OXFORD UNIVERSITY PRESS | SLEEP

Are sleep problems a risk factor for the onset of musculoskeletal pain in children and adolescents? A systematic review.

Journal:	*Sleep*
Manuscript ID	SLEEP-2017-0063.R2
Manuscript Type:	Review
Date Submitted by the Author:	08-May-2017
Complete List of Authors:	Andreucci, Alessandro; Arthritis Research UK Primary Care Centre, Research Institute for Primary Care and Health Sciences, Keele University Campbell, Paul; Arthritis Research UK Primary Care Centre, Research Institute for Primary Care and Health Sciences, Keele University Dunn, Kate; Arthritis Research UK Primary Care Centre, Research Institute for Primary Care and Health Sciences, Keele University
Section:	Sleep, Health, and Disease
Keywords Pick List:	Pain, Pediatrics - Adolescents, Pediatrics - Sleep and Arousal, Public Health, Sleep Hygiene
Other Keywords:	Sleep, Systematic review

Reviewer information page

Number of tables: 5

Number of figures: 1

Abstract word count: 234

Statement of significance word count: 120

Word count: 4,156

Are sleep problems a risk factor for the onset of musculoskeletal pain in children and adolescents? A systematic review.

Authors: Alessandro Andreucci[a], Paul Campbell PhD[a], Kate M Dunn PhD[a]

Authors' affiliation: [a] Arthritis Research UK Primary Care Centre, Research Institute for Primary Care and Health Sciences, Keele University, UK

Institution where the work was performed: Arthritis Research UK Primary Care Centre, Research Institute for Primary Care and Health Sciences, Keele University, UK

Corresponding author:

Alessandro Andreucci, Arthritis Research UK Primary Care Centre, Research Institute for Primary Care and Health Sciences, Keele University, Staffordshire ST5 5BG, UK. +44 (0) 1782 734889 a.andreucci@keele.ac.uk

Corresponding author's current email: a.andreucci@keele.ac.uk

Abstract

Study objectives

Musculoskeletal pain is a major burden on society. Adults with sleep problems are at higher risk for musculoskeletal pain onset, but there is no evidence for this relationship in children and adolescents. This study aimed to systematically review prospective studies on the risk for musculoskeletal pain onset in children and adolescents with sleep problems.

Methods

Five databases (MEDLINE, PsycINFO, AMED, EMBASE, HMIC) were systematically searched to identify prospective studies that investigated if children and adolescents (aged 6-19 years) with sleep problems are at higher risk for musculoskeletal pain onset. Included studies were assessed for study quality and a best evidence synthesis was carried out on extracted data.

Results

Thirteen prospective studies were identified. Overall, evidence indicates that sleep problems (quality, quantity, day-time tiredness) are not risk factors for musculoskeletal pain onset. Further analysis on specific body regions show strong evidence that sleep problems are a risk factor for neck pain onset (only in girls), and strong evidence that sleep problems are not a risk factor for the onset of widespread pain.

Conclusions

Overall sleep problems are not a risk factor for musculoskeletal pain onset in children and adolescents. Increased risk was found for some specific body regions and sub-groups but the evidence base was less strong and generally inconsistent. This review found a lack of quality in research methodology compared to research in adults and further research with improved methodology is required.

Keywords:

Pain
Sleep
Pediatrics - Adolescent
Pediatrics - Sleep and Arousal
Public Health
Sleep Hygiene
Systematic review

Statement of significance

Musculoskeletal pain is a major burden on society and there is a need to identify risk factors for the onset of musculoskeletal pain. Research carried out in adults has shown a link between sleep problems and the onset of musculoskeletal pain, but evidence is lacking about this relationship in younger populations. This is the first systematic review that has summarized prospective studies on the risk between sleep problems and the onset of musculoskeletal pain in children and adolescents. Our findings show that sleep problems are not risk factors for musculoskeletal pain onset in children and adolescents, although further analysis did reveal sub-groups at some increased risk. Further research is now required to understand why particular sub-groups are at increased risk.

Introduction

Musculoskeletal pain is a major concern worldwide. In developed countries, the proportion of the global disability-adjusted life years (DALYs) due to musculoskeletal pain is 13% [1], and musculoskeletal conditions rank first, fourth and sixth among the top 10 diseases in terms of global years lived with disability [2]. Musculoskeletal conditions have a significant economic burden, with the mean cost of chronic pain estimated at $560-635 billion in the US (2010 figures) [3] and 3-10% of gross domestic product in Europe in 2008 [4]. Consequences of musculoskeletal pain include psychological distress, disability, limitation of activities, limitation in social participation and burden on the family [5,6]. Individuals who experience musculoskeletal pain during adolescence are more likely to have musculoskeletal pain in adulthood [7–10]. Studies investigating the course of pain over time, report that lifelong patterns of musculoskeletal pain that can appear stable and unchanging in adulthood, may begin in childhood [11,12]. However, to date, research on the epidemiology of musculoskeletal conditions has focused mainly on adult populations [11,13–15], which are likely to identify risk factors for new episodes of musculoskeletal pain (often confounded by the experience of previous pain) rather than true risk factors for the first initial onset of musculoskeletal pain. Gaining knowledge of the factors predictive of musculoskeletal pain in childhood is important as such knowledge could provide information on potential targets for intervention to prevent or reduce risk for child musculoskeletal pain onset, and potentially avert or alter the trajectory of long-term painful musculoskeletal conditions among adults. One specific area with growing research interest and evidence from research on adults with musculoskeletal pain is the role of sleep, more specifically sleep problems (quality, quantity, resulting day time tiredness), as both a risk factor and prognostic factor [16]. Recent reviews, both in adult and child populations, show that sleep problems are common in those with pain [16,17] and that in adults sleep problems are more likely to precede pain (risk of new episodes of pain) in contrast to

pain as a predictor of sleep problems [16]. Previous systematic reviews [18–23] on risk factors for musculoskeletal pain onset in children and adolescents have been carried out, but have not yet considered the potential role of sleep problems as a risk factor for musculoskeletal pain onset in these populations. The aim of this systematic review is to evaluate evidence from prospective studies that investigated if children and adolescents with sleep problems are at higher risk for the onset of musculoskeletal pain.

Methods

Selection of the literature

A systematic search of the literature was carried out by one reviewer (AA) with the support of another reviewer (PC). Two approaches were used to search the literature. A broad search was carried out on risk factors for musculoskeletal pain onset in general in order to retrieve articles that may report data on sleep where sleep was not the main focus of the study. A more specific search was also carried out using appropriate sleep terms to increase specificity. Databases were searched from inception to the 8th November 2016. The following databases were searched through the OVID and NSH HDAS interfaces: Medline, PsycINFO, Allied and Complementary Medicine Database (AMED), Excerpta Medica dataBASE (EMBASE), and Health Management Information Consortium (HMIC). A combination of keywords for each database (see appendix 1) was used to retrieve the papers. Keywords were identified by the principal investigator (AA) after consulting similar systematic reviews and discussion with other reviewers (PC, KD). An additional search was employed by consulting local experts (e.g. accessing and searching personal databases of senior colleagues within the Research Institute, contacting other research experts within the field of childhood musculoskeletal pain), as well as consulting previous relevant reviews in adult populations.

Inclusion/exclusion criteria

Studies had to report data on musculoskeletal pain presence as the outcome and use a prospective design conducted in general population, school or primary care settings, in order to retrieve results that were generalizable to the overall population. Studies had to include individuals aged 6 to 19 years; this age criteria was chosen as the age of six has been reported to be the starting point for children to use the word “pain” and age nineteen is defined by the World Health Organization as the start of adulthood [24–26]. Articles were considered regardless

of the language, and date of publication in order to minimise publication bias. Studies were not included if they had a sample size ≤30 as they provide unreliable risk estimates, and studies were not included if they did not report separate data on children or adolescents. Randomized controlled trials (RCTs) were excluded as their focus is on intervention not observation, and RCTs often employ more stringent selection criteria which can compromise generalisability. Studies of populations with specific diseases or conditions where pain is assessed and reported but is a result of the disease or underlying condition (e.g. cancer pain), were also excluded, as well as studies where translation was not possible.

Selection process

All the titles and abstracts of papers identified through the search process were checked to include potentially relevant studies by two authors of the review team (AA, PC). The two authors randomly checked 20% of each other's assigned titles and abstract to ensure reliability, similar checks were also carried out on the full-text papers. In the case of disagreement or inconsistency between reviewers for inclusion of a paper, the third reviewer (KD) was consulted and consensus achieved.

Data extraction

Data were extracted by the first reviewer (AA) using a standardised data extraction form (Appendix 2). Random samples of 20% of the full-texts were cross-checked by the second reviewer (PC) in order to assess consistency in the extraction process, and any disagreements were resolved through discussion and consultation with the third reviewer (KD).

Quality assessment

The assessment of study quality was carried out using a structured assessment tool. This tool was chosen based on previous systematic reviews with a similar focus to this current review (prospective studies, focus on musculoskeletal pain as outcome [27,28]). The tool reports on 15

items relative to both internal and external validity [27,28]. Each item was assessed to check if the criteria was met or not and a score was given (table 1). This enabled the classification of articles according to methodological quality, and to weight the results of the studies (best evidence synthesis). Each item was scored positive (+) if present and a point awarded, negative (–) if absent (no point was given), or (na) if not applicable (no point was given). It follows that the highest possible score was 15. For ease of interpretation the quality of the articles was rated in three categories: 'high' (11-15 items); 'moderate' (6-10 items), and 'low' (1-5 or no items).

Analysis of risk

For each finding, three possible effects were reported: significant effect (+, if significant effect reported), no effect (x, no significant effect present), mixed (#, where significant and non-significant effects are reported for the same body site, e.g. stratified analysis on gender where an effect is reported for males but not females, or different levels of exposure e.g. mixed findings from low, medium, high levels of sleep problems). Each effect was counted within an overall assessment of risk on onset of musculoskeletal pain (i.e. all findings from all body sites). Secondary analysis was carried out stratified by body pain sites reported (back pain, neck pain, shoulder pain, general musculoskeletal pain, widespread pain). A level of evidence approach was used for the analysis (see Table 2) where the combined evidence is assessed in terms of the direction of effect, and the quality of each individual study [29,30]. The levels of evidence analysis applies greater weighting to those findings of high quality. As Table 2 outlines, strength of evidence is determined by the consistency of direction of findings and study quality. Evidence of risk was explored across all body sites to give an overall estimation of consistency, and then for each body site in turn. The risk for the onset of musculoskeletal pain was reported using definitive categories of sleep problems retrieved from the review data (sleep quality, sleep quantity and day time tiredness). Information on effect size (e.g. odds ratio, relative risk) was reported if presented in the results of each paper.

Results

Study selection

The broad electronic search (all risk factors regardless of type) yielded a total of 35,167 references. After screening of titles and abstracts, 156 full-text articles were assessed for eligibility, of which 145 were excluded because they did not meet the inclusion criteria (see appendix 3). Finally, 11 studies met the eligibility criteria and were included. The second specific search (using specific sleep terms) yielded 3,065 references. After screening of titles and abstracts, ten full-text articles were assessed for eligibility, of which eight were excluded because they did not meet the inclusion criteria and two articles selected for inclusion. These two searches led to the inclusion of 13 articles overall (Figure 1). Seven articles were identified in both searches; four were identified from the broad search, and two within the specific sleep term search.

Quality and characteristics of the studies

Table 3 describes the quality and characteristics of the included studies. Overall, eight articles (62%) out of 13 were defined as high quality and five (38%) as medium quality; no studies were included in the low quality criteria. Included studies were from six different countries with a total population of 18,888 (range from 191 to 4161 individuals). The samples were recruited from schools or school settings in six studies, from the general population in six articles and from a primary care/hospital interface setting in one study. Some cohorts were reported in more than one article. Three studies were drawn from the Northern Finland Birth Cohort [31–33], while four studies were drawn from a cohort in southern Finland [34–37].

Evidence

Sleep quality

Overall ten findings were reported, with two findings [34,38] showing that children with poor sleep quality are significantly at higher risk (both findings in the direction of poor sleep quality predictive of musculoskeletal pain), one finding [31] showing mixed evidence, and seven findings [31,35–37,39,40] showing no significant higher risk (Please see Table 4 for a full description of effect sizes). When considering only high quality evidence, similar rates are found (high quality findings; two studies [34,38] reported significant higher risk, one study [31] mixed, five findings [31,35–37] no higher risk). Overall this indicates a trend toward strong evidence of no effect of poor sleep quality as a risk factor for the onset of musculoskeletal pain. Further inspection at each body site was carried out. For back pain onset there were two non-significant effect, one from a medium quality study [39] and one from a high quality study [31], resulting in a moderate evidence of no higher risk. For neck pain onset the findings shows one mixed [31] and one significant effect [34], resulting in strong evidence that girls with low sleep quality are at higher risk for neck pain onset, but inconsistent evidence of risk in boys. Shoulder pain shows a non-significant effect in one high quality study [31], indicating weak evidence of no higher risk. For general musculoskeletal pain onset there are two findings (one high quality). Both report no significant effects. In the high quality study [37] no one of the ORs provided was significant, and the medium quality study [40] reported no statistically significant difference in the sleep quality score between children with new-onset pain and healthy children. This resulted in a moderate evidence of no risk of musculoskeletal pain onset in children with low sleep quality. For widespread pain onset, three high quality findings are reported. While one study [38] reported significant findings, two studies [35,36] reported no significant effects indicating inconclusive evidence.

Sleep quantity

Overall eight findings were reported with two of those findings [7,41] (medium quality) showing a significant effect (both findings in the direction of low sleep quantity predictive of musculoskeletal pain), two [31,32] (high quality) showing mixed evidence, and four [31,33,38] (one medium, three high quality) showing no significant effect. This indicates inconsistent evidence, though considering only high quality evidence suggests a trend toward no higher risk for musculoskeletal pain onset in children with low sleep quantity. Inspection at each body site revealed for back pain onset, two study findings, one medium quality [7], indicating a significant effect, and one high quality [31] reporting a mixed effect. Closer inspection of this mixed result showed no higher risk in girls but higher risk in boys (albeit within only one sleep quantity category). Overall this indicates inconsistent evidence of the effect of sleep quantity on back pain onset. Both neck pain onset and shoulder pain onset show no significant higher risk from one high quality study [31] indicating weak evidence of no higher risk. Two findings are reported for general musculoskeletal pain onset with one high quality study [32] reporting mixed findings and one medium quality [41] study reporting a significant effect. This indicates a moderate evidence of higher risk in boys, but inconsistent evidence in girls. For widespread pain two studies (one high quality [38], one medium quality [33]) report no significant higher risk, indicating moderate evidence that sleep quantity is not a risk factor for onset of widespread pain.

Daytime tiredness

Out of eight findings, two [34,37] (high quality) report a significant effect (both findings in the direction of daytime tiredness predictive of musculoskeletal pain), three [31] (high quality) report mixed effects, and three [36,39,42] (two high quality) report no significant effect indicating inconsistency, with a similar conclusion if only high quality evidence is considered.

Examination by body site revealed one high quality [31] study reporting mixed evidence and one medium quality [39] study reporting no effect for back pain onset. This indicates a moderate evidence that boys with daytime tiredness are not at higher risk for back pain onset, but an inconsistent evidence in girls. Similarly for neck pain, one high quality study [34] found a significant effect, and one high quality study [31] reported mixed effects. This indicates strong evidence that girls with daytime tiredness are at higher risk for neck pain onset, but inconsistent evidence in boys. For widespread pain, two findings [36,42] (high quality) report that children with day time tiredness are not at higher risk for widespread pain onset, indicating strong evidence of no risk. Evidence is inconclusive for shoulder pain as there is only one (high quality) mixed finding [31]. For general musculoskeletal pain onset there is weak evidence (one high quality finding [37]) that children with day time tiredness are at higher risk of onset.

Discussion

This is the first systematic review that has synthesised evidence on the risk for the onset of musculoskeletal pain in children and adolescents with sleep problems (quality, quantity) or day-time tiredness. The main finding of this review is that sleep quality, sleep quantity and day-time tiredness are not risk factors for the onset of musculoskeletal pain for children or adolescents. Further analysis at each body site revealed similar trends of no effect or inconsistent results, though some mixed findings suggest some risk for particular body regions (e.g. neck pain onset) dependent on gender.

Comparison with existing literature

Findings from this review are in contrast with those reported in adult populations. A recent review [16] has investigated the prospective and experimental research on the relationship between sleep and pain. Within that review findings from two prospective studies conducted in adult populations are reported and both studies show that individuals with sleep problems were at higher risk of developing fibromyalgia [43] or chronic (both widespread and regional) musculoskeletal pain [44] at follow-up. The results from adult population studies oppose the findings within this current review, which suggest no or little risk for children and adolescents. Examination of the literature on adults does shows that most reported evidence of risk are for chronic musculoskeletal outcomes or for widespread pain, which is suggestive of a higher level of pain severity or severity threshold (i.e. chronic pain samples and those with widespread pain often report higher levels of pain severity [45]), and secondly outcomes such as chronic pain may include populations where pain was present before the measurement of outcome and therefore potentially enable a reciprocal relationship to establish between sleep and pain [46,47]. Taking a wider epidemiological view, there is estimations of 75-80% lifetime prevalence of musculoskeletal pain in adult populations [48],

and therefore it may be difficult to assert within those populations that this would be their first ever experience of musculoskeletal pain as they may have experienced musculoskeletal pain before. If this is the case, the well reported reciprocal effects between sleep and pain (once both are established) may partly explain effects within adults [16,48]. For example, evidence suggests that potential changes to dopaminergic and opiodergic signalling can occur in the presence of sleep and pain, which may then influence subsequent pain episodes [16]. This potential difference in case mix may explain the difference in the results found in children and adolescents (who generally would be less likely than adults to have already experienced musculoskeletal pain). Though, prospective studies carried out within adult populations have shown that individuals with sleep problems were still at higher risk for the onset of chronic musculoskeletal pain after adjustment for baseline pain [5,49]. This may suggest that previous reciprocal relationships between sleep and pain are not factors in new onset but perhaps factors for persistence. This viewpoint on the influence of sleep on pain persistence highlights an important limitation within the current literature in this area, namely the need to measure the relationship between pain and sleep more frequently. Findings of adult research, investigating the day-to-day relationship between sleep and pain, show that sleep is a reliable predictor of subsequent pain, but pre-sleep pain has less of an effect, and that there is variation in pain severity on a day to day basis [50]. At present it is not clear whether we can understand the relationships between pain and sleep in children and adolescents in a "like for like" comparison to findings in the adult literature, until similar sophisticated measurement and study quality is obtained (e.g. frequent measurement stages, objective measures such as polysomnography, actigraphy [51] or sleep diaries [50]).

Analysis of study heterogeneity

The overall trend found within this review is that there is no effect of sleep problems on musculoskeletal pain onset. However, some inconsistencies and opposing results are reported when examining different pain sites, and heterogeneity may explain some of this variation. Different measures were used for both exposure and outcome between studies (See table 5) and this made comparison between studies complex. For example, in one [34] of the two studies that reported a significant finding between low sleep quality and day-time tiredness and the onset of neck pain, sleep quality and day-time tiredness were part of a variable that also included other physical and psychological symptoms. Therefore the effect reported may be also attributable to the other symptoms included in the variable, this limits the strength of this finding somewhat. Also, in one [41] of the two studies that provided moderate evidence of risk for the onset of general musculoskeletal pain in children with low sleep quantity, the measure of pain also included abdominal pain, headaches and/or pains in other parts of the body occurring at least weekly. This highlights the difficulty in the ability to distinguish musculoskeletal pain from other type of pain with this measure, which may have potentially influenced the reported evidence of risk.

Strengths and weaknesses of the study

Five databases were systematically searched without any language or time restrictions, to encompass the widest range of literature. Also, the use of a broad search (non-restrictive search without specific sleep search terms) and a more specific search enabled the identification of additional literature (four articles were identified in the broad search, two in the specific search and seven in both searches). Another strength is the focus solely on studies employing prospective designs. This produces the best evidence as it provides estimates of incidence, enables the assessment of temporal sequence between exposure and the outcome,

and avoids recall bias that may occur with retrospective or case-control studies [52]. The review also incorporated the use of levels of evidence, basing conclusions not only on results presented but also the quality of studies, to account for the potential effect of bias. However, it is recognised that use of total score for study quality can be overly blunt, and does not account for key elements of bias within each study (e.g. response rate) and we have attempted to overcome these issues where possible. For example, two studies had a dropout rate of over 20%, which may raise the possibility of bias from loss to follow-up. However, in one of these studies, sensitivity analyses were carried out to compare the baseline characteristics of the subjects who dropped out the study to those who completed the study, and results commented [34]. There are some limitations. First, no one study used objective measures of sleep (e.g. polysomnography, actigraphy) [51], which may have provided more accurate results, and the variation of definitions used for both the exposure and musculoskeletal pain outcome in the included studies limited the comparison and analysis. Second, some flaws were present in the design of the studies. In one study [38] pain was only measured at follow-up, thus limiting the inference of causality. In another study [40], the group with new-onset musculoskeletal pain consisted of children presenting to emergency medicine, and this may have represented a more severe cohort. Thirdly, identified studies were predominantly from developed countries (i.e. no studies from South America, Africa, or Asia were retrieved), so the results may be not generalizable to different social/cultural environments. Studies that do not find evidence of risk and papers in a language other than English are less likely to be published or be within the databases searched (grey literature). Whilst we translated three papers produced in German, which did not meet the inclusion criteria, we were unable to translate six additional papers (1 paper in Swedish, 1 paper in Norwegian, 1 paper in Czech, 1 paper in Finnish and 2 papers in Chinese) and so they were excluded. Though the reference lists of the included papers were searched, other alternative sources such as registers for unpublished studies and

PhD thesis were not explored. Therefore publication bias is a possible limitation (although no language restrictions were applied). Finally, due to the heterogeneity in both exposure and outcome measure (see table 5), it was not possible to perform a meta-analysis, which would have provided an accurate estimate of the effect of sleep problems on the onset of musculoskeletal pain.

Implications for clinical practice and future research

This systematic review provides evidence that children and adolescents with sleep problems are not at higher risk for the onset of musculoskeletal pain. These findings are opposed to the findings within the adult population literature, and this paper argues that a potential reason is that in adults there may be an already established sleep/pain relationship due to prior experience of pain, or that alternatively such findings are due to the measures and populations used within the studies. Therefore whilst this paper would not recommend routine screenings of sleep problems in children/adolescents as a way of identifying at risk individuals, it may be important to monitor children with both pain and sleep problems, as once both are established may make treatment more challenging. This review does report some subgroups more at risk of developing musculoskeletal pain (e.g. girls with low sleep quality and day-time tiredness more at risk of the onset of neck pain). This paper recommends more research on at risk subgroups to understand potential mechanisms and this would lay the foundation for designing interventions on the direct treatment of sleep problems to avert musculoskeletal outcomes. For example, there may be a place for routine sleep screenings in some subgroups of children who could benefit from education on sleep hygiene to reduce risk of musculoskeletal pain problems [41]. Future research recommendations are a need to explore potential risk in sub-groups of children and adolescents and the need for more objective measures (e.g. polysomnography, actigraphy) [51] to be used in future prospective studies on

sleep and musculoskeletal pain onset in children. Also, given the potential daily variation of pain [50], there may be scope to perform longitudinal studies in children and adolescents using both sleep and pain diaries.

Conclusions

In conclusion, this systematic review has shown no or little risk of musculoskeletal pain onset preceded by sleep problems in children and adolescents, although some subgroups at heightened risk were identified. Given the heterogeneity of the measures used among studies, the use of more objective measures for both sleep and musculoskeletal pain is recommended. Future research exploring the daily variation in the relationship between sleep and pain may help to shed further light on the effect of sleep problems on the onset of musculoskeletal pain in children.

Acknowledgments

We thank Mrs. Jo Jordan, Ms. Opeyemi Babatunde and Ms. Nadia Corp for their support in developing the search strategy for the systematic review. This study was supported by the Keele University ACORN funding.

Disclosure statement

Mr. Andreucci has nothing to disclose.

References

1. Murray CJ, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet (London, England)*. 2012;380(9859):2197–2223. doi:10.1016/S0140-6736(12)61689-4 [doi].

2. Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet (London, England)*. 2012;380(9859):2163–2196. doi:10.1016/S0140-6736(12)61729-2 [doi].

3. Gaskin DJ, Richard P. The economic costs of pain in the United States. *J Pain*. 2012;13(8):715–724. doi:10.1016/j.jpain.2012.03.009.

4. Breivik H, Eisenberg E, O'Brien T. The individual and societal burden of chronic pain in Europe: the case for strategic prioritisation and action to improve knowledge and availability of appropriate care. *BMC Public Health*. 2013;13:1229. doi:10.1186/1471-2458-13-1229 [doi].

5. Gupta A, Silman AJ, Ray D, et al. The role of psychosocial factors in predicting the onset of chronic widespread pain: results from a prospective population-based study. *Rheumatology (Oxford)*. 2007;46(4):666–671. doi:kel363 [pii].

6. Hunfeld JA, Perquin CW, Duivenvoorden HJ, et al. Chronic pain and its impact on quality of life in adolescents and their families. *J Pediatr Psychol*. 2001;26(3):145–153. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=11259516.

7. Brattberg G. The incidence of back pain and headache among Swedish school children. *Qual Life Res*. 1994;3(Suppl 1):S27–31. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med3&AN=7866367.

8. Brink Y, Crous LC, Louw QA, Grimmer-Somers K, Schreve K. The association between postural alignment and psychosocial factors to upper quadrant pain in high school students: A prospective study. *Man Ther*. 2009;14(6):647–653. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed9&AN=2009576583.

9. Feldman DE, Rossignol M, Shrier I, Abenhaim L. Smoking. A risk factor for development of low back pain in adolescents. *Spine (Phila Pa 1976)*. 1999;24(23):2492–2496. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=10626312.

10. Gill DK, Davis MC, Smith AJ, Straker LM. Bidirectional relationships between cigarette use and spinal pain in adolescents accounting for psychosocial functioning. *Br J Health Psychol*. 19(1):113–131. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc11&AN=2014-00741-008.

11. Dunn KM, Hestbaek L, Cassidy JD. Low back pain across the life course. *Best Pract Res Rheumatol*. 2013;27(5):591–600. doi:10.1016/j.berh.2013.09.007 [doi].

12. Dunn KM, Jordan KP, Mancl L, Drangsholt MT, Le Resche L. Trajectories of pain in adolescents: a prospective cohort study. *Pain*. 2011;152(1):66–73.

doi:10.1016/j.pain.2010.09.006 [doi].

13. Pinheiro MB, Ferreira ML, Refshauge K, et al. Symptoms of Depression and Risk of New Episodes of Low Back Pain: A Systematic Review and Meta-Analysis. *Arthritis Care Res (Hoboken)*. 2015;67(11):1591–1603. doi:10.1002/acr.22619 [doi].

14. Ramond A, Bouton C, Richard I, et al. Psychosocial risk factors for chronic low back pain in primary care--a systematic review. *Fam Pract*. 2011;28(1):12–21. doi:10.1093/fampra/cmq072 [doi].

15. Taylor JB, Goode AP, George SZ, Cook CE. Incidence and risk factors for first-time incident low back pain: a systematic review and meta-analysis. *Spine J*. 2014;14(10):2299–2319. doi:10.1016/j.spinee.2014.01.026 [doi].

16. Finan PH, Goodin BR, Smith MT. The association of sleep and pain: An update and a path forward. *J Pain*. 2013;14(12):1539–1552.

17. Valrie CR, Bromberg MH, Palermo T, Schanberg LE. A systematic review of sleep in pediatric pain populations. *J Dev Behav Pediatr*. 2013;34(2):120–8. doi:10.1097/DBP.0b013e31827d5848.

18. Hill JJ, Keating JL. Risk factors for the first episode of low back pain in children are infrequently validated across samples and conditions: a systematic review. *J Physiother*. 2010;56(4):237–244.

19. King S, Chambers CT, Huguet A, et al. The epidemiology of chronic pain in children and adolescents revisited: a systematic review. *Pain*. 2011;152(12):2729–2738. doi:10.1016/j.pain.2011.07.016 [doi].

20. Lardon A, Leboeuf-Yde C, Le Scanff C, Wedderkopp N. Is puberty a risk factor for

back pain in the young? a systematic critical literature review. *Chiropr Man Therap*. 2014;22(1):27. doi:10.1186/s12998-014-0027-6.

21. Paulis WD, Silva S, Koes BW, Van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: A systematic review. *Obes Rev*. 2014;15(1):52–67. doi:10.1111/obr.12067.

22. Prins Y, Crous L, Louw Q a. A systematic review of posture and psychosocial factors as contributors to upper quadrant musculoskeletal pain in children and adolescents. *Physiother Theory Pract*. 2008;24(4):221–242. doi:10.1080/09593980701704089.

23. Huguet A, Tougas ME, Hayden J, McGrath PJ, Stinson JN, Chambers CT. A Systematic Review with Meta-analysis of Childhood and Adolescent Risk and Prognostic Factors for Musculoskeletal Pain. *Pain*. 2016;157:1. doi:10.1097/j.pain.0000000000000685.

24. Stanford EA, Chambers CT, Craig KD. A normative analysis of the development of pain-related vocabulary in children. *Pain*. 2005;114(1-2):278–284. doi:S0304-3959(04)00616-5 [pii].

25. von Baeyer CL. Children's self-reports of pain intensity: scale selection, limitations and interpretation. *Pain Res Manag*. 2006;11(3):157–162.

26. World Health Organization. WHO - Definition of key terms.

27. Mallen CD, Peat G, Thomas E, Dunn KM, Croft PR. Prognostic factors for musculoskeletal pain in primary care: a systematic review. *Br J Gen Pract*. 2007;57(541):655–661.

28. Shraim M, Mallen CD, Dunn KM. GP consultations for medically unexplained

physical symptoms in parents and their children: a systematic review. *Br J Gen Pract*. 2013;63(610):e318–25. doi:10.3399/bjgp13X667178 [doi].

29. D S, S S, W R. *How to Practice and Teach EBM*.; 2000.

30. Ariëns GAM, Van Mechelen W, Bongers PM, Bouter LM, Van Der Wal G. Physical risk factors for neck pain. *Scand J Work Environ Heal*. 2000;26(1):7–19. doi:10.5271/sjweh.504.

31. Auvinen JP, Tammelin TH, Taimela SP, et al. Is insufficient quantity and quality of sleep a risk factor for neck, shoulder and low back pain? A longitudinal study among adolescents. *Eur Spine J*. 2010;19(4):641–649. doi:10.1007/s00586-009-1215-2 [doi].

32. Jussila L, Paananen M, Nayha S, et al. Psychosocial and lifestyle correlates of musculoskeletal pain patterns in adolescence: A 2-year follow-up study. *Eur J Pain*. 2014;18(1):139–146. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc11&AN=2013-43374-016.

33. Paananen M V, Taimela SP, Auvinen JP, et al. Risk factors for persistence of multiple musculoskeletal pains in adolescence: A 2-year follow-up study. *Eur J Pain*. 14(10):1026–1032. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc7&AN=2010-23980-009.

34. Ståhl M, Kautiainen H, El-Metwally A, et al. Non-specific neck pain in schoolchildren: Prognosis and risk factors for occurrence and persistence. A 4-year follow-up study. *Pain*. 2008;137(2):316–322. doi:10.1016/j.pain.2007.09.012.

35. Mikkelsson M, Sourander A, Salminen JJ, Kautiainen H, Piha J. Widespread pain and

neck pain in schoolchildren. A prospective one-year follow-up study. *Acta Paediatr Int J Paediatr*. 1999;88(10):1119–1124. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed4&AN=1999363928.

36. Mikkelsson M, ElMetwally A, Kautiainen H, Auvinen A, Macfarlane GJ, Salminen JJ. Onset, prognosis and risk factors for widespread pain in schoolchildren: A prospective 4-year follow-up study. *Pain*. 2008;138(3):681–687. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc6&AN=2008-12957-005.

37. El-Metwally A, Salminen JJ, Auvinen A, MacFarlane G, Mikkelsson M. Risk factors for development of non-specific musculoskeletal pain in preteens and early adolescents: A prospective 1-year follow-up study. *BMC Musculoskelet Disord*. 2007;8. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed8&AN=2007286187.

38. Harrison L, Wilson S, Munafo MR. Exploring the associations between sleep problems and chronic musculoskeletal pain in adolescents: A prospective cohort study. *Pain Res Manag*. 2014;19(5):e139–e145. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed12&AN=2014825638.

39. Szpalski M, Gunzburg R, Balague F, Nordin M, Melot C. A 2-year prospective longitudinal study on low back pain in primary school children. *Eur Spine J*. 2002;11(5):459–464. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=

emed5&AN=2002383790.

40. Lewandowski Holley A, Wilson AC, Cho E, Palermo TM. Clinical Phenotyping of Youth With New-Onset Musculoskeletal Pain. *Clin J Pain*. 2016;00(00):1. doi:10.1097/AJP.0000000000000371.

41. Incledon E, O'Connor M, Giallo R, Chalkiadis GA, Palermo TM. Child and Family Antecedents of Pain During the Transition to Adolescence: A Longitudinal Population-based Study. *J Pain*. 2016;17(11):1174–1182. doi:http://dx.doi.org/10.1016/j.jpain.2016.07.005.

42. Jones GT, Silman AJ, Macfarlane GJ. Predicting the onset of widespread body pain among children. *Arthritis Rheum*. 2003;48(9):2615–2621. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed6&AN=2003377470.

43. Mork PJ, Nilsen TI. Sleep problems and risk of fibromyalgia: longitudinal data on an adult female population in Norway. *Arthritis Rheum*. 2012;64(1):281–284. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=22081440.

44. Nitter AK, Pripp AH, Forseth K. Are sleep problems and non-specific health complaints risk factors for chronic pain? A prospective population-based study with 17 year follow-up. *Scand J Pain*. 2012;3(4):210–217. doi:10.1016/j.sjpain.2012.04.001.

45. Vasseljen O, Woodhouse A, Bjørngaard JH, Leivseth L. Natural course of acute neck and low back pain in the general population: The HUNT study. *Pain*. 2013;154(8):1237–1244. doi:10.1016/j.pain.2013.03.032.

46. Bergman S. A General Practice Approach To Management of Chronic Widespread Musculoskeletal Pain and Fibromyalgia. *Rheum Dis*. 2005;4.

47. Larsson B, Björk J, Börsbo B, Gerdle B. A systematic review of risk factors associated with transitioning from regional musculoskeletal pain to chronic widespread pain. *Eur J Pain*. 2012;16(8):1084–93. doi:10.1002/j.1532-2149.2012.00117.x.

48. Kelly GA, Blake C, Power CK, O'keeffe D, Fullen BM. The association between chronic low back pain and sleep: a systematic review. *Clin J Pain*. 2011;27(2):169–81. doi:10.1097/AJP.0b013e3181f3bdd5.

49. McBeth J, Lacey RJ, Wilkie R. Predictors of new-onset widespread pain in older adults: results from a population-based prospective cohort study in the UK. *Arthritis Rheumatol (Hoboken, NJ)*. 2014;66(3):757–767. doi:10.1002/art.38284 [doi].

50. Tang NKY, Goodchild CE, Sanborn AN, Howard J, Salkovskis PM. Deciphering the temporal link between pain and sleep in a heterogeneous chronic pain patient sample: A multilevel daily process study. *Sleep*. 2012;35(5):675–87A. doi:10.5665/sleep.1830.

51. Meltzer LJ, Walsh CM, Traylor J, Westin AML. Direct comparison of two new actigraphs and polysomnography in children and adolescents. *Sleep*. 2012;35(1):159–66. doi:10.5665/sleep.1608.

52. Delgado-Rodriguez M, Llorca J. Bias. *J Epidemiol Community Health*. 2004;58(8):635–641. doi:10.1136/jech.2003.008466 [doi].

Reviewer information page

Number of tables: 5

Number of figures: 1

Abstract word count: 234

Statement of significance word count: 120

Word count: 4,15936

Are sleep problems a risk factor for the onset of musculoskeletal pain in children and adolescents? A systematic review.

Authors: Alessandro Andreucci[a], Paul Campbell PhD[a], Kate M Dunn PhD[a]

Authors' affiliation: [a] Arthritis Research UK Primary Care Centre, Research Institute for Primary Care and Health Sciences, Keele University, UK

Institution where the work was performed: Arthritis Research UK Primary Care Centre, Research Institute for Primary Care and Health Sciences, Keele University, UK

Corresponding author:

Alessandro Andreucci, Arthritis Research UK Primary Care Centre, Research Institute for Primary Care and Health Sciences, Keele University, Staffordshire ST5 5BG, UK. +44 (0) 1782 734889 a.andreucci@keele.ac.uk

Corresponding author's current email: a.andreucci@keele.ac.uk

Abstract

Study objectives

Musculoskeletal pain is a major burden on society. Adults with sleep problems are at higher risk for musculoskeletal pain onset, but there is no evidence for this relationship in children and adolescents. This study aimed to systematically review prospective studies on the risk for musculoskeletal pain onset in children and adolescents with sleep problems.

Methods

Five databases (MEDLINE, PsycINFO, AMED, EMBASE, HMIC) were systematically searched to identify prospective studies that investigated if children and adolescents (aged 6-19 years) with sleep problems are at higher risk for musculoskeletal pain onset. Included studies were assessed for study quality and a best evidence synthesis was carried out on extracted data.

Results

Thirteen prospective studies were identified. Overall, evidence indicates that sleep problems (quality, quantity, day-time tiredness) are not risk factors for musculoskeletal pain onset. Further analysis on specific body regions show strong evidence that sleep problems are a risk factor for neck pain onset (only in girls), and strong evidence that sleep problems are not a risk factor for the onset of widespread pain.

Conclusions

Overall sleep problems are not a risk factor for musculoskeletal pain onset in children and adolescents. Increased risk was found for some specific body regions and sub-groups but the evidence base was less strong and generally inconsistent. This review found a lack of quality in research methodology compared to research in adults and further research with improved methodology is required.

Keywords:

Pain
Sleep
Pediatrics - Adolescent
Pediatrics - Sleep and Arousal
Public Health
Sleep Hygiene
Systematic review

Statement of significance

Musculoskeletal pain is a major burden on society and there is a need to identify risk factors for the onset of musculoskeletal pain. Research carried out in adults has shown a link between sleep problems and the onset of musculoskeletal pain, but evidence is lacking about this relationship in younger populations. This is the first systematic review that has summarized prospective studies on the risk between sleep problems and the onset of musculoskeletal pain in children and adolescents. Our findings show that sleep problems are not risk factors for musculoskeletal pain onset in children and adolescents, although further analysis did reveal sub-groups at some increased risk. Further research is now required to understand why particular sub-groups are at increased risk.

Introduction

Musculoskeletal pain is a major concern worldwide. In developed countries, the proportion of the global disability-adjusted life years (DALYs) due to musculoskeletal pain is 13% [1], and musculoskeletal conditions rank first, fourth and sixth among the top 10 diseases in terms of global years lived with disability [2]. Musculoskeletal conditions have a significant economic burden, with the mean cost of chronic pain estimated at $560-635 billion in the US (2010 figures) [3] and 3-10% of gross domestic product in Europe in 2008 [4]. Consequences of musculoskeletal pain include psychological distress, disability, limitation of activities, limitation in social participation and burden on the family [5,6]. Individuals who experience musculoskeletal pain during adolescence are more likely to have musculoskeletal pain in adulthood [7–10]. Studies investigating the course of pain over time, report that lifelong patterns of musculoskeletal pain that can appear stable and unchanging in adulthood, may begin in childhood [11,12]. However, to date, research on the epidemiology of musculoskeletal conditions has focused mainly on adult populations [11,13–15], which are likely to identify risk factors for new episodes of musculoskeletal pain (often confounded by the experience of previous pain) rather than true risk factors for the first initial onset of musculoskeletal pain. Gaining knowledge of the factors predictive of musculoskeletal pain in childhood is important as such knowledge could provide information on potential targets for intervention to prevent or reduce risk for child musculoskeletal pain onset, and potentially avert or alter the trajectory of long-term painful musculoskeletal conditions among adults. One specific area with growing research interest and evidence from research on adults with musculoskeletal pain is the role of sleep, more specifically sleep problems (quality, quantity, resulting day time tiredness), as both a risk factor and prognostic factor [16]. Recent reviews, both in adult and child populations, show that sleep problems are common in those with pain [16,17] and that in adults sleep problems are more likely to precede pain (risk of new episodes of pain) in contrast to

pain as a predictor of sleep problems [16]. Previous systematic reviews [18–23] on risk factors for musculoskeletal pain onset in children and adolescents have been carried out, but have not yet considered the potential role of sleep problems as a risk factor for musculoskeletal pain onset in these populations. The aim of this systematic review is to evaluate evidence from prospective studies that investigated if children and adolescents with sleep problems are at higher risk for the onset of musculoskeletal pain.

Methods

Selection of the literature

A systematic search of the literature was carried out by one reviewer (AA) with the support of another reviewer (PC). Two approaches were used to search the literature. A broad search was carried out on risk factors for musculoskeletal pain onset in general in order to retrieve articles that may report data on sleep where sleep was not the main focus of the study. A more specific search was also carried out using appropriate sleep terms to increase specificity. Databases were searched from inception to the 8th November 2016. The following databases were searched through the OVID and NSH HDAS interfaces: Medline, PsycINFO, Allied and Complementary Medicine Database (AMED), Excerpta Medica dataBASE (EMBASE), and Health Management Information Consortium (HMIC). A combination of keywords for each database (see appendix 1) was used to retrieve the papers. Keywords were identified by the principal investigator (AA) after consulting similar systematic reviews and discussion with other reviewers (PC, KD). An additional search was employed by consulting local experts (e.g. accessing and searching personal databases of senior colleagues within the Research Institute, contacting other research experts within the field of childhood musculoskeletal pain), as well as consulting previous relevant reviews in adult populations.

Inclusion/exclusion criteria

Studies had to report data on musculoskeletal pain presence as the outcome and use a prospective design conducted in general population, school or primary care settings, in order to retrieve results that were generalizable to the overall population. Studies had to include individuals aged 6 to 19 years; this age criteria was chosen as the age of six has been reported to be the starting point for children to use the word “pain” and age nineteen is defined by the World Health Organization as the start of adulthood [24–26]. Articles were considered regardless

of the language, and date of publication in order to minimise publication bias. Studies were not included if they had a sample size ≤30 as they provide unreliable risk estimates, and studies were not included if they did not report separate data on children or adolescents. Randomized controlled trials (RCTs) were excluded as their focus is on intervention not observation, and RCTs often employ more stringent selection criteria which can compromise generalisability. Studies of populations with specific diseases or conditions where pain is assessed and reported but is a result of the disease or underlying condition (e.g. cancer pain), were also excluded, as well as studies where translation was not possible.

Selection process

All the titles and abstracts of papers identified through the search process were checked to include potentially relevant studies by two authors of the review team (AA, PC). The two authors randomly checked 20% of each other's assigned titles and abstract to ensure reliability, similar checks were also carried out on the full-text papers. In the case of disagreement or inconsistency between reviewers for inclusion of a paper, the third reviewer (KD) was consulted and consensus achieved.

Data extraction

Data were extracted by the first reviewer (AA) using a standardised data extraction form (Appendix 2). Random samples of 20% of the full-texts were cross-checked by the second reviewer (PC) in order to assess consistency in the extraction process, and any disagreements were resolved through discussion and consultation with the third reviewer (KD).

Quality assessment

The assessment of study quality was carried out using a structured assessment tool. This tool was chosen based on previous systematic reviews with a similar focus to this current review (prospective studies, focus on musculoskeletal pain as outcome [27,28]). The tool reports on 15

items relative to both internal and external validity [27,28]. Each item was assessed to check if the criteria was met or not and a score was given (table 1). This enabled the classification of articles according to methodological quality, and to weight the results of the studies (best evidence synthesis). Each item was scored positive (+) if present and a point awarded, negative (–) if absent (no point was given), or (na) if not applicable (no point was given). It follows that the highest possible score was 15. For ease of interpretation the quality of the articles was rated in three categories: 'high' (11-15 items); 'moderate' (6-10 items), and 'low' (1-5 or no items).

Analysis of risk

For each finding, three possible effects were reported: significant effect (+, if significant effect reported), no effect (x, no significant effect present), mixed (#, where significant and non-significant effects are reported for the same body site, e.g. stratified analysis on gender where an effect is reported for males but not females, or different levels of exposure e.g. mixed findings from low, medium, high levels of sleep problems). Each effect was counted within an overall assessment of risk on onset of musculoskeletal pain (i.e. all findings from all body sites). Secondary analysis was carried out stratified by body pain sites reported (back pain, neck pain, shoulder pain, general musculoskeletal pain, widespread pain). A level of evidence approach was used for the analysis (see Table 2) where the combined evidence is assessed in terms of the direction of effect, and the quality of each individual study [29,30]. The levels of evidence analysis applies greater weighting to those findings of high quality. As Table 2 outlines, strength of evidence is determined by the consistency of direction of findings and study quality. Evidence of risk was explored across all body sites to give an overall estimation of consistency, and then for each body site in turn. The risk for the onset of musculoskeletal pain was reported using definitive categories of sleep problems retrieved from the review data (sleep quality, sleep quantity and day time tiredness). Information on effect size (e.g. odds ratio, relative risk) was reported if presented in the results of each paper.

Results

Study selection

The broad electronic search (all risk factors regardless of type) yielded a total of 35,167 references. After screening of titles and abstracts, 156 full-text articles were assessed for eligibility, of which 145 were excluded because they did not meet the inclusion criteria (see appendix 3). Finally, 11 studies met the eligibility criteria and were included. The second specific search (using specific sleep terms) yielded 3,065 references. After screening of titles and abstracts, ten full-text articles were assessed for eligibility, of which eight were excluded because they did not meet the inclusion criteria and two articles selected for inclusion. These two searches led to the inclusion of 13 articles overall (Figure 1). Seven articles were identified in both searches; four were identified from the broad search, and two within the specific sleep term search.

Quality and characteristics of the studies

Table 3 describes the quality and characteristics of the included studies. Overall, eight articles (62%) out of 13 were defined as high quality and five (38%) as medium quality; no studies were included in the low quality criteria. Included studies were from six different countries with a total population of 18,888 (range from 191 to 4161 individuals). The samples were recruited from schools or school settings in six studies, from the general population in six articles and from a primary care/hospital interface setting in one study. Some cohorts were reported in more than one article. Three studies were drawn from the Northern Finland Birth Cohort [31–33], while four studies were drawn from a cohort in southern Finland [34–37].

Evidence

Sleep quality

Overall ten findings were reported, with two findings [34,38] showing that children with poor sleep quality are significantly at higher risk (both findings in the direction of poor sleep quality predictive of musculoskeletal pain), one finding [31] showing mixed evidence, and seven findings [31,35–37,39,40] showing no significant higher risk (Please see Table 4 for a full description of effect sizes). When considering only high quality evidence, similar rates are found (high quality findings; two studies [34,38] reported significant higher risk, one study [31] mixed, five findings [31,35–37] no higher risk). Overall this indicates a trend toward strong evidence of no effect of poor sleep quality as a risk factor for the onset of musculoskeletal pain. Further inspection at each body site was carried out. For back pain onset there were two non-significant effects. One was from a medium quality study [39] (estimate not provided in the multivariate analysis) and one was from a high quality study [31] (Boys adjusted Odds Ratios: 1.14, 95% Confidence Interval 0.66, 2.00; Girls adj. OR: 1.48, 95% CI 0.97, 2.24), resulting in a moderate evidence of no higher risk. For neck pain onset the findings shows one mixed [31] (Boys adj. OR: 0.83, 95% CI 0.48, 1.44; Girls adj. OR: 1.67, 95% CI 1.00, 2.78) and one significant effect [34] (Boys adj. OR: 1.25, 95% CI 1.11, 1.41; Girls adj. OR: 1.14, 95% CI 1.03, 1.26), resulting in strong evidence that girls with low sleep quality are at higher risk for neck pain onset, but inconsistent evidence of risk in boys. Shoulder pain shows a non-significant effect in one high quality study [31] (Boys adj. OR: 1.32, 95% CI 0.77, 2.25; Girls adj. OR: 1.47, 95% CI 0.91, 2.39), indicating weak evidence of no higher risk. For general musculoskeletal pain onset there are two findings (one high quality). Both report no significant effects. In the high quality study [37] no one of the ORs provided was significant (difficulty falling asleep and non-traumatic musculoskeletal pain Adj. OR: 1.48, 95% CI 0.99, 2.23; waking up during nights and non-traumatic musculoskeletal pain Adj. OR: 1.31,

95% CI 0.82, 2.08; difficulty falling asleep and traumatic musculoskeletal pain Adj. OR: 1.47, 95% CI 0.67, 3.24; waking up during nights and traumatic musculoskeletal pain Adj. OR: 1.64, 95% CI 0.70, 3.85), and. tThe medium quality study [40] reported no statistically significant difference in the sleep quality score between children with new-onset pain (Mean 3.96, Standard Deviation 0.58) and healthy children (Mean 4.13, SD 0.69). This resulted in a moderate evidence of no risk of musculoskeletal pain onset in children with low sleep quality. For widespread pain onset, three high quality findings are reported. While one study [38] reported significant findings (problems with hypersomnolence Adj. OR: 2.76, 95% CI 1.05, 7.25; Waking up 2-3 times/ > 3 times a night Adj. OR: 2.13, 95% CI 1.22, 3.74), two studies [35,36] reported no significant effects (difficulty falling asleep [36] Adj. OR: 1.2, 95% CI 0.9, 1.7; waking up during nights [36] Adj. OR: 1.1, 95% CI 0.8, 1.6; Higher sleep score [35] Adj. OR: 1.23, 95% CI 0.98, 1.54) indicating inconclusive evidence.

Sleep quantity

Overall eight findings were reported with two of those findings [7,41] (medium quality) showing a significant effect (both findings in the direction of low sleep quantity predictive of musculoskeletal pain), two [31,32] (high quality) showing mixed evidence, and four [31,33,38] (one medium, three high quality) showing no significant effect. This indicates inconsistent evidence, though considering only high quality evidence suggests a trend toward no higher risk for musculoskeletal pain onset in children with low sleep quantity. Inspection at each body site revealed for back pain onset, two study findings, one medium quality [7], indicating a significant effect (those with trouble getting enough sleep had more pain but no estimate was reported), and one high quality [31] reporting a mixed effect. Closer inspection of this mixed result showed no higher risk in girls (Sleeping 7 hour or less a day adj. OR: 1.45, 95% CI 0.96, 2.19; sleeping 9-10 hours a day adj. OR: 0.86, 95% CI 0.58, 1.27; sleeping 10 hours or more a day adj. OR: 0.87, 95% CI 0.52, 1.47) but higher risk in boys (albeit within only one

sleep quantity category~~); 9-10 hours a day adj. OR: 1.59, 95% CI 1.03, 2.44; but not for sleeping 7 hours or less a day adj. OR: 1.42, 95% CI 0.86, 2.33 or sleeping 10 hours or more a day adj. OR: 0.93, 95% CI 0.56, 1.54)~~. Overall this indicates inconsistent evidence of the effect of sleep quantity on back pain onset. Both neck pain onset ~~(Girls: Sleeping 7 hour or less a day adj. OR: 1.44, 95% CI 0.90, 2.32; sleeping 9-10 hours a day adj. OR: 1.02, 95% CI 0.66, 1.57; sleeping 10 hours or more a day adj. OR: 1.55, 95% CI 0.84, 2.87; Boys: Sleeping 7 hour or less a day adj. OR: 1.40, 95% CI 0.86, 2.30; sleeping 9-10 hours a day adj. OR: 0.98, 95% CI 0.64, 1.50; sleeping 10 hours or more a day adj. OR: 0.86, 95% CI 0.52, 1.44)~~, and shoulder pain onset ~~(Girls: Sleeping 7 hour or less a day adj. OR: 1.36, 95% CI 0.85, 2.17; sleeping 9-10 hours a day adj. OR: 1.17, 95% CI 0.76, 1.81; sleeping 10 hours or more a day adj. OR: 1.08, 95% CI 0.61, 1.93; Boys: Sleeping 7 hour or less a day adj. OR: 1.05, 95% CI 0.66, 1.69; sleeping 9-10 hours a day adj. OR: 0.84, 95% CI 0.55, 1.29; sleeping 10 hours or more a day adj. OR: 0.85, 95% CI 0.51, 1.39)~~ show no significant higher risk from one high quality study [31] indicating weak evidence of no higher risk. Two findings are reported for general musculoskeletal pain onset with one high quality study [32] reporting mixed findings ~~(boys with shorter sleeping time were more likely to be in a cluster of pain, P = 0.001, but not girls, P = 0.100)~~ and one medium quality [41] study reporting a significant effect ~~(Adj. OR: 1.86, 95% CI 1.16, 2.97)~~. This indicates a moderate evidence of higher risk in boys, but inconsistent evidence in girls. For widespread pain two studies (one high quality [38], one medium quality [33]) report no significant higher risk. ~~(High quality study [38]: rarely/never enough sleep adj. OR: 1.20, 95% CI 0.55, 2.62; Medium quality study [33], boys: sleeping < 7 hours a day adj. OR: 1.15, 95% CI 0.66, 1.98; sleeping ≥ 10 hours a day adj. OR: 1.14, 95% CI 0.69, 1.88; girls: sleeping < 7 hours a day adj. OR: 0.93, 95% CI 0.54, 1.61; sleeping ≥ 10 hours a day adj. OR: 1.12, 95% CI 0.56, 2.27)~~ indicating moderate evidence that sleep quantity is not a risk factor for onset of widespread pain.

Daytime tiredness

Out of eight findings, two [34,37] (high quality) report a significant effect (both findings in the direction of daytime tiredness predictive of musculoskeletal pain), three [31] (high quality) report mixed effects, and three [36,39,42] (two high quality) report no significant effect indicating inconsistency, with a similar conclusion if only high quality evidence is considered.

Examination by body site revealed one high quality [31] study reporting mixed evidence ~~(Boys often too tired adj. OR: 1.46, 95% CI 0.61, 3.45; sometimes too tired adj. OR: 1.16, 95% CI 0.80, 1.68; Girls often too tired adj. OR: 2.42, 95% CI 1.24, 4.71; sometimes too tired adj. OR: 1.32, 95% CI 0.93, 1.85)~~, and one medium quality [39] study reporting no effect ~~(estimate not provided in the multivariate analysis)~~ for back pain onset. This indicates a moderate evidence that boys with daytime tiredness are not at higher risk for back pain onset, but an inconsistent evidence in girls. Similarly for neck pain, one high quality study [34] found a significant effect ~~(Boys Adj. OR: 1.25, 95% CI 1.11, 1.41; Girls Adj. OR: 1.14, 95% CI 1.03, 1.26)~~, and one high quality study [31] reported mixed effects ~~(Boys often too tired adj. OR 1.15, 95% CI 0.48, 2.74; sometimes too tired adj. OR 1.28, 95% CI 0.88, 1.85; Girls often too tired adj. OR 3.92, 95% CI 1.55, 9.90; sometimes too tired adj. OR 1.46, 95% CI 1.00, 2.13)~~. This indicates strong evidence that girls with daytime tiredness are at higher risk for neck pain onset, but inconsistent evidence in boys. For widespread pain, two findings [36,42] (high quality) report that children with day time tiredness are not at higher risk for widespread pain onset ~~(adj. OR: 1.1, 95% CI 0.8, 1.6 [36]; adj. OR: 1.41, 95% CI 0.84, 2.40 [42])~~, indicating strong evidence of no risk. Evidence is inconclusive for shoulder pain as there is only one (high quality) mixed finding [31] ~~(Boys often too tired adj. OR: 1.36, 95% CI 0.60, 3.13; sometimes too tired adj. OR: 1.57, 95% CI 1.10, 2.25; Girls often too tired adj. OR: 1.78, 95% CI 0.83, 3.83; sometimes too tired adj. OR: 1.21, 95% CI 0.83, 1.76)~~. For general musculoskeletal

pain onset there is weak evidence (one high quality finding [37]~~: day time tiredness and non-traumatic musculoskeletal pain Adj. OR: 1.53, 95% CI 1.03, 2.26; day time tiredness and traumatic musculoskeletal pain Adj. OR: 2.97, 95% CI 1.41, 6.26~~) that children with day time tiredness are at higher risk of onset.

Discussion

This is the first systematic review that has synthesised evidence on the risk for the onset of musculoskeletal pain in children and adolescents with sleep problems (quality, quantity) or day-time tiredness. The main finding of this review is that sleep quality, sleep quantity and day-time tiredness are not risk factors for the onset of musculoskeletal pain for children or adolescents. Further analysis at each body site revealed similar trends of no effect or inconsistent results, though some mixed findings suggest some risk for particular body regions (e.g. neck pain onset) dependent on gender.

Comparison with existing literature

Findings from this review are in contrast with those reported in adult populations. A recent review [16] has investigated the prospective and experimental research on the relationship between sleep and pain. Within that review findings from two prospective studies conducted in adult populations are reported and both studies show that individuals with sleep problems were at higher risk of developing fibromyalgia [43] or chronic (both widespread and regional) musculoskeletal pain [44] at follow-up. The results from adult population studies oppose the findings within this current review, which suggest no or little risk for children and adolescents. Examination of the literature on adults does shows that most reported evidence of risk are for chronic musculoskeletal outcomes or for widespread pain, which is suggestive of a higher level of pain severity or severity threshold (i.e. chronic pain samples and those with widespread pain often report higher levels of pain severity [45]), and secondly outcomes such as chronic pain may include populations where pain was present before the measurement of outcome and therefore potentially enable a reciprocal relationship to establish between sleep and pain [46,47]. Taking a wider epidemiological view, there is estimations of 75-80% lifetime prevalence of musculoskeletal pain in adult populations [48],

and therefore it may be difficult to assert within those populations that this would be their first ever experience of musculoskeletal pain as they may have experienced musculoskeletal pain before. If this is the case, the well reported reciprocal effects between sleep and pain (once both are established) may partly explain effects within adults [16,48]. For example, evidence suggests that potential changes to dopaminergic and opiodergic signalling can occur in the presence of sleep and pain, which may then influence subsequent pain episodes [16]. This potential difference in case mix may explain the difference in the results found in children and adolescents (who generally would be less likely than adults to have already experienced musculoskeletal pain). Though, prospective studies carried out within adult populations have shown that individuals with sleep problems were still at higher risk for the onset of chronic musculoskeletal pain after adjustment for baseline pain [5,49]. This may suggest that previous reciprocal relationships between sleep and pain are not factors in new onset but perhaps factors for persistence. This viewpoint on the influence of sleep on pain persistence highlights an important limitation within the current literature in this area, namely the need to measure the relationship between pain and sleep more frequently. Findings of adult research, investigating the day-to-day relationship between sleep and pain, show that sleep is a reliable predictor of subsequent pain, but pre-sleep pain has less of an effect, and that there is variation in pain severity on a day to day basis [50]. At present it is not clear whether we can understand the relationships between pain and sleep in children and adolescents in a "like for like" comparison to findings in the adult literature, until similar sophisticated measurement and study quality is obtained (e.g. frequent measurement stages, objective measures such as polysomnography, actigraphy [51] or sleep diaries [50]).

Analysis of study heterogeneity

The overall trend found within this review is that there is no effect of sleep problems on musculoskeletal pain onset. However, some inconsistencies and opposing results are reported when examining different pain sites, and heterogeneity may explain some of this variation. Different measures were used for both exposure and outcome between studies (See table 5) and this made comparison between studies complex. For example, in one [34] of the two studies that reported a significant finding between low sleep quality and day-time tiredness and the onset of neck pain, sleep quality and day-time tiredness were part of a variable that also included other physical and psychological symptoms. Therefore the effect reported may be also attributable to the other symptoms included in the variable, this limits the strength of this finding somewhat. Also, in one [41] of the two studies that provided moderate evidence of risk for the onset of general musculoskeletal pain in children with low sleep quantity, the measure of pain also included abdominal pain, headaches and/or pains in other parts of the body occurring at least weekly. This highlights the difficulty in the ability to distinguish musculoskeletal pain from other type of pain with this measure, which may have potentially influenced the reported evidence of risk.

Strengths and weaknesses of the study

Five databases were systematically searched without any language or time restrictions, to encompass the widest range of literature. Also, the use of a broad search (non-restrictive search without specific sleep search terms) and a more specific search enabled the identification of additional literature (four articles were identified in the broad search, two in the specific search and seven in both searches). Another strength is the focus solely on studies employing prospective designs. This produces the best evidence as it provides estimates of incidence, enables the assessment of temporal sequence between exposure and the outcome,

and avoids recall bias that may occur with retrospective or case-control studies [52]. The review also incorporated the use of levels of evidence, basing conclusions not only on results presented but also the quality of studies, to account for the potential effect of bias. However, it is recognised that use of total score for study quality can be overly blunt, and does not account for key elements of bias within each study (e.g. response rate) and we have attempted to overcome these issues where possible. For example, two studies had a dropout rate of over 20%, which may raise the possibility of bias from loss to follow-up. However, in one of these studies, sensitivity analyses were carried out to compare the baseline characteristics of the subjects who dropped out the study to those who completed the study, and results commented [34]. There are some limitations. First, no one study used objective measures of sleep (e.g. polysomnography, actigraphy) [51], which may have provided more accurate results, and the variation of definitions used for both the exposure and musculoskeletal pain outcome in the included studies limited the comparison and analysis. Second, some flaws were present in the design of the studies. In one study [38] pain was only measured at follow-up, thus limiting the inference of causality. In another study [40], the group with new-onset musculoskeletal pain consisted of children presenting to emergency medicine, and this may have represented a more severe cohort. Thirdly, identified studies were predominantly from developed countries (i.e. no studies from South America, Africa, or Asia were retrieved), so the results may be not generalizable to different social/cultural environments. Studies that do not find evidence of risk and papers in a language other than English are less likely to be published or be within the databases searched (grey literature). Whilst we translated three papers produced in German, which did not meet the inclusion criteria, we were unable to translate six additional papers (1 paper in Swedish, 1 paper in Norwegian, 1 paper in Czech, 1 paper in Finnish and 2 papers in Chinese) and so they were excluded. Though the reference lists of the included papers were searched, other alternative sources such as registers for unpublished studies and

PhD thesis were not explored. Therefore publication bias is a possible limitation (although no language restrictions were applied). Finally, due to the heterogeneity in both exposure and outcome measure (see table 5), it was not possible to perform a meta-analysis, which would have provided an accurate estimate of the effect of sleep problems on the onset of musculoskeletal pain.

Implications for clinical practice and future research

This systematic review provides evidence that children and adolescents with sleep problems are not at higher risk for the onset of musculoskeletal pain. These findings are opposed to the findings within the adult population literature, and this paper argues that a potential reason is that in adults there may be an already established sleep/pain relationship due to prior experience of pain, or that alternatively such findings are due to the measures and populations used within the studies. Therefore whilst this paper would not recommend routine screenings of sleep problems in children/adolescents as a way of identifying at risk individuals, it may be important to monitor children with both pain and sleep problems, as once both are established may make treatment more challenging. This review does report some subgroups more at risk of developing musculoskeletal pain (e.g. girls with low sleep quality and day-time tiredness more at risk of the onset of neck pain). This paper recommends more research on at risk subgroups to understand potential mechanisms and this would lay the foundation for designing interventions on the direct treatment of sleep problems to avert musculoskeletal outcomes. For example, there may be a place for routine sleep screenings in some subgroups of children who could benefit from education on sleep hygiene to reduce risk of musculoskeletal pain problems [41]. Future research recommendations are a need to explore potential risk in sub-groups of children and adolescents and the need for more objective measures (e.g. polysomnography, actigraphy) [51] to be used in future prospective studies on

sleep and musculoskeletal pain onset in children. Also, given the potential daily variation of pain [50], there may be scope to perform longitudinal studies in children and adolescents using both sleep and pain diaries.

Conclusions

In conclusion, this systematic review has shown no or little risk of musculoskeletal pain onset preceded by sleep problems in children and adolescents, although some subgroups at heightened risk were identified. Given the heterogeneity of the measures used among studies, the use of more objective measures for both sleep and musculoskeletal pain is recommended. Future research exploring the daily variation in the relationship between sleep and pain may help to shed further light on the effect of sleep problems on the onset of musculoskeletal pain in children.

Acknowledgments

We thank Mrs. Jo Jordan, Ms. Opeyemi Babatunde and Ms. Nadia Corp for their support in developing the search strategy for the systematic review. This study was supported by the Keele University ACORN funding.

Disclosure statement

Mr. Andreucci has nothing to disclose.

References

1. Murray CJ, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet (London, England)*. 2012;380(9859):2197–2223. doi:10.1016/S0140-6736(12)61689-4 [doi].

2. Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet (London, England)*. 2012;380(9859):2163–2196. doi:10.1016/S0140-6736(12)61729-2 [doi].

3. Gaskin DJ, Richard P. The economic costs of pain in the United States. *J Pain*. 2012;13(8):715–724. doi:10.1016/j.jpain.2012.03.009.

4. Breivik H, Eisenberg E, O'Brien T. The individual and societal burden of chronic pain in Europe: the case for strategic prioritisation and action to improve knowledge and availability of appropriate care. *BMC Public Health*. 2013;13:1229. doi:10.1186/1471-2458-13-1229 [doi].

5. Gupta A, Silman AJ, Ray D, et al. The role of psychosocial factors in predicting the onset of chronic widespread pain: results from a prospective population-based study. *Rheumatology (Oxford)*. 2007;46(4):666–671. doi:kel363 [pii].

6. Hunfeld JA, Perquin CW, Duivenvoorden HJ, et al. Chronic pain and its impact on quality of life in adolescents and their families. *J Pediatr Psychol*. 2001;26(3):145–153. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=11259516.

7. Brattberg G. The incidence of back pain and headache among Swedish school children. *Qual Life Res*. 1994;3(Suppl 1):S27–31. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med3&AN=7866367.

8. Brink Y, Crous LC, Louw QA, Grimmer-Somers K, Schreve K. The association between postural alignment and psychosocial factors to upper quadrant pain in high school students: A prospective study. *Man Ther*. 2009;14(6):647–653. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed9&AN=2009576583.

9. Feldman DE, Rossignol M, Shrier I, Abenhaim L. Smoking. A risk factor for development of low back pain in adolescents. *Spine (Phila Pa 1976)*. 1999;24(23):2492–2496. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=10626312.

10. Gill DK, Davis MC, Smith AJ, Straker LM. Bidirectional relationships between cigarette use and spinal pain in adolescents accounting for psychosocial functioning. *Br J Health Psychol*. 19(1):113–131. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc11&AN=2014-00741-008.

11. Dunn KM, Hestbaek L, Cassidy JD. Low back pain across the life course. *Best Pract Res Rheumatol*. 2013;27(5):591–600. doi:10.1016/j.berh.2013.09.007 [doi].

12. Dunn KM, Jordan KP, Mancl L, Drangsholt MT, Le Resche L. Trajectories of pain in adolescents: a prospective cohort study. *Pain*. 2011;152(1):66–73.

doi:10.1016/j.pain.2010.09.006 [doi].

13. Pinheiro MB, Ferreira ML, Refshauge K, et al. Symptoms of Depression and Risk of New Episodes of Low Back Pain: A Systematic Review and Meta-Analysis. *Arthritis Care Res (Hoboken)*. 2015;67(11):1591–1603. doi:10.1002/acr.22619 [doi].

14. Ramond A, Bouton C, Richard I, et al. Psychosocial risk factors for chronic low back pain in primary care--a systematic review. *Fam Pract*. 2011;28(1):12–21. doi:10.1093/fampra/cmq072 [doi].

15. Taylor JB, Goode AP, George SZ, Cook CE. Incidence and risk factors for first-time incident low back pain: a systematic review and meta-analysis. *Spine J*. 2014;14(10):2299–2319. doi:10.1016/j.spinee.2014.01.026 [doi].

16. Finan PH, Goodin BR, Smith MT. The association of sleep and pain: An update and a path forward. *J Pain*. 2013;14(12):1539–1552.

17. Valrie CR, Bromberg MH, Palermo T, Schanberg LE. A systematic review of sleep in pediatric pain populations. *J Dev Behav Pediatr*. 2013;34(2):120–8. doi:10.1097/DBP.0b013e31827d5848.

18. Hill JJ, Keating JL. Risk factors for the first episode of low back pain in children are infrequently validated across samples and conditions: a systematic review. *J Physiother*. 2010;56(4):237–244.

19. King S, Chambers CT, Huguet A, et al. The epidemiology of chronic pain in children and adolescents revisited: a systematic review. *Pain*. 2011;152(12):2729–2738. doi:10.1016/j.pain.2011.07.016 [doi].

20. Lardon A, Leboeuf-Yde C, Le Scanff C, Wedderkopp N. Is puberty a risk factor for

back pain in the young? a systematic critical literature review. *Chiropr Man Therap*. 2014;22(1):27. doi:10.1186/s12998-014-0027-6.

21. Paulis WD, Silva S, Koes BW, Van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: A systematic review. *Obes Rev*. 2014;15(1):52–67. doi:10.1111/obr.12067.

22. Prins Y, Crous L, Louw Q a. A systematic review of posture and psychosocial factors as contributors to upper quadrant musculoskeletal pain in children and adolescents. *Physiother Theory Pract*. 2008;24(4):221–242. doi:10.1080/09593980701704089.

23. Huguet A, Tougas ME, Hayden J, McGrath PJ, Stinson JN, Chambers CT. A Systematic Review with Meta-analysis of Childhood and Adolescent Risk and Prognostic Factors for Musculoskeletal Pain. *Pain*. 2016;157:1. doi:10.1097/j.pain.0000000000000685.

24. Stanford EA, Chambers CT, Craig KD. A normative analysis of the development of pain-related vocabulary in children. *Pain*. 2005;114(1-2):278–284. doi:S0304-3959(04)00616-5 [pii].

25. von Baeyer CL. Children's self-reports of pain intensity: scale selection, limitations and interpretation. *Pain Res Manag*. 2006;11(3):157–162.

26. World Health Organization. WHO - Definition of key terms.

27. Mallen CD, Peat G, Thomas E, Dunn KM, Croft PR. Prognostic factors for musculoskeletal pain in primary care: a systematic review. *Br J Gen Pract*. 2007;57(541):655–661.

28. Shraim M, Mallen CD, Dunn KM. GP consultations for medically unexplained

physical symptoms in parents and their children: a systematic review. *Br J Gen Pract*. 2013;63(610):e318–25. doi:10.3399/bjgp13X667178 [doi].

29. D S, S S, W R. *How to Practice and Teach EBM*.; 2000.

30. Ariëns GAM, Van Mechelen W, Bongers PM, Bouter LM, Van Der Wal G. Physical risk factors for neck pain. *Scand J Work Environ Heal*. 2000;26(1):7–19. doi:10.5271/sjweh.504.

31. Auvinen JP, Tammelin TH, Taimela SP, et al. Is insufficient quantity and quality of sleep a risk factor for neck, shoulder and low back pain? A longitudinal study among adolescents. *Eur Spine J*. 2010;19(4):641–649. doi:10.1007/s00586-009-1215-2 [doi].

32. Jussila L, Paananen M, Nayha S, et al. Psychosocial and lifestyle correlates of musculoskeletal pain patterns in adolescence: A 2-year follow-up study. *Eur J Pain*. 2014;18(1):139–146. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc11&AN=2013-43374-016.

33. Paananen M V, Taimela SP, Auvinen JP, et al. Risk factors for persistence of multiple musculoskeletal pains in adolescence: A 2-year follow-up study. *Eur J Pain*. 14(10):1026–1032. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc7&AN=2010-23980-009.

34. Ståhl M, Kautiainen H, El-Metwally A, et al. Non-specific neck pain in schoolchildren: Prognosis and risk factors for occurrence and persistence. A 4-year follow-up study. *Pain*. 2008;137(2):316–322. doi:10.1016/j.pain.2007.09.012.

35. Mikkelsson M, Sourander A, Salminen JJ, Kautiainen H, Piha J. Widespread pain and

neck pain in schoolchildren. A prospective one-year follow-up study. *Acta Paediatr Int J Paediatr*. 1999;88(10):1119–1124. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed4&AN=1999363928.

36. Mikkelsson M, ElMetwally A, Kautiainen H, Auvinen A, Macfarlane GJ, Salminen JJ. Onset, prognosis and risk factors for widespread pain in schoolchildren: A prospective 4-year follow-up study. *Pain*. 2008;138(3):681–687. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc6&AN=2008-12957-005.

37. El-Metwally A, Salminen JJ, Auvinen A, MacFarlane G, Mikkelsson M. Risk factors for development of non-specific musculoskeletal pain in preteens and early adolescents: A prospective 1-year follow-up study. *BMC Musculoskelet Disord*. 2007;8. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed8&AN=2007286187.

38. Harrison L, Wilson S, Munafo MR. Exploring the associations between sleep problems and chronic musculoskeletal pain in adolescents: A prospective cohort study. *Pain Res Manag*. 2014;19(5):e139–e145. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed12&AN=2014825638.

39. Szpalski M, Gunzburg R, Balague F, Nordin M, Melot C. A 2-year prospective longitudinal study on low back pain in primary school children. *Eur Spine J*. 2002;11(5):459–464. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=

emed5&AN=2002383790.

40. Lewandowski Holley A, Wilson AC, Cho E, Palermo TM. Clinical Phenotyping of Youth With New-Onset Musculoskeletal Pain. *Clin J Pain*. 2016;00(00):1. doi:10.1097/AJP.0000000000000371.

41. Incledon E, O'Connor M, Giallo R, Chalkiadis GA, Palermo TM. Child and Family Antecedents of Pain During the Transition to Adolescence: A Longitudinal Population-based Study. *J Pain*. 2016;17(11):1174–1182. doi:http://dx.doi.org/10.1016/j.jpain.2016.07.005.

42. Jones GT, Silman AJ, Macfarlane GJ. Predicting the onset of widespread body pain among children. *Arthritis Rheum*. 2003;48(9):2615–2621. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed6&AN=2003377470.

43. Mork PJ, Nilsen TI. Sleep problems and risk of fibromyalgia: longitudinal data on an adult female population in Norway. *Arthritis Rheum*. 2012;64(1):281–284. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=22081440.

44. Nitter AK, Pripp AH, Forseth K. Are sleep problems and non-specific health complaints risk factors for chronic pain? A prospective population-based study with 17 year follow-up. *Scand J Pain*. 2012;3(4):210–217. doi:10.1016/j.sjpain.2012.04.001.

45. Vasseljen O, Woodhouse A, Bjørngaard JH, Leivseth L. Natural course of acute neck and low back pain in the general population: The HUNT study. *Pain*. 2013;154(8):1237–1244. doi:10.1016/j.pain.2013.03.032.

46. Bergman S. A General Practice Approach To Management of Chronic Widespread Musculoskeletal Pain and Fibromyalgia. *Rheum Dis*. 2005;4.

47. Larsson B, Björk J, Börsbo B, Gerdle B. A systematic review of risk factors associated with transitioning from regional musculoskeletal pain to chronic widespread pain. *Eur J Pain*. 2012;16(8):1084–93. doi:10.1002/j.1532-2149.2012.00117.x.

48. Kelly GA, Blake C, Power CK, O'keeffe D, Fullen BM. The association between chronic low back pain and sleep: a systematic review. *Clin J Pain*. 2011;27(2):169–81. doi:10.1097/AJP.0b013e3181f3bdd5.

49. McBeth J, Lacey RJ, Wilkie R. Predictors of new-onset widespread pain in older adults: results from a population-based prospective cohort study in the UK. *Arthritis Rheumatol (Hoboken, NJ)*. 2014;66(3):757–767. doi:10.1002/art.38284 [doi].

50. Tang NKY, Goodchild CE, Sanborn AN, Howard J, Salkovskis PM. Deciphering the temporal link between pain and sleep in a heterogeneous chronic pain patient sample: A multilevel daily process study. *Sleep*. 2012;35(5):675–87A. doi:10.5665/sleep.1830.

51. Meltzer LJ, Walsh CM, Traylor J, Westin AML. Direct comparison of two new actigraphs and polysomnography in children and adolescents. *Sleep*. 2012;35(1):159–66. doi:10.5665/sleep.1608.

52. Delgado-Rodriguez M, Llorca J. Bias. *J Epidemiol Community Health*. 2004;58(8):635–641. doi:10.1136/jech.2003.008466 [doi].

Figure 1. Flowchart showing the process of selection/exclusion of studies

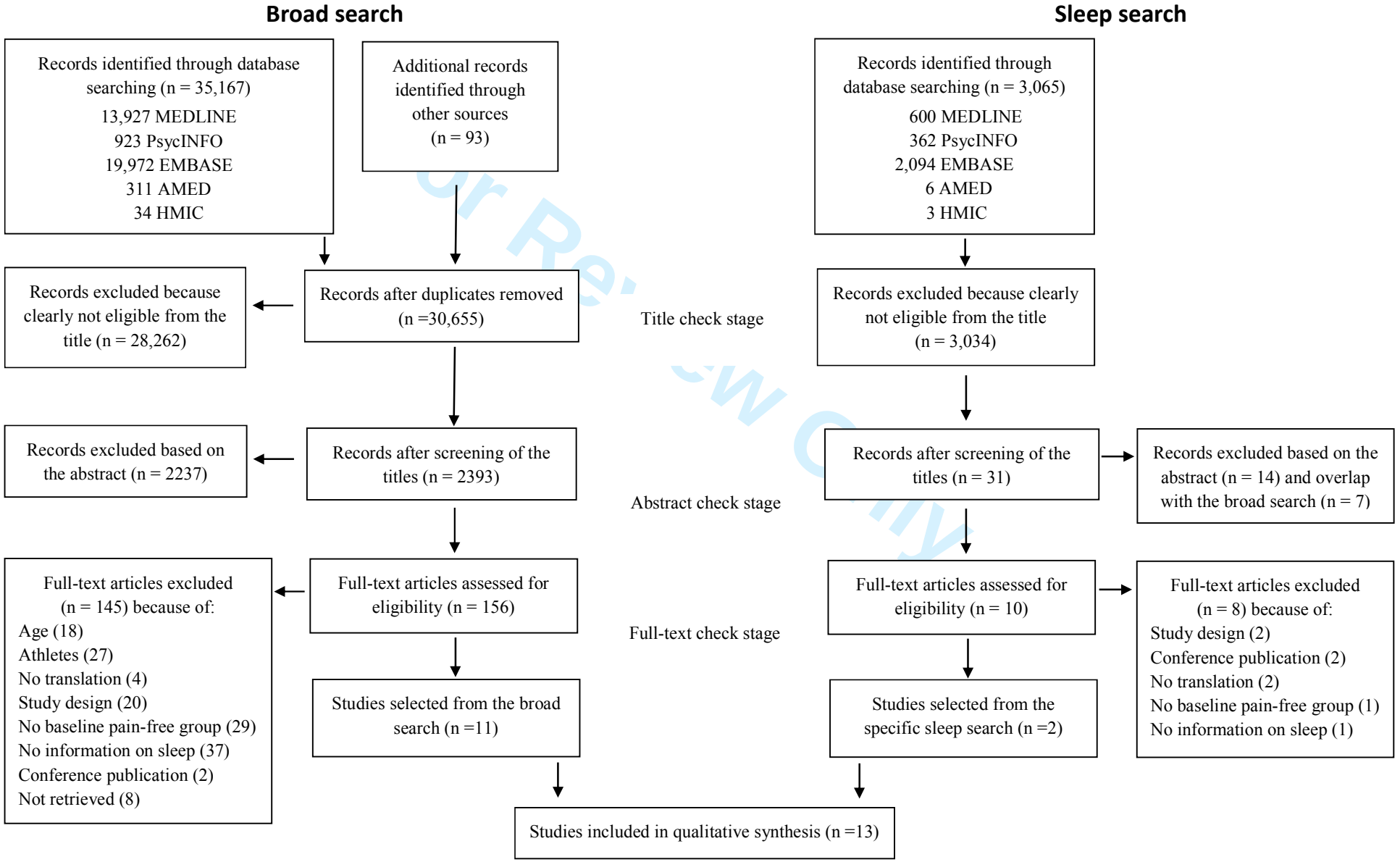

Table 1. Quality assessment checklist
Item
A. Clearly defined study objective
B. Appropriate design for study question
C. Inclusion and exclusion criteria clear and appropriate
D. Representative sample (and comparison)
E. Sample size calculation presented
F. Appropriate selection of outcome
G. Appropriate measurement of outcome
H. Standardised collection of data
I. Adequate length of follow-up for research question
J. Baseline participation >70% (all groups)
K. Losses and dropouts <20%
L. Adequate description of losses and completers
M. Appropriate analysis of outcomes measured
N. Numerical description of important outcomes given
O. Adjusted and unadjusted calculations provided (with confidence interval if appropriate)

Table 2 Levels of evidence for association of risk factors for musculoskeletal pain onset in children and adolescents

Level of evidence	
Strong	Consistent findings (≥ 75%) in studies of high quality, at least 2 studies
Moderate	Consistent findings (≥ 75%) in studies of high and medium/low quality with at least one study of high quality in the direction of consistent findings
Weak	Findings of only one study of high quality or consistent findings (≥ 75%) in studies of medium/low quality
Inconclusive	Findings in less than 3 studies of medium/low quality, or inconsistent findings (regardless of quality)

Table 3. Articles reporting on the risk for the onset of musculoskeletal pain in children and adolescents with sleep problems

Author, year	Country	Setting	Sample size (baseline)	Age (baseline), years	Length of follow-up	Drop-out rate	Quality (Score)
Auvinen et al., 2010 [31]	Finland	Birth Cohort	1773	15-16	2 years	N/A	High (11)
Brattberg, 1994 [7]	Sweden	School	597	8-13	2 years	21.1%	Medium (9)
El-Metwally et al., 2007 [37]	Finland	School	1192	9.8-11.8	1 year	6.6%	High (12)
Harrison et al., 2014 [38]	England	Birth Cohort	2493	15	2 years	N/A	High (11)
Incledon et al., 2016 [41]	Australia	General population	4161	10-11	2 years	8.2%	Medium (10)
Jones et al., 2003 [42]	England	General population	1440	11-14	1 year	12%	High (12)
Jussila et al., 2014 [32]	Finland	Birth Cohort	1773	16	2 years	N/A	High (11)
Lewandoski Holley et al., 2016 [40]	U.S.A.	Academic medical center	191	10-17	4 months	N/A	Medium (9)
Mikkelsson et al., 2008 [36]	Finland	School	1756	9.8-11.8	4 years	3%	High (12)
Mikkelsson et al., 1999 [35]	Finland	School	363	9.8-11.8	1 year	10%	High (11)
Paananen et al., 2010 [33]	Finland	Birth Cohort	1594	16	2 years	N/A	Medium (9)
Ståhl et al., 2008 [34]	Finland	School	1268	9.8-11.8	4 years	38.5%	High (13)
Szpalski et al., 2002 [39]	Belgium	School	287	9	2 years	N/A	Medium (8)

Legend
N/A = Analysis on subjects who responded to both baseline and follow-up questionnaires

Table 4. Risk for the onset of musculoskeletal pain

Baseline factor	Outcome				
	Back pain	Neck pain	Shoulder pain	Musculoskeletal pain	Widespread pain
Sleep quality					
+		**34** Boys: OR: 1.25, 95% CI 1.11, 1.41 Girls: OR: 1.14, 95% CI 1.03, 1.26			**38** Hypersomnolence problems: OR: 2.76, 95% CI 1.05, 7.25 Waking up ≥ 2-3 times a night: OR: 2.13, 95% CI 1.22, 3.74
#		**31** Boys: OR: 0.83, 95% CI 0.48, 1.44 Girls: OR: 1.67, 95% CI 1.00, 2.78			
x	39 (estimate not provided in multivariate analysis) **31** Boys: OR: 1.14, 95% CI 0.66, 2.00 Girls: OR: 1.48, 95% CI 0.97, 2.24		**31** Boys: OR: 1.32, 95% CI 0.77, 2.25 Girls: OR: 1.47, 95% CI 0.91, 2.39	**37** Non-traumatic: - Difficulty falling asleep: OR: 1.48, 95% CI 0.99, 2.23 - Waking up during nights: OR: 1.31, 95% CI 0.82, 2.08 Traumatic: - Difficulty falling asleep: OR: 1.47, 95% CI 0.67, 3.24 - Waking up during nights: OR: 1.64, 95% CI 0.70, 3.85 40 Sleep quality score - Children with new-onset pain: Mean 3.96, SD 0.58 - Healthy children: Mean 4.13, SD 0.69	**35** Higher sleep score: OR: 1.23, 95% CI 0.98, 1.54 **36** Difficulty falling asleep: OR: 1.2, 95% CI 0.9, 1.7 Waking up during nights: OR: 1.1, 95% CI 0.8, 1.6
Sleep quantity					
+	7 Those with trouble getting enough sleep had more pain but no estimate was reported			41 Sleep deficiency: OR: 1.86, 95% CI 1.16, 2.97	
#	**31** Sleeping time in girls: - 7 hour or less a day: OR: 1.45, 95% CI 0.96, 2.19 – 9/10 hours a day: OR: 0.86, 95% CI 0.58, 1.27			**32** Shorter sleeping time and probability to have pain: - Boys P = 0.001 - Girls, P = 0.100	

	- 10 hours or more a day: OR: 0.87, 95% CI 0.52, 1.47 Sleeping time in boys: - 7 hours or less a day: OR: 1.42, 95% CI 0.86, 2.33 - 9/10 hours a day: OR: 1.59, 95% CI 1.03, 2.44 - 10 hours or more a day: OR: 0.93, 95% CI 0.56, 1.54				
x		**31** Sleeping time in girls: - 7 hour or less a day: OR: 1.44, 95% CI 0.90, 2.32 - 9/10 hours a day: OR: 1.02, 95% CI 0.66, 1.57 - 10 hours or more a day: OR: 1.55, 95% CI 0.84, 2.87 Sleeping time in boys: - 7 hour or less a day: OR: 1.40, 95% CI 0.86, 2.30 - 9/10 hours a day: OR: 0.98, 95% CI 0.64, 1.50 - 10 hours or more a day: OR: 0.86, 95% CI 0.52, 1.44	**31** Sleeping time in girls : - 7 hour or less a day: OR: 1.36, 95% CI 0.85, 2.17 - 9/10 hours a day: OR: 1.17, 95% CI 0.76, 1.81 - 10 hours or more a day: OR: 1.08, 95% CI 0.61, 1.93 Sleeping time in boys: - 7 hour or less a day: OR: 1.05, 95% CI 0.66, 1.69 - 9/10 hours a day: OR: 0.84, 95% CI 0.55, 1.29 - 10 hours or more a day: OR: 0.85, 95% CI 0.51, 1.39		33 Sleeping time in boys: - < 7 hours a day: OR: 1.15, 95% CI 0.66, 1.98 - ≥ 10 hours a day: OR: 1.14, 95% CI 0.69, 1.88 Sleeping time in girls: - < 7 hours a day: OR: 0.93, 95% CI 0.54, 1.61 - ≥ 10 hours a day: OR: 1.12, 95% CI 0.56, 2.27 **38** Rarely/never enough sleep: OR: 1.20, 95% CI 0.55, 2.62
Day-time tiredness					
+		**34** Boys: OR: 1.25, 95% CI 1.11, 1.41 Girls: OR: 1.14, 95% CI 1.03, 1.26		**37** Non-traumatic: OR: 1.53, 95% CI 1.03, 2.26 Traumatic: OR: 2.97, 95% CI 1.41, 6.26	
#	**31** Boys: - often too tired: OR: 1.46, 95% CI 0.61, 3.45 - sometimes too tired: OR: 1.16, 95% CI 0.80, 1.68 Girls: - often too tired OR: 2.42, 95% CI 1.24, 4.71	**31** Boys: - often too tired: OR 1.15, 95% CI 0.48, 2.74 - sometimes too tired OR 1.28, 95% CI 0.88, 1.85 Girls: - often too tired: OR 3.92, 95% CI 1.55, 9.90	**31** Boys: - often too tired: OR: 1.36, 95% CI 0.60, 3.13 - sometimes too tired: OR: 1.57, 95% CI 1.10, 2.25 Girls: - often too tired: OR: 1.78, 95% CI 0.83, 3.83		

	- sometimes too tired: OR: 1.32, 95% CI 0.93, 1.85	- sometimes too tired: OR 1.46, 95% CI 1.00, 2.13	- sometimes too tired: OR: 1.21, 95% CI 0.83, 1.76		
x	39 (estimate not provided in multivariate analysis)				**36** OR: 1.1, 95% CI 0.8, 1.6 **42** OR: 1.41, 95% CI 0.84, 2.40

Legend
+ significant effect x no effect # mixed effect
Numbers in the table represent the study reference numbers. Numbers in bold represent the studies of high quality.
OR = Odds Ratios. All the Odds Ratios provided are for adjusted analysis
95% CI = 95% Confidence Interval
SD = Standard Deviation

Table 5. Definitions of exposure and outcome used in the studies

Author, year	Exposure	Outcome
Auvinen et al., 2010 [31]	Poor sleep quality: having sleeping problems "sometimes or often" (reference category was "not at all"), Day-time tiredness: being too tired "often" or "sometimes" (reference category was "never")	Any aches or pain in the last 6 months in the following areas: - Neck or occipital area - Shoulders - Low back
Brattberg, 1994 [7]	Sleep quantity	Back pain often
El-Metwally et al., 2007 [37]	Sleep quality: Difficulties falling asleep and waking up during the night present at least once a week during the preceding 3 months	Pain in any musculoskeletal locations with a frequency of at least once a week during the previous 3 months
Harrison et al., 2014 [38]	Sleep quality: Frequency of problems with hypersomnolence and waking up during the night Sleep quantity (enough sleep): Always (Reference) Usually Sometimes Rarely/Never	Pain on both sides of the body, above and below the waist and in the axial skeleton that had been present for more than 3 months
Incledon et al., 2016 [41]	Sleep deficiency: "not quite" or "not nearly enough sleep" in the last month (reference categories: "plenty" or "just enough")	Abdominal pain, headaches and/or pains in other parts of the body occurring at least weekly
Jones et al., 2003 [42]	Day-time tiredness measured with a visual analog scale (VAS)	ACR definition of criteria for fibromyalgia to define widespread pain
Jussila et al., 2014 [32]	Sleeping time, hours a day	Any aches or pain in the last 6 months in the following areas: - Neck or occipital area - Shoulders - Low back - Elbows - Wrists - Knees Ankle/foot area
Lewandoski Holley et al., 2016 [40]	Sleep quality: Adolescent Sleep-Wake Scale (total score was used in the analysis)	New-onset musculoskeletal pain: children presenting to an orthopaedic clinic or emergency medicine
Mikkelsson et al., 2008 [36]	Day-time tiredness, difficulty falling asleep and waking up during night at least once a week for the preceding 3 months	ACR definition of criteria for fibromyalgia to define widespread pain
Mikkelsson et al., 1999 [35]	Day-time tiredness, difficulty falling asleep and waking up during night at least once a week for the preceding 3 months	Pain above and below the waist, on both sides of the body and in the axial skeleton at least once a week during the preceding 3

		months
Paananen et al., 2010 [33]	Sleeping time: 7 hours a day or less 8-9 hours a day (Reference) 10 or more hours a day	Any aches or pain in the last 6 months in more than one of the following areas: - Neck or occipital area - Shoulders - Low back - Elbows - Wrists - Knees - Ankle/foot area
Ståhl et al., 2008 [34]	Physical and psychological symptoms (abdominal pain, headache, depressive mood, daytime tiredness, difficulty falling asleep, waking up during the night) at least once a week	Neck pain at least once a week
Szpalski et al., 2002 [39]	Quality of sleep, quality of falling asleep and being tired without any reason measured with a visual analog scale (VAS)	Back pain prevalence and disability of back pain

Appendix 1

Search strategies

Here below are listed the two search strategies used within the systematic review. The search strategies listed are those used for the MEDLINE database. For other databases similar search strategies were used with the specific search terms adapted for each specific database.

Specific search using specific sleep terms	
Number	Search term
1	INCIDENCE/
2	(inciden*).ti,ab,af
3	RISK FACTORS/
4	(risk ADJ3 factor*).ti,ab,af
5	(Risk ADJ3 score).ti,ab,af
6	exp COHORT STUDIES/
7	(cohort ADJ3 stud*).ti,ab,af
8	PROSPECTIVE STUDIES/
9	(prospective ADJ3 stud*).ti,ab,af
10	FOLLOW UP STUDIES/
11	(Follow up ADJ3 stud*).ti,ab,af
12	(onset).ti,ab,af
13	(predict*).ti,ab,af
14	(1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13)
15	ADOLESCENT/
16	(adolescen*).ti,ab,af
17	exp CHILD/
18	(child*).ti,ab,af
19	(youth).ti,ab,af
20	SCHOOLS/
21	(school*).ti,ab,af
22	PEDIATRICS/
23	(pediatric*).ti,ab,af
24	(paediatric*).ti,ab,af
25	(young*).ti,ab,af
26	(boy*).ti,ab,af

27	(girl*).ti,ab,af
28	exp PUBERTY/
29	(pubescent*).ti,ab,af
30	(pubert*).ti,ab,af
31	(prepubert*).ti,ab,af
32	(juvenile*).ti,ab,af
33	(teenage*).ti,ab,af
34	(15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33)
35	PAIN/
36	exp BACK/
37	KNEE/
38	NECK/
39	exp HAND/
40	SHOULDER/
41	HIP/
42	exp FOOT/
43	ELBOW/
44	ARM/
45	FOREARM/
46	WRIST/
47	LEG/
48	ANKLE/
49	exp SPINE/
50	(36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49)
51	(35 AND 50)
52	(back ADJ3 pain).ti,ab,af
53	(knee ADJ3 pain).ti,ab,af
54	(neck ADJ3 pain).ti,ab,af
55	(hand ADJ3 pain).ti,ab,af
56	(shoulder ADJ3 pain).ti,ab,af
57	(hip ADJ3 pain).ti,ab,af
58	(foot ADJ3 pain).ti,ab,af
59	(elbow ADJ3 pain).ti,ab,af
60	(arm ADJ3 pain).ti,ab,af
61	(forearm ADJ3 pain).ti,ab,af
62	(wrist ADJ3 pain).ti,ab,af

63	(leg ADJ3 pain).ti,ab,af
64	(ankle ADJ3 pain).ti,ab,af
65	(spinal ADJ3 pain).ti,ab,af
66	(backache).ti,ab,af
67	LOW BACK PAIN/
68	(low back ADJ3 pain).ti,ab,af
69	CHRONIC PAIN/
70	(chronic ADJ3 pain).ti,ab,af
71	MUSCULOSKELETAL PAIN/
72	(musculoskeletal ADJ3 pain).ti,ab,af
73	(widespread ADJ3 pain).ti,ab,af
74	(multisite ADJ3 pain).ti,ab,af
75	(regional ADJ3 pain).ti,ab,af
76	(juvenile ADJ3 fibromyalgia).ti,ab,af
77	*(52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69 OR 70 OR 71 OR 72 OR 73 OR 74 OR 75 OR 76)*
78	(35 OR 51 OR 77)
79	exp SLEEP DISORDERS, CIRCADIAN RHYTHM/
80	exp SLEEP AROUSAL DISORDERS/
81	exp REM SLEEP PARASOMNIAS/
82	exp SLEEP, REM/
83	exp REM SLEEP BEHAVIOR DISORDER/
84	exp SLEEP STAGES/
85	exp SLEEP PHASE CHRONOTHERAPY/
86	exp "SLEEP INITIATION AND MAINTENANCE DISORDERS"/
87	exp SLEEP APNEA SYNDROMES/
88	(apnea OR apnoea).ti,ab,af
89	exp SLEEP/
90	exp SLEEP DEPRIVATION/
91	exp SLEEP DISORDERS, INTRINSIC/
92	exp SLEEP PARALYSIS/
93	exp SLEEP MEDICINE SPECIALTY/
94	exp SLEEP BRUXISM/
95	exp SLEEP APNEA, CENTRAL/
96	exp SLEEP-WAKE TRANSITION DISORDERS/
97	exp SLEEP APNEA, OBSTRUCTIVE/
98	(hypersomnia).ti,ab,af

99	exp "DISORDERS OF EXCESSIVE SOMNOLENCE"/
100	(narcolepsy).ti,ab,af
101	exp NARCOLEPSY/
102	(dyssomnia).ti,ab,af
103	exp DYSSOMNIAS/
104	exp AIRWAY RESISTANCE/
105	(upper airway resistance).ti,ab,af
106	exp CHEYNE-STOKES RESPIRATION/
107	(Cheyne Stokes).ti,ab,af
108	exp SLEEP/ AND exp HYPOVENTILATION/
109	(sleep hypoventilation).ti,ab,af
110	exp SLEEP/ AND exp ANOXIA/
111	(sleep hypoxemia).ti,ab,af
112	(nightmare).ti,ab,af
113	exp DREAMS/
114	exp SLEEP/ AND exp ENURESIS/
115	(sleep enuresis).ti,ab,af
116	(sleep bruxism).ti,ab,af
117	exp SLEEP BRUXISM/
118	(snoring).ti,ab,af
119	exp SNORING/
120	(Nocturnal paroxysmal dystonia).ti,ab,af
121	exp NOCTURNAL PAROXYSMAL DYSTONIA/
122	(Restless legs syndrome).ti,ab,af
123	exp RESTLESS LEGS SYNDROME/
124	(periodic limb movement disorder).ti,ab,af
125	exp NOCTURNAL MYOCLONUS SYNDROME/
126	(rhythmic movement disorder).ti,ab,af
127	(sleep walking).ti,ab,af
128	exp SOMNAMBULISM/
129	(sleep talking).ti,ab,af
130	exp SLEEP/ AND exp MYOCLONUS/
131	(sleep myoclonus).ti,ab,af
132	exp SLEEP/ AND exp HYPERHIDROSIS/
133	(sleep hyperhidrosis).ti,ab,af
134	exp SLEEP/ AND exp HALLUCINATIONS/
135	(hypnagogic hallucinations).ti,ab,af

136	(insomnia).ti,ab,af
137	POLYSOMNOGRAPHY/
138	ACTIGRAPHY/
139	(polysomnogr* OR actigr* OR accelerom*).ti,ab,af
140	(Sleep* ADJ3 (report OR questionnaire* OR index OR eval* OR diary OR diaries OR log* OR journal*)).ti,ab,af
141	(sleep ADJ3 duration).ti,ab,af
142	(sleep).ti,ab
143	(sleep*).ti,ab
144	*(79 OR 80 OR 81 OR 82 OR 83 OR 84 OR 85 OR 86 OR 87 OR 88 OR 89 OR 90 OR 91 OR 92 OR 93 OR 94 OR 95 OR 96 OR 97 OR 98 OR 99 OR 100 OR 101 OR 102 OR 103 OR 104 OR 105 OR 106 OR 107 OR 108 OR 109 OR 110 OR 111 OR 112 OR 113 OR 114 OR 115 OR 116 OR 117 OR 118 OR 119 OR 120 OR 121 OR 122 OR 123 OR 124 OR 125 OR 126 OR 127 OR 128 OR 129 OR 130 OR 131 OR 132 OR 133 OR 134 OR 135 OR 136 OR 137 OR 138 OR 139 OR 140 OR 141 OR 142 OR143)*
145	*(14 AND 34 AND 78 AND 145)*

Broad search	
Number	Search term
1	Incidence/
2	risk factors/
3	(risk adj3 factor$).ti,ab.
4	(Risk adj3 score).ti,ab.
5	exp Cohort Studies/
6	(cohort adj3 stud$).ti,ab.
7	Prospective Studies/
8	(prospective adj3 stud$).ti,ab.
9	Follow-Up Studies/
10	(Follow up adj3 stud$).ti,ab.
11	onset.ti,ab.
12	predict$.ti,ab.
13	inciden$.ti,ab.
14	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15	Adolescent/
16	adolescen$.ti,ab.
17	exp Child/
18	child$.ti,ab.
19	youth.ti,ab.
20	Schools/
21	school$.ti,ab.
22	Pediatrics/
23	pediatric$.ti,ab.
24	paediatric$.ti,ab.
25	young$.ti,ab.
26	boy$.ti,ab.
27	girl$.ti,ab.
28	exp Puberty/
29	pubescent$.ti,ab.
30	pubert$.ti,ab.
31	prepubert$.ti,ab.
32	juvenile$.ti,ab.
33	teenage$.ti,ab.
34	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or

	31 or 32 or 33
35	Pain/
36	exp Back/
37	Knee/
38	Neck/
39	exp Hand/
40	Shoulder/
41	Hip/
42	exp Foot/
43	Elbow/
44	Arm/
45	Forearm/
46	Wrist/
47	Leg/
48	Ankle/
49	exp Spine/
50	36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49
51	35 and 50
52	(back adj3 pain).ti,ab.
53	(knee adj3 pain).ti,ab.
54	(neck adj3 pain).ti,ab.
55	(hand adj3 pain).ti,ab.
56	(shoulder adj3 pain).ti,ab.
57	(hip adj3 pain).ti,ab.
58	(foot adj3 pain).ti,ab.
59	(elbow adj3 pain).ti,ab.
60	(arm adj3 pain).ti,ab.
61	(forearm adj3 pain).ti,ab.
62	(wrist adj3 pain).ti,ab.
63	(leg adj3 pain).ti,ab.
64	(ankle adj3 pain).ti,ab.
65	(spinal adj3 pain).ti,ab.
66	backache.ti,ab.
67	Low Back Pain/
68	(low back adj3 pain).ti,ab.
69	Chronic Pain/
70	(chronic adj3 pain).ti,ab.

71	Musculoskeletal Pain/
72	(musculoskeletal adj3 pain).ti,ab.
73	(widespread adj3 pain).ti,ab.
74	(multisite adj3 pain).ti,ab.
75	(regional adj3 pain).ti,ab.
76	(juvenile adj3 fibromyalgia).ti,ab.
77	52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76
78	35 or 51 or 77
79	**14 and 34 and 78**

Appendix 2

Data extraction form

Date of extraction
ID number
Article title
Authors
Date
Country
Aim of the study
Study design
Study setting
Inclusion/exclusion criteria
"Recruitment procedures used"
N participants
Age range
Sex ratio
Ethnicity
Response rate
"Information about non-responders"
Pain definition
Pain Location
Exposures analysed
Questionnaire used
Prevalence
Incidence
Length of follow-up
Statistical analyses performed
Results
Conclusions
Notes

Appendix 3

Articles excluded with reason for exclusion

Broad search		
	Article reference	**Reason for exclusion**
1	Aartun, Ellen et al. "Spinal Pain In Adolescents: Prevalence, Incidence, And Course: A School-Based Two-Year Prospective Cohort Study In 1,300 Danes Aged 11–13". *BMC Musculoskeletal Disorders* 15.1 (2014): n. pag. Web.	No information on sleep as a risk factor
2	Aggarwal, Vishal R. et al. "Risk Factors For Onset Of Chronic Oro-Facial Pain – Results Of The North Cheshire Oro-Facial Pain Prospective Population Study". *Pain* 149.2 (2010): 354-359. Web.	Age (18-75 years old)
3	Bakker, R. J. et al. "Risk Factors For Persistent Fatigue With Significant School Absence In Children And Adolescents". *PEDIATRICS* 124.1 (2009): e89-e95. Web.	Study design (Somatic complaints were assessed at baseline only)
4	Auvinen, Juha et al. "MUSCULOSKELETAL PAIN COMBINATIONS IN ADOLESCENTS". *Spine* &NA; (2008): 44. Web.	No information on sleep as a risk factor
5	Balagué F, Dutoit G, Waldburger M. Low back pain in schoolchildren. An epidemiological study. Scand J Rehabil Med. 1988;20(4):175-9.	Study design (Retrospective study)
6	Foss, Kim D. Barber et al. "Is Body Composition Associated With An Increased Risk Of Developing Anterior Knee Pain In Adolescent Female Athletes?". *The Physician and Sportsmedicine* 40.1 (2012): 13-19. Web.	Athletes
7	Bishop, Jackie L et al. "Parental Accounts Of The Prevalence, Causes And Treatments Of Limb Pain In Children Aged 5 To 13 Years: A Longitudinal Cohort Study". *Archives of Disease in Childhood* 97.1 (2010): 52-53. Web.	No information on sleep as a risk factor

8	Campbell, Tavis S. et al. "A Longitudinal Study Of Pain Sensitivity And Blood Pressure In Adolescent Boys: Results From A 5-Year Follow-Up.". *Health Psychology* 21.6 (2002): 594-600. Web.	No baseline pain-free group
9	Brattberg G, Wickman V. Longitudinell studie avskolelever Rehabilitera tidigt vid ryggont/huvudv¨ark.L¨akartidningen. 1993;90(15):1452-1460	No translation available (Article in Swedish)
10	Campbell, Tavis S. et al. "A Longitudinal Study Of Pain Sensitivity And Blood Pressure In Adolescent Boys: Results From A 5-Year Follow-Up.". *Health Psychology* 21.6 (2002): 594-600. Web.	No baseline pain-free group
11	Cottalorda J, Bourelle S, Gautheron V. Effects of backpack carrying in children. Orthopedics. 2004 Nov;27(11):1172-5; quiz 1176-7. Review.	No information on sleep as a risk factor
12	Crow, Justin F. et al. "Hip Adductor Muscle Strength Is Reduced Preceding And During The Onset Of Groin Pain In Elite Junior Australian Football Players". *Journal of Science and Medicine in Sport* 13.2 (2010): 202-204. Web.	Athletes
13	Diepenmaat AC, van der Wal MF, de Vet HC, Hirasing RA. Neck/shoulder, low back, and arm pain in relation to computer use, physical activity, stress, and depression among Dutch adolescents. Pediatrics. 2006 Feb;117(2):412-6.	Study design (Cross-sectional study)
14	Diniz MR, Sabadin PA, Leite FP, Kamizaki R. Psychological factors related to temporomandibular disorders: an evaluation of students preparing for college entrance examinations. Acta Odontol Latinoam. 2012;25(1):74-81.	Age (18-25 years old)
15	Driscoll, D. J., Glicklich, L. B., & Gallen, W. J. (1976). Chest pain in children: a prospective study. *Pediatrics*, *57*(5), 648–651.	No information on sleep as a risk factor
16	Drouin, Sammantha and Jennifer J. McGrath. "Blood Pressure And Pain Sensitivity In Children And Adolescents". *Psychophysiology* 50.6 (2013): 513-520. Web.	No baseline pain-free group

17	Dunn, Kate M. et al. "Trajectories Of Pain In Adolescents: A Prospective Cohort Study". *Pain* 152.1 (2011): 66-73. Web.	No information on sleep as a risk factor
18	EGGER, HELEN LINK et al. "Somatic Complaints And Psychopathology In Children And Adolescents: Stomach Aches, Musculoskeletal Pains, And Headaches". *Journal of the American Academy of Child & Adolescent Psychiatry* 38.7 (1999): 852-860. Web.	No baseline pain-free group
19	El-Metwally, Ashraf et al. "Prognosis Of Non-Specific Musculoskeletal Pain In Preadolescents: A Prospective 4-Year Follow-Up Study Till Adolescence". *Pain* 110.3 (2004): 550-559. Web.	No baseline pain-free group
20	El-Metwally, A. "Lower Limb Pain In A Preadolescent Population: Prognosis And Risk Factors For Chronicity--A Prospective 1- And 4-Year Follow-Up Study". *PEDIATRICS* 116.3 (2005): 673-681. Web.	No baseline pain-free group
21	Finnoff, Jonathan T. et al. "Hip Strength And Knee Pain In High School Runners: A Prospective Study". *PM&R* 3.9 (2011): 792-801. Web.	Athletes
22	Finnoff, Jonathan T. et al. "Hip Strength And Knee Pain In High School Runners: A Prospective Study". *PM&R* 3.9 (2011): 792-801. Web.	Athletes
23	Baker, A. D. L. (2014). Risk Factors in Low-back Pain. An Epidemiological Survey. In P. A. Banaszkiewicz & D. F. Kader (Eds.), *Classic Papers in Orthopaedics* (pp. 261–263). London: Springer London. doi:10.1007/978-1-4471-5451-8_64	Age (18-55 years old)
24	Fyfe, D. A. and D. S. Moodie. "Chest Pain In Pediatric Patients Presenting To A Cardiac Clinic". *Clinical Pediatrics* 23.6 (1984): 321-324. Web.	No information on sleep as a risk factor

25	Geldhof, Elisabeth et al. "Back Posture Education In Elementary Schoolchildren: A 2-Year Follow-Up Study". *European Spine Journal* 16.6 (2006): 841-850. Web.	Study design (Back education programme)
26	McCrory, P. "Neovascularisation And Pain In Jumper's Knee: A Prospective Clinical And Sonographic Study In Elite Junior Volleyball Players". *Yearbook of Sports Medicine* 2006 (2006): 63-64. Web.	Athletes
27	Grimmer, K, L Nyland, and S Milanese. "Repeated Measures Of Recent Headache, Neck And Upper Back Pain In Australian Adolescents". *Cephalalgia* 26.7 (2006): 843-851. Web.	No information on sleep as a risk factor
28	Grimmer, Karen, Leah Nyland, and Steve Milanese. "Longitudinal Investigation Of Low Back Pain In Australian Adolescents: A Five-Year Study". *Physiotherapy Research International* 11.3 (2006): 161-172. Web.	No information on sleep as a risk factor
29	Iwamoto, J. et al. "Relationship Between Radiographic Abnormalities Of Lumbar Spine And Incidence Of Low Back Pain In High School Rugby Players: A Prospective Study". *Scandinavian Journal of Medicine and Science in Sports* 15.3 (2005): 163-168. Web.	Athletes
30	Hanvold, Therese N., Kaj B. Veiersted, and Morten Wærsted. "A Prospective Study Of Neck, Shoulder, And Upper Back Pain Among Technical School Students Entering Working Life". *Journal of Adolescent Health* 46.5 (2010): 488-494. Web.	Age (17 at baseline, 20 at follow-up)
31	Hanvold TN, Wærsted M, Veiersted KB. Long periods with uninterrupted muscle activity related to neck and shoulder pain. Work. 2012;41 Suppl 1:2535-8. doi: 10.3233/WOR-2012-0494-2535.	Age (Mean age 22 years old)

32	Harringe, M. L. et al. "Low Back Pain In Young Female Gymnasts And The Effect Of Specific Segmental Muscle Control Exercises Of The Lumbar Spine: A Prospective Controlled Intervention Study". *Knee Surgery, Sports Traumatology, Arthroscopy* 15.10 (2007): 1264-1271. Web.	Athletes
33	Hickey, Gregory J., Peter A. Fricker, and Warren A. McDonald. "Injuries To Young Elite Female Basketball Players Over A Six-Year Period". *Clinical Journal of Sport Medicine* 7.4 (1997): 252-256. Web.	Athletes
34	Hjelm, N., S. Werner, and P. Renstrom. "Injury Risk Factors In Junior Tennis Players: A Prospective 2-Year Study". *Scandinavian Journal of Medicine & Science in Sports* 22.1 (2010): 40-48. Web.	Athletes
35	Hjelm, Nina, Suzanne Werner, and Per Renstrom. "Injury Profile In Junior Tennis Players: A Prospective Two Year Study". *Knee Surgery, Sports Traumatology, Arthroscopy* 18.6 (2010): 845-850. Web.	Athletes
36	Iwamoto, J. et al. "Relationship Between Radiographic Abnormalities Of Lumbar Spine And Incidence Of Low Back Pain In High School Rugby Players: A Prospective Study". *Scandinavian Journal of Medicine and Science in Sports* 15.3 (2005): 163-168. Web.	Athletes
37	Iwamoto, J. "Relationship Between Radiographic Abnormalities Of Lumbar Spine And Incidence Of Low Back Pain In High School And College Football Players: A Prospective Study". *American Journal of Sports Medicine* 32.3 (2004): 781-786. Web.	Athletes
38	Jacchia GE, Butler UP, Innocenti M, Capone A. Low back pain in athletes: pathogenetic mechanisms and therapy. Chir Organi Mov. 1994 Jan-Mar;79(1):47-53	Athletes

39	Janssens, Karin A.M. et al. "An Inactive Lifestyle And Low Physical Fitness Are Associated With Functional Somatic Symptoms In Adolescents. The TRAILS Study". *Journal of Psychosomatic Research* 76.6 (2014): 454-457. Web.	No information on sleep as a risk factor
40	Jones, Gareth T. and Gary J. Macfarlane. "Predicting Persistent Low Back Pain In Schoolchildren: A Prospective Cohort Study". *Arthritis & Rheumatism* 61.10 (2009): 1359-1366. Web.	No baseline pain-free group
41	Juul-Kristensen, B. et al. "Generalized Joint Hypermobility In Childhood Is Both A Contributive And Predictive Risk Factor For Pain Development In Adolescence: A Cohort Study". *Osteoarthritis and Cartilage* 22 (2014): S216. Web.	No information on sleep as a risk factor
42	Karjalainen, Ulla et al. "Role Of Environmental Factors And History Of Low Back Pain In Sciatica Symptoms Among Finnish Adolescents". *Spine* 38.13 (2013): 1105-1111. Web.	No information on sleep as a risk factor
43	Karterud, S., & Kogstad, O. (1978). [Low back pain. Diagnostic, therapeutic and prognostic aspects]. *Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke*, *98*(25), 1215–1217.	No translation available (Article in Norwegian)
44	Kashikar-Zuck, S. et al. "Controlled Follow-Up Study Of Physical And Psychosocial Functioning Of Adolescents With Juvenile Primary Fibromyalgia Syndrome". *Rheumatology* 49.11 (2010): 2204-2209. Web.	Age (Age range 15-23 years old)
45	Kaspiris A, Grivas TB, Zafiropoulou C, Vasiliadis E, Tsadira O. Nonspecific low back pain during childhood: a retrospective epidemiological study of risk factors. J Clin Rheumatol. 2010 Mar;16(2):55-60. doi: 10.1097/RHU.0b013e3181cf3527.	Study design (Retrospective study)
46	Kjaer, Per et al. "Prevalence And Tracking Of Back Pain From Childhood To Adolescence". *BMC Musculoskeletal Disorders* 12.1 (2011): n. pag. Web.	No information on sleep as a risk factor

47	Koh, Min Jung et al. "The Effect Of Education On Decreasing The Prevalence And Severity Of Neck And Shoulder Pain: A Longitudinal Study In Korean Male Adolescents". *Korean Journal of Anesthesiology* 67.3 (2014): 198. Web.	Study design (Back programme)
48	Kola, I. et al. "Vertebral Column Deformities In Obese Children In Albania". *Annals of Physical and Rehabilitation Medicine* 57 (2014): e322. Web.	Not retrieved
49	Korovessis, P., Repantis, T., & Baikousis, A. (2010). Factors affecting low back pain in adolescents. *Journal of Spinal Disorders & Techniques*, *23*(8), 513–520	No information on sleep as a risk factor
50	Kriegeskorte V. Back pain: Children and adolescents are also affected. [in German] Kompendium Orthop. Unfallchir. Rheumatol.. 2008;1(1):7	Not retrieved
51	Kujala UM, Taimela S, Oksanen A, Salminen JJ. "Lumbar mobility and low back pain during adolescence. A longitudinal three-year follow-up study in athletes and controls". Am J Sports Med. 1997 May-Jun;25(3):363-8.	No information on sleep as a risk factor
52	Kujala, U. M. et al. "Baseline Anthropometry, Flexibility And Strength Characteristics And Future Low-Back Pain In Adolescent Athletes And Nonathletes". *Scandinavian Journal of Medicine & Science in Sports* 4.3 (2007): 200-205. Web.	No information on sleep as a risk factor
53	KUJALA, URHO M. et al. "Low-Back Pain In Adolescent Athletes". *Medicine &amp Science in Sports &amp Exercise* 28.2 (1996): 165-170. Web.	Athletes
54	Lebkowski WJ. ["Back pain" in teenagers and young adults]. Pol Merkur Lekarski. 1997 Feb;2(8):111-2.	Age (Age range 17 - 24 years old)
55	Lee, Joon-Hee et al. "Trunk Muscle Weakness As A Risk Factor For Low Back Pain". *Spine* 24.1 (1999): 54-57. Web.	Age (Age range 17 - 22 years old)

56	Logan, Deirdre E. et al. "Changes In Sleep Habits In Adolescents During Intensive Interdisciplinary Pediatric Pain Rehabilitation". *Journal of Youth and Adolescence* 44.2 (2014): 543-555. Web.	Study design (Rehabilitation program)
57	Lyman S, Fleisig GS, Andrews JR, Osinski ED. Effect of pitch type, pitch count, and pitching mechanics on risk of elbow and shoulder pain in youth baseball pitchers. Am J Sports Med. 2002 Jul-Aug;30(4):463-8.	Athletes
58	Lyman S, Fleisig GS, Waterbor JW, Funkhouser EM, Pulley L, Andrews JR, Osinski ED, Roseman JM. Longitudinal study of elbow and shoulder pain in youth baseball pitchers. Med Sci Sports Exerc. 2001 Nov;33(11):1803-10.	Athletes
59	MacDonald, James and Pierre D'Hemecourt. "Back Pain In The Adolescent Athlete". *Pediatric Annals* 36.11 (2007): 703-712. Web.	Athletes
60	Magni, G., G. Canton, and L. Gallimberti. "Pain Symptoms In An Adolescent Italian Population". *European Journal of Pediatrics* 149.8 (1990): 592-593. Web.	Study design (Cross-sectional study)
61	Shrier I, Ehrmann-Feldman D, Rossignol M, Abenhaim L. Risk factors for development of lower limb pain in adolescents. J Rheumatol. 2001 Mar;28(3):604-9.	No information on sleep as a risk factor
62	Mattila, Ville M. et al. "Predictors Of Low Back Pain Hospitalization – A Prospective Follow-Up Of 57,408 Adolescents". *Pain* 139.1 (2008): 209-217. Web.	Age (Age at baseline 14-18 and 25-29 years old at follow-up).
63	McKenna, Leanda, Leon Straker, and Anne Smith. "Can Scapular And Humeral Head Position Predict Shoulder Pain In Adolescent Swimmers And Non-Swimmers?". *Journal of Sports Sciences* 30.16 (2012): 1767-1776. Web.	Athletes

64	Meienburg M., Kjaer P., Lebouef-Yde C., Wedderkopp N. "Low back pain and physical activity in childhood and youth: Longitudinal associations." Scand. J. Rheumatol.. 2012;41:36-37.	No information on sleep as a risk factor
65	Mikkelsson, Marja et al. "Contributing Factors To The Persistence Of Musculoskeletal Pain In Preadolescents: A Prospective 1-Year Follow-Up Study". *Pain* 77.1 (1998): 67-72. Web.	No baseline pain-free group
66	Mikkelsson, Marja, Jouko J Salminen, and Hannu Kautiainen. "Non-Specific Musculoskeletal Pain In Preadolescents. Prevalence And 1-Year Persistence". *Pain* 73.1 (1997): 29-35. Web.	No information on sleep as a risk factor
67	Milicić G, Krolo I, Anticević D, Roić G, Zadravec D, Bojić D, Fattorini MZ, Bumci I. Causal connection of non-specific low back pain and disc degeneration in children with transitional vertebra and/or Spina bifida occulta: role of magnetic resonance--prospective study. Coll Antropol. 2012 Jun;36(2):627-33	No baseline pain-free group
68	Mirovsky, Yigal et al. "Non-Specific Back Pain In Children And Adolescents: A Prospective Study Until Maturity". *Journal of Pediatric Orthopaedics, Part B* 11.4 (2002): 275-278. Web.	No baseline pain-free group
69	Murray, Caitlin B. et al. "Pain And Sleep–Wake Disturbances In Adolescents With Depressive Disorders". *Journal of Clinical Child & Adolescent Psychology* 41.4 (2012): 482-490. Web.	Study design (Cross-sectional study)
70	Nagashima, Masaki et al. "Risk Factors For Lumbar Disc Degeneration In High School American Football Players". *The American Journal of Sports Medicine* 41.9 (2013): 2059-2064. Web.	Athletes
71	Nelson-Wong, Erika and Jack P. Callaghan. "Transient Low Back Pain Development During Standing Predicts Future Clinical Low Back Pain In Previously Asymptomatic Individuals". *Spine* 39.6 (2014): E379-E383. Web.	Age (Age range 18-50 years old)

72	Nemec V. Growth pain and articular hypermobility in children. [in Czech] Cesko-Slov. Pediatr.. 2005;60(11):606-611	No translation available (Article in Czech)
73	Nilsson IM. Reliability, validity, incidence and impact of temporormandibular pain disorders in adolescents. Swed Dent J Suppl. 2007;(183):7-86.	Not retrieved
74	G. Dahmen H. Gehring T. Meier P. Schmucker A. Ziegler A. Roth-Isigkeit. Pain in boys and girls: Preliminary results of a 1-year follow-up survey. Monatsschrift Kinderheilkunde vol. 157 issue 4 pp: 361-367	No information on sleep as a risk factor
75	Poussa, Mikko S. et al. "Predictors Of Neck Pain: A Cohort Study Of Children Followed Up From The Age Of 11 To 22 Years". *European Spine Journal* 14.10 (2005): 1033-1036. Web.	Age (Age at follow-up 22 years old)
76	Poussa, Mikko S. et al. "Anthropometric Measurements And Growth As Predictors Of Low-Back Pain: A Cohort Study Of Children Followed Up From The Age Of 11 To 22 Years". *European Spine Journal* 14.6 (2005): 595-598. Web.	Age (Age at follow-up 23 years old)
77	Prendeville K, Dockrell S: A pilot survey to investigate the incidence of low back pain in school children. Physiotherapy Ireland. 1998, 19: 3-7	No information on sleep as a risk factor
78	Purcell L. Causes and prevention of low back pain in young athletes. Paediatr Child Health. 2009 Oct;14(8):533-8	Athletes
79	Rabbitts, J. et al. "Bidirectional Associations Between Pain And Physical Activity In Adolescents". *The Journal of Pain* 13.4 (2012): S33. Web.	Study design (Case-control study)
80	Rathleff CR, Olesen JL, Roos EM, Rasmussen S, Rathleff MS. Half of 12-15-year-olds with knee pain still have pain after one year. Dan Med J. 2013 Nov;60(11):A4725	No baseline pain-free group

81	Reinking, Mark F., Tricia M. Austin, and Ann M. Hayes. "Risk Factors For Self-Reported Exercise-Related Leg Pain In High School Cross-Country Athletes". *Journal of Athletic Training* 45.1 (2010): 51-57. Web.	Athletes
82	Reinking, Mark F., Tricia M. Austin, and Ann M. Hayes. "Exercise-Related Leg Pain In Collegiate Cross-Country Athletes: Extrinsic And Intrinsic Risk Factors". *Journal of Orthopaedic & Sports Physical Therapy* 37.11 (2007): 670-678. Web.	Athletes
83	Rocha, E. M. and K. M. Prkachin. "Temperament And Pain Reactivity Predict Health Behavior Seven Years Later". *Journal of Pediatric Psychology* 32.4 (2006): 393-399. Web.	No information on sleep as a risk factor
84	Rozenberg S, Bourgeois P. "Are children also fated to develop back pain?" Rev Rhum Engl Ed. 1999 Jul-Sep;66(7-9):365-6.	Not retrieved
85	Salminen JJ. Low back pain: prevalence and risk factors in children and adolescents. Eur J Chiropractic. 2002;49(1):18-22	Study design (Review)
86	Salminen, Jouko J. et al. "Recurrent Low Back Pain And Early Disc Degeneration In The Young". *Spine* 24.13 (1999): 1316. Web.	Age (Age at follow-up 23 years old)
87	Salminen JJ, Kujala U. [Frequency and back ground of back pains in young persons]. Duodecim. 1999;115(16):1773-8	No translation available (Article in Finnish)
88	Sano, Atsuki et al. "Body Mass Index Is Associated With Low Back Pain In Childhood And Adolescence: A Birth Cohort Study With A 6-Year Follow-Up In Niigata City, Japan". *European Spine Journal* 24.3 (2014): 474-481. Web.	No information on sleep as a risk factor

89	Sato, T., Ito, T., Hirano, T., Morita, O., Kikuchi, R., Endo, N., & Tanabe, N. (2008). Low back pain in childhood and adolescence: A cross-sectional study in Niigata City. *European Spine Journal*, *17*(11), 1441–1447. doi:10.1007/s00586-008-0788-5	Study design (Cross-sectional study)
90	Ledig T. Chest pain in general practice. [in German] MMW-Fortschr. Med.. 2013;155(12):35-37.	Not retrieved
91	Selbst SM, Ruddy R, Clark BJ. Chest pain in children. Follow-up of patients previously reported. Clin Pediatr (Phila). 1990 Jul;29(7):374-7.	Not retrieved
92	Sil, S. et al. "A Controlling Family Environment Predicts Long-Term Emotional And Social Functioning In Adolescents With Juvenile Fibromyalgia". *The Journal of Pain* 13.4 (2012): S104. Web.	No baseline pain-free group
93	Sil, Soumitri et al. "Influence Of Family Environment On Long-Term Psychosocial Functioning Of Adolescents With Juvenile Fibromyalgia". *Arthritis Care & Research* 65.6 (2013): 903-909. Web.	No baseline pain-free group
94	Sjolie, Astrid Noreng. "Persistence And Change In Nonspecific Low Back Pain Among Adolescents: A 3-Year Prospective Study". *Spine* 29.21 (2004): 2452-2457. Web.	No baseline pain-free group
95	Skaggs, David L. et al. "Back Pain And Backpacks In School Children". *Journal of Pediatric Orthopaedics* 26.3 (2006): 358-363. Web.	Study design (Cross-sectional study)
96	Sokol L., Zurakowski D., Hemecour H.D., Micheli L., Treves T. Back pain in children less than 10 years of age: High incidence of abnormalities detected on skeletal single photon emission computed tomography (SPECT). Pediatr. Radiol.. 2010;40(4):539	Not retrieved

97	Sperotto, F et al. "Pres-FINAL-2004: Musculoskeletal Pain In Schoolchildren Across Puberty: A 3-Year Follow-Up Study". *Pediatric Rheumatology* 11.Suppl 2 (2013): O7. Web.	Conference publication
98	Sperotto, F et al. "Pres-FINAL-2005: Prevalence Of Antinuclear Antibodies In Schoolchildren Across Puberty And Possible Relationship With Musculoskeletal Pain. A Longitudinal Study". *Pediatric Rheumatology* 11.Suppl 2 (2013): P18. Web.	Conference publication
99	Stanford, E. A. (2006). *The prevalence, trajectories and predictors of recurrent pain among adolescents: A population-based approach*. University of British Columbia, Vancouver, BC.	No baseline pain-free group
100	Straker, Leon M. et al. "Neck/Shoulder Pain, Habitual Spinal Posture And Computer Use In Adolescents: The Importance Of Gender". *Ergonomics* 54.6 (2011): 539-546. Web.	Study design (Cross-sectional study)
101	Suvinen TI, Nyström M, Evälahti M, Kleemola-Kujala E, Waltimo A, Könönen M. "An 8-year follow-up study of temporomandibular disorder and psychosomatic symptoms from adolescence to young adulthood." J Orofac Pain. 2004 Spring;18(2):126-30.	No information on sleep as a risk factor
102	Temizturk F., Temizturk S., Ozguzel M.H. "Determination of the prevalence of benign joint hypermobility syndrome in secondary school children", Ortaokul Cocuklarinda Bening Eklem Hipermobilite Sendromu Siklitinin Arastirilmasi. Turk. Fiz. Tip Rehab. Derg.. 2013;59:278.	Not retrieved
103	Tyrdal, S. and R. Bahr. "High Prevalence Of Elbow Problems Among Goalkeepers In European Team Handball - 'Handball Goalie's Elbow'". *Scandinavian Journal of Medicine & Science in Sports* 6.5 (2008): 297-302. Web.	Athletes

104	Uziel Y, Chapnick G, Oren-Ziv A, Jaber L, Nemet D, Hashkes PJ. Bone strength in children with growing pains: long-term follow-up. Clin Exp Rheumatol. 2012 Jan-Feb;30(1):137-40.	No baseline pain-free group
105	VALOIS, TERESA et al. "Incidence Of Self-Limiting Back Pain In Children Following Caudal Blockade: An Exploratory Study". *Pediatric Anesthesia* 20.9 (2010): 844-850. Web.	Study design (Surgical cohort)
106	van Gessel, Hester, Jennifer Gaßmann, and Birgit Kröner-Herwig. "Children In Pain: Recurrent Back Pain, Abdominal Pain, And Headache In Children And Adolescents In A Four-Year-Period". *The Journal of Pediatrics* 158.6 (2011): 977-983.e2. Web.	No baseline pain-free group
107	Walker, Helen et al. "Shoulder Pain In Swimmers: A 12-Month Prospective Cohort Study Of Incidence And Risk Factors". *Physical Therapy in Sport* 13.4 (2012): 243-249. Web.	Athletes
108	Widhe, Torulf. "Spine: Posture, Mobility And Pain. A Longitudinal Study From Childhood To Adolescence". *European Spine Journal* 10.2 (2001): 118-123. Web.	No information on sleep as a risk factor
109	Wilkerson, Gary B., Jessica L. Giles, and Dustin K. Seibel. "Prediction Of Core And Lower Extremity Strains And Sprains In Collegiate Football Players: A Preliminary Study". *Journal of Athletic Training* 47.3 (2012): 264-272. Web.	Athletes
110	WILLEMS, TINE MARIEKE et al. "Gait-Related Risk Factors For Exercise-Related Lower-Leg Pain During Shod Running". *Medicine & Science in Sports & Exercise* 39.2 (2007): 330-339. Web.	Athletes
111	Wojtys EM, Ashton-Miller JA, Huston LJ, Moga PJ. "The association between athletic training time and the sagittal curvature of the immature spine." Am J Sports Med. 2000 Jul-Aug;28(4):490-8.	Athletes

112	Wolff, N. J. et al. "Concurrent And Longitudinal Bidirectional Relationships Between Toddlers' Chronic Pain And Mental Health: The Generation R Study". *Journal of Pediatric Psychology* 37.5 (2012): 546-556. Web.	Age (Age of the children 3 years old)
113	Campbell, Tavis S. et al. "A Longitudinal Study Of Pain Sensitivity And Blood Pressure In Adolescent Boys: Results From A 5-Year Follow-Up.". *Health Psychology* 21.6 (2002): 594-600. Web.	No baseline pain-free group
114	Janssens, Karin A.M. et al. "An Inactive Lifestyle And Low Physical Fitness Are Associated With Functional Somatic Symptoms In Adolescents. The TRAILS Study". *Journal of Psychosomatic Research* 76.6 (2014): 454-457. Web.	No information on sleep as a risk factor
115	Poussa, Mikko S. et al. "Anthropometric Measurements And Growth As Predictors Of Low-Back Pain: A Cohort Study Of Children Followed Up From The Age Of 11 To 22 Years". *European Spine Journal* 14.6 (2005): 595-598. Web.	No information on sleep as a risk factor
116	Geldhof, Elisabeth et al. "Back Posture Education In Elementary Schoolchildren: A 2-Year Follow-Up Study". *European Spine Journal* 16.6 (2006): 841-850. Web.	Study design (Back education programme)
117	Drouin, Sammantha and Jennifer J. McGrath. "Blood Pressure And Pain Sensitivity In Children And Adolescents". *Psychophysiology* 50.6 (2013): 513-520. Web.	No baseline pain-free group
118	Sano, Atsuki et al. "Body Mass Index Is Associated With Low Back Pain In Childhood And Adolescence: A Birth Cohort Study With A 6-Year Follow-Up In Niigata City, Japan". *European Spine Journal* 24.3 (2014): 474-481. Web.	No information on sleep as a risk factor

119	Logan, Deirdre E. et al. "Changes In Sleep Habits In Adolescents During Intensive Interdisciplinary Pediatric Pain Rehabilitation". *Journal of Youth and Adolescence* 44.2 (2014): 543-555. Web.	Study design (Rehabilitation program)
120	van Gessel, Hester, Jennifer Gaßmann, and Birgit Kröner-Herwig. "Children In Pain: Recurrent Back Pain, Abdominal Pain, And Headache In Children And Adolescents In A Four-Year-Period". *The Journal of Pediatrics* 158.6 (2011): 977-983.e2. Web.	No baseline pain-free group
121	Mikkelsson, Marja et al. "Contributing Factors To The Persistence Of Musculoskeletal Pain In Preadolescents: A Prospective 1-Year Follow-Up Study". *Pain* 77.1 (1998): 67-72. Web.	No baseline pain-free group
122	Kashikar-Zuck, S. et al. "Controlled Follow-Up Study Of Physical And Psychosocial Functioning Of Adolescents With Juvenile Primary Fibromyalgia Syndrome". *Rheumatology* 49.11 (2010): 2204-2209. Web.	Age (Age range 15-23)
123	Uziel Y, Chapnick G, Jaber L, Nemet D, Hashkes PJ. Five-year outcome of children with "growing pains": correlations with pain threshold. J Pediatr. 2010 May;156(5):838-40. doi:10.1016/j.jpeds.2009.11.078	No information on sleep as a risk factor
124	Rathleff CR, Olesen JL, Roos EM, Rasmussen S, Rathleff MS. Half of 12-15-year-olds with knee pain still have pain after one year. Dan Med J. 2013 Nov;60(11):A4725	No baseline pain-free group
125	Tsao, Jennie C.I. et al. "Healthcare Utilization For Pain In Children And Adolescents: A Prospective Study Of Laboratory And Non-Laboratory Predictors Of Care-Seeking". *International Journal of Adolescent Medicine and Health* 23.3 (2011): n. pag. Web.	No information on sleep as a risk factor

126	Sil, Soumitri et al. "Influence Of Family Environment On Long-Term Psychosocial Functioning Of Adolescents With Juvenile Fibromyalgia". *Arthritis Care & Research* 65.6 (2013): 903-909. Web.	No baseline pain-free group
127	Grimmer, Karen, Leah Nyland, and Steve Milanese. "Longitudinal Investigation Of Low Back Pain In Australian Adolescents: A Five-Year Study". *Physiotherapy Research International* 11.3 (2006): 161-172. Web.	No information on sleep as a risk factor
128	Auvinen, Juha et al. "MUSCULOSKELETAL PAIN COMBINATIONS IN ADOLESCENTS". *Spine* &NA; (2008): 44. Web.	No information on sleep as a risk factor
129	Mikkelsson, Marja, Jouko J Salminen, and Hannu Kautiainen. "Non-Specific Musculoskeletal Pain In Preadolescents. Prevalence And 1-Year Persistence". *Pain* 73.1 (1997): 29-35. Web.	No information on sleep as a risk factor
130	Jones, Gareth T. and Gary J. Macfarlane. "Predicting Persistent Low Back Pain In Schoolchildren: A Prospective Cohort Study". *Arthritis & Rheumatism* 61.10 (2009): 1359-1366. Web.	No baseline pain-free group
131	Mattila, Ville M. et al. "Predictors Of Low Back Pain Hospitalization – A Prospective Follow-Up Of 57,408 Adolescents". *Pain* 139.1 (2008): 209-217. Web.	Age (Age at baseline 14-18 and 25-29 years old at follow-up).
132	Poussa, Mikko S. et al. "Predictors Of Neck Pain: A Cohort Study Of Children Followed Up From The Age Of 11 To 22 Years". *European Spine Journal* 14.10 (2005): 1033-1036. Web.	Age (Age at follow-up 22 years old)
133	El-Metwally, Ashraf et al. "Prognosis Of Non-Specific Musculoskeletal Pain In Preadolescents: A Prospective 4-Year Follow-Up Study Till Adolescence". *Pain* 110.3 (2004): 550-559. Web.	No baseline pain-free group

134	Diniz MR, Sabadin PA, Leite FP, Kamizaki R. Psychological factors related to temporomandibular disorders: an evaluation of students preparing for college entrance examinations. Acta Odontol Latinoam. 2012;25(1):74-81.	Age (Age 18-25 years old)
135	Grimmer, K, L Nyland, and S Milanese. "Repeated Measures Of Recent Headache, Neck And Upper Back Pain In Australian Adolescents". *Cephalalgia* 26.7 (2006): 843-851. Web.	No information on sleep as a risk factor
136	Widhe, Torulf. "Spine: Posture, Mobility And Pain. A Longitudinal Study From Childhood To Adolescence". *European Spine Journal* 10.2 (2001): 118-123. Web.	No information on sleep as a risk factor
137	Rocha, E. M. and K. M. Prkachin. "Temperament And Pain Reactivity Predict Health Behavior Seven Years Later". *Journal of Pediatric Psychology* 32.4 (2006): 393-399. Web.	No information on sleep as a risk factor
138	Koh, Min Jung et al. "The Effect Of Education On Decreasing The Prevalence And Severity Of Neck And Shoulder Pain: A Longitudinal Study In Korean Male Adolescents". *Korean Journal of Anesthesiology* 67.3 (2014): 198. Web.	Study design (Pain education programme)
139	Dunn, Kate M. et al. "Trajectories Of Pain In Adolescents: A Prospective Cohort Study". *Pain* 152.1 (2011): 66-73. Web.	No information on sleep as a risk factor
140	Rathleff CR, Olesen JL, Roos EM, Rasmussen S, Rathleff MS. Half of 12-15-year-olds with knee pain still have pain after one year. Dan Med J. 2013 Nov;60(11):A4725	No baseline pain-free group
141	Geldhof, Elisabeth et al. "Back Posture Education In Elementary Schoolchildren: A 2-Year Follow-Up Study". *European Spine Journal* 16.6 (2006): 841-850. Web.	Study design (Back education programme)

142	Mikkelsson, Marja et al. "Contributing Factors To The Persistence Of Musculoskeletal Pain In Preadolescents: A Prospective 1-Year Follow-Up Study". *Pain* 77.1 (1998): 67-72. Web.	No baseline pain-free group
143	Campbell, Tavis S. et al. "A Longitudinal Study Of Pain Sensitivity And Blood Pressure In Adolescent Boys: Results From A 5-Year Follow-Up.". *Health Psychology* 21.6 (2002): 594-600. Web.	No baseline pain-free group
144	Logan, Deirdre E. et al. "Changes In Sleep Habits In Adolescents During Intensive Interdisciplinary Pediatric Pain Rehabilitation". *Journal of Youth and Adolescence* 44.2 (2014): 543-555. Web.	Study design (Rehabilitation program)
145	van Gessel, Hester, Jennifer Gaßmann, and Birgit Kröner-Herwig. "Children In Pain: Recurrent Back Pain, Abdominal Pain, And Headache In Children And Adolescents In A Four-Year-Period". *The Journal of Pediatrics* 158.6 (2011): 977-983.e2. Web.	No baseline pain-free group
Search with specific sleep terms		
146	Norell-Clarke A.; Hagquist C. Adolescent sleep duration in relation to psychosomatic complaints: Development between 1985 and 2013 in Sweden. Journal of Sleep Research. Conference: 23rd Congress of the European Sleep Research Society, ESRS 2016. Italy. Conference Start: 20160913. Conference End: 20160916. 25 (pp 139), 2016	Conference publication
147	Groenewald C.B.; Rabbitts J.A.; Palermo T.M. Associations between sleep disturbance and health services use among adolescents: Results from the national health interview survey. Sleep. Conference: 29th Annual Meeting of the Associated Professional Sleep Societies, LLC, SLEEP 2015. Seattle, WA United States. Conference Start: 20150606. Conference End: 20150610. Conference Publication: (var.pagings). 38 (pp A394), 2015.	Conference publication

148	Zhao Q, Zhang Y, Deng G, Jiang W, Zhang L, Di L, Su Y, Du X, Wu X, Che Q, Chen K. [Relationship between the incidence of chronic pain and academic pressure in high school students]. Zhonghua Yi Xue Za Zhi. 2014 Dec 30;94(48):3831-5.	No translation available (Article in Chinese)
149	Zhang Y, Deng G, Zhao S, Zhou Q, Gao X, Wang H, Zhang Z, Ju Y, Wang R, Wang Y, Zhao Q. [Effects of non-physical factors on neck and shoulder pain and low back pain of adolescents]. Zhonghua Yi Xue Za Zhi. 2014 Oct 14;94(37):2923-8.	No translation available (Article in Chinese)
150	Gunzburg, R. et al. "Low Back Pain In A Population Of School Children". *European Spine Journal* 8.6 (1999): 439-443. Web.	Study design (Cross-sectional study)
151	Firestone K, Jones K, Wilson A. Functional Disability in Adolescents Is Predicted By Self-Report of Sleep Problems, Depressive Symptoms, Low Physical Activity and Worst Pain Intensity Levels [abstract]. Arthritis Rheumatol. 2015; 67 (suppl 10).	No baseline pain-free group
152	Roth-Isigkeit, A. "Pain Among Children And Adolescents: Restrictions In Daily Living And Triggering Factors". *PEDIATRICS* 115.2 (2005): e152-e162. Web.	Study design (Cross-sectional study)
153	Mikkonen, Paula et al. "Accumulation Of Psychosocial And Lifestyle Factors And Risk Of Low Back Pain In Adolescence: A Cohort Study". *European Spine Journal* 25.2 (2015): 635-642. Web.	No information on sleep as a risk factor