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Adverse childhood experiences and bodily pain at 10 years of age: Findings from the Generation XXI cohort

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ABSTRACT

Background: Youth and young adults with pain conditions report having a history of adverse childhood experiences (ACEs) more frequently than their healthy peers. The relationship between ACEs and pain before adolescence in population-based settings is not extensively researched.
Objective: To examine the association between the history of ACEs and bodily pain at 10 years of age.
Participants and setting: Cross-sectional analysis of 4738 participants of Generation XXI population-based birth cohort, recruited in 2005–06 in Porto, Portugal.
Methods: Study includes self-reported data on ACEs exposures and bodily pain (pain presence, sites, and intensity a week prior to the interview). Adjusted odds ratios (AOR) and 95% confidence intervals (CI) were obtained from binary and multinomial logistic regression analyses to estimate the likelihood of various pain features according to the extent of exposure to ACEs (i.e., 0 ACEs, 1–3 ACEs, 4–5 ACEs, and $\geq$ 6 ACEs).
Results: Prevalence of pain, multisite, and high-intensity pain a week prior to the interview increased with increasing exposure to ACEs. After controlling for sociodemographic characteristics, children who had experienced $\geq$6 ACEs were more likely to report pain [AOR 3.18 (95% CI 2.19, 4.74)], multisite pain [AOR 2.45 (95% CI 1.37, 4.40)], and high-intensity pain [AOR 4.27 (95% CI 2.56, 7.12)] compared with children with no ACEs.
Conclusions: A dose-response association was observed between the cumulative number of ACEs and reports of pain in 10-year-old children, suggesting that embodiment of ACEs starts as early as childhood and that pain related to ACEs begins earlier than previously reported.

1. Introduction

Adverse childhood experiences (ACEs) are traumatic situations perpetrated against the child or acts of neglect directed at the child, before the age of 18 years, as well as any other conditions that affect the family environment, making it dysfunctional (Felitti et al., 1998).

A landmark study by Felitti et al. (1998) reported a strong dose-dependent association between the cumulative number of ACEs and an array of poor health and behavioral outcomes in adulthood. Subsequent research broadened the content of the adverse experience and showed that increased number of ACEs was associated with a higher risk of adverse health outcomes, including health risk

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behaviors (Garrido et al., 2018), mental health problems (Fuller-Thomson et al., 2016; Kerker et al., 2015), physiologic disruptions (i.e., alterations in immune function and increases in inflammatory markers) (Danese & McEwen, 2012; Fraga et al., 2014; Miller et al., 2011), consequently chronic disease development (Felitti et al., 1998; Miller et al., 2011), and ultimately premature mortality (Brown et al., 2009).

Evidence also suggests that exposure to childhood adversity is a vulnerability factor for chronic pain in adulthood (Anda et al., 2010; Tietjen et al., 2012). Among the potential mechanisms that link childhood adversity to the onset of chronic pain is a dysregulation of centrally mediated stress-response processes: exposure to chronic stress may induce significant biological changes (biological embedding) and modify the maturation and responsiveness of allostatic systems (namely the nervous, endocrine, and immune systems) (Danese & McEwen, 2012; McEwen & Kalia, 2010). Over-activation of the hypothalamic-pituitary-adrenal (HPA) axis has been directly implicated in increasing risk for the development and/or maintenance of long-term detrimental effects on health (Danese & McEwen, 2012), including chronic pain (McEwen & Kalia, 2010).

In the pain literature, the relationship between ACEs and pain is less well researched and primarily based on reports of adults who have experienced adversity for years (Anda et al., 2010; Felitti et al., 1998; Kalmakis & Chandler, 2015). The evidence available also suggests that youth and young adults with certain pain conditions (including migraine, recurrent headaches, abdominal pain, and fibromyalgia) report having a history of ACEs more frequently than their healthy peers (Groenewald et al., 2020; Nelson et al., 2017; Stensland et al., 2013). Understanding the association between exposure to ACEs and pain early in life is particularly relevant to clarify the roots of lifelong pain syndromes. Although previous research is compelling, to date the relationship between ACEs and pain has mainly been examined in established pain conditions (King et al., 2011; Nelson et al., 2017) and/or using a limited assessment of ACEs exposure (i.e., only sexual and/or physical abuse) (Groenewald et al., 2020; Stensland et al., 2013).

Thus, we aimed to examine the association between the history of ACEs and pain reports in 10-year-old children from the Generation XXI birth cohort. We hypothesized that children with a history of ACEs would have an increased likelihood of reporting pain history, even after controlling for sociodemographic context. We also expected that children with cumulative exposure to multiple ACEs would experience more adverse pain when compared to children with fewer ACEs or no history of ACEs.

2. Methods

2.1. Study design and participants

Participants in this study are from the Generation XXI population-based birth cohort (Alves et al., 2012), which was assembled in 2005–06 from the five public maternity units providing obstetrical and neonatal care covering the metropolitan area of Porto, Portugal. Data collection procedures and measures have been described in detail elsewhere (Alves et al., 2012). Briefly, of the invited mothers, 91.4% accepted to participate, and their 8647 infants were enrolled in the cohort. Since then, the entire cohort was invited to attend the first (2009–2011), second (2012–2014), and third (2016–2017) follow-ups, when children were four, seven, and ten years of age, respectively. The study protocol complied with the ethical principles outlined in the Declaration of Helsinki and was approved by the joint Ethics Committee of the São João Hospital and University Centre and the University of Porto Medical School (CES-01/2017). It is also registered with the Portuguese Authority of Data Protection (Authorization n° 5833/2011). Written informed consent was obtained from all parents or legal guardians and oral assent was obtained from children at each evaluation.

The present study is a cross-sectional study based on the 10-year follow-up evaluation ($n = 6397$, participation rate 76%). Adverse childhood experiences were reported by 5366 children. Our final sample consisted of 4738 children with complete information on pain and adverse childhood experiences (2317 girls and 2421 boys; 628 children did not complete the pain assessment questionnaire). Children who participated in the present study did not differ from the remaining cohort participants with respect to sex (48.9% girls vs. 49.0% girls) and family structure (77.6% vs. 79.5% living with both parents). However, they belonged to families with a lower monthly disposable household income (27.4% vs. 24.7% with income ≤1000€/month), and were less likely to report no history of ACEs (0.4% vs. 7.5% reporting 0 ACEs) (Supplementary Table 1).

2.2. Exposure

2.2.1. Adverse childhood experiences

To assess the exposure to lifetime ACEs in children, we used 15 questions adapted from the ACEs study (Felitti et al., 1998). The questionnaire was handed out to the children, who answered in private in the presence of a trained interviewer if they needed any assistance. The children included in this study come from the third wave of the Generation XXI cohort. A familiar and safe environment was ensured by conducting the interviews in the same facilities and having the same interviewers administering the questionnaires during the third wave as in the baseline. Exposure to childhood adversity was calculated by summing the occurrences among the adversities assessed, each classified as binary (0/1). Subsequently, total childhood adversity was categorized into 0 ACEs, 1–3 ACEs, 4–5 ACEs, and ≥ 6 ACEs. The prevalence of child-reported ACEs is presented in Supplementary Table 2.

2.3. Outcomes

2.3.1. Pain in children

A structured questionnaire was applied to collect information on children's pain experience in a week prior to the interview. Children aged 10 were asked *"During the last week, did you feel pain in any region of your body?"*. Those who answered affirmatively were asked to indicate in a body chart the area(s) where they felt pain. Children could select more than one area from the head, neck, back, shoulders, upper limbs, hands, chest, abdomen, hips, lower limbs, and feet. Pain experienced in any other body site (i.e., face, eyes, nose, mouth, teeth, gums, tongue, chin, throat, ears, genitals, groin, bladder, anus) was counted for 1 site. *The number of pain sites* was categorized as 0 (no pain), 1 site, and ≥ 2 sites (multisite pain). Children were also asked to select the pain that bothered them the most in the previous week. For the pain that was described as the main source of discomfort, the children were asked to specify the *intensity of the pain* using the original Wong-Baker Faces Pain Scale (FPS) (Bieri et al., 1990) that consists of 6 faces, with each face representing an increasing pain intensity. *The intensity of pain* was categorized as no pain, low (FPS 1–3), and high (FPS 4–6).

2.3.2. Covariates

Data were collected on the following sociodemographic characteristics: sex at birth (classified as girls vs. boys), family structure (classified as "living with both parents" vs. "living in lone parenthood or with others", if the child is living only with the mother, or only with the father, or with other family members), and monthly household income (classified as ≤1000€/month vs. 1001–2000€/month vs. >2000€/month).

Table 1
Sample characteristics, N = 4738

	n (%)
Sex	
girls	2317 (48.9)
boys	2421 (51.1)
BMI z-score[a]	
Underweight and normal weight	2753 (58.1)
Overweight	1208 (25.5)
Obese	776 (16.4)
missings	1 (0.0)
History of child chronic disease[b]	
no	4068 (85.9)
yes	670 (14.1)
Family structure	
living in lone parenthood or with others	1063 (22.4)
living with both parents	3675 (77.6)
Disposable household income (€/month)	
≤1000	1252 (27.4)
1001–2000	2187 (47.8)
>2000	1134 (24.8)
Adverse childhood experiences	
0	187 (3.9)
1–3	1898 (40.1)
4–5	1377 (29.1)
≥6	1274 (26.9)
Pain in the week before the interview	
no	3073 (64.9)
yes	1665 (35.1)
Pain sites in the week before the interview[c]	
no pain	3073 (64.9)
1 site	1208 (25.5)
≥2 sites	457 (9.6)
Intensity of pain in the week before the interview[d]	
no pain	3073 (64.9)
low	628 (13.3)
high	1035 (21.8)

[a] BMI z-score was recoded as Underweight/Normal weight (≤1Standard Deviation (SD)); Overweight (>1SD to <2SD), and Obesity (≥2SD) based on the World Health Organization recommendations.

[b] History of child chronic disease was recoded based on the following predefined diagnosis (asthma, epilepsy, diabetes, heart disease, and kidney failure) as "no" if child does not have any of these diagnoses and "yes" if at least one diagnosis was present).

[c] Pain sites were recoded from the children's selection of anatomical sites where they felt the pain in the week before the interview, from a body chart that included: head, neck, back, shoulders, upper limbs, hands, chest, abdomen, hips, lower limbs, feet, and other sites (i.e., face, eyes, nose, mouth, teeth, gums, tongue, chin, throat, ears, genitals, groin, bladder, anus). Pain experienced in other body sites counted for 1 site.

[d] Intensity of pain was recoded as follows: no pain, low (FPS 1–3), and high (FPS ≥ 4).

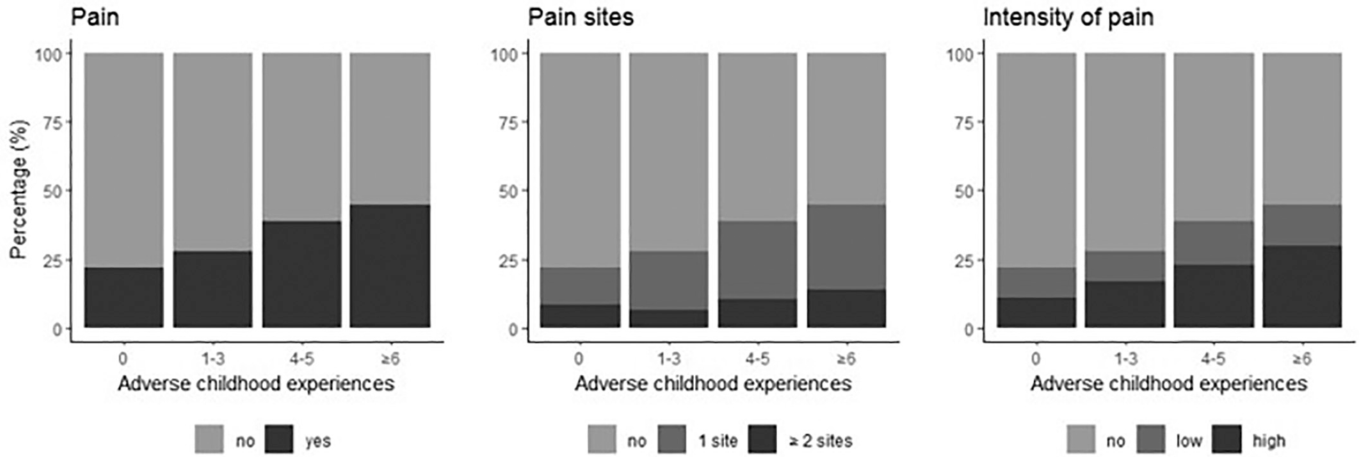

Fig. 1. Distribution (%), of pain a week before the interview, pain sites, and intensity of pain by the number of adverse childhood experiences, $N = 4738$.

2.4. Statistical analysis

Sample characteristics were summarized descriptively using counts and percentages. A Chi-square test was used to test for associations between ACEs and sociodemographic characteristics; reports of pain and sociodemographic characteristics; and reports of ACEs and pain. Binary logistic regression was used to assess the associations between pain a week before the interview and the four categories of exposure to ACEs. Multinomial logistic regression was employed to model the relationship between the number of ACEs and pain sites and intensity of pain. We also tested whether adjustment for selected sociodemographic characteristics altered the estimated strength of associations between ACEs and pain. A sensitivity analysis was conducted by modifying the three response variables related to pain to only track non-specific pain reports (i.e., head, back, neck, shoulders, and abdomen). All statistical analyses were performed in R version 3.6.1 (R Core Team, 2020).

3. Results

Characteristics of the 4738 children included in our study are summarized in Table 1. Prevalence of pain in a week before the interview was 35.1%. Two or more pain sites were reported by 9.6% of children, and the prevalence of high intensity pain was 21.8%. The most frequently reported pain was located in the lower limb (31.9%), followed by the abdomen (19.0%), and head (12.1%) (Supplementary Table 3).

The prevalence of experienced pain varied according to exposure to ACEs: among children with no history of ACEs, the prevalence of any pain a week before the interview was 21.9%, compared to 38.6% among those who experienced 4–5 ACEs. The prevalence of pain increased to 44.7% for children who experienced ≥6 ACEs. With an increasing number of ACEs, the report of pain at 1 site increases (21.1% for 1–3 ACEs, 28.1% for 4–5 ACEs, and 31.1% for ≥6 ACEs). A similar trend was observed for both low and high intensity pain and exposure to ACEs (Fig. 1).

A higher number of ACEs (≥4 ACEs) was observed in boys, children living in lone parenthood or with others (40.6% vs. 22.9%), those from low household income (≤1000€/mo = 34.9% vs. 1001–2000€/mo = 24.8% vs. >2000€/mo = 21.8%) (Table 2). The prevalence of pain a week before the interview was higher among girls (36.1% vs. 34.2%), those living in lone parenthood or with others (40.5% vs. 33.6%), and those from low household income (≤1000€/mo = 35.3% vs. 1001–2000€/mo = 34.9% vs. >2000€/mo =34.9%). Similar trend was found for the prevalence of high intensity pain. The prevalence of multisite pain (≥2 sites) was higher among boys than girls (9.8% vs. 9.5%) (Table 3).

When compared to children with no pain in the previous week, the most commonly reported ACEs for children with pain were "household member shout, yelled or screamed at the child" (53.9% vs. 64.6%), "witnessing parents arguing or fighting" (41.9% vs. 49.2%), bullying victimization at school (40.0% vs. 48.1%), "death of a family member" (41.6% vs. 47.9%), and the least commonly reported ACE was "household member alcohol abuse or drug addiction" (1.4% vs. 2.3%) (Supplementary Table 2).

Logistic regression analyses revealed that after controlling for sociodemographic variables, children who had experienced ACEs were more likely to report pain a week before the interview than those without ACEs [aOR 1.46 for 1–3 ACEs (95% CI 1.01, 2.15) vs. aOR 2.40 for 4–5 ACEs (95% CI 1.66, 3.56) vs. aOR 3.18 for ≥6 ACEs (95% CI 2.19, 4.74)]. Similarly, a strong association was observed between exposure to ACEs and high intensity pain (FPS ≥ 4). Even after controlling for covariates, children who had reported a history of ACEs were more likely to report high intensity pain as compared to those with no ACEs history [aOR 1.80 for 1–3 ACEs (95% CI 1.08, 2.98) vs. aOR 2.82 for 4–5 ACEs (95% CI 1.69, 4.71) vs. aOR 4.27 for ≥6 ACEs (95% CI 2.56, 7.12)]. Similar trends were observed for the associations between exposure to ACEs and one pain site. We observed associations between exposure to ACEs and multisite pain (≥2 sites) in children who had been exposed to ≥6 ACEs [aOR 2.45 (95% CI 1.37, 4.40)], even after controlling for child sex, family structure, and monthly disposable household income (Table 4). As a sensitivity analysis, we re-ran the analysis by modifying the three response variables related to pain to only track non-specific pain reports (i.e., head, back, neck, shoulders, and abdomen), the estimates remained very similar to our first analysis (Supplementary Table 4).

Table 2
Prevalence of number of adverse childhood experiences by sociodemographic characteristics, $N = 4738$

Number of adverse childhood experiences, n (%)				
	0 ACEs	1–3 ACEs	4–5 ACEs	≥6 ACEs
Sex				
girls	115 (5.0)	1040 (44.9)	667 (28.8)	493 (21.3)
boys	72 (3.0)	858 (35.4)	710 (29.3)	781 (32.3)
Family structure				
living in lone parenthood or with others	3 (0.3)	264 (24.8)	364 (34.2)	432 (40.6)
living with both parents	184 (5.0)	1634 (44.5)	1013 (27.6)	842 (22.9)
Disposable household income (€/month)				
≤1000	27 (2.2)	409 (32.7)	379 (30.3)	437 (34.9)
1001–2000	97 (4.4)	923 (42.2)	623 (28.5)	543 (24.8)
>2000	55 (4.9)	509 (44.9)	322 (28.4)	247 (21.8)

Table 3
Prevalence of pain a week before the interview, pain sites, and intensity of pain by sociodemographic characteristics, N = 4738

	Pain, n (%)		Pain sites, n (%)			Intensity of pain, n (%)		
	no	yes	no pain	1 site	≥2 sites	no pain	low	high
Sex								
girls	1480 (63.9)	837 (36.1)	1480 (63.9)	618 (26.7)	219 (9.5)	1480 (63.9)	300 (13.0)	536 (23.1)
boys	1593 (65.8)	828 (34.2)	1593 (65.8)	590 (24.4)	238 (9.8)	1593 (65.8)	328 (13.6)	499 (20.6)
Family structure								
living in lone parenthood or with others	633 (59.5)	430 (40.5)	633 (59.5)	308 (29.0)	122 (11.5)	633 (59.7)	140 (13.2)	288 (27.1)
living with both parents	2440 (66.4)	1235 (33.6)	2440 (66.4)	900 (24.5)	335 (9.1)	2440 (66.4)	488 (13.3)	747 (20.3)
Disposable household income (€/month)								
≤1000	810 (64.7)	442 (35.3)	810 (64.7)	319 (25.5)	123 (9.8)	810 (64.7)	319 (25.5)	123 (9.8)
1001–2000	1424 (65.1)	763 (34.9)	1424 (65.1)	553 (25.3)	210 (9.6)	1424 (65.1)	553 (25.3)	210 (9.6)
>2000	738 (65.1)	396 (34.9)	738 (65.1)	292 (25.7)	104 (9.2)	738 (65.1)	292 (25.7)	104 (9.2)

4. Discussion

In our study, most of the children reported at least one adverse event during childhood. The high frequency of these events is attributable to the definition adopted, the measurements, and the methodology used. The prevalence of ACEs varies considerably across studies. According to the recent systematic review of evidence (includes international samples ($N = 44$) and samples from the United States ($N = 52$)) published between 1990 and 2015 the prevalence of multiple ACEs in school-aged youth is ranging from 41% to 97%) (Carlson et al., 2020). Around 85% of Brazilian adolescents have reported at least one adverse event during childhood (Soares et al., 2016). One third of children in our sample reported experiencing pain a week prior to the interview. Pain prevalence, number of sites, and intensity of pain varied according to the increasing exposure to ACEs, with children experiencing the most ACEs reporting more adverse pain experiences. Specifically, after controlling for sex, family structure, and monthly disposable household income, the number of childhood adverse events predicted the report of adverse pain experiences at 10 years of age. Our results are consistent with prior studies carried out in children and adolescent populations (Groenewald et al., 2020; Stensland et al., 2013) and indicate that children with a history of ACEs have an increased risk for experiencing pain, and that this association increased in a dose-dependent manner. The present findings are all the more critical given that this is a population-based investigation where children were selected independently of ACEs and pain complaints, and therefore both the spectrum of pain experiences and the variability of ACEs are expected to reflect the general population of 10-year-old children.

Consistent with prior research (Bakoula et al., 2006; Boey et al., 2000; Huguet & Miró, 2008; Nelson et al., 2018; Petersen et al., 2003), no sex differences were observed, whether in the prevalence of experienced pain a week before the interview, or in the number of pain sites, or intensity of pain. These results were similar to those reported by Boey et al. (2000) that the prevalence of abdominal pain in Malaysian children and adolescents (aged 11–16 years) did not differ by sex. Similarly, Petersen et al. (2003) reported no sex difference for backache among young school children (aged 6–13 years) in Sweden. Nelson et al. (2018) reported no differences in the ratings of pain intensity related to sex. Yet, some studies observed sex differences in the prevalence of reported pain and its intensity (King et al., 2011; Vierhausl et al., 2011). The explanation for this inconsistency of results may to some extent be the differences in definitions of pain, single vs. multiple pain sites, age of the respondents, methodology applied, as well as the recall period (King et al., 2011). Also, both biological and psychosocial mechanisms may play a fundamental role in sex-related differences in pain perception and reporting, such as significantly higher pain threshold and pain tolerance in boys than in girls (Boerner et al., 2014), onset of pubertal development (Hoyt et al., 2020) stereotypical gender roles (i.e., pain expression is generally more socially acceptable among girls than boys) (Alabas et al., 2012).

The prevalence of bodily pain (i.e., pain a week before the interview, number of pain sites, and intensity of pain) was found to be higher in children from low-income households, and those living in lone parenthood or with others. Across studies, the findings were mixed concerning the sociodemographic factors associated with pain in children and adolescents (Bakoula et al., 2006; Bugdayci et al., 2005; Huguet & Miró, 2008; King et al., 2011). Bugdayci et al. (2005) reported that lower socioeconomic status (SES) was associated with higher pain prevalence for headache in school children (aged 8–16 years) when mothers had a low level of education and when there was a family history of headache. Our results are in line with those from Bakoula et al. (2006) who observed that in a sample of Greek children (7 years old), no association was determined between SES and recurrent complaints of pain. The contribution of SES to the development of long-term pain complaints requires further investigation (King et al., 2011).

Regarding the different ACEs, children who reported that the household member shouted, yelled, or screamed at them, those who witnessed parents arguing or fighting, experienced the death of a family member, or suffered bullying at school, or changed house, school, or neighborhood were more likely to experience pain a week before the interview as compared to children experiencing other type of ACEs. Thus, living in dysfunctional and/or conflictual home environments, as well as having school-related social difficulties

Table 4
Associations (Odds Ratios; 95% Confidence Intervals) between adverse childhood experiences and pain a week before the interview, pain sites, and intensity of pain, $N = 4738$

	Pain		Pain sites				Intensity of pain			
	OR (95% CI)	AOR (95% CI)[a]	OR (95% CI)		AOR (95% CI)[a]		OR (95% CI)		AOR (95% CI)[a]	
	yes	yes	1 site	≥2 sites	1 site	≥2 sites	low	high	low	high
0 ACEs	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
1–3 ACEs	1.35 (0.95, 1.96)	1.46 (1.01, 2.15)	1.70 (1.10, 2.63)	0.82 (0.47, 1.41)	1.78 (1.13, 2.82)	0.92 (0.52, 1.65)	1.03 (0.64, 1.67)	1.69 (1.05, 2.75)	1.14 (0.69, 1.88)	1.80 (1.08, 2.98)
4–5 ACEs	2.24 (1.57, 3.25)	2.40 (1.66, 3.56)	2.67 (1.71, 4.15)	1.55 (0.90, 2.68)	2.85 (1.80, 4.51)	1.66 (0.93, 2.99)	1.77 (1.09, 2.86)	2.72 (1.67, 4.41)	2.00 (1.21, 3.32)	2.82 (1.69, 4.71)
≥6 ACEs	2.88 (2.02, 4.19)	3.18 (2.19, 4.74)	3.29 (2.11, 5.11)	2.25 (1.31, 3.88)	3.62 (2.28, 5.76)	2.45 (1.37, 4.40)	1.86 (1.14, 3.02)	3.95 (2.44, 4.41)	2.14 (1.28, 3.58)	4.27 (2.56, 7.12)

[a] Adjusted for child sex, family structure, and disposable household income.

seem to play an important role in the onset of pain development in childhood. Each adversity may have a different impact on child's development and wellbeing but it is not expected to have a different effect on the direction of the association. In the scope of this study, we examined the cumulative effect of these experiences in child's pain.

Drawing from a biopsychosocial model of pain (Gatchel, 2004; Gatchel et al., 2007), Nelson et al. (2017) suggested a conceptual framework that highlights the potential exacerbating influence of ACEs on the development of chronic pain in youth. Specifically, biological (i.e., allostatic load), psychological (i.e., cognitive processes, psychological comorbidities), and social (i.e., family and peer/social environment) factors may impact the pain experience (Gatchel, 2004; Gatchel et al., 2007), but also many of the above-noted constructs may influence ACEs experienced in youth (Kerker et al., 2015). In the context of evidence suggesting a relationship between ACEs and increased risk for pain, more attention needs to be focused on the potentially complex interplay within ACEs and biopsychosocial factors to better understand the specific nature and magnitude of the risk that ACEs may have on the development and/or exacerbation of pain in children.

4.1. Study strengths and limitations

Most prior studies have examined the association between ACEs and pain among adults who have lived with the effects of their adverse experiences for years (Anda et al., 2010; Felitti et al., 1998; Kalmakis & Chandler, 2015). Further, much of the research to date only examines established pain conditions (King et al., 2011; Nelson et al., 2017) and/or is restricted in scope by only assessing limited ACEs (Groenewald et al., 2020; Stensland et al., 2013). In the current study, we measured the associations between several types of ACEs and pain located in multiple sites in a large sample of children, using data from a population-based birth cohort. Additionally, since pain is a subjective experience, self-reported measures are considered vital (von Baeyer, 2009; von Baeyer & Spagrud, 2007), taking into account that most children older than six years of age are already able to provide estimates of their pain using developmentally appropriate scales (Birnie et al., 2019; Boey et al., 2000).

Despite these strengths, limitations are also present in the design of the study. The cross-sectional nature of this study limits our ability to infer the direction of causality. The temporal sequence between pain and ACEs is unclear. We speculate that adverse events preceded the onset of pain, as adults' reports (Anda et al., 2010; Craner & Lake, 2021; Dennis et al., 2019) demonstrated a cumulative or "dose-response" relationship between the number of ACEs (that occurred before the age of 18) and pain in adulthood. It is also unclear whether associations between ACEs and pain experiences result from common susceptibility (confounding) or misclassification. Nevertheless, we adjusted for income as a proxy of socioeconomic confounders and tested several ACEs that are objective experiences, not likely subject to misclassification. Also, many of the ACEs in the Generation XXI cohort are objective experiences, that are much less subject to misreporting and confounding.

One of the most significant adverse experiences causing a lot of suffering relates to sexual abuse. However, this experience was deliberately excluded from the questionnaire administered to the children. Speaking to children themselves about sexual abuse is a complex task, and fraught with ethical, and methodological challenges (Merg, 2012). However, questions on this traumatic experience will be asked in adolescence.

Another limitation concerns reported pain. In our study, the pain was quantified in terms of presence, location, and intensity. We did not assess the frequency and duration of pain, as well as its impact pain on the child's well-being, namely on physical functioning or limitations due to pain. Even though it is important to assess all the dimensions of pain, pain intensity has been suggested to be one of the core outcome domains to be used in pediatric pain research (McGrath et al., 2008). Furthermore, in the current study we assessed pain in children that occurred one week before the interview, which is subject to fluctuations over time. Although the recent evidence confirms that there is already some stability of pain experience in the first decade according to maternal reports (Lucas et al., 2021). To provide a more accurate picture of the pattern of a child's pain, future investigation is required to track the pain experience over time.

5. Conclusions

This study shows a dose-response association between the number of ACEs and bodily pain in 10 years old children suggesting that embodiment of ACEs starts already in childhood and ACE-related pain begins earlier than previously reported.

The onset of pain early in life may indicate the precursor of pain-related problems later in life, which suggests that preventive measures should be taken at a young age. Additionally, screening for the presence of stressful or traumatic events should be considered for the children presenting pain experiences.

Drawing from biopsychosocial models of pain, future research needs to more fully explore the underlying mechanisms that may explain the link between ACEs and pain, including modifiable familial and socio-environmental factors to improve prevention and treatment approaches.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chiabu.2022.105620.

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