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Poor prognosis of child and adolescent Musculoskeletal Pain - a Systematic Literature Review

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Abstract

Objectives

To identify baseline patient characteristics that are: (i) associated with a poor outcome on follow up regardless of which treatment was provided (prognosis); or (ii) associated with a successful outcome to a specific treatment (treatment effect modifiers).

Design

Systematic literature review according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines.

Data sources

Medline, Embase, Cinahl, Web of Science, Cochrane, SportDiscus, OT Seeker, and PsychInfo were searched for prospective cohort studies up to May 2017 without limitation in publication date.

Eligibility criteria

Prospective cohort studies reporting either prognostic factors or treatment effect modifiers on persistent musculoskeletal pain in 0- to 19-year-old children and adolescents.

Outcome measures

Our primary outcome was musculoskeletal pain at follow-up and identification of any baseline characteristics that were associated with this outcome (prognostic factors). No secondary outcomes were declared.

Method

Two reviewers independently screened abstracts and titles. We included prospective cohort studies that investigated the prognosis or treatment effect modifiers of 0- to 19-year-old children and adolescents with self-reported musculoskeletal pain. Risk of bias assessment was conducted with the QUIPS tool.

Results

Twenty-five studies yielding a total of 109 unique prognostic factors were included. Female sex and psychological symptoms were the most frequent investigated prognostic factors. Increasing age, generalised pain, longer pain duration, and smoking were other identified prognostic factors.

Conclusion

Several prognostic factors are associated with a poor prognosis in children and adolescents with musculoskeletal pain. These prognostic factors may help guide clinical practice and shared decision-making. None of the included studies was conducted within a general practice setting which highlights an area in need of research.

Registration

The protocol for this review was developed using the PRISMA-P 2015 statement, inspired by the Cochrane Central Register of Controlled Trials, and registered prospectively in the International Prospective Register of Systematic Reviews (PROSPERO, ID: CRD42016041378).

Strengths and limitations of this study

- No previous review has aimed to identify prognostic factors in children and adolescents with musculoskeletal pain with the purpose of informing clinical practice.
- In collaboration with a research librarian we developed a highly sensitive search for each of the eight databases to ensure an inclusion of the totality of previous research.
- Two reviewers independently carried out the screening and data extraction was executed in the same manner for all included studies.
- No meta-analysis was conducted due to a heterogeneity of patient population, setting, and endpoints.

Keywords

musculoskeletal pain; adolescents; children; prognosis; general practice

Introduction

General practice is often the point of first contact into the health care system and musculoskeletal pain complaints are the most common cause of contact. The case workload due to musculoskeletal pain complaints in children and adolescents is estimated to be 4-8% of the UK general practice (1).

Musculoskeletal pain affects half of all children and adolescents, and increases exponentially in frequency around the age of 10 (2-6). A recent systematic review reported that 40% of an adolescent population had experienced pain during the past six months (3). The most common pain sites are the knee and back (7). Musculoskeletal pain has a detrimental impact on the adolescents' quality of life and may cause them to withdraw from school, social, and athletic activities (8, 9).

Musculoskeletal pain in children and adolescents has previously been considered a self-limiting condition without long-term impact (10). Recent cohort studies show that 16-32% of patients with knee pain still report knee pain one year later (10, 11) and that 21% of 12-35-year-olds had persistent knee pain six years after initial contact to their general practitioner (10). Collectively, these studies highlight that a significant proportion of adolescents will report pain even years later. Who are the children and adolescents with a particularly high risk of long-lasting musculoskeletal pain? This is one of the most common questions from our stakeholder interviews with general practitioners [*unpublished stakeholder event*].

Knowledge of prognostic factors can inform the general practitioner of the prognosis of their patients and enable them to identify those with a poor prognosis to stratify care, address modifiable risk factors and better understand chronic pain conditions. So far, no systematic reviews have aimed to inform clinical practice of prognostic factors in children, and adolescents with musculoskeletal pain. Therefore, we aimed to identify baseline patient characteristics associated with a (i) poor outcome on follow-up (prognosis) or (ii) successful outcome of a treatment (treatment effect modifiers).

Methods

Literature search

We searched in Medline, Embase, Cinahl, Web of Science, Cochrane, SportDiscus, OT Seeker, and PsychInfo from their inception until September 2017 without limitation on date. An experienced research librarian collaborated in the production of individual search strategies for each of the eight databases (Appendix 1).

Eligibility criteria

Study population and design

We included prospective studies that investigated prognostic factors or treatment effect modifiers in children and adolescents 0- to 19-years-old, with any type and location of musculoskeletal pain. Musculoskeletal pain was defined as pain in muscle, tendon, bone, and joint (12). We included musculoskeletal pain types, reported in each of our included studies, without further definition of or changes in the designations chosen by the respective authors. We excluded pain knowingly caused by tumours, fractures, infections, systemic and neurological conditions, and stomach pain, because of insufficient differentiation between musculoskeletal stomach pain and stomach pain by other causes. Furthermore, we included all prospective studies, independent of intervention and randomised trials including all types of comparators. As expected, most studies did not use a comparator because they were prospective cohort studies. Similar to intervention, these studies were included independent of comparators. There were no restrictions on the type of setting or language.

Review process

Two reviewers (NP and AR) independently screened titles and abstracts for studies addressing the question: What are the prognostic factors and treatment effect modifiers for children and adolescents with musculoskeletal pain? Full-text articles were then screened, adding primary reasons for exclusion.

There was no blinding of the review authors to the journal titles, authors, or institutions. Reference lists of all included studies were screened for eligible publications that may have been missed during the initial search. The study selection process was finalised without any disagreements on included studies. EndNote was used to remove duplicates and NP manually checked for duplicates afterwards.

Data extraction

Study details and results were extracted using a pre-defined data extraction form inspired by The Cochrane Collaboration (13). We extracted the prognostic factors from the included papers and used the following estimates: odds ratios (OR), relative risks (RR), and/or P-values. If possible, we extracted the adjusted associations.

Outcomes and endpoints

Our primary outcome of interest was musculoskeletal pain at follow-up and identification of any baseline characteristics that were associated with this outcome (prognostic factors). We used the term "pain persistence" to describe participants who had pain at both baseline and follow-up, without applying restrictions on either pain measurement or on follow-up time points.

Risk of bias

Risk of bias was assessed using the Quality in Prognostic Studies (QUIPS) tool (14). On the study level, NP and AR independently rated the 25 included studies and reached consensus on all risk of bias assessments (table 1). Prognostic factors from studies with a high risk of bias, were excluded from figure 3.

Table 1 Risk of bias in included studies. With the Quality in Prognostic Studies (QUIPS) tool studies were assessed on the overall risk of bias within each of the six domains and rated as low, moderate or high risk of bias. Three studies were rated with high risk of bias, and hence excluded from the final results.

Study author year	Design	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and presentation
Blauuw et al 2015	Prospective cohort	Low	Moderate	Low	Low	Moderate	Low
Brattberg et al 1993	Prospective cohort	Moderate	Moderate	Low	Low	Moderate	High
Brattberg et al 2004	Prospective cohort	Low	Moderate	Low	Low	Low	Low
El-Metwally et al 2004	Prospective cohort	Low	Low	Low	Low	Low	Low
El-Metwally et al 2005	Prospective cohort	Low	Low	Low	Low	Low	Low
Flato et al 1997	Prospective cohort	Low	Low	Low	Low	Low	Low
Jones et al 2009	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Jussila et al 2014	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Laimi et al 2007	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Lunde et al 2015	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Mikkelsson et al 1997	Prospective cohort	Low	Low	Low	Low	Moderate	Moderate
Mikkelsson et al 1998	Prospective cohort	Low	Low	Low	Low	Low	Moderate
Mikkelsson et al 1999	Prospective cohort	Low	Low	Low	Low	Low	Low
Mikkonen et al 2008	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Mikkonen et al 2012	Prospective cohort	Moderate	Low	Low	Low	Low	Low
Mikkonen et al 2013	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Paananen et al 2010	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Rathleff et al 2013	Prospective cohort and nested case-control	Moderate	Low	Low	Low	Low	Low
Rathleff et al 2016*	Prospective cohort	Low	Low	Low	Low	Low	Low
Rathleff et al 2016	Prospective cohort	Low	Low	Low	Low	Low	Low
Sjolie et al 2001	Prospective cohort study with a cross sectional part	Low	Low	Low	Low	Low	Low
Sperotto et al 2015	Prospective cohort	Low	Moderate	Low	Low	High	Moderate
Stanford et al 2007	Prospective cohort	Low	Moderate	Low	Low	Low	Low

Ståhl et al 2008	Prospective cohort	Low	Moderate	Low	Low	Moderate	Low
Uziel et al 2010	Prospective cohort	Moderate	Low	Low	Low	High	Moderate

**Is knee pain during adolescence a self-limiting condition?*

Risk of bias in included studies. With the Quality in Prognostic Studies (QUIPS) tool studies were assessed on the overall risk of bias within each of the six domains and rated as low, moderate or high risk of bias. Three studies were rated with high risk of bias, and hence excluded from the final results

Involvement of general practitioners

With stakeholder involvement and input from a panel of general practice researchers experienced in musculoskeletal research, we sub-grouped our identified prognostic factors in accordance with the biopsychosocial model (15, 16):

Biological prognostic factors:
-Female sex
-Older age
-Body measurement factors
-Physical functioning
-Pain characteristics

Psychological prognostic factors
-General psychological factors
-Depressive factors

Social prognostic factors:
-General social factors
-Sleep-related factors
-Physical activity/inactivity
-Alcohol
-Smoking

Reporting of results

We were not able to conduct our a priori planned meta-analysis because of heterogeneity in terms of patient population, setting, and time points for follow-up. The evidence on included prognostic factors was reported with odds ratios (OR), relative risks (RR), and/or P-values. As OR and RR may differ in interpretation, we reported them separately. A statistically significant association between a patient characteristic and an outcome was defined as an RR or OR above or below 1 that did not include 1 in the 95% confidence interval. As for P-value, a statistically significant association was defined as $P < 0.05$.
We used the PRISMA checklist when writing our report (17).

Patient involvement

No patients or public were involved in the present study.

RESULTS

Included studies

Figure 1 reports the results of the search strategy. Of the 37,884 titles identified, 36,224 studies were screened, and 25 studies (9, 11, 16, 18-39) were included. All included studies were prospective studies. The included studies used a mix of different measures to capture pain at follow-up. Musculoskeletal pain types included in our search were: general musculoskeletal pain, neck, back, lower back, stomach, lower limb, knee, and growing pain. No treatment effect modifiers were identified.

Risk of bias

The most common reasons for a moderate or high risk of bias were inadequately described study participation and statistical analyses (n=6, 23%), attrition rates (n=5, 20%), and poor adjustment for confounders (n=11, 42%).

Prognosis

Figure 2 highlights the persistence of musculoskeletal pain in all included studies at different follow-up time points. On average, 54% with general musculoskeletal pain, 49% with knee pain and 42% with neck pain also reported pain at follow-up. A complete report of all the identified prognostic factors is listed in supplementary table 1. Figure 3 depicts the majority of these prognostic factors, stratified in pain type, sex, study population size, and follow-up (please see web supplemental document for explanatory notes).

Very few prognostic factors were reported on back pain, growing pain, lower limb pain, and widespread musculoskeletal pain (supplementary table 1); consequently, they were excluded from figure 3. Table 2 condenses the results from supplementary table 1 and highlights four prognostic factors on four different musculoskeletal pain types. Below each factor are suggestive questions to provide the general practitioner with insight into the patient's prognosis. Table 2 and figure 3 can be printed and used by a general practitioner at time of initial consultation with a 0-19-year-old patient with musculoskeletal pain.

	General musculoskeletal pain	Low back pain	Neck pain	Knee pain
Prognostic factors	-Female sex and female smokers -Day tiredness/fatigue -Physical activity vs. none -Depressive symptoms	-Higher lumbar mobility* -Longer pain duration -Peer problems -Smoking	-Female sex -Depressive symptoms -Multisite pain vs. localized -Day tiredness	-Increasing age -Daily pain -Sport > 2t/week -Low quality of life
Questions	-Do you smoke? -Do you get enough sleep? -Do you do sport? -Are you feeling mentally well?	-Clinical examination -How long have you had pain? -Do you have friends? -Do you smoke?	-Are you feeling mentally well? -Do you have pain in more than one musculoskeletal region? -Do you feel tired during the day?	-Do you experience daily pain -Do you do practice sport frequently? -Are you feeling mentally well?

Table 2 What to ask in clinical practice? *4* prognostic factors belonging to *4* frequent musculoskeletal pain types in general practice: General musculoskeletal-, Low back-, Neck-, and Knee Pain.
The questions are proposals towards assessment of prognosis on musculoskeletal pain.
** to be evaluated by clinical examination*

Prognostic factors associated with pain at follow-up

A total of 109 prognostic factors were associated with musculoskeletal pain at follow-up, of which most were on general musculoskeletal pain and low back pain (table 3). Supplementary table 1 includes these results and further detailed depiction of prognostic factors.

Table 3 Included studies described by musculoskeletal pain type, baseline age, size of study population, and follow-up.

Study author (reference)	Musculoskeletal pain type	Baseline age (years)	Study population (n)	Follow-up (years)	Persistent pain at follow-up Female (%)	Persistent pain at follow-up Male (%)	Persistent pain at follow-up combined (%)
Blaauw BA (18)	Headache	12 to 16	1586	4	45.7	22.7	35.1
Brattberg G 93 (19)	Back, Head	8, 11, 13	471	2	Back 15, Head 40	Back 4, Head 20	Back 9.3, Head 30.7
Brattberg G 04 (20)	General musculoskeletal	10, 13, 16	597	11	59	39	20
El-Metwally A 04 (21)	General musculoskeletal	9 to 12	1756	1 and 4	4 years: 56.2	4 years: 43.8	1 years: 53.8, 4 years: 63.5
El-Metwally A 05 (11)	Lower limb	9 to 12	1756	1 and 4	1 year: 29.4, 4 years 31.9	1 year 55.8, 4 years 48.6	1 year: 32, 4 years 31
Flato B (22)	General musculoskeletal	2 to 17	37	9	13	N/A	59
Jones GT (23)	Low back	11 to 14	330	4	N/A	N/A	26
Jussila L (24)	General musculoskeletal	16 to 18	1773	2	N/A	N/A	N/A

Laimi K (25)	Headache[a]	13	311	3	54	70.5	48
Lunde LK (26)	Low back	15 to 19	420	6.5	N/A	N/A	39
Mikkelsson M 97 (27)	Neck, Widespread, low back	9 to 12	1756	1	N/A	N/A	Neck 48.3, WSP[b] 29.7, Low back 34.4
Mikkelsson M 98 (28)	General musculoskeletal	9 to 12	1756	1	N/A	N/A	52.9
Mikkelsson M 99 (29)	Neck, Widespread	9 to 12	464	1	Neck 70.4, WSP 62.5	Neck 41, WSP 62.5	Neck 29, WSP 28.6
Mikkonen P 08 (30)	Low back	16	2969	2	N/A	N/A	27.1
Mikkonen P 11 (31)	Low back	16	728	2	53	46	50.4
Mikkonen P 13 (32)	Low back	7 to 19	1660	2 and 3	2 years 68, 3 years 63	2 years 62, 3 years 47	N/A
Paananen MV (33)	General musculoskeletal	16	1594	2	N/A	75	88
Rathleff CR (9)	Knee	12 to 15	768	1	N/A	N/A	48.8
Rathleff MS 16 (34)	Knee	16 to 18	504	2	N/A	N/A	55.9
Rathleff MS 16 (35)	Knee (PFP)	15 to 19	121	3 months	N/A	N/A	74.4
Sjolie AN (36)	Low back	14 to 16	88	3	N/A	N/A	39
Sperotto F (37)	General musculoskeletal	8 to 13	289	3	N/A	N/A	54.3
Stanford EA (39)	Head, Back, Stomachache	10 to 11	2488[c]	2	N/A	N/A	Head 29, Back 21.7
Ståhl M (38)	Neck	9 to 12	1756	1 and 4	N/A	N/A	1 year: 48.2, 4 years: 33.5
Uziel Y (40)	Growing pain	10 to 16	35	5	N/A	N/A	48.6

N/A = not applicable
A = Headache: non migrainous
b = Widespread pain
c = included stomachache participants

Extracted data from the Included studies were all musculoskeletal pain types investigated in the individual included studies together with baseline age, size of study population, follow-up and percentage of study participants who represented persistent pain at follow-up, -both stratified by gender and combined.

Female sex was the most frequently identified prognostic factor associated with musculoskeletal pain at follow-up. Eleven studies identified psychological factors (e.g. depression, anxiety, and low self-esteem) to be associated with pain at follow-up in seven out of nine musculoskeletal pain types (9, 16, 18, 20, 21, 23, 24, 28, 33, 34, 38).
Longer pain duration was associated with pain at follow-up across four musculoskeletal pain types: musculoskeletal, low back, knee, and back pain (20, 22, 23, 34).
Five studies identified sleep-related problems associated with outcome (21, 24, 28, 33, 38).
Other indicators for musculoskeletal pain at follow-up were increasing age (9, 21, 25, 28), smoking (30, 33), parental pain (16, 22, 39), and multisite pain (21, 22, 38).
Figure 3 summarises all identified prognostic factors for musculoskeletal pain at follow-up, stratified in pain type, study population size, sex, and follow-up.

Non-significant prognostic factors

We identified a total of 134 patient characteristics across nine musculoskeletal pain types and different follow-up time points with a non-significant association with musculoskeletal pain at follow-up (supplementary table 1).
Increasing age (11, 20, 22, 27, 29, 34, 39, 40) was the most frequently identified baseline factor with a non-significant association to musculoskeletal pain at follow-up. Multiple studies reported non-significant evidence on higher body mass index (22, 24, 40) and hypermobility (11, 28, 38).

DISCUSSION

Principal findings

Female sex was consistently associated with an increased risk of pain at follow-up across six different musculoskeletal pain types. Depressive symptoms (9, 16, 18, 21, 24, 28, 33, 34, 38), sleep-related factors (21, 24, 28, 33, 38), and parental pain condition (16, 22, 39) were all associated with a higher risk of pain at follow-up. Collectively, the identified studies included prognostic factors across all aspects of the

biopsychosocial model, despite a main focus on biological factors. Increasing age was identified as both a significant and a non-significant prognostic factor in the included studies. This conflicting finding reflects the uncertainty surrounding the importance of age as a prognostic factor.

Strengths and limitations in comparison with existing literature

The latest systematic review on prognostic factors for children and adolescents with musculoskeletal pain ended their search in July 2015 which makes for a timely update (41). In addition to adding newer studies, our review differs from the previous with search in more databases, no restriction on publication language, and no restriction on pain duration (41). Despite methodology differences, we did not identify additional studies from inception to 2015, but identified two new studies from January 2016 to 2017. These studies added important knowledge of female sex, pain frequency, and the prognosis of knee pain. Thereby, supporting the previous research. Despite the commonality of children and adolescents with musculoskeletal pain in general practice (6), we did not identify a single study with a population of children or adolescents recruited from general practice.

A previous review on prognostic factors for adults with musculoskeletal pain in primary care was published in 2017 (42) with findings similar to ours i.e., female gender, older age, depression/anxiety, and long pain duration was found associated with an increased risk of musculoskeletal pain at follow-up. This suggest that some of the prognostic factors function well across the age range and their use is not isolated to specific age groups.

Explanation of findings and implications for clinical practice

Our findings suggest that females are at higher risk of persistent pain. Previous research highlights potential sex differences in pain responses by assessing pain intensity and threshold and conclude that females display greater sensitivity to multiple pain modalities compared with males (43). Importantly, pain-coping strategies have been found to differ between the sexes (44, 45). Females make use of social support, cognitive reinterpretation, and positive self-statements, while males use behavioural distraction and problem-focused tactics to manage pain. This could partly explain the sex-difference in prognosis and may open new opportunities for targeted treatment to improve long-term outcomes of young females with musculoskeletal pain.

The current results point towards both modifiable (psychological factors, smoking, and peer problems) and non-modifiable (sex, age, and pain duration) factors associated with prognosis. Despite time constraints in general practice, most of these factors can be extracted from electronic stored patient data, psychometric tests, and examination in a clinical general practice setting.

By asking your patient a few questions at the first consultation of musculoskeletal pain, the general practitioner may improve their understanding of their patients` risk of pain in the future. In the case of a present, baseline factor with a poor prognosis e.g. smoking among low back pain patients, the general practitioner now both has a scientific reason for and the clinical tool to modulate this factor. By prescribing cessation of smoking, thus, making an effort to improve the outcome for this patient.

Treatment of musculoskeletal pain requires the general practitioner to apply a multifactorial rather than a single-factor approach, hence, including the entire person and their life-circumstances when treating patients with pain (15, 46, 47). Clinicians must be aware of the multifactorial aetiology and consider biological-, psychological-, and social factors of musculoskeletal pain when addressing patient's coping behaviour and cognitive appraisal (48).

Implications for future research

Most of our included studies investigated biological prognostic factors (52 factors). Fewer investigated social (35 factors) and even fewer psychological prognostic factors (22 factors). Future research should include the entire patient, in terms of biological, psychological, and social-related components and aim to study these prognostic factors in a general practice setting. There is a dearth of knowledge of how psycho-social factors are associated with prognosis and how general practitioners can harness this information to tailor treatment and information to their patients. Despite the potential importance of pain, "who" the patient is should not be discounted. Geographical location of home, parental -pain, -profession and -income, and social identity in

terms of cultural differences, religious beliefs, and relations could be important because we know from the biopsychosocial model that social background is important in relation to pain coping.
Only one study did follow-up after 4, 6.5, 9, and 11 years, respectively, which highlights the lack of long-term cohort studies on prognosis and impact of musculoskeletal pain in youth.
Almost one in every two children and adolescents still reported pain even years later (10, 11, 49). This highlights the importance of prognosis of pain in children and adolescents. Health care practitioners should be cognisant not to assume that musculoskeletal pain during childhood or adolescence is transient or self-limiting.

Supplementary information
Additional information accompanies this paper in the form of Appendix 1: Search string, Appendix 2: Completed PRISMA checklist, Appendix 3: Protocol, Figure 1: PRISMA Flow chart, Figure 2: Persistent musculoskeletal pain, stratified in pain type and follow-up, Figure 3: Prognostic factors for persistent musculoskeletal pain, according to pain type, population size, sex, follow-up, and the biopsychosocial model, Supplementary table 1: Estimates on prognostic factors specified according to musculoskeletal pain type, baseline age, and follow-up in the included studies, and an animation showing how our findings can be used in a clinical setting, go to: https://youtu.be/raltzsgkTHc

Author contributions
NP conducted the systematic literature search. NP and AR independently carried out the screening, study inclusion, and study bias assessment. NP and MSR led writing of both the protocol and manuscript and all authors contributed with important reflections and revisions to both.

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Ethical approval
Not applicable.

Competing interests
The authors have declared no competing interests.

Data sharing statement
All data and results presented within this systematic review can be obtained, on reasonable request, by contacting the corresponding author.

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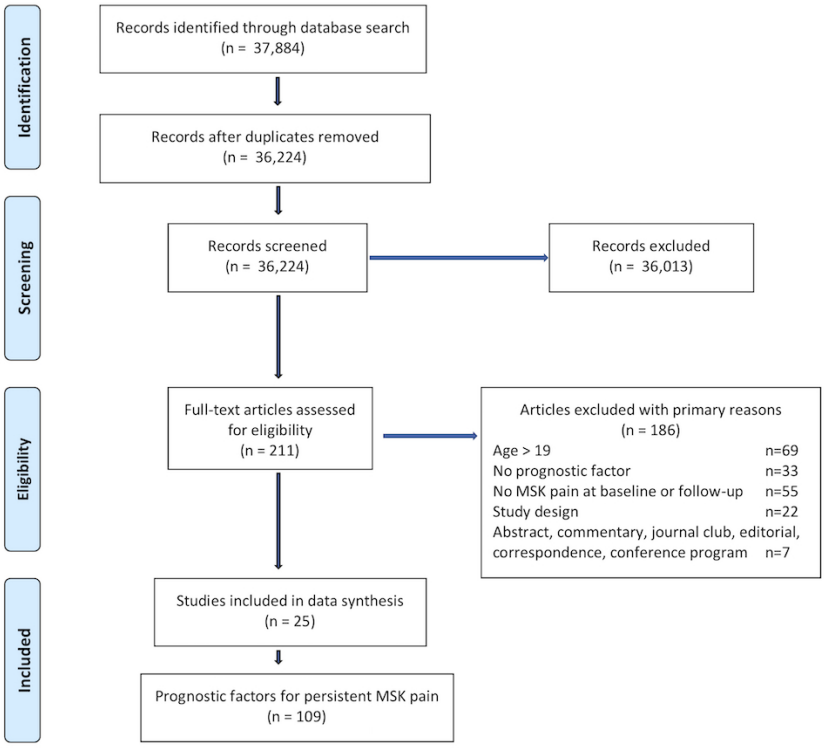
Figure 1 PRISMA Flow Chart presenting the flow of citations reviewed in the course of the systematic review
37,884 articles were identified through search in eight databases, resulting in 211 articles for full-text eligibility screen and a final number of 25 studies for inclusion yielding 109 prognostic factors on musculoskeletal pain.



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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PRISMA Flow Chart presenting the flow of citations reviewed in the course of the systematic review.

37,884 articles were identified through search in eight databases, resulting in 211 articles for full-text eligibility screen and a final number of 25 studies for inclusion yielding 109 prognostic factors on musculoskeletal pain.

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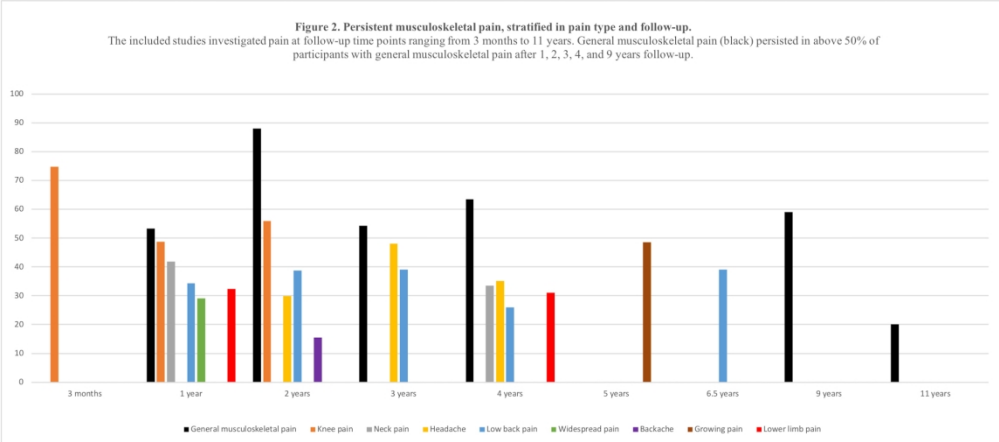

Persistent musculoskeletal pain, stratified in pain type and follow-up.

The included studies investigated pain at follow-up time points ranging from 3 months to 11 years. General musculoskeletal pain (black) persisted in above 50% of participants after 1, 2, 3, 4, and 9 years follow-up.

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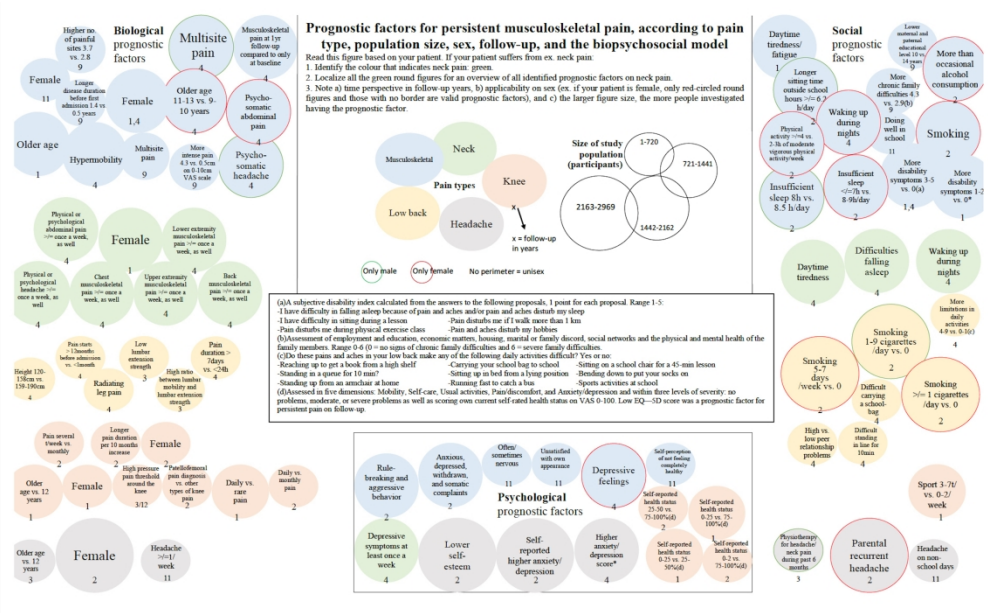

Caption and legend embedded in figure.

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Table 2. Estimates on prognostic factors specified according to musculoskeletal pain type, baseline age, and follow-up in the included studies

Musculoskeletal pain	Neck pain	
Low back pain	Low limb pain	Headache
Knee pain	Back pain	Growing pain

Baseline age	Prognostic factors subgrouped according to the biopsychosocial model	Study ID (Follow-up, yrs)	RR (95% CI)	OR (95% CI)	p-value	Adjusted for
	BIOLOGICAL PROGNOSTIC FACTORS					
	Female sex compared to male					
8 to 13		37 (3)			0.038	
10 to 16		20 (11)		M 1.8 (1.1-2.9)		
9 to 12		21 (4)	U 1.24 (1.07-1.44)			age
9 to 12		28 (1)		1.78 (1.18-2.69)	0.006	
9 to 12		27 (1)			0.001	
12 to 15		34 (2)	CR 1.29 (1.02-1.63)		0.08	
12 to 15		9 (1)		3.66 (1.09-12.33)	0.04	
10 to 11		39 (2)			M < 0.001	
10 to 11		39 (2)			M < 0.001	
8, 11, 14		20 (11)		2.24 (1.24-4.20)		
	Older age					
9 to 12	Older age	28 (1)		1.24 (1.02-1.50)	0.031	
9 to 12 F	11 to 13 years vs. 9-10 years	21 (4)	M 1.40 (1.17-1.67)			
12 to 15	Older age, increase per year, 12 years as referent	9 (1)		M 1.45 (1.07-1.95)	0.01	
13	Older age	25 (3)			0.04	
	Body measurement factors					
8 to 13	Higher pubertal group (a) group 2 and 3 vs. group 1	37 (3)			0.022	
9 to 12 F	Beighton score 6-9 vs. score < 6	21 (4)	M 1.31 (1.18-1.46)			age
11 to 14	Height < 158cm	23 (4)	2.2 (1.2-3.8)			age, sex
9 to 12	Hypermobility score >/=6 vs. <6	11 (4)		M 2.93 (1.13-7.70)		
	Physical functioning					
14 to 16	Ratio flexion mobility (cm)/extension strength (min) (b)	36 (3)		1.9 (1.1-3.2)	0.02	gender, well being, physical activity
14 to 16	Ratio extension mobility cm/extension strength (min) (b)	36 (3)		3.2 (1.3-8.3)	0.02	gender
14 to 16	Ratio flexion + extension mobility (cm)/extension strenght (min) (b)	36 (3)		1.5 (1.1-2.2)	0.02	gender, well being, physical activity
	Pain characteristics					
2 to 17	Higher number of painful sites (mean 3.7 vs. 2.8) range 0-6	22 (9)			0.04	
2 to 17	More frequent generalised vs. localised pain (86 vs. 47%)	22 (9)		84.0 (2.1-3000)	0.02	
2 to 17	More intense pain (median 4.3 vs. 0.5cm) range 0-10cm VAS	22 (9)			0.03	
2 to 17	Longer disease duration before first admission (median 1.4 vs. 0.5 years)	22 (9)			<0.01	
9 to 12	Pain at both baseline and 1 year follow-up vs. only baseline	21 (4)		2.9 (1.9-4.4)		age
9 to 12 M	Multisite vs. localised pain	21 (4)	U 1.32 (1.04-1.66)			age
9 to 12 M	Headache (psychosomatic symptom (c))	21 (4)	M 1.43 (1.12-1.83)			age
9 to 12 F	Abdominal pain (psychosomatic symptom (c))	21 (4)	U 1.20 (1.03-1.40)			age
11 to 14	Radiating leg pain vs. no radiating pain	23 (4)	2.2 (1.4-3.6)			age, sex
11 to 14	Low back pain start > 12 month prior to admission	23 (4)	2.4 (1.3-4.4)			age, sex
11 to 14	Pain episode > 7 days vs < 24h	23 (4)	2.6 (1.4-4.9)			age, sex
15 to 19	Patellofemoral pain diagnosis vs. other types of knee pain	34 (2)	1.24 (1.04-1.49)		0.01	age, sex, BMI
15 to 19	High pressure pain threshold (PPT) around the knee	35 (3mo)			0.03	
12 to 15	Daily vs. rare pain	9 (1)		M 6.31 (1.21-33.01)	0.03	
12 to 15	Pain several times/week vs. monthly	34 (2)	CR 1.58 (1.15-2.17)		0.005	
16 to 18	Daily pain frequency vs. monthly	34 (2)	1.58 (1.17-2.14)		0.003	
16 to 18	Longer pain duration per 10-months increase	34 (2)	CR 1.04 (1.01-1.07)		0.01	
9 to 12 M	Also headache (d) at least once a week	38 (4)			<0.001	

9 to 12 M	Also abdominal pain (d) at least a week	38 (4)			<0.001			
9 to 12 F	Also headache (d) at least once a week	38 (4)			<0.001			
9 to 12 F	Also abdominal pain (d) at least a week	38 (4)			<0.001			
9 to 12	Other musculoskeletal symptoms: upper extremities at least once a week	38 (4)			<0.001			
9 to 12 M	Other musculoskeletal symptoms: chest at least once a week	38 (4)			0.008			
9 to 12 F	Other musculoskeletal symptoms: chest at least once a week	38 (4)			0.001			
9 to 12	Other musculoskeletal symptoms: back at least once a week	38 (4)			<0.001			
9 to 12 M	Other musculoskeletal symptoms as well: lower extremities at least once a week	38 (4)			<0.001			
9 to 12 F	Other musculoskeletal symptoms as well: lower extremities at least once a week	38 (4)			0.003			
8, 11, 14	Headache >/= 1time/week	20 (11)		2.3 (1.1-4.5)				
10 to 16	Duration of pain episodes > 3 hours vs. < 3 hours	20 (11)		U 3.1 (1.1-8.2)				
10 to 16	Lower pain threshhold	40 (5)			<0.05			
10 to 16	Lower pain threshold at anterior tibial region (pressure level < 5kg/cm2)	40 (5)			<0.01			
	PSYCHOLOGICAL PROGNOSTIC FACTORS							
	General psychological factors							
16 M	Internalization (e)	33 (2)		2.32 (1.23-4.37)				
16 M	Externalization (e)	33 (2)		2.17 (1.24-3.81)				
16 F	Internalization (e)	33 (2)		3.70 (1.88-7.27)				
10 to 16	Often/sometimes nervous	20 (11)		M 2.1 (1.3-3.4)				
16 to 18 M	Internalization (e)	24 (2)			< 0.001			
16 to 18 M	Externalization (e)	24 (2)			< 0.001			
16 to 18 F	Higher internalization score (e)	24 (2)			< 0.001			
16 to 18 F	Higher externalization score (e)	24 (2)			< 0.001			
10 to 16	Self-perception of not feeling completely healthy	20 (11)		U 1.7 (1.1-2.8)				
10 to 16	Unsatisfied with own appearance	20 (11)		U 1.6 (1.1-2.5)				
12 to 15	EQ-5D index score 0-25 vs. 75-100% quartiles (f)	9 (1)		U 0.08	<0.001			
12 to 15	EQ-5D index score 0-25 vs. 25-50% quartiles (f)	9 (1)		U 0.29	<0.001			
12 to 15	EQ-5D index score 25-50th % vs. 75th-100th % (f)	34 (2)	CR 1.81 (1.14-2.85)		0.01			
12 to 15	EQ-5D index score 0-25th % vs. 75th-100th % (f)	34 (2)	CR 2.00 (1.28-3.12)		0.002			
10 to 11	Self reported low self esteem	39 (2)			U < 0.01			
10 to 11	Parent reported adolescent low self esteem	39 (2)			U < 0.01			
	Depressive factors							
9 to 12 F	Depressive feelings	21 (4)	U 1.21 (1.03-1.42)				age	
9 to 12 F	Depressive symptoms in a frequency of at least once a week	38 (4)			<0.001			
9 to 12 M	Depressive symptoms in a frequency of at least once a week	38 (4)			<0.001			
12 to 16	Higher score of anxiety and depressive symptoms (g)	18 (4)		1.4 (1.03-1.90)	0.032			
10 to 11	Self reported anxiety/depression	39 (2)			M <0.01			
10 to 11	Parent reported adolescent anxiety/depression	39 (2)			< 0.05			
	SOCIAL PROGNOSTIC FACTORS							
	General social factors							
2 to 17	Lower paternal educational level (median 10 vs. 14 years education)	22 (9)			p<0.01			
2 to 17	Lower maternal educational level (median 10 vs. 14 years education)	22 (9)			p<0.01			
2 to 17	More chronic family difficulties (mean 4.3 vs. 2.9) (h)	22 (9)			p<0.01			
10 to 16	Doing well in school	20 (11)		U 1.8 (1.1-2.9)				
9 to 12	Higher disability index (i) 1-2 vs 0	28 (1)	1.72 (1.09-2.73)		0.005			
9 to 12	Higher disability index (i) 3-5 vs 0	28 (1)	3.17 (1.54-6.55		0.005			
9 to 12	Higher disability index (i) 3-5 vs. 0	21 (4)	U 1.23 (1.02-1.49)				age	
11 to 14	High vs. low peer relationship problems	23 (4)	2.4 (1.3-4.2)				age, sex	
11 to 14	Difficulty standing in line for 10 minutes	23 (4)	2.7 (1.5-4.9)					
11 to 14	Difficulties carrying a schoolbag	23 (4)	2.1 (1.1-4.0)					
11 to 14	High limitation level HFAQ (j) 4-9 vs. 0-1 limitations	23 (4)	4.1 (1.05-16.2)					
8, 11, 14	Headache on non-school days	20 (11)		3.1 (1.3-7.3)				
13 M	Use of physiotherapy for headache or neck pain during the past 6 months	25 (3)			0.004			

10 to 11 F	Parental recurrent headache	39 (2)			p<0.05			
10 to 16	At least one parent with a pain syndrome	40 (5)			0.047			
	Sleep related factors							
9 to 12 F	Waking up during nights	21 (4)	U 1.18 (1.01-1.37)			age		
16 F	Sleep </= 7h vs. 8-9 h/day	33 (2)		1.68 (1.05-2.68)				
9 to 12	Day tiredness, fatigue	28 (1)		1.86 (1.16-3.00)	0.010			
16 to 18 M	Insufficient sleeping time h/day (mean 8 vs. 8.5 h/day)	24 (2)			0.001			
9 to 12 M	Difficulties falling asleep	38 (4)			<0.001			
9 to 12 M	Daytime tiredness	38 (4)			<0.001			
9 to 12 M	Walking up during nights	38 (4)			0.001			
9 to 12 F	Difficulties falling asleep	38 (4)			<0.001			
9 to 12 F	Daytime tiredness	38 (4)			<0.001			
9 to 12 F	Walking up during nights	38 (4)			<0.001			
	Physical activity / inactivity							
16 F	>/=4 vs. 2-3 hours of moderate-to-vigorous physical activity/week	33 (2)		1.63 (1.04-2.56)				
16 to 18 M	Longer sitting time outside school hours (mean 6.2 h/day)	24 (2)			0.004			
12 to 15	Sports participation 3-7 t/wk vs. 0-2 t/wk	9 (1)		M 2.01 (1.20-3.36)	0.008			
9 to 12	Exercise frequency 5-7 t vs. 0-2/week	11 (1)		M 2.43 (1.16-5.05)				
	Alcohol							
16 to 18 F	More than occasional consumption	24 (2)			0.038			
	Smoking							
16 F	Smoking vs. nonsmoking	33 (2)		1.89 (1.23-2.90)				
16 F	Smoking 5-7 days/week vs. nonsmoking	30 (2)		2.52 (1.40-4.53)		family's SES, physical activity, BMI, depressive mood		
16 F	Smoking 1-9 cigarettes/day vs. nonsmoking	30 (2)		2.39 (1.40-4.08)		family's SES, physical activity, BMI, depressive mood		
16 F	Smoking > 9 cigarettes/day vs. nonsmoking	30 (2)		2.57 (1.03-6.46)		family's SES, physical activity, BMI, depressive mood		
16 M	Smoking 1-9 cigarettes/day vs. nonsmoking	30 (2)		2.68 (1.35-5.32)		family's SES, physical activity, BMI, depressive mood		

Explanatory notes

F = prognostic factor only applicable for female participants, **M** = Male, when nonspecified = unisex

RR > 1 or < 1, OR > 1 or < 1, p < 0.05 indicate that the prognostic factor is associated with a higher risk of persistent MSK pain.

CI = confidence interval **M** = Multivariate analysis **U** = Univariate analysis CR = Crude

a = Group 1: prepubertal, group 2: became pubertal during 3 years follow-up, and group 3: pubertal at baseline. The pubertal stage was assessed by the presence of secondary signs of pubertal development. For females, puberty was defined by the stage of breast development (Tanner stage >/= 3) and menarche. For males, puberty was defined in presence of a testicles volume >/= 12 ml and presence of pubic and underarm hair.

b = Low lumbar extension strenght and high ratios between lumbar mobility and lumbar extension strenght predicts future low back pain

c = childhood abdominal pain, headache, depressive symptoms, day tiredness, difficulties in falling asleep, waking up during nghts are believed to be having a psychosomatic origin in the great majority of cases.

d = Classified as: other physical and psychological symptoms, without further definition

e = Internalizing score calculated from subscales: anxious/depressed, sithdrawn/depressed symptoms, and somatic complaints. Externalizing from rule-breaking and aggressive behaviour.

f = EQ-5D assesses self-reported health status in 5 dimensions: mobility, self-care, usual activitied, pain/discomfort, anxiety/depression and within 3 levels of severity: no problems, moderate or severe problems as well as scoring own current self-rated health status on VAS 0-100.

g = Anxiety symptoms: been constantly scared and uneasy, felt tense and restless, worried too much about different matters. Depressive symptoms: felt hopeless when thinking of the future, felt down or sad.

h = Assessment of information about employment and education, economic matters, housing, marital or family discord, social networks and the physical and mental health of the family members. Score range 0-6, 6=severe family difficulties.

i = Subjective disability index calculated from answers to the following proposals: difficulty in falling asleep because of pain, difficulty sitting during a lesson, pain disturbs a walk more than 1km, pain disturbs physical exercise, pain disturbs hobbies. Range 0-5.

j = The modified Hannover functional ability Questionnaire HFAQ assesses whether pain and ache in low back make any of the following daily activities difficult: reaching up to get a book from a high shelf, carrying your school bag to school, sitting on a school chair for a 45-min lesson, standing in a queue for 10 min, sitting up in bed from a lying position, bending down to put your socks on, standing up from an armchair at home, running fast to catch a bus, and sports activities at school. Low = 0-1 limitation, moderate = 2-3 limitations or high = 4-9 limitations (23).

k = Yunus criteria: pain modulation by physical activity, by weather, by anxiety and stress, poor sleep, headache, irritable bowel, soft tissue swelling in hands and feet, fatigue, numbness in hands and feet, feeling excited and nervous. Yes to minimum 3 symptoms to meet the Yunus criteria.

l = SES: Socioeconomic status

m = CDI: Children's depression Inventory. Cut off point >/= 13 indicating depressive symptoms

Identified baseline factors without association to persistent musculoskeletal pain, divided in pain type (study ID)	
Musculoskeletal	Female: sitting h/day, sleep h/day, Male: physical activity MET-h/week and above occasional alcohol consumption, unisex: smoking pack years, body mass index (BMI) (24)
	Exercise frequency >3 vs. <3t/week, disability index 1-5 vs. 0 (i), waking up during nights (Male), day tiredness, difficulty falling asleep, depressive feelings (Male), headache (Female), abscence one day or more from school vs. never being asbcent due to pain, maximum volume O2 intake (per unit increase) measured during a shuttle run test (21)
	Headache, stomachache, depressive feelings, difficulty falling asleep, waking up during nights, Yunus criteria (k), increasing exercise amount, and hypermobility (28)
	Male: physical activity level, sitting >4 h/day, sleep </= 7 h/day, smoking and overweight. Female: externalization, sitting > 4h/day, overweight (33)
	Increasing age (20, 27)

	Increasing age, sex, family history of related diseases, VAS score assessed by physicians, elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), platelet count, lower score in psychosocial functioning reflecting mental health and functioning at school/work, within the family, with friends and in other social activities (Children's Global Assessment Scale, CGAS) (22)
Low back	Extension strength (minutes) and plain saggital mobility (36)
	Akward trunk postures, physically demanding job (working hands above shoulders, awkward trunk posture and standing or walking), working regularly or irregularly, duration of work, work with specific physical load factors (31)
	BMI (32)
	Male: smoking 5-7 d/week vs. no smoking, smoking <9 cigarettes/day (30)
	High emotional vs. low emotional problems, reaching to a high shelf, sitting up in bed, bending down to put on socks, high conduct problems, high hyperactivity, high prosocial behavior, widespread pain, headache, stomachache in the past month compared to none, daytime tiredness on a scale 0-10, 5-10 vs. 0-4, pain start < 12 months ago, pain lasts </= 7 days, pain today, pain severity on a scale 0-10, 4-10 vs. 0-3, Hannover 2-3 vs. 0-1 (23)
	Sex, increasing age, tobacco, profession: hairdresser and media/design compared to electrician, western ethnicity compared to non-western ethnicity, moderate/high vs. low socio-economic status (SES) (l), moderate/high vs. low physical activity level, BMI, moderate/high physical work demand vs. low (26)
Knee	Increasing age compared to 15, participation in sports, BMI, EQ-5D index score 50-75th percentile compared to 75-100th, weekly pain frequency compared to monthly (34)
	BMI, EQ-5D 50-75th percentile compared to 0-25th, monthly, weekly, several times a week pain frequency compared to rarely (9)
Lower limb	After 1 year follow-up: traumatic limb at baseline, exercise 3-4 t/week vs. 0-2 t, hypermobility score >/= 6 vs. < 6. After 4 years follow-up: exercise frequency 5-7 t/week vs. 0-2 t, lower limb trauma at baseline. Common after both 1 and 4 years follow-up: age 11-14 vs. 9-11, frequency of exercise 2-4 times vs. once a week, multisite pain, female sex, headache, stomachache, depressive feelings, difficulty falling asleep, day tiredness, waking up during nights, school abscence due to pain vs. never abscent, disability symptoms >/=3 vs. </=2, volume ..O2 max average or above, exercise frequency 3-4 t/week vs. 0-2 t (11)
Neck	Joint hypermobility Beighton 6-9, physical activity at least half and hour more than 3 times a week (38)
Growing pain	Sex, ethnicity, increasing age (40)
Headache	Sex (19)
	Pain frequency, pain in daily activities, physiotherapy, relaxation therapy, sport activity, stress at home or in hobbies, pain on palpation, pain threshold measured by dolorimeter, depressive symptoms, temporomandibular disorder, stress at school, use of computer (25)
	Stress (20)
Widespread	Female sex, increasing age, tender point count, CDI > 13 (m), Yunus criteria >/=3, sleep score, disability index (f), psychosomatic symptoms (29)
Back	Stress (20)

Prognostic factors are divided primarily in biological, psychological, and social factors and secondary according to musculoskeletal pain type. The prognostic value were reported with RR, OR, and/or p-value.

Appendix 1

Search history

Medline Ovid May 30th 2017

1	back pain/ or headache/ or exp musculoskeletal pain/ or Abdominal Pain/ or Back Pain/ or Low Back Pain/ or exp Arthralgia/ or Chest Pain/ or Facial Pain/ or Flank Pain/ or Metatarsalgia/ or Neck Pain/	110,274
2	Acute Pain/ or Chronic Pain/ or Breakthrough Pain/ or Pain, Intractable/ or Pain, Referred/	16,079
3	(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann).mp.	1,960,816
4	2 and 3	4,733
5	(backache or headache).mp.	78,052
6	((pain or ache) adj3 (musculoskeletal or back or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann)).mp.	103,970
7	1 or 4 or 5 or 6	217,985
8	limit 7 to "all child (0 to 18 years)"	41,139
9	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager).mp.	3,721,647
10	7 and 9	54,465
11	8 or 10	55,016
12	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*).mp.	4,208,880
13	11 and 12	20,363
14	(systematic reviews or meta analysis).pt.	80,495
15	case report/ or (case reports or letter or historical article or comment or editorial).pt.	3,595,207
16	limit 13 to (systematic reviews or meta analysis)	466
17	14 or 15	3,674,563
18	13 not (16 or 17)	17,183

EMBASE Ovid May 31st 2017

1	exp *musculoskeletal pain/	40,261
2	exp *"headache and facial pain"/	73,629
3	exp *abdominal pain/	10,492
4	*arthralgia/	4,782
5	*thorax pain/	9,691
6	*flank pain/	245
7	*metatarsalgia/	522
8	1 or 2 or 3 or 4 or 5 or 6 or 7	137,602
9	*chronic pain/	20,500
10	*breakthrough pain/	346
11	*intractable pain/	2,166
12	*referred pain/	233
13	or/9-12	23,135
14	(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann).mp.	2,678,325
15	13 and 14	8,147
16	(backache or headache).mp.	261,495
17	((pain or ache) adj3 (musculoskeletal or back or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann)).mp.	171,769
18	8 or 15 or 16 or 17	450,426
19	limit 18 to (infant <to one year> or child <unspecified age> or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	54,948
20	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager).mp.	3,594,291
21	18 and 20	79,053
22	19 or 21	79,102

23	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*).mp.	5,319,110
24	22 and 23	28,128
25	limit 24 to ("systematic review" or meta analysis)	497
26	case report/ or (letter or editorial or conference*).pt.	6,706,285
27	25 or 26	6,706,709
28	24 not 27	17,726

CINAHL Ebsco May 31st 2017

I	Search Terms	Search Options	Results
S18	S16 not S17	Search modes - Boolean/Phrase	3,716
S17	PT (Systematic Review or Meta Analysis)	Search modes - Boolean/Phrase	41,837
S16	S14 AND S15	Search modes - Boolean/Phrase	3,802
S15	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*)	Search modes - Boolean/Phrase	530,171
S14	S11 OR S13	Search modes - Boolean/Phrase	11,516
S13	S10 AND S12	Search modes - Boolean/Phrase	11,425
S12	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager)	Search modes - Boolean/Phrase	590,118
S11	S1 OR S7 OR S8 OR S9	Limiters - Age Groups: Infant, Newborn: birth-1 month, Infant: 1-23 months, Child, Preschool: 2-5 years, Child: 6-12 years, Adolescent: 13-18 years Search modes - Boolean/Phrase	8,712
S10	S1 OR S7 OR S8 OR S9	Search modes - Boolean/Phrase	64,982
S9	((pain or ache) N3 (musculoskeletal or back or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann))	Search modes - Boolean/Phrase	37,883
S8	backache or headache	Search modes - Boolean/Phrase	16,417
S7	S5 AND S6	Search modes - Boolean/Phrase	4,707

S6	(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann)	Search modes - Boolean/Phrase	312,634
S5	S2 OR S3 OR S4	Search modes - Boolean/Phrase	12,235
S4	(MH "Referred Pain")	Search modes - Boolean/Phrase	284
S3	(MH "Breakthrough Pain")	Search modes - Boolean/Phrase	58
S2	(MH "Chronic Pain")	Search modes - Boolean/Phrase	11,921
S1	(MH "Back Pain") OR (MH "Low Back Pain") OR (MH "Facial Pain") OR (MH "Headache") OR (MH "Knee Pain+") OR (MH "Metatarsalgia") OR (MH "Muscle Pain") OR (MH "Neck Pain") OR (MH "Arthralgia") OR (MH "Shoulder Pain") OR (MH "Chest Pain") OR (MH "Elbow Pain") OR (MH "Heel Pain") OR (MH "Abdominal Pain")	Search modes - Boolean/Phrase	40,609

Cochrane June 9th 2017

Search Name:
Date Run: 09/06/17 10:28:15.152
Description:

ID	Search Hits
#1	((pain or ache) next/3 (musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann)) 7405
#2	(backache or headache) 26356
#3	#1 or #2 32236
#4	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager) 243010
#5	#3 and #4 8870
#6	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*) 399020
#7	#5 and #6 4430

All Results (4430)

- Cochrane Reviews (1311)
  - All
  - Review
  - Protocol
- Other Reviews (66)
- Trials (3002)
- Methods Studies (0)
- Technology Assessments (4)
- Economic Evaluations (34)
- Cochrane Groups (13)

Imported: Trial, Technology, Economic

Web of Science June 9th 2017

Set	Results	Save History / Create Alert / Open Saved History	Edit Sets	Combine Sets AND OR Combine	Delete Sets Select All Delete
# 9	11,624	#8 AND #7 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 8	5,905,200	ts=(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 7	29,467	#6 AND #5 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 6	2,457,687	ts=(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 5	240,860	#4 OR #3 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 4	66,234	ts=(backache or headache) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 3	191,133	#2 AND #1 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 2	2,616,397	TS=(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 1	491,777	ts=(pain or ache) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
				AND OR Combine	Select All Delete

SportDiscus June 9th 2017

S7	((predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*)) AND (S5 AND S6)	Search modes - Boolean/Phrase	843
S6	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*)	Search modes - Boolean/Phrase	118,227
S5	S3 AND S4	Search modes - Boolean/Phrase	2,876
S4	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager)	Search modes - Boolean/Phrase	200,385
S3	(S1 OR S2)	Search modes - Boolean/Phrase	25,984
S2	backache or headache	Search modes - Boolean/Phrase	12,066
S1	((pain or ache) N3 (musculoskeletal or back or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann))	Search modes - Boolean/Phrase	18,440

OT-seeker June 9th 2017

((pain or ache)
AND
(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann))
AND
juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager

PsychInfo June 9th 2017

1	exp Musculoskeletal Disorders/	15,728
2	headache/ or muscle contraction headache/	7,110
3	myofascial pain/	317
4	back pain/	3,411
5	or/1-4	25,776
6	chronic pain/	11,631
7	pain/	22,243
8	6 or 7	33,184
9	(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann).mp.	220,772
10	8 and 9	9,266
11	(backache or headache).mp.	18,772
12	((pain or ache) adj3 (musculoskeletal or back or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann)).mp.	9,290
13	5 or 10 or 11 or 12	43,824
14	limit 13 to (100 childhood <birth to age 12 yrs> or 200 adolescence <age 13 to 17 yrs>)	5,603
15	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager).mp.	895,379
16	13 and 15	5,465
17	14 or 16	7,676
18	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*).mp.	723,493
19	17 and 18	2,119
20	(((systematic or method*) adj3 (review* or overview* or study or studies or search* or approach*)) or meta analy* or meta-analy* or metaanaly*).ti,ab,id.	142,307
21	limit 19 to ("0830 systematic review" or 1200 meta analysis)	36
22	21 or 20	142,310

23	19 not 22	1,971
1	exp Musculoskeletal Disorders/	15,728

Reporting checklist for systematic review and meta-analysis.

Based on the PRISMA guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA reporting guidelines, and cite them as:

Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement

		Reporting Item	Page Number
	#1	Identify the report as a systematic review, meta-analysis, or both.	1
Structured summary	#2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number	2
Rationale	#3	Describe the rationale for the review in the context of what is already known.	3
Objectives	#4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
Protocol and	#5	Indicate if a review protocol exists, if and where it can be	3

registration		accessed (e.g., Web address) and, if available, provide registration information including the registration number.	
Eligibility criteria	#6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rational	3
Information sources	#7	Describe all information sources in the search (e.g., databases with dates of coverage, contact with study authors to identify additional studies) and date last searched.	3
Search	#8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	3
Study selection	#9	State the process for selecting studies (i.e., for screening, for determining eligibility, for inclusion in the systematic review, and, if applicable, for inclusion in the meta-analysis).	3
Data collection process	#10	Describe the method of data extraction from reports (e.g., piloted forms, independently by two reviewers) and any processes for obtaining and confirming data from investigators.	4
Data items	#11	List and define all variables for which data were sought (e.g., PICOS, funding sources), and any assumptions and simplifications made.	4
Risk of bias in individual studies	#12	Describe methods used for assessing risk of bias in individual studies (including specification of whether this was done at the study or outcome level, or both), and how this information is to be used in any data synthesis.	4
Summary measures	#13	State the principal summary measures (e.g., risk ratio, difference in means).	4
Planned methods of analyis	#14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.	5
Risk of bias across studies	#15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5
Additional	#16	Describe methods of additional analyses (e.g., sensitivity or	5

analyses		subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
Study selection	#17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	#18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citation.	5
Risk of bias within studies	#19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	5
Results of individual studies	#20	For all outcomes considered (benefits and harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	5
Synthesis of results	#21	Present the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency.	5
Risk of bias across studies	#22	Present results of any assessment of risk of bias across studies (see Item 15).	5
Additional analysis	#23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	5
Summary of Evidence	#24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers	7
Limitations	#25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	7
Conclusions	#26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	7
Funding	#27	Describe sources of funding or other support (e.g., supply of data) for the systematic review; role of funders for the systematic review.	8

PROSPERO
International prospective register of systematic reviews

NHS National Institute for Health Research

UNIVERSITY of York
Centre for Reviews and Dissemination

Systematic review

Please complete all mandatory fields below (marked with an asterisk *) and as many of the non-mandatory fields as you can then click *Submit* to submit your registration. You don't need to complete everything in one go, this record will appear in your *My PROSPERO* section of the web site and you can continue to edit it until you are ready to submit. Click *Show help* below or click on the icon
to see guidance on completing each section.
This record cannot be edited because it has been rejected

1. * Review title.

Give the working title of the review, for example the one used for obtaining funding. Ideally the title should state succinctly the interventions or exposures being reviewed and the associated health or social problems. Where appropriate, the title should use the PI(E)COS structure to contain information on the Participants, Intervention (or Exposure) and Comparison groups, the Outcomes to be measured and Study designs to be included.

Prognostic factors and treatment effect modifiers for children and adolescents with musculoskeletal pain: a protocol for a systematic literature review

2. Original language title.

For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3. * Anticipated or actual start date.

Give the date when the systematic review commenced, or is expected to commence.

21/06/2016

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

01/12/2017

5. * Stage of review at time of this submission.

Indicate the stage of progress of the review by ticking the relevant Started and Completed boxes. Additional information may be added in the free text box provided.
Please note: Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. Should evidence of incorrect status and/or completion date being supplied at the time of submission come to light, the content of the PROSPERO record will be removed leaving only the title and named contact details and a statement that inaccuracies in the stage of the review date had been identified.
This field should be updated when any amendments are made to a published record and on completion and publication of the review.

The review has not yet started: No

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Review stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	Yes
Data analysis	Yes	Yes

Provide any other relevant information about the stage of the review here (e.g. Funded proposal, protocol not yet finalised).

6. * Named contact.

The named contact acts as the guarantor for the accuracy of the information presented in the register record.

Negar Pourbordbari

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

7. * Named contact email.

Give the electronic mail address of the named contact.

negar@dcm.aau.dk

8. Named contact address

Give the full postal address for the named contact.

Dr. Negar Pourbordbari
Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University
Fyrkildevej 7, 9220 Aalborg
Denmark

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

004527914224

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University, Denmark

Organisation web address:

11. Review team members and their organisational affiliations.

Give the title, first name, last name and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong.

Dr Negar Pourbordbari. Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University, Denmark
Mr Allan Riis. Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University, Denmark
Professor Martin Bach Jensen. Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University, Denmark
Dr Jens Lykkegaard Olesen. The Faculty of Medicine Department of Clinical Medicine, Aalborg University, Denmark
Dr Michael Skovdal Rathleff. Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University, Denmark

12. * Funding sources/sponsors.

Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Include any unique identification numbers assigned to the review by the individuals or bodies listed.

Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University, Denmark

13. * Conflicts of interest.

List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members.

15. * Review question.

State the question(s) to be addressed by the review, clearly and precisely. Review questions may be specific or broad. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS where relevant.

The aim of this study is to conduct a systematic review on children and adolescents with musculoskeletal pain with a view to determining which baseline patient characteristics are associated with a poor outcome in follow-up regardless of which treatment has been provided (prognosis) or are associated with a successful outcome to a specific treatment (treatment effect modifiers).
Review question: What are the prognostic factors and treatment effect modifiers for children and adolescents with musculoskeletal pain?

16. * Searches.

Give details of the sources to be searched, search dates (from and to), and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.

This systematic review search will be conducted in the following electronic databases: MEDLINE, Embase, CINAHL, Web of Science, Cochrane and SPORTDiscus without limitations on dates.
Articles reported in English, German, Danish, Norwegian, Swedish, French, Spanish, Japanese, Chinese, Thai, Arabic, Persian, Turkish and Hindi will be included.
The search strategy will be divided into seven parts. 1. Pain; 2. Musculoskeletal defined in components; 3. Anatomic regions; 4. Musculoskeletal conditions in general and those common among children and adolescents; 5. Children and adolescents and synonyms; 6. Predictive factors and synonyms; and 7. Final search string to be applied in above mentioned electronic databases and also tested in MEDLINE with 5336 hits.
Additional details about the search strategy can be found in the attached PDF document (link provided

below).

17. URL to search strategy.

Give a link to the search strategy or an example of a search strategy for a specific database if available (including the keywords that will be used in the search strategies).

https://www.crd.york.ac.uk/PROSPEROFILES/41378_STRATEGY_20170613.pdf

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Yes I give permission for this file to be made publicly available

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

Children and adolescents aged 0-19 years with musculoskeletal pain.

19. * Participants/population.

Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.

The participants must all have some form of self-reported musculoskeletal pain at recruitment. Musculoskeletal pain is defined according to the International Association for the Study of Pain, IASP as: “pain arisen from muscle, tendon, bone and joint. Excluded from the definition is pain due to serious local causes, such as tumors, fractures, or infections, and systemic and neurological causes”. Types of pain are named according to the region affected, e.g. back pain, neck pain, shoulder pain, elbow pain, buttock pain, hip pain, knee pain, and ankle pain.
Inclusion criteria: 0 to 19 years of age, self-reported musculoskeletal pain.
Exclusion criteria: Older than 19 years of age.

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the nature of the interventions or the exposures to be reviewed.

All interventions used to treat musculoskeletal pain in children and adolescents are eligible, including conservative as well as non-conservative interventions. Conservative intervention is defined as: utilization of non-surgical treatment options, such as, but not limited to, the following: physiotherapy, immobilization, bandaging, drug therapy, wait and see and intraarticular, intramuscular and intratendinous injections with NSAID/glucocorticoid/steroid. We will also include studies that do not contain interventions.

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

We expect that most studies will not have used a comparator as they are prospective cohort studies. If the study design is a randomized trial, we will include all types of comparators.

22. * Types of study to be included.

Give details of the types of study (study designs) eligible for inclusion in the review. If there are no restrictions on the types of study design eligible for inclusion, or certain study types are excluded, this should be stated. The preferred format includes details of both inclusion and exclusion criteria.

Prospective cohort studies (including randomized trials) with a population of children and adolescents aged 0-19 years will be included in this systematic review if they report prognostic factors or treatment effect

modifiers (e.g. baseline variables that are associated with the outcome).

23. Context.

Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

There will be no restrictions on the type of setting.

24. * Primary outcome(s).

Give the pre-specified primary (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

We will search for all baseline patient characteristics that are: (i) associated with a poor outcome on follow-up regardless of which treatment has been provided (prognosis); or ii) associated with a successful outcome to a specific treatment (treatment effect modifiers). These may include intrinsic variables (such as age, height, weight, pain intensity, pain duration and similar) or extrinsic variables (such as social status, parental education, sports participation and similar).

Timing and effect measures

We will include patient characteristics that are associated with both short- and long-term outcomes. These will be divided into three endpoints, i.e. short-term (3 months), medium-term (3-12 months) and long-term (more than 12 months).

25. * Secondary outcome(s).

List the pre-specified secondary (additional) outcomes of the review, with a similar level of detail to that required for primary outcomes. Where there are no secondary outcomes please state 'None' or 'Not applicable' as appropriate to the review

The proportion of patients that report themselves free of musculoskeletal pain at follow-up in the included studies.

Timing and effect measures

We will include patient characteristics that are associated with both short- and long-term outcomes. These will be divided into three endpoints, i.e. short-term (3 months), medium-term (3-12 months) and long-term (more than 12 months).

26. Data extraction (selection and coding).

Give the procedure for selecting studies for the review and extracting data, including the number of researchers involved and how discrepancies will be resolved. List the data to be extracted.

The process of study selection will be conducted by two reviewers (NP and AR). They will independently identify studies from the electronic database search and will screen the titles and/or abstracts that have relevance to the question: what are the prognostic factors for children and adolescents with musculoskeletal pain? Studies kept after the primary assessment will be screened by full text and then selected for a final inclusion.
Any excluded studies will be recorded, along with a reason for the exclusion. There will be no blinding of the review authors to the journal titles, authors or institutions. Reference lists of all included studies will be screened for additional eligible publications that may have been missed during the initial search.
Any disagreements inside the reviewer group will lead to the involvement of a third reviewer (MSR).
NP will extract data using a pre-defined data extraction form (see Appendix 1 in the full protocol), inspired by The Cochrane Collaboration, Data collection form for intervention reviews: RCTs and non-RCTs (3). All the extracted data will then be validated by a second person (MSR). The collected data will include a description of the participants, setting (e.g. general practice or population-based cohort) and results (including all patient characteristics tested for association with outcome).

We will contact the corresponding author with a request for information, if any data concerning the intervention or outcome is missing from an included study, the intention being to increase the thoroughness of the descriptions of interventions and outcomes in this study.

Studies examining children and adolescents with musculoskeletal pain aged 0 to 19 years will be included in this review. If a study reports on an age range that exceeds this, we will contact the corresponding author and ask for data on the 0-19 year olds. The requested data will be included if it can be retrieved within one month of the inquiry.

27. * Risk of bias (quality) assessment.

State whether and how risk of bias will be assessed (including the number of researchers involved and how discrepancies will be resolved), how the quality of individual studies will be assessed, and whether and how this will influence the planned synthesis.

The QUIPS risk of bias tool for prognostic studies will be used to assess the quality of each paper (4). This tool contains items and considerations for six bias domains i.e. study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, statistical analysis and reporting (see Appendix 2 in full protocol). Each of the six potential bias domains will be rated by NP as high, moderate, or low risk of bias. When assessing the overall risk of bias in each study, a study will be described with a low risk of bias when either a) most of or b) the most important (determined a priori) or c) all of the six bias domains are rated with a low risk of bias. The same applies to moderate and high risk of bias.

28. * Strategy for data synthesis.

Give the planned general approach to synthesis, e.g. whether aggregate or individual participant data will be used and whether a quantitative or narrative (descriptive) synthesis is planned. It is acceptable to state that a quantitative synthesis will be used if the included studies are sufficiently homogenous.

A narrative synthesis is planned, the reason being the expected substantial heterogeneity in our results. If the prognostic factors or treatment effect modifiers are adequately homogenous, we will conduct a meta-analysis and pool the individual variables.

29. * Analysis of subgroups or subsets.

Give details of any plans for the separate presentation, exploration or analysis of different types of participants (e.g. by age, disease status, ethnicity, socioeconomic status, presence or absence or co-morbidities); different types of intervention (e.g. drug dose, presence or absence of particular components of intervention); different settings (e.g. country, acute or primary care sector, professional or family care); or different types of study (e.g. randomised or non-randomised).

Data will be divided into two main separate groups: prognostic factors and treatment effect modifiers and then sub-grouped into regions of musculoskeletal pain, gender and age.

30. * Type and method of review.

Select the type of review and the review method from the lists below. Select the health area(s) of interest for your review.

Type of review

Cost effectiveness
No

Diagnostic
No

Epidemiologic
No

Individual patient data (IPD) meta-analysis
No

Intervention

No

Meta-analysis
No

Methodology
No

Network meta-analysis
No

Pre-clinical
No

Prevention
No

Prognostic
Yes

Prospective meta-analysis (PMA)
No

Qualitative synthesis
No

Review of reviews
No

Service delivery
No

Systematic review
Yes

Other
No

Health area of the review

Alcohol/substance misuse/abuse
No

Blood and immune system
No

Cancer
No

Cardiovascular
No

Care of the elderly
No

Child health
No

Complementary therapies
No

Crime and justice
No

Dental
No

Digestive system
No

Ear, nose and throat
No

Education

No

Endocrine and metabolic disorders
No

Eye disorders
No

General interest
No

Genetics
No

Health inequalities/health equity
No

Infections and infestations
No

International development
No

Mental health and behavioural conditions
No

Musculoskeletal
No

Neurological
No

Nursing
No

Obstetrics and gynaecology
No

Oral health
No

Palliative care
No

Perioperative care
No

Physiotherapy
No

Pregnancy and childbirth
No

Public health (including social determinants of health)
No

Rehabilitation
No

Respiratory disorders
No

Service delivery
No

Skin disorders
No

Social care
No

Surgery
No

Tropical Medicine
No

Urological
No

Wounds, injuries and accidents
No

Violence and abuse
No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.
English

There is an English language summary.

32. Country.

Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved.

Denmark

33. Other registration details.

Give the name of any organisation where the systematic review title or protocol is registered (such as with The Campbell Collaboration, or The Joanna Briggs Institute) together with any unique identification number assigned. (N.B. Registration details for Cochrane protocols will be automatically entered). If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

34. Reference and/or URL for published protocol.

Give the citation and link for the published protocol, if there is one

Give the link to the published protocol.

http://www.crd.york.ac.uk/PROSPEROFILES/41378_PROTOCOL_20160520.pdf

Alternatively, upload your published protocol to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Yes I give permission for this file to be made publicly available

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

35. Dissemination plans.

Give brief details of plans for communicating essential messages from the review to the appropriate audiences.

The manuscript will be submitted for publication in an appropriate peer-reviewed journal. In addition to this we will produce material to be distributed to general practitioners and other health care providers, who manage children and adolescents with musculoskeletal pain. This will be done in the form of a short animation video, visualizing the main study results from the systematic review. The animation will be distributed through social media, websites and patient associations. This will ensure dissemination of our results to our target audience.

Do you intend to publish the review on completion?

Yes

PROSPERO
International prospective register of systematic reviews

NHS National Institute for Health Research

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords will help users find the review in the Register (the words do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

systematic review
children
adolescence
musculoskeletal pain
prognosis
treatment effect modifier

37. Details of any existing review of the same topic by the same authors.

Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

38. * Current review status.

Review status should be updated when the review is completed and when it is published.
Please provide anticipated publication date

Review_Ongoing

39. Any additional information.

Provide any other information the review team feel is relevant to the registration of the review.

References:
1. http://www.iasp-pain.org/files/Content/ContentFolders/GlobalYearAgainstPain2/MusculoskeletalPainFactSheets/AcutePain_Final.pdf
2. http://www.spine-health.com/glossary/conservative-treatment.
3. Cochrane Training, Data collection form for intervention reviews: RCTs and non-RCTs. http://training.cochrane.org/resource/data-collection-forms-intervention-reviews 2014.
4. Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing bias in studies of prognostic factors. Ann Intern Med. 2013;158(4):280-6.

40. Details of final report/publication(s).

This field should be left empty until details of the completed review are available.

Give the link to the published review.

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Poor prognosis of child and adolescent Musculoskeletal Pain - a Systematic Literature Review

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Systematic-review-animation-final.mp4	

Poor prognosis of child and adolescent Musculoskeletal Pain - a Systematic Literature Review

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Abstract

Objectives

To identify baseline patient characteristics that are: (i) associated with a poor outcome on follow up regardless of which treatment was provided (prognosis); or (ii) associated with a successful outcome to a specific treatment (treatment effect modifiers).

Design

Systematic literature review according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines.

Data sources

Medline, Embase, Cinahl, Web of Science, Cochrane, SportDiscus, OT Seeker, and PsychInfo were searched for prospective cohort studies up to February 2019 without limitation in publication date.

Eligibility criteria

Prospective cohort studies reporting either prognostic factors or treatment effect modifiers on persistent musculoskeletal pain in 0- to 19-year-old children and adolescents. Pain caused by tumours, fractures, infections, systemic and neurological conditions were excluded.

Outcome measures

Our primary outcome was musculoskeletal pain at follow-up and identification of any baseline characteristics that were associated with this outcome (prognostic factors). No secondary outcomes were declared.

Method

Two reviewers independently screened abstracts and titles. We included prospective cohort studies investigating the prognosis or treatment effect modifiers of 0- to 19-year-old children and adolescents with self-reported musculoskeletal pain. Risk of bias assessment was conducted with the QUIPS tool.

Results

Twenty-six studies yielding a total of 111 unique prognostic factors were included. Female sex and psychological symptoms were the most frequent investigated prognostic factors. Increasing age, generalised pain, longer pain duration, and smoking were other identified prognostic factors. No treatment effect modifiers were identified.

Conclusion

Several prognostic factors are associated with a poor prognosis in children and adolescents with musculoskeletal pain. These prognostic factors may help guide clinical practice and shared decision-making. None of the included studies was conducted within a general practice setting which highlights an area in need of research.

Registration

The protocol for this review was developed using the PRISMA-P 2015 statement, inspired by the Cochrane Central Register of Controlled Trials, and registered prospectively in the International Prospective Register of Systematic Reviews (PROSPERO, ID: CRD42016041378).

Strengths and limitations of this study

- This review is highly updated with a search up to February 2019.
- No previous review has aimed to identify prognostic factors in children and adolescents with musculoskeletal pain with the purpose of informing clinical practice.
- In collaboration with a research librarian a highly sensitive search for each of the eight databases was developed to ensure an inclusion of the totality of previous research.
- Two reviewers independently carried out the screening and data extraction was executed in the same manner for all included studies.
- No meta-analysis was conducted due to a heterogeneity of patient population, setting, and endpoints.

Keywords

musculoskeletal pain; adolescents; children; prognosis; general practice

Introduction

General practice is often the point of first contact into the health care system and musculoskeletal pain complaints are the most common cause of contact. The case workload due to musculoskeletal pain complaints in children and adolescents is estimated to be 4-8% of the UK general practice (1) and musculoskeletal pain is known to affect half of all children and adolescents, increasing exponentially in frequency around the age of 10 (2-6). A recent systematic review reported that 40% of an adolescent population had experienced pain during the past six months (3). The most common pain sites are the knee and back (7). Musculoskeletal pain has a detrimental impact on the adolescents' quality of life and may cause them to withdraw from school, social, and athletic activities (8, 9).

Musculoskeletal pain in children and adolescents has previously been considered a self-limiting condition without long-term impact (10). Recent cohort studies show that 16-32% of patients with knee pain still report knee pain one year later (10, 11) and that 21% of 12-35-year-olds had persistent knee pain six years after initial contact to their general practitioner (10). Collectively, these studies highlight that a significant proportion of adolescents will report pain even years later. Who are the children and adolescents with a particularly high risk of long-lasting musculoskeletal pain? This is one of the most common questions from our stakeholder interviews with general practitioners [*unpublished stakeholder event*].

Knowledge of prognostic factors can inform the general practitioner of the prognosis of their patients and enable them to identify those with a poor prognosis to stratify care, address modifiable risk factors and better understand chronic pain conditions. The latest systematic review on prognostic factors for adolescents with musculoskeletal pain (12) ended their literature search in July 2015 which makes for a timely update. So far, no systematic reviews have aimed to inform clinical practice of prognostic factors in children, and adolescents with musculoskeletal pain. Therefore, we aimed to identify baseline patient characteristics associated with a (i) poor outcome on follow-up (prognosis) or (ii) successful outcome of a treatment (treatment effect modifiers).

Methods

Literature search

We searched in Medline, Embase, Cinahl, Web of Science, Cochrane, SportDiscus, OT Seeker, and PsychInfo from their inception until February 2019 without limitation on date. An experienced research librarian collaborated in the production of individual search strategies for each of the eight databases (Appendix 1).

Eligibility criteria

Study population and design

We included prospective studies that investigated prognostic factors or treatment effect modifiers in children and adolescents 0- to 19-years-old, with any type and location of musculoskeletal pain. Musculoskeletal pain was defined as pain in muscle, tendon, bone, and joint (13). We included musculoskeletal pain types, reported in each of our included studies, without further definition of or changes in the designations chosen by the respective authors. We excluded pain knowingly caused by tumours, fractures, infections, systemic and neurological conditions, and stomach pain, because of insufficient differentiation between musculoskeletal stomach pain and stomach pain by other causes. Furthermore, we included all prospective studies, independent of intervention and randomised trials including all types of comparators. As expected, most studies did not use a comparator because they were prospective cohort studies. Similar to intervention, these studies were included independent of comparators. There were no restrictions on the type of setting or language.

Review process

Two reviewers (NP and AR) independently screened titles and abstracts for studies addressing the question: What are the prognostic factors and treatment effect modifiers for children and adolescents with musculoskeletal pain? Full-text articles were then screened, adding primary reasons for exclusion.
There was no blinding of the review authors to the journal titles, authors, or institutions. Reference lists of all included studies were screened for eligible publications that may have been missed during the initial search.

The study selection process was finalised without any disagreements on included studies. EndNote was used to remove duplicates and NP manually checked for duplicates afterwards.

Data extraction

Data for the included studies were extracted by NP in the form of: *study characteristics* (study design, recruitment setting, and duration of follow-up), *participant characteristics* (musculoskeletal pain type, baseline age, study population, and persistent pain at follow-up in females, males, and combined) (Table 1), and *prognostic factors* with their reported estimates: odds ratios (OR), relative risks (RR), (95% confidence intervals (95%CI)), and/or P-values. If possible, we extracted the adjusted associations.
Data were extracted with a pre-defined data extraction form inspired by The Cochrane Collaboration (14).

Outcomes and endpoints

Our primary outcome of interest was musculoskeletal pain at follow-up. We wanted to identify any baseline characteristics that were associated with this outcome (prognostic factors). We used the term "pain persistence" to describe participants who had pain at both baseline and follow-up, without applying restrictions on either pain measurement or on follow-up time points.

Risk of bias

Risk of bias was assessed using the Quality in Prognostic Studies (QUIPS) tool (15). On the study level, NP and AR independently rated the 26 included studies and reached consensus on all risk of bias assessments (Table 2). Prognostic factors from studies with a high risk of bias, were excluded from Figure 1.

Involvement of general practitioners

With stakeholder involvement and input from a panel of general practice researchers experienced in musculoskeletal research, we sub-grouped our identified prognostic factors in accordance with the biopsychosocial model (16, 17):

Biological prognostic factors:
-Female sex
-Older age
-Body measurement factors
-Physical functioning
-Pain characteristics

Psychological prognostic factors
-General psychological factors
-Depressive factors

Social prognostic factors:
-General social factors
-Factors related to sleep/daytime tiredness
-Physical activity/inactivity
-Alcohol
-Smoking

Reporting of results

We were not able to conduct our a priori planned meta-analysis because of heterogeneity in terms of patient population, setting, and time points for follow-up. The evidence on included prognostic factors was reported with odds ratios (OR), relative risks (RR), and/or P-values. As OR and RR may differ in interpretation, we reported them separately. A statistically significant association between a patient characteristic and an outcome was defined as an RR or OR above or below 1 that did not include 1 in the 95% confidence interval. As for P-value, a statistically significant association was defined as $P < 0.05$. Average on pain at follow-up was

calculated as average of individual studies reporting same musculoskeletal pain type at same follow-up duration (Figure 2).
We used the PRISMA checklist when writing our report (18) (Appendix 2).

Patient involvement
No patients or public were involved in the present study.

RESULTS

Included studies

Figure 3 reports the results of the search strategy. Of the 48,538 titles identified, 41,735 studies were screened, and 26 studies (9, 11, 17, 19-41) were included. All included studies were prospective studies. The included studies used a mix of different measures to capture pain at follow-up. Musculoskeletal pain types included in our search were: general musculoskeletal pain, neck, back, lower back, lower limb, knee, and growing pain. No treatment effect modifiers were identified.

Table 1 Included studies described by musculoskeletal pain type, baseline age, size of study population, and follow-up.

Study (reference)	MSK pain type	Baseline age (years)	Recruitment setting	Study population (n)	Follow-up (years)	Persistent pain at follow-up Female (%)	Persistent pain at follow-up Male (%)	Persistent pain at follow-up combined (%)
Blaauw (19)	Headache	12 - 16	School	1586	4	45.7	22.7	35.1
Brattberg 93 (20)	Back, Head	8, 11, 13	School	471	2	Back 15 Head 40	Back 4 Head 20	Back 9.3 Head 30.7
Brattberg 04 (21)	General MSK	10, 13, 16	School	597	11	59	39	20
El-Metwally 04 (22)	General MSK	9 - 12	School	1756	1 and 4	4 years: 56.2	4 years: 43.8	1 years: 53.8 4 years: 63.5
El-Metwally 05 (11)	Lower limb	9 - 12	School	1756	1 and 4	1 year: 29.4 4 years: 31.9	1 year: 55.8 4 years: 48.6	1 year: 32 4 years 31
Flato (23)	General MSK	2 - 17	Clinical	37	9	13	N/A	59
Holley (24)	General MSK	10 - 17	Clinical	88	3 months	87,1	12,9	35,2
Jones (25)	Low back	11 - 14	School	330	4	N/A	N/A	26
Jussila (26)	General MSK	16 - 18	Community	1773	2	N/A	N/A	N/A
Laimi (27)	Headache[a]	13	School	311	3	54	70.5	48
Lunde (28)	Low back	15 - 19	School	420	6.5	N/A	N/A	39
Mikkelsson 97 (29)	Neck, WSP, low back	9 - 12	School	1756	1	N/A	N/A	Neck 48.3 WSP 29.7 Low back 34.4
Mikkelsson 98 (30)	General MSK	9 - 12	School	1756	1	N/A	N/A	52.9
Mikkelsson 99 (31)	Neck, WSP	9 - 12	School	464	1	Neck 70.4 WSP 62.5	Neck 41 WSP 62.5	Neck 58,1 WSP 62,5
Mikkonen 08 (32)	Low back	16	Community	2969	2	N/A	N/A	27.1
Mikkonen 11 (33)	Low back	16	Community	728	2	53	46	50.4
Mikkonen 13 (34)	Low back	7 - 19	Community	1660	2 and 3	2 years: 68 3 years: 63	2 years: 62 3 years: 47	N/A
Paananen (35)	General MSK	16	Community	1594	2	N/A	75	88
Rathleff (9)	Knee	12 - 15	School	768	1	N/A	N/A	48.8
Rathleff 16 (36)	Knee	16 - 18	School	504	2	N/A	N/A	55.9
Rathleff 16 (37)	Knee (PFP)	15 - 19	School	121	3 months	N/A	N/A	74.4
Sjolie (38)	Low back	14 - 16	Community	88	3	N/A	N/A	39
Sperotto (39)	General MSK	8 - 13	School	289	3	N/A	N/A	54.3
Stanford (17)	Head, Back, Stomachache	10 - 11	Community	2488[b]	2	N/A	N/A	Head 29 Back 21.7
Ståhl (40)	Neck	9 - 12	School	1756	1 and 4	N/A	N/A	1 year: 48.2 4 years: 33.5
Uziel (41)	Growing pain	10 - 16	Clinical	35	5	N/A	N/A	48.6

MSK = Musculoskeletal
N/A = not applicable
A = Headache: non migrainous
WSP = Widespread pain
b = included stomachache participants

Extracted data from the included studies: MSK pain type, baseline age, recruitment setting, size of study population, follow-up and percentage of study participants who represented persistent pain at follow-up, -both stratified by gender and combined.

Risk of bias

The most common reasons for a moderate or high risk of bias were inadequately described study participation and statistical analyses (n=6, 23%), attrition rates (n=5, 20%), and poor adjustment for confounders (n=11, 42%). Three studies were rated with high risk of bias. With the purpose of filtering the results of prognostic factors, we excluded these studies from the final results depicted in Figure 1.

Table 2 Risk of bias in included studies. With the Quality in Prognostic Studies (QUIPS) tool studies were assessed on the overall risk of bias within each of the six domains and rated as low, moderate or high risk of bias.

Study author year	Design	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and presentation
Blauuw et al 2015	Prospective cohort	Low	Moderate	Low	Low	Moderate	Low
Brattberg et al 1993	Prospective cohort	Moderate	Moderate	Low	Low	Moderate	High
Brattberg et al 2004	Prospective cohort	Low	Moderate	Low	Low	Low	Low
El-Metwally et al 2004	Prospective cohort	Low	Low	Low	Low	Low	Low
El-Metwally et al 2005	Prospective cohort	Low	Low	Low	Low	Low	Low
Flato et al 1997	Prospective cohort	Low	Low	Low	Low	Low	Low
Holley et al 2017	Prospective cohort	Low	Low	Low	Low	Low	Low
Jones et al 2009	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Jussila et al 2014	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Laimi et al 2007	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Lunde et al 2015	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Mikkelsson et al 1997	Prospective cohort	Low	Low	Low	Low	Moderate	Moderate
Mikkelsson et al 1998	Prospective cohort	Low	Low	Low	Low	Low	Moderate
Mikkelsson et al 1999	Prospective cohort	Low	Low	Low	Low	Low	Low
Mikkonen et al 2008	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Mikkonen et al 2012	Prospective cohort	Moderate	Low	Low	Low	Low	Low
Mikkonen et al 2013	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Paananen et al 2010	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Rathleff et al 2013	Prospective cohort and nested case-control	Moderate	Low	Low	Low	Low	Low
Rathleff et al 2016*	Prospective cohort	Low	Low	Low	Low	Low	Low
Rathleff et al 2016	Prospective cohort	Low	Low	Low	Low	Low	Low
Sjolie et al 2001	Prospective cohort study with a cross sectional part	Low	Low	Low	Low	Low	Low
Sperotto et al 2015	Prospective cohort	Low	Moderate	Low	Low	High	Moderate
Stanford et al 2007	Prospective cohort	Low	Moderate	Low	Low	Low	Low
Ståhl et al 2008	Prospective cohort	Low	Moderate	Low	Low	Moderate	Low
Uziel et al 2010	Prospective cohort	Moderate	Low	Low	Low	High	Moderate

**"Is knee pain during adolescence a self-limiting condition?"*

Risk of bias in included studies. With the Quality in Prognostic Studies (QUIPS) tool studies were assessed on the overall risk of bias within each of the six domains and rated as low, moderate or high risk of bias. Three studies were rated with high risk of bias, and hence excluded from the final results.

Prognosis

Figure 2 highlights the persistence of musculoskeletal pain in all included studies at different follow-up time points and is calculated based on persistent pain at follow-up in Table 1.

At one-year follow-up, an average of 54,4% with general musculoskeletal pain, an average of 41,8% with neck pain, and 48,8% with knee pain reported pain. At four-year follow-up 63,5% with general musculoskeletal pain, 33,5% with neck pain, and 26% with low back pain reported pain. At nine-year follow-up 59% with general musculoskeletal pain reported pain. A complete report of all the identified prognostic factors is listed in Supplementary Table 1. Figure 1 depicts the majority of these prognostic factors, stratified by pain type, sex, study population size, and follow-up (please see Supplemental Table 1 for explanatory notes).

Very few prognostic factors were reported on back pain, growing pain, lower limb pain, and widespread musculoskeletal pain (Supplementary Table 1); consequently, they were excluded from Figure 1. Table 3

condenses the results from Supplementary Table 1 and highlights four prognostic factors on four different musculoskeletal pain types. Below each factor are suggestive questions to provide the general practitioner with insight into the patient's prognosis. Table 3 and Figure 1 can be printed and used by a general practitioner at time of initial consultation with a 0-19-year-old patient with musculoskeletal pain.
Please see the Supplementary file – video for an animation showing how our findings can be used in a clinical setting.

Table 3 What to ask in clinical practice? *4* prognostic factors belonging to *4* frequent musculoskeletal pain types in general practice: General musculoskeletal-, Low back-, Neck-, and Knee Pain.

The questions are proposals towards assessment of prognosis on musculoskeletal pain.

	General musculoskeletal pain	Low back pain	Neck pain	Knee pain
Prognostic factors	-Female sex and female smokers -Day tiredness/fatigue -Physical activity vs. none -Depressive symptoms	-Higher lumbar mobility(a) -Longer pain duration -Peer problems -Smoking	-Female sex -Depressive symptoms -Multisite pain vs. localized -Day tiredness	-Increasing age -Daily pain -Sport > 2t/week -Low quality of life
Questions	-Do you smoke?(F) -Do you feel tired during the day? -Do you do sport? -Are you feeling mentally well?	-Clinical examination -How long have you had pain? -Do you have friends/do you experience bullying? -Do you smoke?	-Are you feeling mentally well? -Do you have pain in more than one musculoskeletal region? -Do you feel tired during the day?	-Do you experience daily pain -Do you do practice sport frequently? -How are things at school and at home?(b)

a = to be evaluated by clinical examination
b = this question is a suggestion for use in evaluation of quality of life
F Female patients

Prognostic factors associated with pain at follow-up
A total of 111 prognostic factors were associated with musculoskeletal pain at follow-up, of which most were on general musculoskeletal pain and low back pain (Table 3). Supplementary table 1 includes these results and further detailed depiction of prognostic factors.

Female sex was the most frequently identified prognostic factor associated with musculoskeletal pain at follow-up. Eleven studies identified psychological factors (e.g. depression, anxiety, and low self-esteem) to be associated with pain at follow-up in seven out of nine musculoskeletal pain types (9, 17, 19, 21, 22, 25, 26, 30, 35, 36, 40).
Longer pain duration was associated with pain at follow-up across four musculoskeletal pain types: musculoskeletal, low back, knee, and back pain (21, 23, 25, 36).
Five studies identified sleep-related problems associated with outcome (22, 26, 30, 35, 40).
Other indicators for musculoskeletal pain at follow-up were increasing age (9, 22, 27, 30), smoking 32, 35), parental pain (17, 23, 41), and multisite pain (22, 23, 40).
Figure 1 summarises all identified prognostic factors for musculoskeletal pain at follow-up, stratified by pain type, study population size, sex, and follow-up.

Non-significant prognostic factors
We identified a total of 134 patient characteristics across nine musculoskeletal pain types and different follow-up time points with a non-significant association with musculoskeletal pain at follow-up (Supplementary Table 1).

Increasing age (11, 21, 23, 28, 29, 31, 36, 41) was the most frequently identified baseline factor with a non-significant association to musculoskeletal pain at follow-up. Multiple studies reported non-significant evidence on higher body mass index (23, 26, 28) and hypermobility (11, 30, 40).

DISCUSSION

Principal findings

Female sex was consistently associated with an increased risk (OR and RR between 1.24 and 3.66) of pain at follow-up across six different musculoskeletal pain types. Depressive symptoms (9, 17, 19, 22, 24, 26, 30, 35, 36, 40), factors related to sleep/daytime tiredness (22, 26, 30, 35, 40), and parental pain condition (17, 23, 41) were all associated with a higher risk of pain at follow-up. Collectively, the identified studies included prognostic factors across all aspects of the biopsychosocial model, despite a main focus on biological factors. Increasing age was identified as both a significant and a non-significant prognostic factor in the included studies. This conflicting finding reflects the uncertainty surrounding the importance of age as a prognostic factor. A complete overview of strength of associations can be found in Supplementary Table 1.

Strengths and limitations in comparison with existing literature

The latest systematic review on prognostic factors for children and adolescents with musculoskeletal pain ended their search in July 2015 which makes for a timely update (12). In addition to adding newer studies, our review differs from the previous with search in more databases, no restriction on publication language, and no restriction on pain duration (41). Furthermore, this review is highly updated with a search up to February 2019 and the protocol for this review was developed using the PRISMA-P 2015 statement (Appendix 3). Despite methodology differences, we did not identify additional studies from inception to 2015, but identified three new studies from January 2016 to 2017. These studies added important knowledge of female sex, pain frequency, and the prognosis of knee pain and general musculoskeletal pain. Thereby, supporting the previous research. Despite the commonality of children and adolescents with musculoskeletal pain in general practice (6), we did not identify a single study with a population of children or adolescents recruited from general practice.

A previous review on prognostic factors for adults with musculoskeletal pain in primary care was published in 2017 (42) with findings similar to ours i.e., female gender, older age, depression/anxiety, and long pain duration was found associated with an increased risk of musculoskeletal pain at follow-up. This suggest that some of the prognostic factors function well across the age range and their use is not isolated to specific age groups.

Explanation of findings and implications for clinical practice

Our findings suggest that females are at higher risk of persistent pain. Previous research highlights potential sex differences in pain responses by assessing pain intensity and threshold and conclude that females display greater sensitivity to multiple pain modalities compared with males (43). Importantly, pain-coping strategies have been found to differ between the sexes (44, 45). Females make use of social support, cognitive reinterpretation, and positive self-statements, while males use behavioural distraction and problem-focused tactics to manage pain. This could partly explain the sex-difference in prognosis and may open new opportunities for targeted treatment to improve long-term outcomes of young females with musculoskeletal pain.

The current results point towards both modifiable (psychological factors, smoking, and peer problems) and non-modifiable (sex, age, and pain duration) factors associated with prognosis. Despite time constraints in general practice, most of these factors can be extracted from electronic stored patient data, psychometric tests, and examination in a clinical general practice setting.

By asking your patient a few questions at the first consultation of musculoskeletal pain, the general practitioner may improve their understanding of their patients` risk of pain in the future. In the case of a present, baseline factor with a poor prognosis e.g. smoking among low back pain patients, the general practitioner now both has a scientific reason for and the clinical tool to modulate this factor. By prescribing cessation of smoking, thus, making an effort to improve the outcome for this patient.

Treatment of musculoskeletal pain requires the general practitioner to apply a multifactorial rather than a single-factor approach, hence, including the entire person and their life-circumstances when treating patients

with pain (16, 46, 47). Clinicians must be aware of the multifactorial aetiology and consider biological-, psychological-, and social factors of musculoskeletal pain when addressing patient's coping behaviour and cognitive appraisal (48).

Implications for future research

Most of our included studies investigated biological prognostic factors (54 factors). Fewer investigated social (35 factors) and even fewer psychological prognostic factors (22 factors). Future research should include the entire patient, in terms of biological, psychological, and social-related components and aim to study these prognostic factors in a general practice setting. There is a dearth of knowledge of how psycho-social factors are associated with prognosis and how general practitioners can harness this information to tailor treatment and information to their patients. Despite the potential importance of pain, "who" the patient is should not be discounted. Geographical location of home, parental -pain, -profession and -income, and social identity in terms of cultural differences, religious beliefs, and relations could be important because we know from the biopsychosocial model that social background is important in relation to pain coping.

Only one study did follow-up after 4, 6.5, 9, and 11 years, respectively, which highlights the lack of long-term cohort studies on prognosis and impact of musculoskeletal pain in youth.

Almost one in every two children and adolescents still reported pain even years later (10, 11, 49). This highlights the importance of prognosis of pain in children and adolescents. Health care practitioners should be cognisant not to assume that musculoskeletal pain during childhood or adolescence is transient or self-limiting.

Supplementary information

Additional information accompanies this paper in the form of Figure 1: Prognostic factors for persistent musculoskeletal pain, according to pain type, population size, sex, follow-up, and the biopsychosocial model, Figure 2: Persistent musculoskeletal pain, stratified by pain type and follow-up: The included studies investigated pain at follow-up time points ranging from 3 months to 11 years. General musculoskeletal pain persisted in above 50% of participants with general musculoskeletal pain after 1, 2, 3, 4, and 9 years follow-up, Figure 3: PRISMA Flow chart presenting the flow of citations reviewed in the course of the systematic review: 48,538 articles were identified through search in eight databases, resulting in 223 articles for full-text eligibility screen and a final number of 26 studies for inclusion yielding 111 prognostic factors on musculoskeletal pain, Appendix 1: Search string, Appendix 2: Completed PRISMA checklist, Appendix 3: Protocol, and Supplementary Table 1: Estimates on prognostic factors specified according to musculoskeletal pain type, baseline age, and follow-up in the included studies, and an animation showing how our findings can be used in a clinical setting, see the Supplementary file: https://youtu.be/raltzsgkTHc

Author contributions

NP conducted the systematic literature search. NP and AR independently carried out the screening, study inclusion, and study bias assessment. NP and MSR led writing of both the protocol and manuscript and all authors NP, AR, MSR, MBJ, and JLO contributed with important reflections and revisions to both.

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Ethical approval

Not applicable.

Competing interests

The authors have declared no competing interests.

Data sharing statement

All data and results presented within this systematic review can be obtained, on reasonable request, by contacting the corresponding author.

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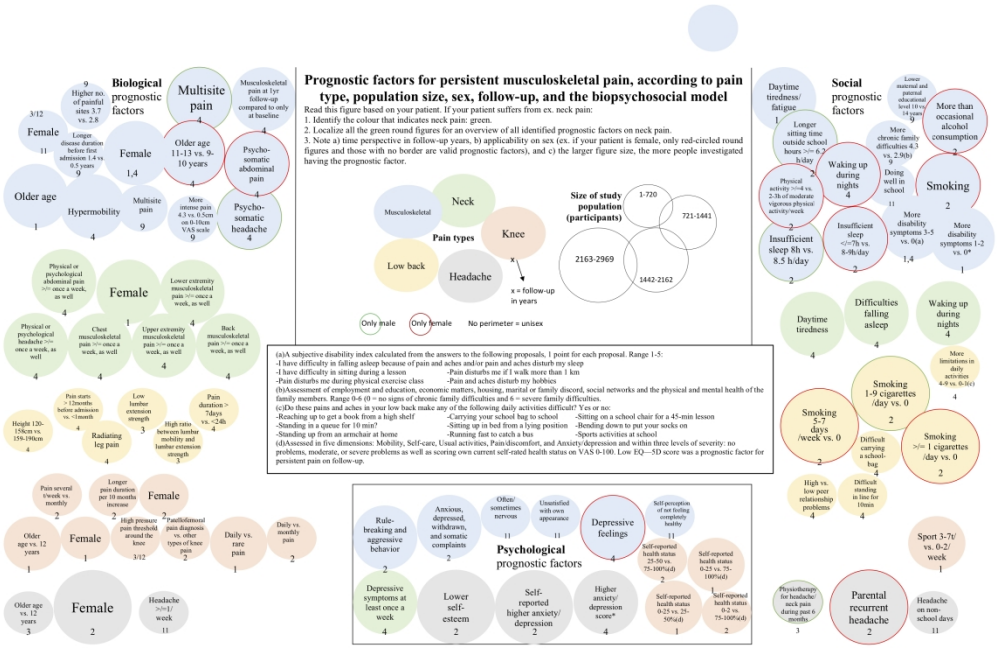

Caption and legend embedded in figure

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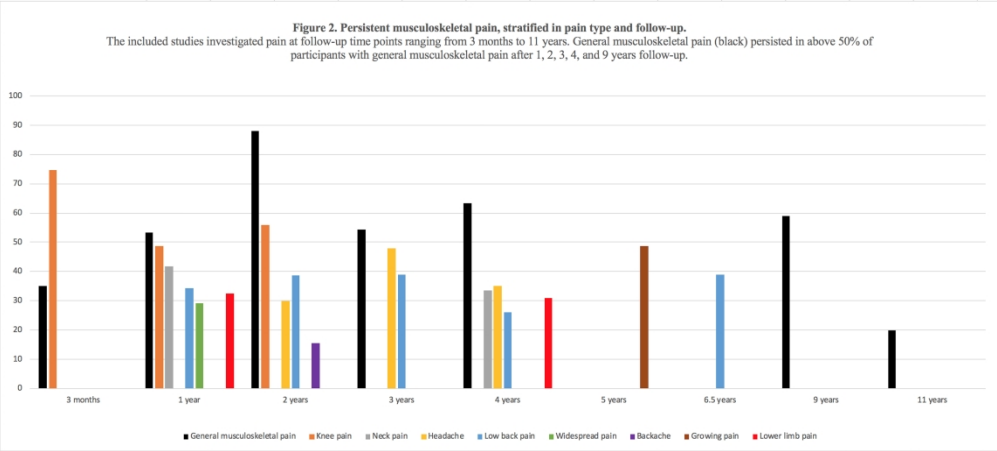
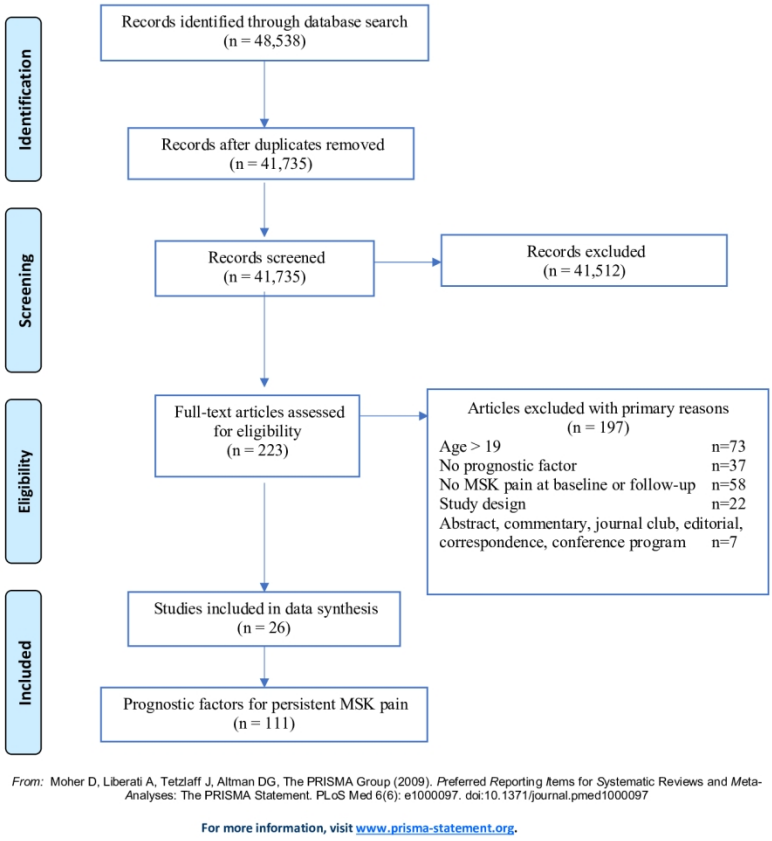


Caption : Persistent musculoskeletal pain, stratified in pain type and follow-up. The included studies investigated pain at follow-up time points ranging from 3 months to 11 years. General musculoskeletal pain (black) persisted in above 50% of participants after 1, 2, 3, 4, and 9 years follow-up.

469x212mm (300 x 300 DPI)

Figure 3 PRISMA Flow Chart presenting the flow of citations reviewed in the course of the systematic review
48,538 articles were identified through search in eight databases, resulting in 223 articles for full-text eligibility screen and a final number of 26 studies for inclusion yielding 111 prognostic factors on musculoskeletal pain.



PRISMA Flow Chart presenting the flow of citations reviewed in the course of the systematic review. 48,538 articles were identified through search in eight databases, resulting in 223 articles for full-text eligibility screen and a final number of 26 studies for inclusion yielding 111 prognostic factors on musculoskeletal pain.

215x279mm (200 x 200 DPI)

Appendix 1

Search history

Medline Ovid May 30th 2017

1	back pain/ or headache/ or exp musculoskeletal pain/ or Abdominal Pain/ or Back Pain/ or Low Back Pain/ or exp Arthralgia/ or Chest Pain/ or Facial Pain/ or Flank Pain/ or Metatarsalgia/ or Neck Pain/	110,274
2	Acute Pain/ or Chronic Pain/ or Breakthrough Pain/ or Pain, Intractable/ or Pain, Referred/	16,079
3	(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann).mp.	1,960,816
4	2 and 3	4,733
5	(backache or headache).mp.	78,052
6	((pain or ache) adj3 (musculoskeletal or back or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann)).mp.	103,970
7	1 or 4 or 5 or 6	217,985
8	limit 7 to "all child (0 to 18 years)"	41,139
9	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager).mp.	3,721,647
10	7 and 9	54,465
11	8 or 10	55,016
12	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*).mp.	4,208,880
13	11 and 12	20,363
14	(systematic reviews or meta analysis).pt.	80,495
15	case report/ or (case reports or letter or historical article or comment or editorial).pt.	3,595,207
16	limit 13 to (systematic reviews or meta analysis)	466
17	14 or 15	3,674,563
18	13 not (16 or 17)	17,183

EMBASE Ovid May 31st 2017

1	exp *musculoskeletal pain/	40,261
2	exp *"headache and facial pain"/	73,629
3	exp *abdominal pain/	10,492
4	*arthralgia/	4,782
5	*thorax pain/	9,691
6	*flank pain/	245
7	*metatarsalgia/	522
8	1 or 2 or 3 or 4 or 5 or 6 or 7	137,602
9	*chronic pain/	20,500
10	*breakthrough pain/	346
11	*intractable pain/	2,166
12	*referred pain/	233
13	or/9-12	23,135
14	(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann).mp.	2,678,325
15	13 and 14	8,147
16	(backache or headache).mp.	261,495
17	((pain or ache) adj3 (musculoskeletal or back or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann)).mp.	171,769
18	8 or 15 or 16 or 17	450,426
19	limit 18 to (infant <to one year> or child <unspecified age> or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	54,948
20	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager).mp.	3,594,291
21	18 and 20	79,053
22	19 or 21	79,102

23	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*).mp.	5,319,110
24	22 and 23	28,128
25	limit 24 to ("systematic review" or meta analysis)	497
26	case report/ or (letter or editorial or conference*).pt.	6,706,285
27	25 or 26	6,706,709
28	24 not 27	17,726

CINAHL Ebsco May 31st 2017

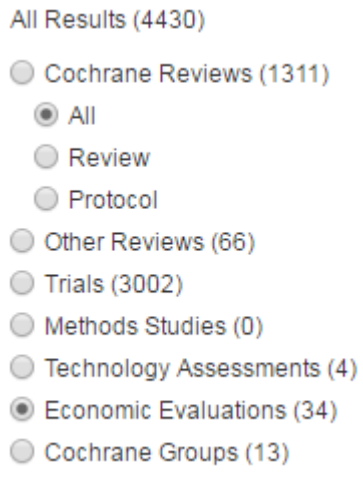
I	Search Terms	Search Options	Results
S18	S16 not S17	Search modes - Boolean/Phrase	3,716
S17	PT (Systematic Review or Meta Analysis)	Search modes - Boolean/Phrase	41,837
S16	S14 AND S15	Search modes - Boolean/Phrase	3,802
S15	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*)	Search modes - Boolean/Phrase	530,171
S14	S11 OR S13	Search modes - Boolean/Phrase	11,516
S13	S10 AND S12	Search modes - Boolean/Phrase	11,425
S12	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager)	Search modes - Boolean/Phrase	590,118
S11	S1 OR S7 OR S8 OR S9	Limiters - Age Groups: Infant, Newborn: birth-1 month, Infant: 1-23 months, Child, Preschool: 2-5 years, Child: 6-12 years, Adolescent: 13-18 years Search modes - Boolean/Phrase	8,712
S10	S1 OR S7 OR S8 OR S9	Search modes - Boolean/Phrase	64,982
S9	((pain or ache) N3 (musculoskeletal or back or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann))	Search modes - Boolean/Phrase	37,883
S8	backache or headache	Search modes - Boolean/Phrase	16,417
S7	S5 AND S6	Search modes - Boolean/Phrase	4,707

S6	(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann)	Search modes - Boolean/Phrase	312,634
S5	S2 OR S3 OR S4	Search modes - Boolean/Phrase	12,235
S4	(MH "Referred Pain")	Search modes - Boolean/Phrase	284
S3	(MH "Breakthrough Pain")	Search modes - Boolean/Phrase	58
S2	(MH "Chronic Pain")	Search modes - Boolean/Phrase	11,921
S1	(MH "Back Pain") OR (MH "Low Back Pain") OR (MH "Facial Pain") OR (MH "Headache") OR (MH "Knee Pain+") OR (MH "Metatarsalgia") OR (MH "Muscle Pain") OR (MH "Neck Pain") OR (MH "Arthralgia") OR (MH "Shoulder Pain") OR (MH "Chest Pain") OR (MH "Elbow Pain") OR (MH "Heel Pain") OR (MH "Abdominal Pain")	Search modes - Boolean/Phrase	40,609

Cochrane June 9th 2017

Search Name:
Date Run: 09/06/17 10:28:15.152
Description:

ID Search Hits
#1 ((pain or ache) next/3 (musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann)) 7405
#2 (backache or headache) 26356
#3 #1 or #2 32236
#4 (juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager) 243010
#5 #3 and #4 8870
#6 (predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*) 399020
#7 #5 and #6 4430



Imported: Trial, Technology, Economic

Web of Science June 9th 2017

Set	Results	Save History / Create Alert / Open Saved History	Edit Sets	Combine Sets (AND / OR) Combine	Delete Sets Select All / Delete
# 9	11,624	#8 AND #7 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 8	5,905,200	ts=(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 7	29,467	#6 AND #5 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 6	2,457,687	ts=(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 5	240,860	#4 OR #3 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 4	66,234	ts=(backache or headache) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 3	191,133	#2 AND #1 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 2	2,616,397	TS=(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 1	491,777	ts=(pain or ache) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
				AND / OR Combine	Select All / Delete

SportDiscus June 9th 2017

S7	((predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*)) AND (S5 AND S6)	Search modes - Boolean/Phrase	843
S6	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*)	Search modes - Boolean/Phrase	118,227
S5	S3 AND S4	Search modes - Boolean/Phrase	2,876
S4	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager)	Search modes - Boolean/Phrase	200,385
S3	(S1 OR S2)	Search modes - Boolean/Phrase	25,984
S2	backache or headache	Search modes - Boolean/Phrase	12,066
S1	((pain or ache) N3 (musculoskeletal or back or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann))	Search modes - Boolean/Phrase	18,440

OT-seeker June 9th 2017

((pain or ache)
AND
(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann))
AND
juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager

PsychInfo June 9th 2017

1	exp Musculoskeletal Disorders/	15,728
2	headache/ or muscle contraction headache/	7,110
3	myofascial pain/	317
4	back pain/	3,411
5	or/1-4	25,776
6	chronic pain/	11,631
7	pain/	22,243
8	6 or 7	33,184
9	(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann).mp.	220,772
10	8 and 9	9,266
11	(backache or headache).mp.	18,772
12	((pain or ache) adj3 (musculoskeletal or back or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann)).mp.	9,290
13	5 or 10 or 11 or 12	43,824
14	limit 13 to (100 childhood <birth to age 12 yrs> or 200 adolescence <age 13 to 17 yrs>)	5,603
15	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager).mp.	895,379
16	13 and 15	5,465
17	14 or 16	7,676
18	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*).mp.	723,493
19	17 and 18	2,119
20	(((systematic or method*) adj3 (review* or overview* or study or studies or search* or approach*)) or meta analy* or meta-analy* or metaanaly*).ti,ab,id.	142,307
21	limit 19 to ("0830 systematic review" or 1200 meta analysis)	36
22	21 or 20	142,310

23	19 not 22	1,971
1	exp Musculoskeletal Disorders/	15,728

Search history 01.02.2019

PubMed 31.05.2017-01.02.2019

History

Download historyClear history

Search	Add to builder	Query	Items found
#60	Add	Search ((((((((((((((((("Back Pain"[Mesh:NoExp]) OR "Musculoskeletal Pain"[Mesh]) OR "Abdominal Pain"[Mesh:NoExp]) OR "Low Back Pain"[Mesh]) OR "Arthralgia"[Mesh]) OR "Chest Pain"[Mesh]) OR "Facial Pain"[Mesh:NoExp]) OR "Flank Pain"[Mesh]) OR "Metatarsalgia"[Mesh:NoExp]) OR "Neck Pain"[Mesh])) OR (((((("Acute Pain"[Mesh]) OR "Chronic Pain"[Mesh]) OR "Breakthrough Pain"[Mesh]) OR "Pain, Intractable"[Mesh]) OR "Pain, Referred"[Mesh])) AND ((musculoskeletal[Text Word] OR back pain[Text Word] OR backache[Text Word] OR headache[Text Word] OR joint[Text Word] OR PFP[Text Word] OR tendinitis[Text Word] OR cervical[Text Word] OR jaw[Text Word] OR limb[Text Word] OR shoulder[Text Word] OR arm[Text Word] OR elbow[Text Word] OR wrist[Text Word] OR carpal[Text Word] OR hand[Text Word] OR finger[Text Word] OR collar[Text Word] OR vertebral[Text Word] OR lumbar[Text Word] OR back[Text Word] OR backache[Text Word] OR back pain[Text Word] OR headache[Text Word] OR hip[Text Word] OR knee[Text Word] OR patella*[Text Word] OR patellofemoral[Text Word] OR retropatellar[Text Word] OR leg[Text Word] OR ankle[Text Word] OR foot[Text Word] OR heel[Text Word] OR arthralgia[Text Word] OR osteochondritis[Text Word] OR osgood[Text Word] OR growing pain*[Text Word] OR scheuermann[Text Word]))))) OR ((backache[Text Word] OR headache[Text Word]))) OR (((pain[Text Word] OR ache[Text Word])) AND (musculoskeletal[Text Word] OR back[Text Word] OR joint[Text Word] OR PFP[Text Word] OR tendinitis[Text Word] OR cervical[Text Word] OR jaw[Text Word] OR limb[Text Word] OR shoulder[Text Word] OR arm[Text Word] OR elbow[Text Word] OR wrist[Text Word] OR carpal[Text Word] OR hand[Text Word] OR finger[Text Word] OR collar[Text Word] OR vertebral[Text Word] OR lumbar[Text Word] OR hip[Text Word] OR knee[Text Word] OR patella*[Text Word] OR patellofemoral[Text Word] OR retropatellar[Text Word] OR leg[Text Word] OR ankle[Text Word] OR foot[Text Word] OR heel[Text Word] OR arthralgia[Text Word] OR osteochondritis[Text Word] OR osgood[Text Word] OR growing pain*[Text Word] OR scheuermann[Text Word]))))) AND ((((juvenile[Text Word] OR adolescen*[Text Word] OR preadolescence[Text Word] OR Preadolescent[Text Word] OR preschool[Text Word] OR child[Text Word] OR children[Text Word] OR prepubertal[Text Word] OR kids[Text Word] OR paediatric[Text Word] OR pediatric[Text Word] OR youth[Text Word] OR young[Text Word] OR childhood[Text Word] OR schoolchild*[Text Word] OR teenager[Text Word]))) OR ((("Adolescent"[Mesh]) OR "Child"[Mesh]) OR "Infant"[Mesh])))) AND ((predict*[Text Word] OR long term[Text Word] OR Follow-up[Text Word] OR Prospective[Text Word] OR cohort[Text Word] OR cluster[Text Word] OR prognosis[Text Word] OR prognostic[Text Word] OR Mediator*[Text Word] OR treatment effect modifier*[Text Word] OR longitudinal*[Text Word])))) NOT (((((("Systematic Review" [Publication Type]) OR "Meta-Analysis" [Publication Type]) OR "Case Reports" [Publication Type]) OR "Letter" [Publication Type]) OR "Historical Article" [Publication Type]) OR	2514

Search	Add to builder	Query	Items found
		"Comment" [Publication Type]) OR "Editorial" [Publication Type]) Filters: Publication date from 2017/05/31 to 2019/12/31	
#59	Add	Search ((((((((((((((((("Back Pain"[Mesh:NoExp]) OR "Musculoskeletal Pain"[Mesh]) OR "Abdominal Pain"[Mesh:NoExp]) OR "Low Back Pain"[Mesh]) OR "Arthralgia"[Mesh]) OR "Chest Pain"[Mesh]) OR "Facial Pain"[Mesh:NoExp]) OR "Flank Pain"[Mesh]) OR "Metatarsalgia"[Mesh:NoExp]) OR "Neck Pain"[Mesh])) OR (((((("Acute Pain"[Mesh]) OR "Chronic Pain"[Mesh]) OR "Breakthrough Pain"[Mesh]) OR "Pain, Intractable"[Mesh]) OR "Pain, Referred"[Mesh])) AND ((musculoskeletal[Text Word] OR back pain[Text Word] OR backache[Text Word] OR headache[Text Word] OR joint[Text Word] OR PFP[Text Word] OR tendinitis[Text Word] OR cervical[Text Word] OR jaw[Text Word] OR limb[Text Word] OR shoulder[Text Word] OR arm[Text Word] OR elbow[Text Word] OR wrist[Text Word] OR carpal[Text Word] OR hand[Text Word] OR finger[Text Word] OR collar[Text Word] OR vertebral[Text Word] OR lumbar[Text Word] OR back[Text Word] OR backache[Text Word] OR back pain[Text Word] OR headache[Text Word] OR hip[Text Word] OR knee[Text Word] OR patella*[Text Word] OR patellofemoral[Text Word] OR retropatellar[Text Word] OR leg[Text Word] OR ankle[Text Word] OR foot[Text Word] OR heel[Text Word] OR arthralgia[Text Word] OR osteochondritis[Text Word] OR osgood[Text Word] OR growing pain*[Text Word] OR scheuermann[Text Word]))))) OR ((backache[Text Word] OR headache[Text Word]))) OR (((pain[Text Word] OR ache[Text Word])) AND (musculoskeletal[Text Word] OR back[Text Word] OR joint[Text Word] OR PFP[Text Word] OR tendinitis[Text Word] OR cervical[Text Word] OR jaw[Text Word] OR limb[Text Word] OR shoulder[Text Word] OR arm[Text Word] OR elbow[Text Word] OR wrist[Text Word] OR carpal[Text Word] OR hand[Text Word] OR finger[Text Word] OR collar[Text Word] OR vertebral[Text Word] OR lumbar[Text Word] OR hip[Text Word] OR knee[Text Word] OR patella*[Text Word] OR patellofemoral[Text Word] OR retropatellar[Text Word] OR leg[Text Word] OR ankle[Text Word] OR foot[Text Word] OR heel[Text Word] OR arthralgia[Text Word] OR osteochondritis[Text Word] OR osgood[Text Word] OR growing pain*[Text Word] OR scheuermann[Text Word]))))) AND ((((juvenile[Text Word] OR adolescen*[Text Word] OR preadolescence[Text Word] OR Preadolescent[Text Word] OR preschool[Text Word] OR child[Text Word] OR children[Text Word] OR prepubertal[Text Word] OR kids[Text Word] OR paediatric[Text Word] OR pediatric[Text Word] OR youth[Text Word] OR young[Text Word] OR childhood[Text Word] OR schoolchild*[Text Word] OR teenager[Text Word])))) OR ((("Adolescent"[Mesh]) OR "Child"[Mesh]) OR "Infant"[Mesh])))) AND ((predict*[Text Word] OR long term[Text Word] OR Follow-up[Text Word] OR Prospective[Text Word] OR cohort[Text Word] OR cluster[Text Word] OR prognosis[Text Word] OR prognostic[Text Word] OR Mediator*[Text Word] OR treatment effect modifier*[Text Word] OR longitudinal*[Text Word]))))) NOT (((((("Systematic Review" [Publication Type]) OR "Meta-Analysis" [Publication Type]) OR "Case Reports" [Publication Type]) OR "Letter" [Publication Type]) OR "Historical Article" [Publication Type]) OR "Comment" [Publication Type]) OR "Editorial" [Publication Type])	29128
#58	Add	Search ((((((("Systematic Review" [Publication Type]) OR "Meta-Analysis" [Publication Type]) OR "Case Reports" [Publication Type]) OR "Letter" [Publication Type]) OR "Historical Article" [Publication Type]) OR "Comment" [Publication Type]) OR "Editorial" [Publication Type]	3926007
#43	Add	Search ((((((((((((((((("Back Pain"[Mesh:NoExp]) OR "Musculoskeletal Pain"[Mesh]) OR "Abdominal Pain"[Mesh:NoExp]) OR "Low Back Pain"[Mesh]) OR "Arthralgia"[Mesh]) OR "Chest Pain"[Mesh]) OR "Facial Pain"[Mesh:NoExp]) OR "Flank Pain"[Mesh]) OR "Metatarsalgia"[Mesh:NoExp]) OR "Neck Pain"[Mesh])) OR (((((("Acute Pain"[Mesh]) OR "Chronic Pain"[Mesh]) OR "Breakthrough Pain"[Mesh]) OR "Pain, Intractable"[Mesh]) OR "Pain, Referred"[Mesh])) AND ((musculoskeletal[Text Word] OR back pain[Text Word] OR backache[Text Word] OR headache[Text Word] OR joint[Text	33553

Search	Add to builder	Query	Items found
		Word] OR PFP[Text Word] OR tendinitis[Text Word] OR cervical[Text Word] OR jaw[Text Word] OR limb[Text Word] OR shoulder[Text Word] OR arm[Text Word] OR elbow[Text Word] OR wrist[Text Word] OR carpal[Text Word] OR hand[Text Word] OR finger[Text Word] OR collar[Text Word] OR vertebral[Text Word] OR lumbar[Text Word] OR back[Text Word] OR backache[Text Word] OR back pain[Text Word] OR headache[Text Word] OR hip[Text Word] OR knee[Text Word] OR patella*[Text Word] OR patellofemoral[Text Word] OR retropatellar[Text Word] OR leg[Text Word] OR ankle[Text Word] OR foot[Text Word] OR heel[Text Word] OR arthralgia[Text Word] OR osteochondritis[Text Word] OR osgood[Text Word] OR growing pain*[Text Word] OR scheuermann[Text Word]))))) OR ((backache[Text Word] OR headache[Text Word]))) OR (((pain[Text Word] OR ache[Text Word])) AND (musculoskeletal[Text Word] OR back[Text Word] OR joint[Text Word] OR PFP[Text Word] OR tendinitis[Text Word] OR cervical[Text Word] OR jaw[Text Word] OR limb[Text Word] OR shoulder[Text Word] OR arm[Text Word] OR elbow[Text Word] OR wrist[Text Word] OR carpal[Text Word] OR hand[Text Word] OR finger[Text Word] OR collar[Text Word] OR vertebral[Text Word] OR lumbar[Text Word] OR hip[Text Word] OR knee[Text Word] OR patella*[Text Word] OR patellofemoral[Text Word] OR retropatellar[Text Word] OR leg[Text Word] OR ankle[Text Word] OR foot[Text Word] OR heel[Text Word] OR arthralgia[Text Word] OR osteochondritis[Text Word] OR osgood[Text Word] OR growing pain*[Text Word] OR scheuermann[Text Word]))))) AND ((((juvenile[Text Word] OR adolescen*[Text Word] OR preadolescence[Text Word] OR Preadolescent[Text Word] OR preschool[Text Word] OR child[Text Word] OR children[Text Word] OR prepubertal[Text Word] OR kids[Text Word] OR paediatric[Text Word] OR pediatric[Text Word] OR youth[Text Word] OR young[Text Word] OR childhood[Text Word] OR schoolchild*[Text Word] OR teenager[Text Word]))) OR ((("Adolescent"[Mesh]) OR "Child"[Mesh]) OR "Infant"[Mesh]))))) AND ((predict*[Text Word] OR long term[Text Word] OR Follow-up[Text Word] OR Prospective[Text Word] OR cohort[Text Word] OR cluster[Text Word] OR prognosis[Text Word] OR prognostic[Text Word] OR Mediator*[Text Word] OR treatment effect modifier*[Text Word] OR longitudinal*[Text Word]))	
#42	Add	Search (predict*[Text Word] OR long term[Text Word] OR Follow-up[Text Word] OR Prospective[Text Word] OR cohort[Text Word] OR cluster[Text Word] OR prognosis[Text Word] OR prognostic[Text Word] OR Mediator*[Text Word] OR treatment effect modifier*[Text Word] OR longitudinal*[Text Word])	4564026
#41	Add	Search ((((((((((((((("Back Pain"[Mesh:NoExp]) OR "Musculoskeletal Pain"[Mesh]) OR "Abdominal Pain"[Mesh:NoExp]) OR "Low Back Pain"[Mesh]) OR "Arthralgia"[Mesh]) OR "Chest Pain"[Mesh]) OR "Facial Pain"[Mesh:NoExp]) OR "Flank Pain"[Mesh]) OR "Metatarsalgia"[Mesh:NoExp]) OR "Neck Pain"[Mesh])) OR (((((((("Acute Pain"[Mesh]) OR "Chronic Pain"[Mesh]) OR "Breakthrough Pain"[Mesh]) OR "Pain, Intractable"[Mesh]) OR "Pain, Referred"[Mesh])) AND ((musculoskeletal[Text Word] OR back pain[Text Word] OR backache[Text Word] OR headache[Text Word] OR joint[Text Word] OR PFP[Text Word] OR tendinitis[Text Word] OR cervical[Text Word] OR jaw[Text Word] OR limb[Text Word] OR shoulder[Text Word] OR arm[Text Word] OR elbow[Text Word] OR wrist[Text Word] OR carpal[Text Word] OR hand[Text Word] OR finger[Text Word] OR collar[Text Word] OR vertebral[Text Word] OR lumbar[Text Word] OR back[Text Word] OR backache[Text Word] OR back pain[Text Word] OR headache[Text Word] OR hip[Text Word] OR knee[Text Word] OR patella*[Text Word] OR patellofemoral[Text Word] OR retropatellar[Text Word] OR leg[Text Word] OR ankle[Text Word] OR foot[Text Word] OR heel[Text Word] OR arthralgia[Text Word] OR osteochondritis[Text Word] OR osgood[Text Word] OR growing pain*[Text Word] OR scheuermann[Text Word]))))) OR ((backache[Text Word] OR headache[Text Word]))) OR (((pain[Text Word] OR ache[Text Word])) AND (musculoskeletal[Text Word] OR back[Text Word] OR joint[Text Word] OR PFP[Text Word] OR tendinitis[Text Word] OR cervical[Text Word] OR jaw[Text Word] OR limb[Text Word] OR shoulder[Text	83258

Search	Add to builder	Query	Items found
		Word] OR arm[Text Word] OR elbow[Text Word] OR wrist[Text Word] OR carpal[Text Word] OR hand[Text Word] OR finger[Text Word] OR collar[Text Word] OR vertebral[Text Word] OR lumbar[Text Word] OR hip[Text Word] OR knee[Text Word] OR patella*[Text Word] OR patellofemoral[Text Word] OR retropatellar[Text Word] OR leg[Text Word] OR ankle[Text Word] OR foot[Text Word] OR heel[Text Word] OR arthralgia[Text Word] OR osteochondritis[Text Word] OR osgood[Text Word] OR growing pain*[Text Word] OR scheuermann[Text Word]))))) AND ((((juvenile[Text Word] OR adolescen*[Text Word] OR preadolescence[Text Word] OR Preadolescent[Text Word] OR preschool[Text Word] OR child[Text Word] OR children[Text Word] OR prepubertal[Text Word] OR kids[Text Word] OR paediatric[Text Word] OR pediatric[Text Word] OR youth[Text Word] OR young[Text Word] OR childhood[Text Word] OR schoolchild*[Text Word] OR teenager[Text Word])))) OR ((("Adolescent"[Mesh]) OR "Child"[Mesh]) OR "Infant"[Mesh]))	
#40	Add	Search (((juvenile[Text Word] OR adolescen*[Text Word] OR preadolescence[Text Word] OR Preadolescent[Text Word] OR preschool[Text Word] OR child[Text Word] OR children[Text Word] OR prepubertal[Text Word] OR kids[Text Word] OR paediatric[Text Word] OR pediatric[Text Word] OR youth[Text Word] OR young[Text Word] OR childhood[Text Word] OR schoolchild*[Text Word] OR teenager[Text Word])))) OR ((("Adolescent"[Mesh]) OR "Child"[Mesh]) OR "Infant"[Mesh])	4321275
#39	Add	Search (juvenile[Text Word] OR adolescen*[Text Word] OR preadolescence[Text Word] OR Preadolescent[Text Word] OR preschool[Text Word] OR child[Text Word] OR children[Text Word] OR prepubertal[Text Word] OR kids[Text Word] OR paediatric[Text Word] OR pediatric[Text Word] OR youth[Text Word] OR young[Text Word] OR childhood[Text Word] OR schoolchild*[Text Word] OR teenager[Text Word])	3920419
#38	Add	Search (("Adolescent"[Mesh]) OR "Child"[Mesh]) OR "Infant"[Mesh]	3366738
#31	Add	Search ((((((((((("Back Pain"[Mesh:NoExp]) OR "Musculoskeletal Pain"[Mesh]) OR "Abdominal Pain"[Mesh:NoExp]) OR "Low Back Pain"[Mesh]) OR "Arthralgia"[Mesh]) OR "Chest Pain"[Mesh]) OR "Facial Pain"[Mesh:NoExp]) OR "Flank Pain"[Mesh]) OR "Metatarsalgia"[Mesh:NoExp]) OR "Neck Pain"[Mesh])) OR (((((((("Acute Pain"[Mesh]) OR "Chronic Pain"[Mesh]) OR "Breakthrough Pain"[Mesh]) OR "Pain, Intractable"[Mesh]) OR "Pain, Referred"[Mesh])) AND ((musculoskeletal[Text Word] OR back pain[Text Word] OR backache[Text Word] OR headache[Text Word] OR joint[Text Word] OR PFP[Text Word] OR tendinitis[Text Word] OR cervical[Text Word] OR jaw[Text Word] OR limb[Text Word] OR shoulder[Text Word] OR arm[Text Word] OR elbow[Text Word] OR wrist[Text Word] OR carpal[Text Word] OR hand[Text Word] OR finger[Text Word] OR collar[Text Word] OR vertebral[Text Word] OR lumbar[Text Word] OR back[Text Word] OR backache[Text Word] OR back pain[Text Word] OR headache[Text Word] OR hip[Text Word] OR knee[Text Word] OR patella*[Text Word] OR patellofemoral[Text Word] OR retropatellar[Text Word] OR leg[Text Word] OR ankle[Text Word] OR foot[Text Word] OR heel[Text Word] OR arthralgia[Text Word] OR osteochondritis[Text Word] OR osgood[Text Word] OR growing pain*[Text Word] OR scheuermann[Text Word])))) OR ((backache[Text Word] OR headache[Text Word]))) OR (((pain[Text Word] OR ache[Text Word])) AND (musculoskeletal[Text Word] OR back[Text Word] OR joint[Text Word] OR PFP[Text Word] OR tendinitis[Text Word] OR cervical[Text Word] OR jaw[Text Word] OR limb[Text Word] OR shoulder[Text Word] OR arm[Text Word] OR elbow[Text Word] OR wrist[Text Word] OR carpal[Text Word] OR hand[Text Word] OR finger[Text Word] OR collar[Text Word] OR vertebral[Text Word] OR lumbar[Text Word] OR hip[Text Word] OR knee[Text Word] OR patella*[Text Word] OR patellofemoral[Text Word] OR retropatellar[Text Word] OR leg[Text Word] OR ankle[Text Word] OR foot[Text Word] OR heel[Text Word] OR arthralgia[Text Word] OR osteochondritis[Text Word] OR osgood[Text Word] OR growing pain*[Text Word] OR scheuermann[Text Word]))	380268

Search	Add to builder	Query	Items found
#30	Add	Search ((pain[Text Word] OR ache[Text Word])) AND (musculoskeletal[Text Word] OR back[Text Word] OR joint[Text Word] OR PFP[Text Word] OR tendinitis[Text Word] OR cervical[Text Word] OR jaw[Text Word] OR limb[Text Word] OR shoulder[Text Word] OR arm[Text Word] OR elbow[Text Word] OR wrist[Text Word] OR carpal[Text Word] OR hand[Text Word] OR finger[Text Word] OR collar[Text Word] OR vertebral[Text Word] OR lumbar[Text Word] OR hip[Text Word] OR knee[Text Word] OR patella*[Text Word] OR patellofemoral[Text Word] OR retropatellar[Text Word] OR leg[Text Word] OR ankle[Text Word] OR foot[Text Word] OR heel[Text Word] OR arthralgia[Text Word] OR osteochondritis[Text Word] OR osgood[Text Word] OR growing pain*[Text Word] OR scheuermann[Text Word])	231899
#29	Add	Search (backache[Text Word] OR headache[Text Word])	81147
#28	Add	Search ((((((("Acute Pain"[Mesh]) OR "Chronic Pain"[Mesh]) OR "Breakthrough Pain"[Mesh]) OR "Pain, Intractable"[Mesh]) OR "Pain, Referred"[Mesh])) AND ((musculoskeletal[Text Word] OR back pain[Text Word] OR backache[Text Word] OR headache[Text Word] OR joint[Text Word] OR PFP[Text Word] OR tendinitis[Text Word] OR cervical[Text Word] OR jaw[Text Word] OR limb[Text Word] OR shoulder[Text Word] OR arm[Text Word] OR elbow[Text Word] OR wrist[Text Word] OR carpal[Text Word] OR hand[Text Word] OR finger[Text Word] OR collar[Text Word] OR vertebral[Text Word] OR lumbar[Text Word] OR back[Text Word] OR backache[Text Word] OR back pain[Text Word] OR headache[Text Word] OR hip[Text Word] OR knee[Text Word] OR patella*[Text Word] OR patellofemoral[Text Word] OR retropatellar[Text Word] OR leg[Text Word] OR ankle[Text Word] OR foot[Text Word] OR heel[Text Word] OR arthralgia[Text Word] OR osteochondritis[Text Word] OR osgood[Text Word] OR growing pain*[Text Word] OR scheuermann[Text Word]))	5826
#27	Add	Search (musculoskeletal[Text Word] OR back pain[Text Word] OR backache[Text Word] OR headache[Text Word] OR joint[Text Word] OR PFP[Text Word] OR tendinitis[Text Word] OR cervical[Text Word] OR jaw[Text Word] OR limb[Text Word] OR shoulder[Text Word] OR arm[Text Word] OR elbow[Text Word] OR wrist[Text Word] OR carpal[Text Word] OR hand[Text Word] OR finger[Text Word] OR collar[Text Word] OR vertebral[Text Word] OR lumbar[Text Word] OR back[Text Word] OR backache[Text Word] OR back pain[Text Word] OR headache[Text Word] OR hip[Text Word] OR knee[Text Word] OR patella*[Text Word] OR patellofemoral[Text Word] OR retropatellar[Text Word] OR leg[Text Word] OR ankle[Text Word] OR foot[Text Word] OR heel[Text Word] OR arthralgia[Text Word] OR osteochondritis[Text Word] OR osgood[Text Word] OR growing pain*[Text Word] OR scheuermann[Text Word])	2077798
#26	Add	Search ((((("Acute Pain"[Mesh]) OR "Chronic Pain"[Mesh]) OR "Breakthrough Pain"[Mesh]) OR "Pain, Intractable"[Mesh]) OR "Pain, Referred"[Mesh]	19040
#19	Add	Search (((((((("Back Pain"[Mesh:NoExp]) OR "Musculoskeletal Pain"[Mesh]) OR "Abdominal Pain"[Mesh:NoExp]) OR "Low Back Pain"[Mesh]) OR "Arthralgia"[Mesh]) OR "Chest Pain"[Mesh]) OR "Facial Pain"[Mesh:NoExp]) OR "Flank Pain"[Mesh]) OR "Metatarsalgia"[Mesh:NoExp]) OR "Neck Pain"[Mesh]	133062

Embase.com 31.05.2017-01.02.2019

No.	Query	Results
#29	#28 AND [31-5-2017]/sd	3306
#28	#24 NOT #27	25542
#27	#25 OR #26	18603
#26	#24 AND ('case report'/de OR 'systematic review'/de OR 'meta analysis'/de)	11517
#25	#24 AND ('Conference Abstract'/it OR 'Editorial'/it OR 'Letter'/it)	9403
#24	#22 AND #23	44145
#23	predict* OR 'long term' OR 'follow-up' OR prospective OR cohort OR cluster OR prognosis OR prognostic OR mediator* OR 'treatment effect modifier*' OR longitudinal*	6151238
#22	#19 OR #21	121885
#21	#18 AND #20	82516
#20	juvenile:ti,ab,kw OR adolescen*:ti,ab,kw OR preadolescence:ti,ab,kw OR preadolescent:ti,ab,kw OR preschool:ti,ab,kw OR child:ti,ab,kw OR children:ti,ab,kw OR prepubertal:ti,ab,kw OR kids:ti,ab,kw OR paediatric:ti,ab,kw OR pediatric:ti,ab,kw OR youth:ti,ab,kw OR young:ti,ab,kw OR childhood:ti,ab,kw OR schoolchild*:ti,ab,kw OR teenager:ti,ab,kw	2498081
#19	#18 AND ([adolescent]/lim OR [child]/lim OR [infant]/lim OR [newborn]/lim OR [preschool]/lim OR [school]/lim)	90443
#18	#8 OR #15 OR #16 OR #17	710948
#17	((pain OR ache) NEAR/3 (musculoskeletal OR 'back pain' OR joint OR pfp OR tendinitis OR cervical OR jaw OR limb OR shoulder OR arm OR elbow OR wrist OR carpal OR hand OR finger OR collar OR vertebral OR lumbar OR back OR backache OR headache OR hip OR knee OR patella* OR patellofemoral OR retropatellar OR leg OR ankle OR foot OR heel OR arthralgia OR osteochondritis OR osgood OR 'growing pain*' OR scheuermann)):ti,ab,kw	150092
#16	backache:ti,ab,kw,de OR headache:ti,ab,kw,de	293040
#15	#13 AND #14	17347
#14	musculoskeletal:ti,ab,kw OR 'back pain':ti,ab,kw OR joint:ti,ab,kw OR pfp:ti,ab,kw OR tendinitis:ti,ab,kw OR cervical:ti,ab,kw OR jaw:ti,ab,kw OR limb:ti,ab,kw OR shoulder:ti,ab,kw OR arm:ti,ab,kw OR elbow:ti,ab,kw OR wrist:ti,ab,kw OR carpal:ti,ab,kw OR hand:ti,ab,kw OR finger:ti,ab,kw OR collar:ti,ab,kw OR vertebral:ti,ab,kw OR lumbar:ti,ab,kw OR back:ti,ab,kw OR backache:ti,ab,kw OR headache:ti,ab,kw OR hip:ti,ab,kw OR knee:ti,ab,kw OR patella*:ti,ab,kw OR patellofemoral:ti,ab,kw OR retropatellar:ti,ab,kw OR leg:ti,ab,kw OR ankle:ti,ab,kw OR foot:ti,ab,kw OR heel:ti,ab,kw OR arthralgia:ti,ab,kw OR osteochondritis:ti,ab,kw OR osgood:ti,ab,kw OR 'growing pain*':ti,ab,kw OR scheuermann:ti,ab,kw	2376662
#13	#9 OR #10 OR #11 OR #12	59894
#12	'referred pain'/exp	1091
#11	'intractable pain'/exp	4650
#10	'breakthrough pain'/exp	1346
#9	'chronic pain'/exp	53614
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	628050
#7	'metatarsalgia'/exp	1188
#6	'arthralgia'/exp	54706
#5	'thorax pain'/exp	79342
#4	'flank pain'/exp	6334
#3	'abdominal pain'/exp	148863
#2	'headache and facial pain'/exp	284304
#1	'musculoskeletal pain'/exp	136136

CINAHL (EBSCONet) 01.06.2017-01.02.2019

Search ID#	Search Terms	Search Options	Results
S19	s16 not s17	Limiters - Published Date: 20170601-20191231 Search modes - Boolean/Phrase	971
S18	s16 not s17	Search modes - Boolean/Phrase	7,109
S17	PT (Systematic Review or Meta Analysis)	Search modes - Boolean/Phrase	87,387
S16	S14 AND S15	Search modes - Boolean/Phrase	7,276
S15	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*)	Search modes - Boolean/Phrase	1,025,399
S14	S11 OR S13	Search modes - Boolean/Phrase	21,414
S13	S10 AND S12	Search modes - Boolean/Phrase	21,266
S12	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager)	Search modes - Boolean/Phrase	1,048,327
S11	S1 OR S7 OR S8 OR S9	Limiters - Age Groups: Infant, Newborn: birth-1 month, Infant: 1-23 months, Child, Preschool: 2-5 years, Child: 6-12 years, Adolescent: 13-18 years Search modes - Boolean/Phrase	15,463
S10	S1 OR S7 OR S8 OR S9	Search modes - Boolean/Phrase	107,547
S9	((pain or ache) N3 (musculoskeletal or back or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann))	Search modes - Boolean/Phrase	61,789
S8	backache or headache	Search modes - Boolean/Phrase	26,017
S7	S5 AND S6	Search modes - Boolean/Phrase	7,112
S6	(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann)	Search modes - Boolean/Phrase	542,363
S5	S2 OR S3 OR S4	Search modes - Boolean/Phrase	18,849
S4	(MH "Referred Pain")	Search modes - Boolean/Phrase	406

S3	(MH "Breakthrough Pain")	Search modes - Boolean/Phrase	128
S2	(MH "Chronic Pain")	Search modes - Boolean/Phrase	18,360
S1	(MH "Back Pain") OR (MH "Low Back Pain") OR (MH "Facial Pain") OR (MH "Headache") OR (MH "Knee Pain+") OR (MH "Metatarsalgia") OR (MH "Muscle Pain") OR (MH "Neck Pain") OR (MH "Arthralgia") OR (MH "Shoulder Pain") OR (MH "Chest Pain") OR (MH "Elbow Pain") OR (MH "Heel Pain") OR (MH "Abdominal Pain")	Search modes - Boolean/Phrase	66,335

Web of Science 2017-11.02.2019

Set	Results	Save History / Create Alert / Open Saved History	Edit Sets	Combine Sets (AND / OR)	Delete Sets
# 10	2,497	#8 AND #7 **Refined by: PUBLICATION YEARS:** (2019 OR 2018 OR 2017) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*		Combine	Select All / Delete
# 9	13,842	#8 AND #7 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 8	6,829,939	**TOPIC:** (predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 7	34,837	#6 AND #5 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 6	2,803,621	**TOPIC:** ((juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager)) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 5	282,070	#4 OR #3 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 4	74,839	**TOPIC:** (backache or headache) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 3	214,291	#2 AND #1 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 2	2,932,366	**TOPIC:** (musculoskeletal or back or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
# 1	573,235	**TOPIC:** (pain OR ache) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Edit		
				AND / OR Combine	Select All / Delete

PsycInfo 2017-11.02.2019

1	exp Musculoskeletal Disorders/	16869
2	headache/ or muscle contraction headache/	7319
3	myofascial pain/	329
4	back pain/	3655
5	1 or 2 or 3 or 4	27350
6	chronic pain/	12511
7	pain/	23687
8	6 or 7	35477
9	(musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or	238846

	patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann).mp.	
10	8 and 9	9902
11	(backache or headache).mp.	19554
12	((pain or ache) adj3 (musculoskeletal or back or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann)).mp.	10225
13	5 or 10 or 11 or 12	46619
14	limit 13 to (100 childhood <birth to age 12 yrs> or 200 adolescence <age 13 to 17 yrs>)	5926
15	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager).mp.	961911
16	13 and 15	5867
17	14 or 16	8172
18	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*).mp.	798327
19	17 and 18	2298
20	(((systematic or method*) adj3 (review* or overview* or study or studies or search* or approach*)) or meta analy* or meta-analy* or metaanaly*).ti,ab,id.	166163
21	limit 19 to ("0830 systematic review" or 1200 meta analysis)	45
22	20 or 21	166166
23	19 not 22	2130
24	limit 23 to yr="2017 -Current"	180

Cochrane Library juni 2017-11.02.2019

ID	Search	Hits
#1	((pain or ache) next/3 (musculoskeletal or back pain or backache or headache or joint or PFP or tendinitis or cervical or jaw or limb or shoulder or arm or elbow or wrist or carpal or hand or finger or collar or vertebral or lumbar or back or backache or back pain or headache or hip or knee or patella* or patellofemoral or retropatellar or leg or ankle or foot or heel or arthralgia or osteochondritis or osgood or growing pain* or scheuermann))	42928
#2	(backache or headache)	27829
#3	#1 OR #2	63886
#4	(juvenile or adolescen* or preadolescence or Preadolescent or preschool or child or children or prepubertal or kids or paediatric or pediatric or youth or young or childhood or schoolchild* or teenager)	270643
#5	#3 AND #4	17122
#6	(predict* or long term or Follow-up or Prospective or cohort or cluster or prognosis or prognostic or Mediator* or treatment effect modifier* or longitudinal*)	453684
#7	#5 AND #6 with Cochrane Library publication date Between Jun 2017 and Feb 2019	1186

Reporting checklist for systematic review and meta-analysis.

Based on the PRISMA guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA reporting guidelines, and cite them as:

Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement

		Reporting Item	Page Number
	#1	Identify the report as a systematic review, meta-analysis, or both.	1
Structured summary	#2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number	2
Rationale	#3	Describe the rationale for the review in the context of what is already known.	3
Objectives	#4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
Protocol and	#5	Indicate if a review protocol exists, if and where it can be	3

registration		accessed (e.g., Web address) and, if available, provide registration information including the registration number.	
Eligibility criteria	#6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rational	3
Information sources	#7	Describe all information sources in the search (e.g., databases with dates of coverage, contact with study authors to identify additional studies) and date last searched.	3
Search	#8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	3
Study selection	#9	State the process for selecting studies (i.e., for screening, for determining eligibility, for inclusion in the systematic review, and, if applicable, for inclusion in the meta-analysis).	3
Data collection process	#10	Describe the method of data extraction from reports (e.g., piloted forms, independently by two reviewers) and any processes for obtaining and confirming data from investigators.	4
Data items	#11	List and define all variables for which data were sought (e.g., PICOS, funding sources), and any assumptions and simplifications made.	4
Risk of bias in individual studies	#12	Describe methods used for assessing risk of bias in individual studies (including specification of whether this was done at the study or outcome level, or both), and how this information is to be used in any data synthesis.	4
Summary measures	#13	State the principal summary measures (e.g., risk ratio, difference in means).	4
Planned methods of analyis	#14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.	5
Risk of bias across studies	#15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5
Additional	#16	Describe methods of additional analyses (e.g., sensitivity or	5

analyses		subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
Study selection	#17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	#18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citation.	5
Risk of bias within studies	#19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	5
Results of individual studies	#20	For all outcomes considered (benefits and harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	5
Synthesis of results	#21	Present the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency.	5
Risk of bias across studies	#22	Present results of any assessment of risk of bias across studies (see Item 15).	5
Additional analysis	#23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	5
Summary of Evidence	#24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers	7
Limitations	#25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	7
Conclusions	#26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	7
Funding	#27	Describe sources of funding or other support (e.g., supply of data) for the systematic review; role of funders for the systematic review.	8

PROSPERO
International prospective register of systematic reviews

NHS National Institute for Health Research

UNIVERSITY of York
Centre for Reviews and Dissemination

Systematic review

Please complete all mandatory fields below (marked with an asterisk *) and as many of the non-mandatory fields as you can then click *Submit* to submit your registration. You don't need to complete everything in one go, this record will appear in your *My PROSPERO* section of the web site and you can continue to edit it until you are ready to submit. Click *Show help* below or click on the icon
to see guidance on completing each section.
This record cannot be edited because it has been rejected

1. * Review title.

Give the working title of the review, for example the one used for obtaining funding. Ideally the title should state succinctly the interventions or exposures being reviewed and the associated health or social problems. Where appropriate, the title should use the PI(E)COS structure to contain information on the Participants, Intervention (or Exposure) and Comparison groups, the Outcomes to be measured and Study designs to be included.

Prognostic factors and treatment effect modifiers for children and adolescents with musculoskeletal pain: a protocol for a systematic literature review

2. Original language title.

For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3. * Anticipated or actual start date.

Give the date when the systematic review commenced, or is expected to commence.

21/06/2016

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

01/12/2017

5. * Stage of review at time of this submission.

Indicate the stage of progress of the review by ticking the relevant Started and Completed boxes. Additional information may be added in the free text box provided.
Please note: Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. Should evidence of incorrect status and/or completion date being supplied at the time of submission come to light, the content of the PROSPERO record will be removed leaving only the title and named contact details and a statement that inaccuracies in the stage of the review date had been identified.
This field should be updated when any amendments are made to a published record and on completion and publication of the review.

The review has not yet started: No

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International prospective register of systematic reviews

National Institute for Health Research

Review stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	Yes
Data analysis	Yes	Yes

Provide any other relevant information about the stage of the review here (e.g. Funded proposal, protocol not yet finalised).

6. * Named contact.

The named contact acts as the guarantor for the accuracy of the information presented in the register record.

Negar Pourbordbari

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

7. * Named contact email.

Give the electronic mail address of the named contact.

negar@dcm.aau.dk

8. Named contact address

Give the full postal address for the named contact.

Dr. Negar Pourbordbari
Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University
Fyrkildevej 7, 9220 Aalborg
Denmark

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

004527914224

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University, Denmark

Organisation web address:

11. Review team members and their organisational affiliations.

Give the title, first name, last name and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong.

Dr Negar Pourbordbari. Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University, Denmark
Mr Allan Riis. Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University, Denmark
Professor Martin Bach Jensen. Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University, Denmark
Dr Jens Lykkegaard Olesen. The Faculty of Medicine Department of Clinical Medicine, Aalborg University, Denmark
Dr Michael Skovdal Rathleff. Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University, Denmark

12. * Funding sources/sponsors.

Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Include any unique identification numbers assigned to the review by the individuals or bodies listed.

Research Unit of General Practice in Aalborg and Department of Clinical Medicine, Aalborg University, Denmark

13. * Conflicts of interest.

List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members.

15. * Review question.

State the question(s) to be addressed by the review, clearly and precisely. Review questions may be specific or broad. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS where relevant.

The aim of this study is to conduct a systematic review on children and adolescents with musculoskeletal pain with a view to determining which baseline patient characteristics are associated with a poor outcome in follow-up regardless of which treatment has been provided (prognosis) or are associated with a successful outcome to a specific treatment (treatment effect modifiers).
Review question: What are the prognostic factors and treatment effect modifiers for children and adolescents with musculoskeletal pain?

16. * Searches.

Give details of the sources to be searched, search dates (from and to), and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.

This systematic review search will be conducted in the following electronic databases: MEDLINE, Embase, CINAHL, Web of Science, Cochrane and SPORTDiscus without limitations on dates.
Articles reported in English, German, Danish, Norwegian, Swedish, French, Spanish, Japanese, Chinese, Thai, Arabic, Persian, Turkish and Hindi will be included.
The search strategy will be divided into seven parts. 1. Pain; 2. Musculoskeletal defined in components; 3. Anatomic regions; 4. Musculoskeletal conditions in general and those common among children and adolescents; 5. Children and adolescents and synonyms; 6. Predictive factors and synonyms; and 7. Final search string to be applied in above mentioned electronic databases and also tested in MEDLINE with 5336 hits.
Additional details about the search strategy can be found in the attached PDF document (link provided

below).

17. URL to search strategy.

Give a link to the search strategy or an example of a search strategy for a specific database if available (including the keywords that will be used in the search strategies).

https://www.crd.york.ac.uk/PROSPEROFILES/41378_STRATEGY_20170613.pdf

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Yes I give permission for this file to be made publicly available

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

Children and adolescents aged 0-19 years with musculoskeletal pain.

19. * Participants/population.

Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.

The participants must all have some form of self-reported musculoskeletal pain at recruitment. Musculoskeletal pain is defined according to the International Association for the Study of Pain, IASP as: “pain arisen from muscle, tendon, bone and joint. Excluded from the definition is pain due to serious local causes, such as tumors, fractures, or infections, and systemic and neurological causes”. Types of pain are named according to the region affected, e.g. back pain, neck pain, shoulder pain, elbow pain, buttock pain, hip pain, knee pain, and ankle pain.
Inclusion criteria: 0 to 19 years of age, self-reported musculoskeletal pain.
Exclusion criteria: Older than 19 years of age.

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the nature of the interventions or the exposures to be reviewed.

All interventions used to treat musculoskeletal pain in children and adolescents are eligible, including conservative as well as non-conservative interventions. Conservative intervention is defined as: utilization of non-surgical treatment options, such as, but not limited to, the following: physiotherapy, immobilization, bandaging, drug therapy, wait and see and intraarticular, intramuscular and intratendinous injections with NSAID/glucocorticoid/steroid. We will also include studies that do not contain interventions.

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

We expect that most studies will not have used a comparator as they are prospective cohort studies. If the study design is a randomized trial, we will include all types of comparators.

22. * Types of study to be included.

Give details of the types of study (study designs) eligible for inclusion in the review. If there are no restrictions on the types of study design eligible for inclusion, or certain study types are excluded, this should be stated. The preferred format includes details of both inclusion and exclusion criteria.

Prospective cohort studies (including randomized trials) with a population of children and adolescents aged 0-19 years will be included in this systematic review if they report prognostic factors or treatment effect

modifiers (e.g. baseline variables that are associated with the outcome).

23. Context.

Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

There will be no restrictions on the type of setting.

24. * Primary outcome(s).

Give the pre-specified primary (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

We will search for all baseline patient characteristics that are: (i) associated with a poor outcome on follow-up regardless of which treatment has been provided (prognosis); or ii) associated with a successful outcome to a specific treatment (treatment effect modifiers). These may include intrinsic variables (such as age, height, weight, pain intensity, pain duration and similar) or extrinsic variables (such as social status, parental education, sports participation and similar).

Timing and effect measures

We will include patient characteristics that are associated with both short- and long-term outcomes. These will be divided into three endpoints, i.e. short-term (3 months), medium-term (3-12 months) and long-term (more than 12 months).

25. * Secondary outcome(s).

List the pre-specified secondary (additional) outcomes of the review, with a similar level of detail to that required for primary outcomes. Where there are no secondary outcomes please state 'None' or 'Not applicable' as appropriate to the review

The proportion of patients that report themselves free of musculoskeletal pain at follow-up in the included studies.

Timing and effect measures

We will include patient characteristics that are associated with both short- and long-term outcomes. These will be divided into three endpoints, i.e. short-term (3 months), medium-term (3-12 months) and long-term (more than 12 months).

26. Data extraction (selection and coding).

Give the procedure for selecting studies for the review and extracting data, including the number of researchers involved and how discrepancies will be resolved. List the data to be extracted.

The process of study selection will be conducted by two reviewers (NP and AR). They will independently identify studies from the electronic database search and will screen the titles and/or abstracts that have relevance to the question: what are the prognostic factors for children and adolescents with musculoskeletal pain? Studies kept after the primary assessment will be screened by full text and then selected for a final inclusion.
Any excluded studies will be recorded, along with a reason for the exclusion. There will be no blinding of the review authors to the journal titles, authors or institutions. Reference lists of all included studies will be screened for additional eligible publications that may have been missed during the initial search.
Any disagreements inside the reviewer group will lead to the involvement of a third reviewer (MSR).
NP will extract data using a pre-defined data extraction form (see Appendix 1 in the full protocol), inspired by The Cochrane Collaboration, Data collection form for intervention reviews: RCTs and non-RCTs (3). All the extracted data will then be validated by a second person (MSR). The collected data will include a description of the participants, setting (e.g. general practice or population-based cohort) and results (including all patient characteristics tested for association with outcome).

We will contact the corresponding author with a request for information, if any data concerning the intervention or outcome is missing from an included study, the intention being to increase the thoroughness of the descriptions of interventions and outcomes in this study.

Studies examining children and adolescents with musculoskeletal pain aged 0 to 19 years will be included in this review. If a study reports on an age range that exceeds this, we will contact the corresponding author and ask for data on the 0-19 year olds. The requested data will be included if it can be retrieved within one month of the inquiry.

27. * Risk of bias (quality) assessment.

State whether and how risk of bias will be assessed (including the number of researchers involved and how discrepancies will be resolved), how the quality of individual studies will be assessed, and whether and how this will influence the planned synthesis.

The QUIPS risk of bias tool for prognostic studies will be used to assess the quality of each paper (4). This tool contains items and considerations for six bias domains i.e. study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, statistical analysis and reporting (see Appendix 2 in full protocol). Each of the six potential bias domains will be rated by NP as high, moderate, or low risk of bias. When assessing the overall risk of bias in each study, a study will be described with a low risk of bias when either a) most of or b) the most important (determined a priori) or c) all of the six bias domains are rated with a low risk of bias. The same applies to moderate and high risk of bias.

28. * Strategy for data synthesis.

Give the planned general approach to synthesis, e.g. whether aggregate or individual participant data will be used and whether a quantitative or narrative (descriptive) synthesis is planned. It is acceptable to state that a quantitative synthesis will be used if the included studies are sufficiently homogenous.

A narrative synthesis is planned, the reason being the expected substantial heterogeneity in our results. If the prognostic factors or treatment effect modifiers are adequately homogenous, we will conduct a meta-analysis and pool the individual variables.

29. * Analysis of subgroups or subsets.

Give details of any plans for the separate presentation, exploration or analysis of different types of participants (e.g. by age, disease status, ethnicity, socioeconomic status, presence or absence or co-morbidities); different types of intervention (e.g. drug dose, presence or absence of particular components of intervention); different settings (e.g. country, acute or primary care sector, professional or family care); or different types of study (e.g. randomised or non-randomised).

Data will be divided into two main separate groups: prognostic factors and treatment effect modifiers and then sub-grouped into regions of musculoskeletal pain, gender and age.

30. * Type and method of review.

Select the type of review and the review method from the lists below. Select the health area(s) of interest for your review.

Type of review

Cost effectiveness
No

Diagnostic
No

Epidemiologic
No

Individual patient data (IPD) meta-analysis
No

Intervention

No

Meta-analysis
No

Methodology
No

Network meta-analysis
No

Pre-clinical
No

Prevention
No

Prognostic
Yes

Prospective meta-analysis (PMA)
No

Qualitative synthesis
No

Review of reviews
No

Service delivery
No

Systematic review
Yes

Other
No

Health area of the review

Alcohol/substance misuse/abuse
No

Blood and immune system
No

Cancer
No

Cardiovascular
No

Care of the elderly
No

Child health
No

Complementary therapies
No

Crime and justice
No

Dental
No

Digestive system
No

Ear, nose and throat
No

Education

No

Endocrine and metabolic disorders
No

Eye disorders
No

General interest
No

Genetics
No

Health inequalities/health equity
No

Infections and infestations
No

International development
No

Mental health and behavioural conditions
No

Musculoskeletal
No

Neurological
No

Nursing
No

Obstetrics and gynaecology
No

Oral health
No

Palliative care
No

Perioperative care
No

Physiotherapy
No

Pregnancy and childbirth
No

Public health (including social determinants of health)
No

Rehabilitation
No

Respiratory disorders
No

Service delivery
No

Skin disorders
No

Social care
No

Surgery
No

Tropical Medicine
No

Urological
No

Wounds, injuries and accidents
No

Violence and abuse
No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.
English

There is an English language summary.

32. Country.

Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved.

Denmark

33. Other registration details.

Give the name of any organisation where the systematic review title or protocol is registered (such as with The Campbell Collaboration, or The Joanna Briggs Institute) together with any unique identification number assigned. (N.B. Registration details for Cochrane protocols will be automatically entered). If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

34. Reference and/or URL for published protocol.

Give the citation and link for the published protocol, if there is one

Give the link to the published protocol.

http://www.crd.york.ac.uk/PROSPEROFILES/41378_PROTOCOL_20160520.pdf

Alternatively, upload your published protocol to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Yes I give permission for this file to be made publicly available

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

35. Dissemination plans.

Give brief details of plans for communicating essential messages from the review to the appropriate audiences.

The manuscript will be submitted for publication in an appropriate peer-reviewed journal. In addition to this we will produce material to be distributed to general practitioners and other health care providers, who manage children and adolescents with musculoskeletal pain. This will be done in the form of a short animation video, visualizing the main study results from the systematic review. The animation will be distributed through social media, websites and patient associations. This will ensure dissemination of our results to our target audience.

Do you intend to publish the review on completion?

Yes

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords will help users find the review in the Register (the words do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

systematic review
children
adolescence
musculoskeletal pain
prognosis
treatment effect modifier

37. Details of any existing review of the same topic by the same authors.

Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

38. * Current review status.

Review status should be updated when the review is completed and when it is published.
Please provide anticipated publication date

Review_Ongoing

39. Any additional information.

Provide any other information the review team feel is relevant to the registration of the review.

References:
1. http://www.iasp-pain.org/files/Content/ContentFolders/GlobalYearAgainstPain2/MusculoskeletalPainFactSheets/AcutePain_Final.pdf
2. http://www.spine-health.com/glossary/conservative-treatment.
3. Cochrane Training, Data collection form for intervention reviews: RCTs and non-RCTs. http://training.cochrane.org/resource/data-collection-forms-intervention-reviews 2014.
4. Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing bias in studies of prognostic factors. Ann Intern Med. 2013;158(4):280-6.

40. Details of final report/publication(s).

This field should be left empty until details of the completed review are available.

Give the link to the published review.

Supplementary table 1. Estimates on prognostic factors specified according to musculoskeletal pain type, baseline age, and follow-up in the included studies

Musculoskeletal pain	Neck pain	
Low back pain	Low limb pain	Headache
Knee pain	Back pain	Growing pain

	Prognostic factors subgrouped according to the biopsychosocial model	Study ID (Follow-up, yrs)	RR (95% CI)	OR (95% CI)	p-value	Adjusted for
	BIOLOGICAL PROGNOSTIC FACTORS					
	Female sex compared to male					
8 to 13		37 (3)			0.038	
10 to 16		20 (11)		M 1.8 (1.1-2.9)		
9 to 12		21 (4)	U 1.24 (1.07-1.44)			age
9 to 12		28 (1)		1.78 (1.18-2.69)	0.006	
10 to 17		50 (3mo)			0.003	
9 to 12		27 (1)			0.001	
12 to 15		34 (2)	CR 1.29 (1.02-1.63)		0.08	
12 to 15		9 (1)		3.66 (1.09-12.33)	0.04	
10 to 11		39 (2)			M < 0.001	
10 to 11		39 (2)			M < 0.001	
8, 11, 14		20 (11)		2.24 (1.24-4.20)		
	Older age					
9 to 12	Older age	28 (1)		1.24 (1.02-1.50)	0.031	
9 to 12 F	11 to 13 years vs. 9-10 years	21 (4)	M 1.40 (1.17-1.67)			
12 to 15	Older age, increase per year, 12 years as referent	9 (1)		M 1.45 (1.07-1.95)	0.01	
13	Older age	25 (3)			0.04	
	Body measurement factors					
8 to 13	Higher pubertal group (a) group 2 and 3 vs. group 1	37 (3)			0.022	
9 to 12 F	Beighton score 6-9 vs. score < 6	21 (4)	M 1.31 (1.18-1.46)			age
11 to 14	Height < 158cm	23 (4)	2.2 (1.2-3.8)			age, sex
9 to 12	Hypermobility score >/=6 vs. <6	11 (4)		M 2.93 (1.13-7.70)		
	Physical functioning					
14 to 16	Ratio flexion mobility (cm)/extension strength (min) (b)	36 (3)		1.9 (1.1-3.2)	0.02	gender, well being, physical activity
14 to 16	Ratio extension mobility cm/extension strength (min) (b)	36 (3)		3.2 (1.3-8.3)	0.02	gender
14 to 16	Ratio flexion + extension mobility (cm)/extension strenght (min) (b)	36 (3)		1.5 (1.1-2.2)	0.02	gender, well being, physical activity
	Pain characteristics					
2 to 17	Higher number of painful sites (mean 3.7 vs. 2.8) range 0-6	22 (9)			0.04	
2 to 17	More frequent generalised vs. localised pain (86 vs. 47%)	22 (9)		84.0 (2.1-3000)	0.02	
2 to 17	More intense pain (median 4.3 vs. 0.5cm) range 0-10cm VAS	22 (9)			0.03	
2 to 17	Longer disease duration before first admission (median 1.4 vs. 0.5 years)	22 (9)			<0.01	
9 to 12	Pain at both baseline and 1 year follow-up vs. only baseline	21 (4)		2.9 (1.9-4.4)		age
9 to 12 M	Multisite vs. localised pain	21 (4)	U 1.32 (1.04-1.66)			age
9 to 12 M	Headache (psychosomatic symptom (c))	21 (4)	M 1.43 (1.12-1.83)			age
10 to 17	Conditioned pain modulation CPM (d)	50(3mo)			0.046	
9 to 12 F	Abdominal pain (psychosomatic symptom (c))	21 (4)	U 1.20 (1.03-1.40)			age
11 to 14	Radiating leg pain vs. no radiating pain	23 (4)	2.2 (1.4-3.6)			age, sex
11 to 14	Low back pain start > 12 month prior to admission	23 (4)	2.4 (1.3-4.4)			age, sex
11 to 14	Pain episode > 7 days vs < 24h	23 (4)	2.6 (1.4-4.9)			age, sex
15 to 19	Patellofemoral pain diagnosis vs. other types of knee pain	34 (2)	1.24 (1.04-1.49)		0.01	age, sex, BMI
15 to 19	High pressure pain threshold (PPT) around the knee	35 (3mo)			0.03	
12 to 15	Daily vs. rare pain	9 (1)		M 6.31 (1.21-33.01)	0.03	
12 to 15	Pain several times/week vs. monthly	34 (2)	CR 1.58 (1.15-2.17)		0.005	
16 to 18	Daily pain frequency vs. monthly	34 (2)	1.58 (1.17-2.14)		0.003	

16 to 18	Longer pain duration per 10-months increase	34 (2)	CR 1.04 (1.01-1.07)		0.01			
9 to 12 M	Also headache (e) at least once a week	38 (4)			<0.001			
9 to 12 M	Also abdominal pain (e) at least a week	38 (4)			<0.001			
9 to 12 F	Also headache (e) at least once a week	38 (4)			<0.001			
9 to 12 F	Also abdominal pain (e) at least a week	38 (4)			<0.001			
9 to 12	Other musculoskeletal symptoms: upper extremities at least once a week	38 (4)			<0.001			
9 to 12 M	Other musculoskeletal symptoms: chest at least once a week	38 (4)			0.008			
9 to 12 F	Other musculoskeletal symptoms: chest at least once a week	38 (4)			0.001			
9 to 12	Other musculoskeletal symptoms: back at least once a week	38 (4)			<0.001			
9 to 12 M	Other musculoskeletal symptoms as well: lower extremities at least once a week	38 (4)			<0.001			
9 to 12 F	Other musculoskeletal symptoms as well: lower extremities at least once a week	38 (4)			0.003			
8, 11, 14	Headache >/= 1time/week	20 (11)		2.3 (1.1-4.5)				
10 to 16	Duration of pain episodes > 3 hours vs. < 3 hours	20 (11)		U 3.1 (1.1-8.2)				
10 to 16	Lower pain threshhold	40 (5)			<0.05			
10 to 16	Lower pain threshold at anterior tibial region (pressure level < 5kg/cm2)	40 (5)			<0.01			
	PSYCHOLOGICAL PROGNOSTIC FACTORS							
	General psychological factors							
16 M	Internalization (f)	33 (2)		2.32 (1.23-4.37)				
16 M	Externalization (f)	33 (2)		2.17 (1.24-3.81)				
16 F	Internalization (f)	33 (2)		3.70 (1.88-7.27)				
10 to 16	Often/sometimes nervous	20 (11)		M 2.1 (1.3-3.4)				
16 to 18 M	Internalization (f)	24 (2)			< 0.001			
16 to 18 M	Externalization (f)	24 (2)			< 0.001			
16 to 18 F	Higher internalization score (f)	24 (2)			< 0.001			
16 to 18 F	Higher externalization score (f)	24 (2)			< 0.001			
10 to 16	Self-perception of not feeling completely healthy	20 (11)		U 1.7 (1.1-2.8)				
10 to 16	Unsatisfied with own appearance	20 (11)		U 1.6 (1.1-2.5)				
12 to 15	EQ-5D index score 0-25 vs. 75-100% quartiles (g)	9 (1)		U 0.08	<0.001			
12 to 15	EQ-5D index score 0-25 vs. 25-50% quartiles (g)	9 (1)		U 0.29	<0.001			
12 to 15	EQ-5D index score 25-50th % vs. 75th-100th % (g)	34 (2)	CR 1.81 (1.14-2.85)		0.01			
12 to 15	EQ-5D index score 0-25th % vs. 75th-100th % (g)	34 (2)	CR 2.00 (1.28-3.12)		0.002			
10 to 11	Self reported low self esteem	39 (2)			U < 0.01			
10 to 11	Parent reported adolescent low self esteem	39 (2)			U < 0.01			
	Depressive factors							
9 to 12 F	Depressive feelings	21 (4)	U 1.21 (1.03-1.42)			age		
9 to 12 F	Depressive symptoms in a frequency of at least once a week	38 (4)			<0.001			
9 to 12 M	Depressive symptoms in a frequency of at least once a week	38 (4)			<0.001			
12 to 16	Higher score of anxiety and depressive symptoms (h)	18 (4)		1.4 (1.03-1.90)	0.032			
10 to 11	Self reported anxiety/depression	39 (2)			M <0.01			
10 to 11	Parent reported adolescent anxiety/depression	39 (2)			< 0.05			
	SOCIAL PROGNOSTIC FACTORS							
	General social factors							
2 to 17	Lower paternal educational level (median 10 vs. 14 years education)	22 (9)			p<0.01			
2 to 17	Lower maternal educational level (median 10 vs. 14 years education)	22 (9)			p<0.01			
2 to 17	More chronic family difficulties (mean 4.3 vs. 2.9) (i)	22 (9)			p<0.01			
10 to 16	Doing well in school	20 (11)		U 1.8 (1.1-2.9)				
9 to 12	Higher disability index (j) 1-2 vs 0	28 (1)	1.72 (1.09-2.73)		0.005			
9 to 12	Higher disability index (j) 3-5 vs 0	28 (1)	3.17 (1.54-6.55		0.005			
9 to 12	Higher disability index (j) 3-5 vs. 0	21 (4)	U 1.23 (1.02-1.49)			age		
11 to 14	High vs. low peer relationship problems	23 (4)	2.4 (1.3-4.2)			age, sex		
11 to 14	Difficulty standing in line for 10 minutes	23 (4)	2.7 (1.5-4.9)					
11 to 14	Difficulties carrying a schoolbag	23 (4)	2.1 (1.1-4.0)					
11 to 14	High limitation level HFAQ (k) 4-9 vs. 0-1 limitations	23 (4)	4.1 (1.05-16.2)					

8, 11, 14	Headache on non-school days	20 (11)		3.1 (1.3-7.3)				
13 M	Use of physiotherapy for headache or neck pain during the past 6 months	25 (3)			0.004			
10 to 11 F	Parental recurrent headache	39 (2)			p<0.05			
10 to 16	At least one parent with a pain syndrome	40 (5)			0.047			
	Factors related to sleep/daytime tiredness							
9 to 12 F	Waking up during nights	21 (4)	U 1.18 (1.01-1.37)			age		
16 F	Sleep </= 7h vs. 8-9 h/day	33 (2)		1.68 (1.05-2.68)				
9 to 12	Day tiredness, fatigue	28 (1)		1.86 (1.16-3.00)	0.010			
16 to 18 M	Insufficient sleeping time h/day (mean 8 vs. 8.5 h/day)	24 (2)			0.001			
9 to 12 M	Difficulties falling asleep	38 (4)			<0.001			
9 to 12 M	Daytime tiredness	38 (4)			<0.001			
9 to 12 M	Walking up during nights	38 (4)			0.001			
9 to 12 F	Difficulties falling asleep	38 (4)			<0.001			
9 to 12 F	Daytime tiredness	38 (4)			<0.001			
9 to 12 F	Walking up during nights	38 (4)			<0.001			
	Physical activity / inactivity							
16 F	>/=4 vs. 2-3 hours of moderate-to-vigorous physical activity/week	33 (2)		1.63 (1.04-2.56)				
16 to 18 M	Longer sitting time outside school hours (mean 6.2 h/day)	24 (2)			0.004			
12 to 15	Sports participation 3-7 t/wk vs. 0-2 t/wk	9 (1)		M 2.01 (1.20-3.36)	0.008			
9 to 12	Exercise frequency 5-7 t vs. 0-2/week	11 (1)		M 2.43 (1.16-5.05)				
	Alcohol							
16 to 18 F	More than occasional consumption	24 (2)			0.038			
	Smoking							
16 F	Smoking vs. nonsmoking	33 (2)		1.89 (1.23-2.90)				
16 F	Smoking 5-7 days/week vs. nonsmoking	30 (2)		2.52 (1.40-4.53)		family's SES, physical activity, BMI, depressive mood		
16 F	Smoking 1-9 cigarettes/day vs. nonsmoking	30 (2)		2.39 (1.40-4.08)		family's SES, physical activity, BMI, depressive mood		
16 F	Smoking > 9 cigarettes/day vs. nonsmoking	30 (2)		2.57 (1.03-6.46)		family's SES, physical activity, BMI, depressive mood		
16 M	Smoking 1-9 cigarettes/day vs. nonsmoking	30 (2)		2.68 (1.35-5.32)		family's SES, physical activity, BMI, depressive mood		

Explanatory notes

F = prognostic factor only applicable for female participants, **M** = Male, when nonspecified = unisex

RR > 1 or < 1, OR > 1 or < 1, p < 0.05 indicate that the prognostic factor is associated with a higher risk of persistent MSK pain.

CI = confidence interval **M** = Multivariate analysis **U** = Univariate analysis CR = Crude

a = Group 1: prepubertal, group 2: became pubertal during 3 years follow-up, and group 3: pubertal at baseline. The pubertal stage was assessed by the presence of secondary signs of pubertal development. For females, puberty was defined by the stage of breast development (Tanner stage >/= 3) and menarche. For males, puberty was defined in presence of a testicles volume >/= 12 ml and presence of pubic and underarm hair.

b = Low lumbar extension strenght and high ratios between lumbar mobility and lumbar extension strenght predicts future low back pain

c = childhood abdominal pain, headache, depressive symptoms, day tiredness, difficulties in falling asleep, waking up during nghts are believed to be having a psychosomatic origin in the great majority of cases.

d = Conditioned pain modulation CPM calculated using a ratio of conditioned heat pain threshold with a conditiones stimulus (cold pressor)(50).

e = Classified as: other physical and psychological symptoms, without further definition

f = Internalizing score calculated from subscales: anxious/depressed, sithdrawn/depressed symptoms, and somatic complaints. Externalizing from rule-breaking and aggressive behaviour.

g = EQ-5D assesses self-reported health status in 5 dimensions: mobility, self-care, usual activitied, pain/discomfort, anxiety/depression and within 3 levels of severity: no problems, moderate or severe problems as well as scoring own current self-rated health status on VAS 0-100.

h = Anxiety symptoms: been constantly scared and uneasy, felt tense and restless, worried too much about different matters. Depressive symptoms: felt hopeless when thinking of the future, felt down or sad.

i = Assessment of information about employment and education, economic matters, housing, marital or family discord, social networks and the physical and mental health of the family members. Score range 0-6, 6=severe family difficulties.

j = Subjective disability index calculated from answers to the following proposals: difficulty in falling asleep because of pain, difficulty sitting during a lesson, pain disturbs a walk more than 1km, pain disturbs physical exercise, pain disturbs hobbies. Range 0-5.

k = The modified Hannover functional ability Questionnaire HFAQ assesses whether pain and ache in low back make any of the following daily activities difficult: reaching up to get a book from a high shelf, carrying your school bag to school, sitting on a school chair for a 45-min lesson, standing in a queue for 10 min, sitting up in bed from a lying position, bending down to put your socks on, standing up from an armchair at home, running fast to catch a bus, and sports activities at school. Low = 0-1 limitation, moderate = 2-3 limitations or high = 4-9 limitations (23).

l = Yunus criteria: pain modulation by physical activity, by weather, by anxiety and stress, poor sleep, headache, irritable bowel, soft tissue swelling in hands and feet, fatigue, numbness in hands and feet, feeling excited and nervous. Yes to minimum 3 symptoms to meet the Yunus criteria.

m = SES: Socioeconomic status

n = CDI: Children's depression Inventory. Cut off point >/= 13 indicating depressive symptoms

Identified baseline factors without association to persistent musculoskeletal pain, divided in pain type (study ID)	
Musculoskeletal	Female: sitting h/day, sleep h/day, Male: physical activity MET-h/week and above occasional alcohol consumption, unisex: smoking pack years, body mass index (BMI) (24)
	Exercise frequency >3 vs. <3t/week, disability index 1-5 vs. 0 (i), waking up during nights (Male), day tiredness, difficulty falling asleep, depressive feelings (Male), headache (Female), abscence one day or more from school vs. never being asbcent due to pain, maximum volume O2 intake (per unit increase) measured during a shuttle run test (21)

	Headache, stomachache, depressive feelings, difficulty falling asleep, waking up during nights, Yunus criteria (l), increasing exercise amount, and hypermobility (28)
	Male: physical activity level, sitting >4 h/day, sleep </= 7 h/day, smoking and overweight. Female: externalization, sitting > 4h/day, overweight (33)
	Increasing age (20, 27)
	Increasing age, sex, family history of related diseases, VAS score assessed by physicians, elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), platelet count, lower score in psychosocial functioning reflecting mental health and functioning at school/work, within the family, with friends and in other social activities (Children's Global Assessment Scale, CGAS) (22)
Low back	Extension strength (minutes) and plain saggital mobility (36)
	Akward trunk postures, physically demanding job (working hands above shoulders, awkward trunk posture and standing or walking), working regularly or irregularly, duration of work, work with specific physical load factors (31)
	BMI (32)
	Male: smoking 5-7 d/week vs. no smoking, smoking <9 cigarettes/day (30)
	High emotional vs. low emotional problems, reaching to a high shelf, sitting up in bed, bending down to put on socks, high conduct problems, high hyperactivity, high prosocial behavior, widespread pain, headache, stomachache in the past month compared to none, daytime tiredness on a scale 0-10, 5-10 vs. 0-4, pain start < 12 months ago, pain lasts </= 7 days, pain today, pain severity on a scale 0-10, 4-10 vs. 0-3, Hannover 2-3 vs. 0-1 (23)
	Sex, increasing age, tobacco, profession: hairdresser and media/design compared to electrician, western ethnicity compared to non-western ethnicity, moderate/high vs. low socio-economic status (SES) (m), moderate/high vs. low physical activity level, BMI, moderate/high physical work demand vs. low (26)
Knee	Increasing age compared to 15, participation in sports, BMI, EQ-5D index score 50-75th percentile compared to 75-100th, weekly pain frequency compared to monthly (34)
	BMI, EQ-5D 50-75th percentile compared to 0-25th, monthly, weekly, several times a week pain frequency compared to rarely (9)
Lower limb	After 1 year follow-up: traumatic limb at baseline, exercise 3-4 t/week vs. 0-2 t, hypermobility score >/= 6 vs. < 6. After 4 years follow-up: exercise frequency 5-7 t/week vs. 0-2 t, lower limb trauma at baseline. Common after both 1 and 4 years follow-up: age 11-14 vs. 9-11, frequency of exercise 2-4 times vs. once a week, multisite pain, female sex, headache, stomachache, depressive feelings, difficulty falling asleep, day tiredness, waking up during nights, school abscence due to pain vs. never abscent, disability symptoms >/=3 vs. </=2, volume ..O2 max average or above, exercise frequency 3-4 t/week vs. 0-2 t (11)
Neck	Joint hypermobility Beighton 6-9, physical activity at least half and hour more than 3 times a week (38)
Growing pain	Sex, ethnicity, increasing age (39)
Headache	Sex (19)
	Pain frequency, pain in daily activities, physiotherapy, relaxation therapy, sport activity, stress at home or in hobbies, pain on palpation, pain threshold measured by dolorimeter, depressive symptoms, temporomandibular disorder, stress at school, use of computer (25)
	Stress (20)
Widespread	Female sex, increasing age, tender point count, CDI > 13 (n), Yunus criteria >/=3, sleep score, disability index (f), psychosomatic symptoms (29)
Back	Stress (20)

Prognostic factors are divided primarily in biological, psychological, and social factors and secondary according to musculoskeletal pain type. The prognostic value were reported with RR, OR, and/or p-value.