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Does birth weight or preterm birth predict worse pain prognosis in adulthood? A Northern Finland Birth Cohort study followed up to 46 years of age

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ABSTRACT

Although pain is a highly common symptom, only a subset of individuals develops chronic and disabling conditions. Delving into the predictors for poor musculoskeletal pain (MSK) outcomes in adulthood may help identify those needing early prevention and intervention. This study aimed to evaluate whether birth weight or preterm birth predicts worse prognosis of MSK pain in adulthood. Participants in the Northern Finland Birth Cohort 1966 were followed from birth to 46 years of age. Associations of birth weight (measured using corrections to gestational age) and preterm birth (<37 completed weeks) with high-risk classification for worse pain using three prognostic tools: the Örebro Musculoskeletal Pain Screening Questionnaire-Short Form (ÖMPSQ-SF), STartT Back Tool (SBT), and Risk of Pain Spreading (ROPS) assessed at 46 years among people reporting MSK pain (n=3200–4525). Log-binomial regression models for dummy outcomes (ÖMPSQ-SF and SBT) and generalized linear regression models for continuous outcomes (ROPS) were employed. Birth weight did not predict high-risk classification by any tool. Compared to full-term participants, those born preterm had higher risk of being classified into the high-risk group only according to ÖMPSQ-SF (relative risk 1.61, 95% confidence interval 1.00–2.59) and SBT (1.61, 1.14–2.28). Adjustments did not change these results. Preterm birth appeared to predict allocation to the group with poorer prognosis of MSK outcomes as measured by ÖMPSQ-SF and SBT, but not by ROPS. This highlights the need for further research into the role of preterm birth in the development or accumulation of adverse pain-related thoughts and experiences in mid-life.
Perspective: Preterm birth tended to predict allocation to the high-risk group for worse pain prognosis in adulthood. Similar was not observed concerning birth weight. Further research is warranted to validate the results and delve into explanatory pathways.

Introduction

Pain is an individual and subjective experience. All individuals experience pain at least once during their life course, but some individuals develop a chronic pain that persists for three months or longer. It is estimated that approximately 20% of individuals in the United

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States suffer from pain on most days or daily.[1] Chronic pain, especially musculoskeletal (MSK) pain, often significantly impairs functional capacity and health-related quality of life to a significant extent.[2,3]

The pathophysiology of many MSK pain conditions remains uncertain. Some suggests that early life conditions, such as preterm birth, may affect pain development[4] and alter modulation systems,[5] for example, through multiple early life invasive procedures (e.g., intubation, intra-arterial cannula insertion) preterm born individuals often are subjected to.[6] Research findings on self-reported pain[7–11] or pain sensitivity[12–15] in individuals born preterm or with very low birth weight are, however, inconsistent and limited in number, leaving room for additional research.

Chronic pain is largely shaped by numerous biopsychosocial factors.[16,17] Therefore, identifying specific prognostic factors or risk factors from this spectrum is crucial to reduce the risk of pain chronification and alleviate its burden. Several validated tools have been developed to this prognostic screening. Among others, Örebro Musculoskeletal Pain Screening Questionnaire-Short Form (ÖMPSQ-SF) and STarT Back Tool (SBT) are widely studied and used for MSK and low back pain (LBP), respectively. Both tools effectively identify psychosocial and symptom-related factors associated with chronic pain and adverse outcomes such as work-related disability.[18–20] Recently, a new instrument, labeled the Risk of Pain Spreading (hereafter ROPS), was introduced to predict the risk of pain chronicity and spreading.[21] This simple six-item tool captures key biopsychosocial factors for chronic pain and worse prognosis.

Individuals with different pain prognosis are likely to be different from their backgrounds. For instance, being in the low-risk group often associates with having more favorable lifestyle profiles and better mental well-being compared to belonging to the high-risk group.[22,23] Also, there are clear discrepancies in the socioeconomic status between the risk groups.[22,23] These findings indicate that there might be potential differences in early backgrounds as well, as factors like depression, obesity, and academic achievement, tend to partly originate from early lifespan, starting from pregnancy period and birth.[24–27] Therefore, investigating birth and pregnancy factors in relation to pain prognostic groups could enhance our understanding of those with the highest vulnerability.

In this population-based study using 46 years of longitudinal data, we aimed to explore the associations between birth weight or preterm birth and high risk for worse pain prognosis using validated prognostic instruments, ÖMPSQ-SF, SBT, and ROPS, among people reporting MSK pain at 46 years. Given the previous inconsistent findings in terms of development of pain symptoms and sensitivity among adolescents and young adults and the study's novelty, no specific a priori hypothesis was given.

Material and methods

Study population

The study population was the Northern Finland Birth Cohort 1966 (NFBC1966), with available prospective data from birth to 46 years of age. The NFBC1966 involves individuals expected to be born between 1st Jan and 31st Dec 1966, and their mothers who resident in the Northernmost provinces of Finland during that period,[28,29] covering 95.6% of all births in the area in 1966 (252 of children in the cohort were born in 1965 or 1967). A total of 12,058 children were live-born and had a birth weight of 600 g or more, formulating the NFBC1966 dataset, which have been followed since then.

In this study, we employed data from questionnaires, maternity cards, birth records, and clinical examinations that were collected during the antenatal period, at birth, and in the 46-year follow-up of the participants. The inclusion criteria for the study sample were the available information on birth weight, gestational age and sex, responding to at least one pain questionnaire and a written consent to use the data. The flowchart for the study is presented in Fig. 1. Of the NFBC1966 members invited to participate in the 46-year follow-up (n=10,331), 4871 (47%) met the inclusion criteria. The study was approved by the Ethics committee of the Northern Ostrobothnia Hospital District (94/2011, 12.12.2011) and followed the Declaration of Helsinki.

Birth weight and gestational age

Birth weight was characterized using birth weight-SD (standard deviation), which was calculated based on recorded birth weight, gestational age, and sex, using a reference of sex-specific birth weight corrected for gestational age in the Finnish population.[30] Birth weight-SD was treated as a continuous variable. The expected date of delivery was estimated based on the last menstruation reported at antenatal visit or on the estimated date from the onset of fetal movements and pregnancy progression.[31] Gestational age was calculated based on this information and the date of birth and was divided into two categories: preterm birth (<37 completed weeks) and full-term birth (≥ 37 completed weeks; the reference).

ÖMPSQ-SF

Participants who had experienced MSK pain in any site within the past 12 months were instructed to complete the ÖMPSQ-SF at the 46-year follow-up. ÖMPSQ-SF is a short version of the original ÖMPSQ, with the Finnish version previously validated.[32] It contains 10 items which enquire about: (i) the duration of pain, (ii) pain rating, (iii) the ability to do light work, (iv) the ability to sleep at night, (v) feelings of anxiety, (vi) feelings of depression, (vii) the perceived risk of pain becoming chronic, (viii) opportunities to return to work, and (ix and x) fear-avoidance beliefs. Each item was scored from 0 to 10, 0 referring to the absence of impairment and 10 to severe impairment. The total scores were summed up and the participants were divided into two groups according to their total score: low risk (0–50 points; the reference) and high risk (51–100 points).[20] The validity of the ÖMPSQ-SF itself has been previously documented in different languages.[33,34]

SBT

Participants who reported having LBP during the preceding year of the 46-year follow-up were asked to complete the validated SBT questionnaire.[18] SBT consists of nine items addressing (i) referred leg pain, (ii) comorbid neck or shoulder pain, (iii-iv) disability (two items), (v) pain catastrophizing, (vi-vii) fear and anxiety, (viii) depressive symptoms, and (ix) bothersomeness. The response alternatives to items 1–8 are "agree = 1 point" or "disagree = 0 point". Item 9 has five response options, of which the two highest responses were counted as one point and the other as zero points. The SBT scores range from 0 to 9, with higher values indicating worse prognosis. The SBT-based risk categories were calculated in accordance with the existing literature[18]: low-risk (3 or less points; the reference) vs high-risk (four or more points). Originally, SBT has three categories, low, medium, and high, but here the medium- and high-risk categories were combined to enhance statistical power in analyses as has been documented before.[23]

ROPS

ROPS includes six binarized and summable variables: mood (two items), sleep (one item), neuroticism (one item), life stressors (one item), and obesity (one item). Each item is recorded as zero or one, resulting in a total score ranging from 0 (lowest risk) to 6 (highest risk). The specific questions and measurements used for formulating ROPS in the NFBC1966 are shown in **Appendix 1**. The original ROPS was validated in the NFBC1966 and was originally constructed based on 99 potential biopsychosocial factors assessed by artificial intelligence.[21]

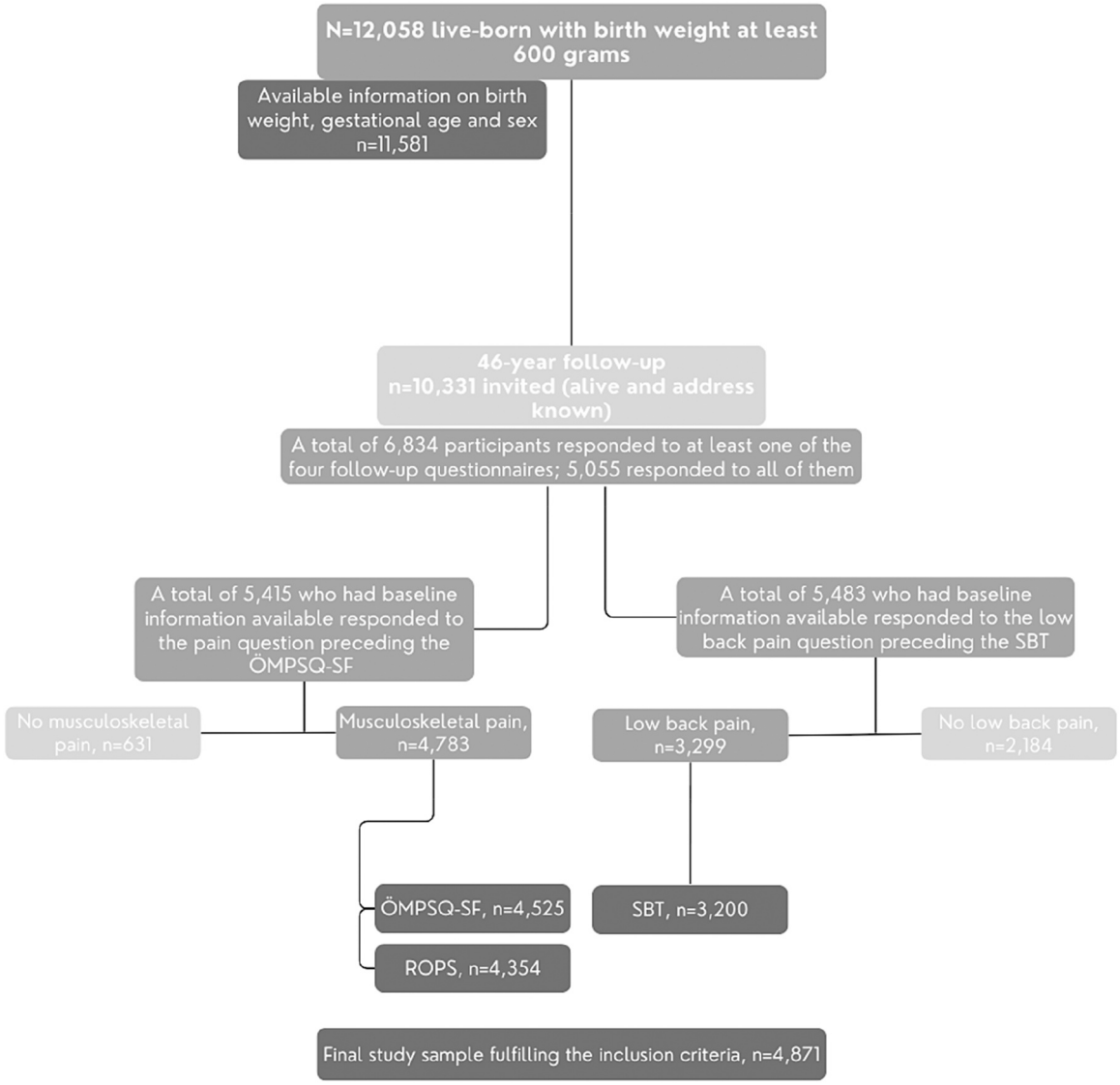

Fig. 1. Flowchart of the study population. Inclusion criteria: available information on birth weight, gestational age and sex, responding to at least one pain questionnaire and a written consent to use the data. ROPS=Risk of Pain Spreading; SBT=Start Back Tool; ÖMPSQ-SF=Örebro Musculoskeletal Pain Screening.

ROPS was evaluated among participants who reported having any MSK pain according to the question preceding the ÖMPSQ-SF at 46 years. In analyses, it was treated as a continuous variable as it had no established cut-offs for high- and low-risk groups.

Potential confounders

Sex, socioeconomic status of childhood family during pregnancy ('antenatal SES'), pregnancy disorders, and mother's age were documented as characteristics and potential confounders. All but sex were selected based on their association with birth weight or gestational age.[35–37] To the authors' knowledge, no literature exists demonstrating a relationship between these potential confounders and pain prognosis. Thus, no specific requirement for their association with pain prognosis could be established.

Data for dichotomized sex variable (males/females) was gathered from birth records, while antenatal SES was determined using several indicators from questionnaires during the antenatal period: mother's marital status, education, and occupation; father's occupation; number of family members and those aged ≤15 years; location of residence, room count, utilities; and family's wealth.[38] The clusters were previously detailed in Oura et al.,[38]: (1) Highest status families (families characterized by high occupational status of the parents, regardless of the number of children; located in cities or population centers; large residences and above-average wealth); (2) Small families (families with ≤2 members and no individuals aged ≤15 at time of pregnancy; living in a small residence in a city or population center; (3) Larger families (families with ≥5 members and ≥ 3 individuals aged ≤15, regardless of utilities); (4) Average wealth families (medium-sized families living in medium-sized residences with average utilities and wealth); and (5) Rural families (relatively large families located in the periphery, with farming as the most common occupation among parents).

Pregnancy disorder included the presence of any the following: (1) diagnosed hypertension during pregnancy, (2) pre-eclampsia (blood pressure >= 140/90 or more after 20th gestational week and proteinuria at least in one sample during pregnancy) and (3) threatening miscarriage (bleeding occurring during pregnancy or being treated due to threatening miscarriage), and thus was divided into yes vs no.[39] Mother's age at birth was calculated based on birth year reported at prenatal period and offspring's birth year and was treated as a continuous variable.

Statistical analysis

Continuous variables were presented as medians and interquartile ranges (IQRs), while categorical variables were presented as frequencies and percentages (%). We utilized log-binomial regression models to obtain relative risks (RRs) and 95% confidence intervals (CIs), to determine the univariate and adjusted associations of birth weight and preterm birth (exposures) with ÖMPSQ-SF and SBT, using low-risk groups as the references. To analyze the unadjusted and adjusted relationships between these exposures and the ROPS, we applied a generalized linear model with gamma log-link. Beta (ß) coefficient and 95% CIs were provided. In the adjusted models, all potential confounders were taken into account.

Univariate log-binomial regression was also used to analyze the association between birth weight and preterm birth, comparing these exposures with dummy single-items of ÖMPSQ-SF, SBT, and ROPS. For the ÖMPSQ-SF, dichotomized single-item variables were formulated according to their distribution in the study sample to achieve a prevalence distribution of approximately 20%/80%. Tertile- or quartile-based categorization was not feasible because the items were skewed and most had a low variation in their scores. All analyses were conducted via SPSS, Version 29 (IBM Corp. Released 2023. IBM SPSS Statistics for Windows, Version 29.0.2.0 Armonk, NY: IBM Corp).

Results

Participants' characteristics

Overall, 4871 participants met the inclusion criteria (Fig. 1). The final sample sizes varied between 3200 and 4525 depending on the outcome of interest. There were slightly less males (42%) than females (58%) in the study sample (Table 1). Their median birth weight-SD was −0.18 (IQR −0.83–0.52). A total of 5% of the participants were born as preterm. Most participants were born into the "Rural families" (25%), while the prevalence of being born into the "Larger families" was the lowest (13%). A quite high percentage of participants' mothers had experienced a pregnancy disorder (45%).

Table 1
Characteristics and distribution of evaluated variables within the study sample (n=4871).

Variables	Distribution % (n) or median (IQR)
Sex	
Males	42 (2056)
Females	58 (2815)
Birth weight-SD, median (IQR)	−0.18 (−0.83–0.52)
Gestational age in weeks	
Preterm (< 37 weeks)	5 (218)
Full-term (≥ 37 weeks)	95 (4653)
Antenatal SES clusters*	
Rural families	25 (1196)
Small families	21 (994)
Larger families	13 (653)
Average wealth families	23 (1133)
Highest status families	18 (847)
Pregnancy disorder*	
Yes	45 (1862)
No	55 (2286)
Mother's age at birth*, median (IQR)	27 (23–32)
SBT at 46 years*	
Low-risk	87 (2801)
High-risk	13 (399)
ÖMPSQ-SF groups at 46 years*	
Low-risk	95 (4286)
High-risk	5 (239)
ROPS score at 46 years*	0 (0–1)

IQR=interquartile range; ROPS=Risk of Pain Spreading; SBT=Start Back Tool; SD=standard deviation; SES=socioeconomic status; ÖMPSQ-SF=Örebro Musculoskeletal Pain Screening Questionnaire-Short Form.
*N varies due to missing data.

Birth weight, ÖMPSQ-SF, SBT and ROPS

Among participants with MSK pain at 46 years, birth weight was not associated with being classified into the high-risk group according to the ÖMPSQ-SF (unadjusted RR 0.98, 95% CI 0.87–1.10) or SBT (unadjusted RR 1.00, 95% CI 0.92–1.09) (Table 2). No associations were found between birth weight and ROPS score (ß 0.001, 95% CI −0.03–0.03). Adjustments for confounders did not alter these results (Supplementary Table 1).

The single-item analyses of the three tools showed that increasing birth weight had a relationship with higher duration of pain (unadjusted RR 1.05, 95% CI 1.00–1.10) (Supplementary Tables 2–4). No other associations with the single items were detected.

Preterm birth, ÖMPSQ-SF, SBT and ROPS

In the univariate analyses (Table 2), participants born preterm had increased risk of being categorized into the high-risk group according to the ÖMPSQ-SF (unadjusted RR 1.61, 95% CI 1.00–2.59) and SBT (unadjusted RR 1.61, 95% CI: 1.14–2.28), compared to those born full-term. In the adjusted analyses (Supplementary Table 1), the relative risks for the association between preterm birth and belonging to the high-risk group according to ÖMPSQ-SF remained nearly the same (adjusted RR 1.62, 95% CI 0.99–2.64). Conversely, the relationships between preterm birth and being classified into high-risk groups based on SBT became slightly stronger after adjustments (adjusted RR 1.74, 95% CI 1.22–2.47). Preterm birth did not predict the ROPS score in any model (Table 1 and Supplementary Table 1).

In the single-item analyses of the ÖMPSQ-SF, we found associations between preterm birth, higher pain rating, lower ability to do light work, and increased fear-avoidance beliefs (Supplementary Table 2). For the SBT, relationships were observed with referred leg pain, disability, depressive symptoms, and bothersomeness (Supplementary Table 3). Additionally, the risk of catastrophizing was higher among preterm birth compared to full-term ones (unadjusted RR 1.72), although the CIs included unity (0.95–3.10). In contrast, no associations were found between preterm birth and the single items of the ROPS (Supplementary Table 4).

Discussion

The present study aimed to describe the associations between birth weight or preterm birth and worse pain prognosis among middle-aged individuals with MSK pain using prospectively collected data. Birth weight was not associated with belonging to the high-risk group or higher number of prognostic factors determined by any evaluated instrument. In contrast, participants born preterm had significantly higher risk of belonging to the high-risk for poorer prognosis at mid-life when screened with either ÖMPSQ-SF or SBT. No significant association was observed between preterm birth and accumulation of ROPS scores in mid-adulthood.

Preterm birth appeared to predict worse pain prognosis in mid-adulthood, although this finding varied depending on the screening tool estimated. Both ÖMPSQ-SF and SBT are primarily symptom-based instruments focusing highly on pain interference while the ROPS captures the key factors from the spectrum of modifiable and non-modifiable biopsychosocial factors that not directly relate to pain symptom itself. This difference may partially explain the observed discrepancy. Collectively, it could be speculated that individuals born preterm birth are likely to be more vulnerable to developing adverse thoughts on pain or experiencing pain more disabling than those born full-term. The single-item analyses suggested that the strongest associations with ÖMPSQ-SF and SBT were related to experienced bothersomeness and disability.

Table 2
Univariate associations between birth weight, gestational age, and ÖMPSQ-SF, SBT, and ROPS at 46 years (n=4525, n=3200 and n=4354, respectively).

	ÖMPSQ-SF			SBT			ROPS	
	High-risk		**Low-risk**	**High-risk**		**Low-risk**		
	RR	95% CI		RR	95% CI		ß	95% CI
Birth weight-SD	0.98	0.87–1.10	Ref.	1.00	0.92–1.09	Ref.	0.01	−0.03–0.01
Preterm (< 37 weeks)	1.61	1.00–2.59	Ref.	1.61	1.14–2.28	Ref.	0.05	−0.05–1.16
Full-term (≥ 37 weeks)	Ref.			Ref.			Ref.	

ß=beta; CI=confidence interval; RR=relative risk; ROPS=Risk of Pain Spreading; SBT=Start Back Tool; SD=standard deviation; ÖMPSQ-SF=Örebro Musculoskeletal Pain Screening Questionnaire-Short Form

Preterm born children often receive intensive and potentially painful medical care[6] that may affect pain development[4] and alter modulation systems.[5] Alterations have been observed not only in biological (e.g., in brain structure) but also in psychological mechanisms (e.g., coping style, parental response).[40] Additionally, preterm infants are born with underdeveloped and immature nervous system, making it more vulnerable to alterations in neural activity. This has been suggested to increase the likelihood of altered pain sensitivity.[40] More specifically, the adverse intrauterine environment associated with preterm fetuses may contribute to the development of chronic pain signaling.[41] These findings support the present observations regarding the role of preterm birth in adverse pain symptom-related thoughts and experiences in mid-life. Obviously, the current study cannot establish any causality but is likely to shed light for further studies and discussions on preterm birth and its potential impact on pain vulnerability. Given that current evidence regarding chronic pain among preterm individuals is very limited and of low quality,[42] more research is needed in the field as a whole.

We found no associations between birth weight and risk groups, which aligns with existing evidence on low birth weight and chronic pain symptoms in later life, although previous studies have primarily focused on early adulthood and used absolute birth weight measurements.[42] In this study, we employed birth weight-SD as an indicator of birth weight instead of absolute birth weight values to account for gestational age in the estimations of participants' size. Interestingly, our results revealed a positive association between increasing birth weight and experiencing pain lasting over a year (vs. pain lasting less than a year). Future pain studies should not only focus on low but also high birth weights.

To our knowledge, this is the first large-scale population-based study to investigate associations between birth weight or preterm birth and the risk groups for worse pain prognosis in mid-adulthood among adults with MSK pain. Another key strength is the use three validated prognostic tools to comprehensively assess the research question.[18,21,33,34] Moreover, data was collected prospectively from the general population, which enhances the accuracy of the findings and facilitates the examination of phenomena at a population-level.

Several limitations of this study should be acknowledged. The NFBC1966, as many other longitudinal birth cohorts, has encountered attrition over the four decades of follow-ups. Therefore, for instance, the distribution of MSK among many original NFBC1966 members is not known. Additionally, at the latest follow-up, a higher percentage of participants were observed to be females and employed compared to non-participants.[28] Moreover, the care of children born preterm or who had low birth weight in the 1960s may have differed significantly from current practices[43] potentially impacting the results and their generalizability. In the 1960s, prenatal ultrasound was not available, which could introduce inaccuracies in estimating gestational age based on the last menstrual period and reduce ability to detect associations. However, in the younger cohort of Northern Finns (the Northern Finland Birth Cohort 1986 [NFBC1986]), early pregnancy ultrasound was available for a proportion of participants and correlated well with gestation age estimates based on the last menstrual period.[44] Also, gestational age has been used in previous publications of the NFBC1966 and NFBC1986.[45] Self-reported data is vulnerable to recall and social desirability biases, which cannot be fully ruled out, even though many of the items considered current status. All study participants were Finns, but we lacked exact data on ethnicity. This affects the generalizability of our findings, and further studies are warranted to validate our findings in different populations. Finally, even though the study employed a prospective study design, any conclusions on cause-and-effect relationships should not be drawn.

Conclusions

Preterm birth seemed to predict allocation to the group with worse pain prognosis in mid-adulthood while measured by the ÖMPSQ-SF and SBT, compared to full-term birth. In contrast, birth weight did not seem to be a relevant predictor of risk group allocation. These findings highlight the need for further studies and discussions on the role of preterm birth in developing and accumulation of adverse pain symptom-related thoughts and experiences in mid-life.

Data availability statement

NFBC data are available from the University of Oulu, Infrastructure for Population Studies. Permission to use the data can be applied for research purposes via an electronic material request portal. In the use of data, we follow the EU general data protection regulation (679/2016) and the Finnish Data Protection Act. The use of personal data is based on a cohort participant's written informed consent in their latest follow-up study, which may cause limitations to its use. Please, contact the NFBC project center (NFBCprojectcenter(at)oulu.fi) and visit the cohort website (www.oulu.fi/nfbc) for more information.

Disclosures

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CRediT authorship contribution statement

EH: Conceptualization; Formal analysis; Methodology; Visualization; Writing – original draft. JRC: Conceptualization; Methodology; Visualization; Writing – review and editing. S-SN: Conceptualization; Writing – review and editing. KV: Conceptualization; Writing – review and editing. EK: Conceptualization; Writing – review and editing. JK: Conceptualization; Writing – review and editing. JM: Conceptualization; Methodology; Writing – review and editing. AYLW: Conceptualization; Methodology; Writing – review and editing.

Declaration of Competing Interest

The authors declare no conflict of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jpain.2024.104773.

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