

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Poor prognosis of child and adolescent Musculoskeletal Pain - a Systematic Literature Review
<b>AUTHORS</b>	Pourbordbari, Negar; Riis, Allan; Jensen, Martin Bach; Olesen, Jens; Rathleff, Michael

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Tie P Yamato University of Sydney
<b>REVIEW RETURNED</b>	09-Nov-2018

<b>GENERAL COMMENTS</b>	<p>Introduction</p> <ul style="list-style-type: none"><li>- In general, references are ok but this section lacks structure and organisation (eg, the first paragraph is too short and has no link with the next one).</li></ul> <p>Methods</p> <ul style="list-style-type: none"><li>- Is there any protocol registered for this review? Otherwise it should be in the limitations.</li><li>- Search strategy must be updated.</li><li>- Data extraction: what about the 95% CI?</li><li>- I think the methods section lacks a "data analysis" subheading and more information on how this was planned.</li></ul> <p>Results</p> <ul style="list-style-type: none"><li>- I would like to see more on the risk of bias incorporated to this section, especially in the interpretation of prognostic factors.</li><li>- I imagine it was hard to get all of this together, but I missed a table with all prognostic factors and their strength of association (eg, OR, RR, 95% CI).</li></ul> <p>Discussion</p> <ul style="list-style-type: none"><li>- Again, the first paragraph summarises results well but there is no information on the strength of the associations.</li><li>- Is it possible that prognostic factors reported by only one included study were due to change only? Or the number of covariates in these studies?</li></ul>
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<b>REVIEWER</b>	Cattram Nguyen MCRI, Australia
<b>REVIEW RETURNED</b>	28-Nov-2018

<b>GENERAL COMMENTS</b>	<p>This article is a systematic review of patient characteristics associated with poor prognosis among child and adolescents with musculoskeletal pain. On the whole, the paper is clearly written and follows PRISMA reporting guidelines. In addition to the main review results, the authors also developed some tools and questions (Table 2 and Figure 3) that may be helpful for general practitioners treating patients with musculoskeletal pain.</p> <p>A few minor comments/suggestions:</p> <ul style="list-style-type: none"> <li>• Abstract (Conclusions). The authors note that “None of the included studies was conducted within a general practice setting which highlights an area in need of research”. I may have missed this, but I couldn’t see this result expanded upon in the main text, nor could I see the settings where the reviewed studies had been conducted.</li> <li>• No treatment modifiers were identified in the review. This result could be mentioned in the abstract, as one of the key research questions concerned treatment modifiers.</li> <li>• Page 4, line 16 (Outcomes and Endpoints). The following sentence doesn’t quite make sense (because the identification of baseline characteristics is not an outcome measure): “Our primary outcome of interest was musculoskeletal pain at follow-up and identification of any baseline characteristics that were associated with this outcome (prognostic factors)”</li> <li>• Page 6, line 10 (Prognosis): “On average, 54% with general musculoskeletal pain, 49% with knee pain and 42% with neck pain also reported pain at follow-up”. Could the authors clarify how these averages were calculated?</li> <li>• Page 6, line 12 (and other places in the manuscript). Very minor suggestion to change the wording “stratified in” to “stratified by”.</li> <li>• Table 3 (Mikkonen M 99). I noticed that the proportion of pain for males and females combined (Neck 29%, WSP 28.6%) is lower than both of the percentages for males and females separately. Are these results correct?</li> <li>• Strengths and Limitations (Page 8). The authors mention a previously published systematic review (the current review only appears to add 2 additional studies). The previous review wasn’t mentioned earlier, and the Introduction gave the sense that the current review was quite novel.</li> </ul>
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**VERSION 1 – AUTHOR RESPONSE**

Reviewer(s)' Comments to Author:

Reviewer: 1  
Reviewer Name: Tie P Yamato  
Institution and Country: University of Sydney  
Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below

#### Introduction

In general, references are ok but this section lacks structure and organization (eg, the first paragraph is too short and has no link with the next one).

Response:

The first two paragraphs of the introduction has been converted into one.

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

#### Methods

Is there any protocol registered for this review? Otherwise it should be in the limitations.

Response:

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

The above mentioned is mentioned in the registration section of the abstract and in the paragraphs supplementary information and author contribution.

Search strategy must be updated.

Response:

Search strategy has been updated to February 2019 and one study has been added to the included studies.

#### Data extraction:

what about the 95% CI?

Response:

In revision of the paragraph Data extraction we think that the mention of the above is needed. Also, please see Supplementary Table 1 for information on strength of associations, including reporting of OR, RR, p-values and the requested 95% CI.

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

Data were extracted with a pre-defined data extraction form inspired by The Cochrane Collaboration (13).

I think the methods section lacks a "data analysis" subheading and more information on how this was planned.

Response:

We agree that the methods section benefits from a more elaborative description of data extraction, why we made the following changes to the paragraph data extraction.

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

No meta-analysis was conducted due to a heterogeneity of patient population, setting, and endpoints. Because of this, we decided not to include such a section.

Data were extracted with a pre-defined data extraction form inspired by The Cochrane Collaboration (13).

Results

I would like to see more on the risk of bias incorporated to this section, especially in the interpretation of prognostic factors.

Response:

Thank you for highlighting a paragraph, which needs further explanation. The following has been added to the risk of bias paragraph in results: Three studies were rated with high risk of bias. Studies with a high risk of bias was excluded from the final results in figure 3. With the purpose of filtering the results of prognostic factors, we excluded these studies from the final results depicted in figure 3. I imagine it was hard to get all of this together, but I missed a table with all prognostic factors and their strength of association (eg, OR, RR, 95% CI).

Response:

Thank you for the acknowledging comment. As part of the original uploaded files, we have Supplementary Table 1, Estimates on prognostic factors specified according to musculoskeletal pain type, baseline age, and follow-up in the included studies. In this table we have all our prognostic factors sub-grouped according to the biopsychosocial model and their strength of association RR, OR, and p-value.

## Discussion

Again, the first paragraph summarizes results well but there is no information on the strength of the associations.

Response:

Thank you for the acknowledging words. We have revised the section to include the strength of associations as suggested. Furthermore, the complete overview can be found in Supplementary Table 1.

Is it possible that prognostic factors reported by only one included study were due to change only? Or the number of covariates in these studies?

Response:

We have respectfully considered this question within the author-group but do not understand the content. We hope the reviewer or editor will elaborate and allow us to edit accordingly.

Reviewer: 2

Reviewer Name: Cattram Nguyen

Institution and Country: MCRI, Australia

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

This article is a systematic review of patient characteristics associated with poor prognosis among child and adolescents with musculoskeletal pain. On the whole, the paper is clearly written and follows PRISMA reporting guidelines. In addition to the main review results, the authors also developed some tools and questions (Table 2 and Figure 3) that may be helpful for general practitioners treating patients with musculoskeletal pain.

Response:

Thank you for your positive feedback and highlighting the tools developed from our study.

A few minor comments/suggestions:

Abstract (Conclusions).

The authors note that "None of the included studies was conducted within a general practice setting which highlights an area in need of research". I may have missed this, but I couldn't see this result expanded upon in the main text, nor could I see the settings where the reviewed studies had been conducted.

Response:

Settings has been added to table 1 in a separate column. We have also added mention of recruitment setting as one of the data we will extract (in the paragraph Data extraction).

No treatment modifiers were identified in the review. This result could be mentioned in the abstract, as one of the key research questions concerned treatment modifiers.

Response:

The following has been added to the results section of the abstract: No treatment effect modifiers were identified.

Page 4, line 16 (Outcomes and Endpoints).

The following sentence doesn't quite make sense (because the identification of baseline characteristics is not an outcome measure): "Our primary outcome of interest was musculoskeletal pain at follow-up and identification of any baseline characteristics that were associated with this outcome (prognostic factors)"

Response:

Thank you for your constructive comment. We changed the above mentioned sentence to the following.

Changes to text: Our primary outcome of interest was musculoskeletal pain at follow-up. We wanted to identify any baseline characteristics that were associated with this outcome (prognostic factors).

Page 6, line 10 (Prognosis):

"On average, 54% with general musculoskeletal pain, 49% with knee pain and 42% with neck pain also reported pain at follow-up". Could the authors clarify how these averages were calculated?

Response:

Thank you for highlighting sentences, with potential cause of confusion for future readers. We decided to change the reporting of the results depicted in figure 2, to the following.

Changes to text: At one-year follow-up, an average of 54,4% with general musculoskeletal pain, an average of 41,83% with neck pain, and 48,8% with knee pain reported pain. At four-year follow-up 63,5% with general musculoskeletal pain, 33,5% with neck pain, and 26% with low back pain reported pain. At nine-year follow-up 59% with general musculoskeletal pain reported pain.

Furthermore, we have added the following to the paragraph, reporting of results: Average on pain at follow-up was calculated as average of individual studies reporting same musculoskeletal pain type at same follow-up duration (figure 2).

Page 6, line 12 (and other places in the manuscript).

Very minor suggestion to change the wording "stratified in" to "stratified by".

Response:

Agreed. Revised as suggested throughout the manuscript.

Table 3 (Mikkonen M 99).

I noticed that the proportion of pain for males and females combined (Neck 29%, WSP 28.6%) is lower than both of the percentages for males and females separately. Are these results correct?

Response:

Thank you for noticing a regrettable miscalculation. We believe you refer to the study by Mikkelsen et al. 1999 (29)? The numbers for persistent pain at follow-up combined (%), has been changed to Neck 58,1 and WSP 62,5.

This notification has led to further changes for improvement in this, now renamed table 1 previously named table 3; the second column: MSK instead of Musculoskeletal, WSP instead of widespread pain, and as mentioned two other places in this response letter the addition of the column named Recruitment setting.

Strengths and Limitations (Page 8).

The authors mention a previously published systematic review (the current review only appears to add 2 additional studies). The previous review wasn't mentioned earlier, and the Introduction gave the sense that the current review was quite novel.

Response:

Thank you for pointing to this. We have added the date of the last systematic review to our introduction to provide a rationale the timely update on this important topic.

Changes to text: The latest systematic review on prognostic factors for adolescents with musculoskeletal pain ref (41) ended their literature search in July 2015 which makes for a timely update.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Tie Parma Yamato University of Sydney - Australia
<b>REVIEW RETURNED</b>	04-Jun-2019
<b>GENERAL COMMENTS</b>	Thank you for addressing my suggestions. I think the manuscript has improved considerably.