosenthal, N., & Zernikow, B. (2020). Prevalence and associated psychosocial and health factors of chronic pain in adolescents: Differences by sex and age. *European Journal of Pain (United Kingdom)*, *24*(4), 761–772. https://doi.org/10.1002/ejp.1526

Wager, J., Hechler, T., Darlington, A. S., Hirschfeld, G., Vocks, S., & Zernikow, B. (2013). Classifying the severity of paediatric chronic pain—An application of the chronic pain grading. *European Journal of Pain (United Kingdom)*, *17*(9), 1393–1402. https://doi.org/10.1002/j.1532-2149.2013.00314.x

Walco, G. A., Gove, N., Phillips, J., & Weisman, S. J. (2017). Opioid Analgesics Administered for Pain in the Inpatient Pediatric Setting. *The Journal of Pain*, *18*(10), 1270–1276. https://doi.org/10.1016/j.jpain.2017.06.001

Walco, G. A., Krane, E. J., Schmader, K. E., & Weiner, D. K. (2016). Applying a lifespan developmental perspective to chronic pain: Pediatrics to geriatrics. *The Journal of Pain*, *17*(9), T108–T117. https://doi.org/10.1016/j.jpain.2015.11.003

Walker, L. S., Dengler-Crish, C. M., Rippel, S., & Bruehl, S. (2010). Functional abdominal pain in childhood and adolescence increases risk for chronic pain in adulthood. *PAIN*, *150*(3), 568–572. https://doi.org/10.1016/j.pain.2010.06.018

References

Walker, L. S., & Greene, J. W. (1991). The functional disability inventory: Measuring a neglected dimension of child health status. *Journal of Pediatric Psychology*, *16*(1), 39–58. https://doi.org/10.1093/jpepsy/16.1.39

Walker, L. S., Sherman, A. L., Bruehl, S., Garber, J., & Smith, C. A. (2012). Functional abdominal pain patient subtypes in childhood predict functional gastrointestinal disorders with chronic pain and psychiatric comorbidities in adolescence and adulthood. *PAIN*, *153*(9), 1798–1806. https://doi.org/10.1016/j.pain.2012.03.026

Walters, C. B., Kynes, J. M., Sobey, J., Chimhundu-Sithole, T., & Kelly Mcqueen, K. A. (2018). Chronic pediatric pain in low-and middle-income countries. *Children*, *5*(9). https://doi.org/10.3390/children5090113

Walters, E. T., & Williams, A. C. de C. (2019). Evolution of mechanisms and behaviour important for pain. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *374*(1785), 20190275. https://doi.org/10.1098/rstb.2019.0275

Weisman, A., Quintner, J., & Masharawi, Y. (2019). Congenital Insensitivity to Pain: A Misnomer. *The Journal of Pain*, *20*(9), 1011–1014. https://doi.org/10.1016/j.jpain.2019.01.331

Werner, M. U., & Kongsgaard, U. E. (2014). I. Defining persistent post-surgical pain: Is an update required? *BJA: British Journal of Anaesthesia*, *113*(1), 1–4. https://doi.org/10.1093/bja/aeu012

Wilson, A. C., & Palermo, T. M. (2012). Physical activity and function in adolescents with chronic pain: A controlled study using actigraphy.

References

The Journal of Pain, *13*(2), 121–130. https://doi.org/10.1016/j.jpain.2011.08.008

World Health Organization. (2007). *International Classification of Functioning, Disability, and Health: Children & Youth Version: ICF-CY.* World Health Organization.

Zhang, C., Brook, J. S., Leukefeld, C. G., De La Rosa, M., & Brook, D. W. (2017). Lack of preventive health behaviors in the early forties: The role of earlier trajectories of cigarette smoking from adolescence to adulthood. *Substance Use & Misuse*, *52*(12), 1527–1537. https://doi.org/10.1080/10826084.2017.1281310