

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

Title (Provisional)

The breadth and visibility of children's lower limb chronic musculoskeletal pain: A scoping review.

Authors

Ilhan, Emre; Davies, Luke; Pacey, Verity; Smith, Mitchell; Munro, Jane; Munns, Craig; Sturgiss, Elizabeth; Williams, Nicole; Tofts, Louise; Locke, Vance; Haines, Terry; Brennan, Sue E.; Maloney, Stephen; Sarkies, Mitchell N; Clavisi, Ornella; Miles, Dan; Nissen, Lisa; Williams, Dr Cylie

VERSION 1 - REVIEW

Reviewer	1
Name	Dunn, Kate
Affiliation Centre	Keele University, Arthritis Research UK Primary Care
Date	08-Feb-2024
COI	None

This scoping review aimed to compare chronic lower limb pain reported in published papers with ICD codes. The review is clearly described and followed prisma guidelines. I have some questions for the authors.

1. It is unclear to me what the authors mean by “articles describing a region of pain without a diagnosis name or term were excluded” – does this mean that an article about e.g. self-reported chronic ‘knee pain’ would be included or excluded? If excluded, this would seem to be a significant exclusion.
2. It would be helpful to describe what a manifestation code is, as some readers will be unfamiliar with this terminology. This is especially important as much of the discussion relates to manifestation codes.
3. In Table 2, what is a Prospective cross-sectional study? Surely studies are either cross-sectional or prospective? What would a non-prospective cross-sectional study be? Were ordinary cross-sectional studies / surveys included?

4. One of your findings was that the most commonly presented health condition identified was juvenile idiopathic arthritis. I wonder if this, which is actually not a common condition in the general population, is as a result of including case reports, which may describe a single case? Did you try stratifying your results by study type? As one of your key conclusions relates to the global burden of chronic musculoskeletal pain of the lower limb in children and adolescents, I am not sure that this conclusion is supported by literature dominated by case reports.

5. I found some of the discussion quite difficult to interpret, as it is almost reported as if the authors were talking about the prevalence of chronic lower limb pain, not the occurrence of publications on it. E.g. how can you conclude that there is an “under-recognition of chronic musculoskeletal pain in children and adolescents” from the results reported in this paper? I am also not sure that this paper supports the notion that “health professionals require training specific to paediatric musculoskeletal health conditions that may result in chronic pain” (I agree with the notion, I am just not sure it’s supported by the results).

Reviewer	2
Name	Riiser, Kirsti
Affiliation	Oslo Metropolitan University, Rehabilitation Science and Health Technology
Date	14-Apr-2024
COI	I have noe competing interests.

Thank you for the opportunity to read this original, interesting, and well-structured scoping review. The authors present a solid rationale and a clear and well-defined objective. It is a particular strength that the authors have included a reference group consisting of experts and user representatives to provide input on the search strategy and coding of conditions. The review is conducted in line with the PRISMA-ScR, with a comprehensive method description, clear synthesis, and discussion. I only have a few minor remarks.

Page 6, line 16: The authors write, "Chronic pain negatively impacts quality of life and increases the risk of psychological disturbances such as anxiety and depression in adulthood" and refer to two studies. One is from 2006 and only includes a small sample from a rare patient population, and the other reference is a protocol for an update of a systematic review. I encourage the authors to find more recent and extensive literature on the associations between pain, quality of life, and mental distress.

Page 8, line 31: The authors should add a reference to how “children” (“peadiatric population”) is defined with regards to age (<18 years).

Page 9, line 3: The sentence, "In studies with mixed populations (...) only data from participants that met this review's eligibility criteria were included", could be elaborated by describing what prerequisites had to be met in order for data to be extracted from such mixed populations.

Page 9, line 29: It has been almost a year since the search was conducted. The authors should briefly argue why an updated search has not been carried out before submission.

Page 13, line 11-20: The authors state that the majority of the studies were conducted in the United States, but at the same time, they report the number to be 139 which cannot be said to be the "majority" of 384. The same applies to the reference to studies that include adolescents between 11 and 17 years old (170/384).

Page 15, line 41: Please remove "the" or "that" in the sentence.

VERSION 1 - AUTHOR RESPONSE

Thank you for the opportunity to revise this manuscript. Detailed responses to reviewers are in the attached file.

Reviewer comments	Response – changes italicised	Location
Professor Kate Dunn, Keele University		
1. It is unclear to me what the authors mean by "articles describing a region of pain without a diagnosis name or term were excluded" – does this mean that an article about e.g. self-reported chronic 'knee pain' would be included or excluded? If excluded, this would seem to	We thank the reviewer for this question. The aim of this scoping review was to determine the types of conditions that may result in chronic musculoskeletal lower limb pain, rather than just the location of pain. Therefore, if an article only reported "knee pain" but not the diagnosis for the knee pain, it was excluded. We have amended this sentence to improve	Methods, Eligibility Criteria, p. 8, para. 1 Discussion, p. 15, para. 5

<p>be a significant exclusion.</p>	<p>clarity in the following manner:</p> <p>“...articles describing a region of pain without a <i>diagnostic</i> name (e.g., juvenile idiopathic arthritis) or <i>condition</i> (e.g., primary chronic musculoskeletal pain) were excluded”.</p> <p>In addition to the above, we have highlighted the potential for under-reporting by only focussing on chronic pain with known conditions associated with it in the Limitation section of the Discussion. We have stated:</p> <p>“This may mean that a large number of region-specific conditions resulting in chronic musculoskeletal lower limb pain in children and adolescents were not captured.”</p>	
<p>2. It would be helpful to describe what a manifestation code is, as some readers will be</p>	<p>We thank the reviewer for the opportunity to provide clarity around this term. We have added the following to define</p>	<p>Methods, Data Charting Process and Data Items, p. 10, para. 2</p>

<p>unfamiliar with this terminology. This is especially important as much of the discussion relates to manifestation codes.</p>	<p>what a manifestation code is:</p> <p><i>“An ICD manifestation code describes the manifestation, symptoms, or signs of the underlying disease (e.g., pain) rather than the disease itself.”</i></p>	
<p>3. In Table 2, what is a Prospective cross-sectional study? Surely studies are either cross-sectional or prospective. What would a non-prospective cross-sectional study be? Were ordinary cross-sectional studies / surveys included?</p>	<p>We thank the reviewer for this suggestion. We have removed the term “prospective” from Table 2 to aid clarity.</p>	<p>Table 2</p>
<p>4. One of your findings was that the most commonly presented health condition identified was juvenile idiopathic arthritis. I wonder if this, which is actually not a common</p>	<p>We agree with the reviewer’s statement that the inclusion of case reports in this review resulted in an over-representation of conditions seen less commonly in the general population.</p> <p>When reporting this finding in the Results section, we have amended the</p>	<p>Abstract, Results, p. 3, para. 1</p> <p>Results, p. 12, para. 3</p> <p>Discussion, p. 14, para. 2</p>

<p>condition in the general population, is as a result of including case reports, which may describe a single case? Did you try stratifying your results by study type? As one of your key conclusions relates to the global burden of chronic musculoskeletal pain of the lower limb in children and adolescents, I am not sure that this conclusion is supported by literature dominated by case reports.</p>	<p>sentence to ensure that readers understand that we evaluated the extent of reporting rather than the prevalence or incidence of the condition:</p> <p>“There were 124 unique conditions associated with chronic lower limb pain, the most commonly <i>reported</i> being chronic widespread musculoskeletal pain (24 studies) and juvenile idiopathic arthritis (26 studies).”</p> <p>“The most commonly <i>reported</i> health conditions identified resulting in chronic lower limb pain in children and adolescents were juvenile idiopathic arthritis (n = 24/384 studies)...”.</p> <p>And in the Discussion section:</p> <p>“These opportunities are in place for conditions such as Juvenile Idiopathic Arthritis, the most <i>commonly reported</i> condition <i>in the literature</i>.”</p>	
<p>5. I found some of the discussion</p>	<p>We would like to thank the reviewer</p>	<p>Discussion, p. 15, para. 3</p>

<p>quite difficult to interpret, as it is almost reported as if the authors were talking about the prevalence of chronic lower limb pain, not the occurrence of publications on it. E.g. how can you conclude that there is an “under-recognition of chronic musculoskeletal pain in children and adolescents” from the results reported in this paper? I am also not sure that this paper supports the notion that “health professionals require training specific to paediatric musculoskeletal health conditions that may result in chronic pain” (I agree with the notion, I am just not sure it’s supported by the results).</p>	<p>for requesting further clarification in the Discussion section.</p> <p>Our intention behind the statement “the under-recognition of chronic musculoskeletal pain...” was to highlight a need for global classification systems, such as the ICD-11, to enable health systems to report chronic pain as a manifestation of many lower limb diseases in children and adolescents. Indeed, our review showed that the ICD-11 does not have chronic pain as a manifestation code in ~89% of health conditions of the lower limb when there should have been one. If there are barriers that prevent health systems from reporting the presence of chronic pain as a result of a disease, then it is unlikely that they will be captured in global statistics. The global burden of chronic lower limb pain in children and adolescents can only be made visible</p>	<p>Discussion, p. 14, para. 2</p>
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	<p>if there are methods of collecting such data. To clarify this argument, we have added the following statement in the Discussion:</p> <p><i>“This review highlights that, due to the lack of manifestation codes, there is potential of the ICD-11 in under-reporting diseases that may result in chronic musculoskeletal pain of the lower limb in children and adolescence. The under-recognition of chronic musculoskeletal pain...”</i></p> <p>We have also amended the statement on training to:</p> <p><i>“Given the breadth of conditions the review found that may result in chronic musculoskeletal lower limb pain, there is a need for health professionals to be aware of multiple paediatric musculoskeletal health conditions that may result in chronic pain.”</i></p>	
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<p>Dr. Kirsti Riiser, Oslo Metropolitan University</p>		
<p>6. Page 6, line 16: The authors write, "Chronic pain negatively impacts quality of life and increases the risk of psychological disturbances such as anxiety and depression in adulthood" and refer to two studies. One is from 2006 and only includes a small sample from a rare patient population, and the other reference is a protocol for an update of a systematic review. I encourage the authors to find more recent and extensive literature on the associations between pain, quality of life, and mental distress.</p>	<p>We agree with the reviewer. We have added more extensive and current literature relating chronic pain to quality of life and mental distress in the paediatric population.</p> <p>We have added the following references after this statement:</p> <p>Chambers CT, Dol J, Tutelman PR, et al. The prevalence of chronic pain in children and adolescents: a systematic review update and meta-analysis. <i>Pain</i>. Published online May 15, 2024.</p> <p>Mikkelsen HT, Haraldstad K, Helseth S, Skarstein S, Småstuen MC, Rohde G. Pain and health-related quality of life in adolescents and the mediating role of self-esteem and self-efficacy: a cross-sectional study including adolescents and parents. <i>BMC Psychol</i>. 2021;9(1):128.</p>	<p>Introduction, p. 6, para. 1</p>

	<p>Miró J, Roman-Juan J, Sánchez-Rodríguez E, Solé E, Castarlenas E, Jensen MP. Chronic pain and high impact chronic pain in children and adolescents: A cross-sectional study. <i>J Pain</i>. 2023;24(5):812-823.</p> <p>Wager J, Brown D, Kupitz A, Rosenthal N, Zernikow B. Prevalence and associated psychosocial and health factors of chronic pain in adolescents: Differences by sex and age. <i>Eur J Pain</i>. 2020;24(4):761-772.</p>	
<p>7. Page 8, line 31: The authors should add a reference to how “children” (“paediatric population”) is defined with regards to age (<18 years).</p>	<p>We thank the reviewer for making this suggestion. We have added the following reference to help define the term “paediatric population”:</p> <p>Hardin AP, Hackell JM; COMMITTEE ON PRACTICE AND AMBULATORY MEDICINE. Age Limit of Pediatrics. <i>Pediatrics</i>. 2017;140(3):e20172151.</p>	<p>Methods, Eligibility Criteria, p. 8, para. 1</p>

<p>8. Page 9, line 3: The sentence, "In studies with mixed populations (...) only data from participants that met this review's eligibility criteria were included", could be elaborated by describing what prerequisites had to be met in order for data to be extracted from such mixed populations.</p>	<p>We thank the reviewer for alerting us of the need for clarification. We have added the following sentence:</p> <p>"...individuals less than 18 years of age with chronic musculoskeletal pain of the lower limb."</p>	<p>Methods, Eligibility Criteria, p. 9, para. 1</p>
<p>9. Page 9, line 29: It has been almost a year since the search was conducted. The authors should briefly argue why an updated search has not been carried out before submission.</p>	<p>We have updated the search. The current review is now up to date from July 25th, 2024. We have also updated the manuscript with the new data.</p>	<p>Throughout</p>
<p>10. Page 13, line 11-20: The authors state that the majority of the studies were conducted in the United States, but at the same time, they report the number to be</p>	<p>We have removed the word "majority" and replaced it with "most studies":</p> <p>"Of the 418 studies included in this review (Supplementary Table 2), <i>most studies</i> were..."</p>	<p>Results, p. 12, para. 2</p>

<p>139 which cannot be said to be the "majority" of 384. The same applies to the reference to studies that include adolescents between 11 and 17 years old (170/384).</p>		
<p>11. Page 15, line 41: Please remove "the" or "that" in the sentence.</p>	<p>We thank the reviewer for pointing out this error. We have removed 'that' and kept 'the' in the sentence.</p>	<p>Discussion, p. 14, para. 1</p>

VERSION 2 - REVIEW

Reviewer **2**

Name **Riiser, Kirsti**

Affiliation **Oslo Metropolitan University, Rehabilitation Science and Health Technology**

Date **31-Aug-2024**

COI **None.**

The authors have done a good job revising the manuscript.

I only have a minor follow-up comment regarding the sentence in the introduction that refers to impact of pain on quality of life, and psychological distress. Here, the authors refer to studies that primarily investigate associations. Moreover, the references do not present data on associations between pain in early age and risk for anxiety and depression in adulthood. The sentence should be corrected to better correspond with the references.

I would like to commend the authors for conducting a nice scoping review, which clearly points to the need of making secondary pain more visible by having the ability to link various conditions to chronic pain manifestation codes. This review may be an important contribution in making researchers, clinicians and policy makers aware of the potential under-reporting of secondary pain in children and young people.

VERSION 2 - AUTHOR RESPONSE

Reviewer 2 comments

I only have a minor follow-up comment regarding the sentence in the introduction that refers to impact of pain on quality of life, and psychological distress. Here, the authors refer to studies that primarily investigate associations. Moreover, the references do not present data on associations between pain in early age and risk for anxiety and depression in adulthood. The sentence should be corrected to better correspond with the references.

Response:

We have removed the link to adulthood and amended the references for this sentence to align with the studies, and how we have described their findings.

I would like to commend the authors for conducting a nice scoping review, which clearly points to the need of making secondary pain more visible by having the ability to link various conditions to chronic pain manifestation codes. This review may be an important contribution in making researchers, clinicians and policy makers aware of the potential under-reporting of secondary pain in children and young people.

Response:

We thank the reviewer for their kind words and also hope for this outcome.

Additional Author comments

During revision we found that a portion of text had not been updated to align with the updated table from the last revision. This has also been updated at this time to align with the updated table.